Challenges for Agricultural Research

OECD

MINISTRY OF AGRICULTURE
OF THE CZECH REPUBLIC

EU2009.CZ

Challenges for Agricultural Research

MINISTRY OF AGRICULTURE
OF THE CZECH REPUBLIC

EU2009.CZ

This work is published on the responsibility of the Secretary-General of the OECD. The opinions expressed and arguments employed herein do not necessarily reflect the official views of the Organisation or of the governments of its member countries.

Please cite this publication as:
OECD (2010), *Challenges for Agricultural Research*, OECD Publishing.
http://dx.doi.org/10.1787/9789264090101-en

ISBN 978-92-64-09009-5 (print)
ISBN 978-92-64-09010-1 (PDF)

Corrigenda to OECD publications may be found on line at: *www.oecd.org/publishing/corrigenda*.

© OECD 2010

You can copy, download or print OECD content for your own use, and you can include excerpts from OECD publications, databases and multimedia products in your own documents, presentations, blogs, websites and teaching materials, provided that suitable acknowledgment of OECD as source and copyright owner is given. All requests for public or commercial use and translation rights should be submitted to *rights@oecd.org*. Requests for permission to photocopy portions of this material for public or commercial use shall be addressed directly to the Copyright Clearance Center (CCC) at *info@copyright.com* or the Centre français d'exploitation du droit de copie (CFC) at *contact@cfcopies.com*.

Foreword

It is a great honour for the Ministry of Agriculture and for me personally to host the Prague OECD Conference "Challenges for Agricultural Research". The conference held from 6 to 8 April 2009 during the Presidency of the Czech Republic (CR) of the EU is among the most important events of the agricultural sector, supporting the Presidency. Its importance is underlined by the participation of the CR Ambassador to the OECD, Mr. Karel Dyba.

The conference brought together outstanding researchers at a time when new targets are evident for European and world agriculture, creating challenges to which agricultural research has to respond. While stocks of non-renewable resources mainly in the field of energy are limited, the problems associated with growing populations, climate change, soil degradation, and shortage of water prevent the use of conventional approaches to increased production as known from the last century as the "Green Revolution". Ecological intensification, *i.e.* employment of methods of sustained agriculture should ensure food sufficiency. It is for this reason that the themes of this conference, such as Protection of Natural Resources, Sustainable Agriculture for Food and the Environment, Competition in Agriculture for Food, Fibre and Fuel, Food Safety, etc., have been chosen for discussion.

The conference programme focuses on the greatest achievements of agricultural research in the past five years and the possibility of further development of these very important scientific issues.

The conclusions of this conference will help in formulating the direction of agricultural research and become a source of inspiration for politicians, scientists and investors, and a rich source of information to the public interested in agricultural research.

Jiří Urban

MINISTERSTVO
ZEMĚDĚLSTVÍ
České republiky
117 05 Praha 1, Těšnov 17
-31-

Former Deputy Minister of Agriculture of the Czech Republic

ACKNOWLEDGEMENTS

The OECD Co-operative Research Programme: Biological Resource Management for Sustainable Agricultural Systems (CRP) expresses its appreciation to all participants for contributing to the success of the Conference on Challenges for Agricultural Research. The Conference was made possible through the generous support of the Ministry of Agriculture of the Czech Republic Ministry of Agriculture. The OECD also greatly acknowledges the former Chair of the Management Committee of the CRP for his input into the organisation of the Conference, the Session Chairs and all the speakers for presenting their work and contributing to this publication. The Conference was organised by Dr. Ervin Balázs, department head of applied genomics at the Agricultural Research Institute, Martonvásár, Hungary, and former Chair of the CRP Management Committee, Dr. Milan Podsednicek, Czech Delegate to the Governing Body of the CRP, Mr. Carl-Christian Schmidt and Ms. Janet Schofield of the OECD Secretariat. The publication has been prepared and edited by Ms Janet Schofield and Ms Nathalie Elisseou Léglise.

Table of contents

Abbreviations **11**

Executive Summary **15**

Report from the CRP Reflection Group meeting on "Vision for the Future" **19**

Part I. Coping with Pressures on Natural Resources (Water and Soil) **27**

Chapter 1. Balancing Global Agricultural Water Supply and Demand **31**

More food 32
More water because of changing diets 34
Scenarios of future water for food demand 35
Role of rainfed agriculture 36
Productivity improvements in irrigated areas 36
Trade 37
Challenges 37

Chapter 2. Effect of Reduced Water Supplies on Food Production Economies **43**

Drivers for water scarcity 44
Importance of "new" challenges for agricultural water availability 44
Role of agricultural productivity 47
Conclusions 49

Chapter 3. Global Soil Resource Base: Degradation and Loss to Other Uses **53**

Introduction 54
World population and soil resources 54
Soil degradation, land degradation and desertification 55
Determinants of soil degradation 55
Processes of soil degradation 56
Cause of soil degradation 57
Assessment of soil degradation, land degradation and desertification 58
Soil degradation by land misuse and soil mismanagement 61
Conversion to other land uses 62
Strategies to reverse soil and land degradation trends 63
Conclusion 65

Chapter 4. Soil Resources: Science-Based Sustainability **71**

Myth 1: Agriculture should mimic natural systems 72
Myth 2: Mineral fertilisers are bad 72

Myth 3: Organic farming can be done anywhere 72
Myth 4: We know quantitatively the effects of soil use on food production, environmental degradation and climate change 73

Part II. Delivering Agriculture for Food and the Environment 75

Chapter 5. Managing Agricultural Landscapes for Production and Biodiversity Outcomes 79

Introduction 80
The ongoing declines in biodiversity 81
Current approaches to managing interactions between agriculture and biodiversity 82
Conclusion 84

Chapter 6. The Role of Genetically Modified Plants in Sustainable Crop Protection 89

Crop losses by pests and food security 90
Sustainable crop protection: the concept of IPM 91
Pest-resistant plants and sustainable crop protection 92
Pest-resistant plants in an IPM perspective 93
Conclusions 100
Challenges to use GM plants in sustainable crop protection 100

Chapter 7. Science-Based Policy Issues to Enable Sustainability on the Ground 109

Food comes from the supermarket 110
Food prices are too high 110
Purchasing seed every year is a conspiracy by multinational corporations 110
Rich country agriculture is extremely efficient and thus sustainable 110
Africa has no chance 111

Part III. Competition in Agriculture for Food, Fibre and Fuel 115

Chapter 8. Economic Balance on Competition for Arable Land between Food and Biofuel: Global Responsibilities of Food, Energy and Environmental Security 117

Food security 120
Energy security 123
Biofuels 123
Challenges 132
Environmental security 134

Chapter 9. Genetic Technology, Sustainable Animal Agriculture and Global Climate Change 145

The global environmental challenge 146
Global pork production 146
Pigs and phosphorus pollution 146
Enhancing phosphorus utilisation and reducing P output in pork production 147
The Enviropig™: a genetic technology for meeting the global environmental challenge 148

Chapter 10. Challenges and Opportunities for Further Improvements in Wheat Yield 153

Introduction 154
Can we breed for yield potential with benefits in realistic growing conditions? 154
What physiological traits may be useful in future improvements of wheat yield potential? 155

Chapter 11. Replacement of Fish Meal in Aquaculture Diets with Plant Ingredients as a Means of Improving Seafood Quality 165

Fish metabolic advantages over terrestrial animals 166
Human health advantages resulting from seafood consumption 166
Cost of feeds in aquaculture 168
Cost of individual dietary components 168
Fish meal replacement 168
Fish oil replacement 171
Plant ingredients with novel functions: gossypol, saponins, quercetin, hydroxytyrosol, steroid-inhibitors 172
Research needs to facilitate wider/larger use of plant ingredients in aquafeeds 172

Part IV. Food Safety Today and Tomorrow: the Challenges in Changing Food and Farming Practices 175

Chapter 12. Major Trends in Mycotoxin Research 177

Introduction 178
History of mycotoxins and mycotoxicoses 178
Major mycotoxins 178
Other important mycotoxins 180
Research and development priorities 180
Conclusions 183

Chapter 13. Food without Zoonotic Agents: Fact or Fiction? 189

Introduction 190
Control of infectious diseases 190
(Re)emerging infectious diseases 191
Challenges in the control of foodborne diseases 192
International co-operation and communication 192
An integrated approach to food safety and zoonoses: global foodborne infections network 193
Conclusion 193

Chapter 14. Altering Foods Derived from Animals for the Future? 197

Decrease production and consumption of animal-derived foods or alter their composition? 198
Gross composition of animal products 199
New genetic selection approaches needed 200
Fatty acid composition of animal-derived foods 200
Side-effects of improved fatty acid composition 202
Altering the content of other minor compounds in animal-derived foods 203
Conclusions and additional considerations 203

Chapter 15. Plants for the Future 209

Ten thousand years of genetically modified plants 210
Biotechnology as a coherent answer to these challenges 210
Policy framework priorities 212
Public perception and regulatory framework 214

Chapter 16. Genetic Resources as the Building Blocks for Breeding: Current Status and Challenges 221

Introduction 222

Current status 228
Challenges ahead 230
Conclusions 235

Part V. Regulatory Challenges 241

Chapter 17. Animal Biotechnology in the United States: the Regulation of Animal Clones and Genetically Engineered Animals 243

Introduction 244
Regulation of animal clones 244
Regulation of genetically engineered animals 249
Summary 253

Chapter 18. Animal Cloning and Transgenesis 255

Introduction 256
Animal cloning 256
Animal transgenesis 265
General conclusions 273

Chapter 19. The Biotechnology and Biosafety Activities at the OECD 281

Introduction 282
Environmental risk/safety assessment of transgenic organisms 282
Risk/safety assessment of foods and feeds derived from transgenic organisms 285
Conclusions 286

Chapter 20. Biosafety Assessment of the EFSA GMO Panel 289

Introduction 290
The role of the scientific panel on GMO 290
Risk assessment of GMO 291
Legal background for the risk assessment of GMOs, GM food and GM feed at European Community level 293
Outlook 298

Tables

Table 3.1. Processes, factors and causes of soil degradation 56
Table 3.2. Estimates of soil degradation by Glasod methodology 58
Table 3.3. Continental distribution of soil degradation by Glasod methodology 59
Table 3.4. Comparison between Glasod estimates of desertification in dry areas with that of UNEP methodology 59
Table 3.5. Estimates of land area under different vulnerability classes of desertification and the number of impacted population 60
Table 3.6. Estimates of land area in human-induced desertification risk classes 60
Table 3.7. Estimates of area affected by land degradation 61
Table 3.8. Estimate of secondary salinisation of irrigated lands in some countries 61
Table 3.9. Extent of urbanisation among other land uses in 2005 63
Table 3.10. Urbanisation in the USA 63
Table 8.1. Transnational land acquisition, 2006-2009 119
Table 8.2. Water security 121
Table 8.3. Scenario of the future: 2050 136

Table 15.1. Plant Biotechnology present and future – Scientific achievements and innovations in plant biotechnology 213

Figures

Figure 1.1. Trends in meat and milk consumption and GDP per capita (1961-2000) 32
Figure 1.2. Per capita cereal consumption by region and by use 33
Figure 1.3. Future crop water requirements under different scenarios and assumptions 36
Figure 2.1. Projected changes in total agricultural water use, global (2000-2050) 46
Figure 2.2. Loss of grain production due to water scarcity, developing countries 47
Figure 2.3. Changes in crop yields versus changes in precipitation: Example of rainfed corn in Illinois, 1955-2008 48
Figure 3.1. Types of soil degradation and contamination 57
Figure 3.2. Reduction in soil resources base through conversion to non-agricultural uses 62
Figure 3.3. Temporal changes in global urban population 63
Figure 3.4. Strategies for reversing soil degradation trends 64
Figure 3.5. Technological options for adaptation to climate change 65
Figure 8.1 Relationships between the long/short term factors and fast/slow-moving drivers 119
Figure 8.2. Trade distortion in the EU and USA in 2009 (Ethanol) 125
Figure 8.3. Global fuel ethanol production, 2009 126
Figure 8.4. Prices of ethanol, crude oil, feed wheat and maize in the EU (July 2007-February 2009) 128
Figure 8.5. Global biodiesel production, 2009 129
Figure 8.6. Prices of biodiesel, crude oil and rapeseed oil in the EU (January 2008-February 2009) 130
Figure 8.7. The economics of ecosystems and biodiversity (TEEB): navigation challenge ahead 137
Figure 11.1. Cost analysis of trout and sea bass production in a Mediterranean country 167
Figure 11.2. Cost analysis of channel catfish production in the USA 169
Figure 11.3. Facilities used in inland aquaculture 170
Figure 11.4. Mean body weight of rainbow trout fed five practical diet formulations for 35 months 171
Figure 18.1. Main steps of somatic cell nucleus transfer (SCNT) 258
Figure 18.2. Different methods to generate transgenic animals 267
Figure 18.3. Elimination of the marker and selectable genes 269

Abbreviations

AI	Artificial Insemination
ARRA	American Recovery and Reinvestment Act
ARTs	Assisted Reproductive Technologies
ATA	Alimentary Toxic Aleukia
BAU	Business As Usual
BIAC	Business and Industry Advisory Committee (to OECD)
BSE	Bovine Spongiform Encephalopathy
C	Carbon
Ca	Calcium
CBD	Convention on Biological Diversity
CBI	Caribbean Basin Initiative
CBSA	Critical Biological Systems Approach
CO_2	Carbon Dioxide
CVM	Center for Veterinary Medicine
DDGS	Dried Distiller Grains
DDT	Dichlorodiphenyltrichloroethane (banned insecticide)
DSI	Drip Subsurface Irrigation
EC	European Commission
EFSA	European Food Safety Authority
ERA	Environmental Risk Assessment/Eicosapentaenoic acid
ETS	European Trading System
EU	European Union
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
Fe	Iron
GDP	Gross Domestic Product
GFN	Global Foodborne Infections Network
GHG	Greenhouse Gases

Glasod	Global Assessment of Soil Degradation
GLEWS	The Global Early Warning and Response System
GM	Genetically Modified
GMHT	Genetically Modified Herbicide Tolerant
GMOs	Genetically Modified Organisms
GMP	Genetically Modified Plants
GRFA	Genetic Resources for Food and Agriculture
ha	hectares
Hg	Mercury
I	Iodine
IARCs	International Agricultural Research Centres
ICID	International Commission on Irrigation and Drainage
IEA	International Energy Agency
IETS	International Embryo Transfer Society
IFPRI	International Food Policy Research Institute
IHR	International Health Regulations
INAD	Investigational New Animal Drug
INFOSAN	International Food Safety Authorities Network
INM	Integrated Nutrient Management
IPCC	Intergovernmental Panel on Climate Change
IPM	Integrated Pest Management
IPR	Intellectual Property Rights
ISRIC	International Soil Reference and Information Centre
ITPGRFA	International Treaty on Plant Genetic Resources for Food and Agriculture
IUSS	International Union of Soil Sciences
IVP	*In Vitro* Production
IWSR	Irrigation Water Supply Reliability Index
K	Potassium
L	Litres
LADA	Land Degradation Assessment in Drylands
LOS	Large Offspring Syndrome
MEA	Millennium Ecosystem Assessment
Mha	Million hectares

Mt	Million tons
Mo	Molybdenum
Mn	Manganese
N	Nitrogen
NADA	New Animal Drug Application
NDVI	Normalised Difference Vegetation Index
NGOs	Non Governmental Organisations
NIH	National Institutes of Health
NM	Natural Mating
NPP	Net Primary Productivity
NUE	Nutrient Use Efficiency
ODA	Official Development Aid
OECD	Organisation for Economic Co-operation and Development
OIE	World Organisation for Animal Health
P	Phosphorous
PGRFA	Plant Genetic Resources for Food and Agriculture
PME	Palm oil methyl ester
QTLs	Quantitative Trait *Loci*
R&D	Research and development
RFS	Renewable Fuel Standard
RMPs	Recommended Management Practices
RNA	Ribonucleic acid
rRNA	Ribosomal ribonucleic acid
SARS	Severe acute respiratory syndrome
Se	Selenium
SME	Soil oil methyl ester
SCNT	Somatic Cell Nuclear Transfer
SOM	Soil Organic Matter
TEEB	The Economics of Ecosystems and Biodiversity
TRIPS	Trade Related Intellectual Property Agreement
TSE	Transmissible Spongiform Encephalopathy
USDA	United States Department of Agriculture
UN	United Nations
UNEP	United Nations Environment Programme

UNIDO	United Nations Industrial Development Organization
UPOV	Union for the Protection of New Varieties of Plants
VMAC	Veterinary Medicine Advisory Committee
WARDA	West Africa Rice Development Association
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization
WUE	Water Use Efficiency
Zn	Zinc

Executive Summary

The OECD Co-operative Research Programme: Biological Resource Management for Sustainable Agricultural Systems (CRP) was established in 1979 to strengthen co-operative efforts among research scientists and institutions. Its main objective is to strengthen scientific knowledge and provide relevant scientific information and advice to inform policy decisions related to the sustainable use of natural resources in the areas of food, agriculture, forestry and fisheries.

The Programme is anchored in both the policy and scientific communities in the fields of food, agriculture, forestry and fisheries, which, more than ever, develop in a multidisciplinary environment. This happens so as to respond to the varied demands from a range of stakeholder groups with interests in these fields, and to take into account an evolving globalised world in which food production systems are interlinked.

The CRP implements its work through two types of activities: Research Fellowships through which it funds scientists to conduct research projects in a different Member country[1] with a view to strengthening the international exchange of ideas and increasing international mobility and co-operation; and Conference sponsorship (or co-sponsorship) of international conferences, workshops, symposia, congresses, (organised by, for example, research institutions, international associations), with a view to informing policy makers, industry and the academic world of current and future research, scientific developments and opportunities.

A meeting of the Bureau of the Governing Body of the CRP and scientific advisors from its Management Committee[2] in Budapest in April 2008 on the theme of "Vision for the Future" discussed the future direction of the CRP. The outcome of that meeting is to be found in the annex to this executive summary. As a follow up, and with the help of the Czech Ministry of Agriculture, the CRP organised a Conference in Prague in 2009 on "Challenges for Agricultural Research". This conference gathered experts from conferences the CRP had sponsored in 2005-2009 to review the progress agricultural science has made over this period, and to identify challenges for the future.

The global drivers were seen to be food security, climate and environmental changes. The Prague Conference was organised in five sessions: (i) Coping with Pressures on Natural Resources (Water and Soil); (ii) Delivering Sustainable Agriculture for Food and the Environment; (iii) Competition in Agriculture for Food, Fibre and Fuel; (iv) Food Safety Today and Tomorrow: the challenges in changing food and farm practices; and (v) Regulatory Challenges.

The session on Coping with Pressures on Natural Resources reviewed the use – and loss – of water in the whole food chain and the effects of a changing climate on the availability and equitable distribution of water. Problems of intersectoral competition, including for biofuel production, the degradation and pollution of water bodies,

unsustainable groundwater use, the need for bold international agreements and the reduction of corruption were discussed.

The importance of soil is often overlooked, especially the consequences of soil degradation and the resultant loss of nutrients, and the effects climate change has on soil, and the effects soil and its use can have on climate change, and the loss of agricultural land to other uses. For example, one ton of carbon is needed to produce, transport and apply one ton of nitrogen in fertilisers. Research is urgently needed to establish credible estimates of soil degradation and its impact on ecosystem services, food security and human nutrition. Policies are needed on land use and its management to minimise and reverse degradation risks. Concurrently, improved communication among all stakeholders is essential.

The session on Delivering Sustainable Agriculture for Food and the Environment looked at various aspects of agricultural management systems: land use to improve productivity and favour biodiversity, the role that genetically modified (GM) plants may play in sustainable crop protection; and how sustainability science can effect change in both developed and developing economies.

It was recognised that effort needs to be put into developing systems and landscapes that will provide ecosystem services such as carbon sequestration, flood control and biodiversity as well as improving production. Sustainable crop protection should use all suitable techniques compatible with economic, ecological and social requirements to improve crop productivity whilst preventing loss both before and after harvest. Integrated pest management is one of the most efficient ways to prevent loss and was examined in the context of the contribution of GM crops. There is an onus on the part of rich countries in particular to examine policies to make agriculture more sustainable, whilst innovative ways of helping to finance sustainable practices in the developing world need to be identified. Above all, sustainability issues must be based on science and agricultural researchers have a responsibility to articulate that science in a simple way.

Session three looked at competing pressures in agriculture to produce food, fibre and fuel and at responses for coping with those pressures. The challenge to food production by biofuels is considerable and the importance of not using agricultural land for crops for biofuels and other bio materials was stressed, particularly if changes in land use cause biofuel production to increase green house gas (GHG) emissions rather than reduce them. Growing global populations with enhanced spending power will increase the demand for meat, necessitating adequate land availability, but at the risk of increased GHGs and pollution of water courses through waste and run-off. Whilst research into technologies to reduce these effects in livestock is being undertaken, more research is needed.

A major use of agricultural land is wheat cultivation, but as a slowdown of yields has been observed, new methodologies and technologies need to be explored to understand why and bring solutions. A significant investment in research funding is needed to cope with the challenge ahead.

Turning to aquaculture to provide a solution to the demand for food and to reduce pressure on the world's fish stocks is not necessarily as straightforward as it seems; aquaculture still takes considerable resources from the seas to feed cultured fish. Important research into using plant protein as a substitute is being carried out and could have great potential.

The main message of this session, however, is that these new technologies and methodologies are important to the global food system and therefore need to be supported and shared globally.

Food safety and the importance of food and farming practices – session four – can be seen from several different angles: from understanding the significance and management of toxic fungi on crops (mycotoxins) in the food chain and their contribution to human health problems; through the importance of research into pathogens transmitted to humans from animals and animal products (zoonoses), both ongoing research into currently known zoonoses and having the structures to cope with new ones which emerge; to using known technologies to produce animals that provide food that is healthier for humans; through to the importance of conserving the world's rich diversity of plants and crops amongst a fast diminishing supply in order to have the greatest bank of genes possible to pick from to improve crop varieties for the pressures of the future.

The key messages emerging from this session are that the importance of animals as part of the food chain is as great as that of plants and that there is an urgent need for research and investment in research into animal breeding and pathologies. There is a worry that the rest of the world will gain from GM technology, but not the European Union (EU). Very closely linked to this is the urgent work that needs to be done with the public on these new technologies, to demystify them and explain clearly and precisely, and engage better with the public.

The final session of the conference looked at the different procedures of transgenesis and cloning and the regimes in place for controlling and certifying the new technologies. This included presentations on the official procedures and regulations in place in the US and Europe, and the work that the OECD is doing on genetically modified organisms.

*

* *

The over-riding message of the conference was that sustainable agriculture requires an integrated approach involving both the public and the private sectors: to harness science, technology, structures and supply chains to ensure productivity; to develop working practices that take environmental outcomes and resource pressures into account; to provide the right signals to farmers through pricing; to ensure a coherent approach to policy making at domestic, regional and global levels; and to pay more attention to considering social and educational issues. Agricultural research needs to be both broader in scope and in scale. Broader in scope to include productivity, environment/biodiversity, food chain and food safety, human nutrition, health, non-food products, climate change and socio-economic issues. Broader in scale to move from studying molecules to landscapes, from local issues to global issues and from the farmer's needs to the needs of all the stakeholders.

These are indeed challenges for agricultural research, which, by 2050, will need to support a doubling of world food production, a reduction in the environmental footprint, the maintenance of economic returns for farmers and landscape managers, and the rationalisation of the allocation of photosynthate into food, fuel and carbon sequestration.

And how can this be achieved? Four main areas emerged from the conference:

(i) productivity gains in major food crops and livestock systems need to be re-invigorated through the application of new technologies and integrated management practices;

(ii) policies and incentives should be developed which recognise and reward the environmental gains made by land holders, particularly in the field of sustainable management of key resources (soil, water, natural vegetation);

(iii) more focus on policies which assist agriculture to adapt to climate change; and

(iv) greater focus on supply chain dynamics, particularly on post-harvest losses and inefficiencies in developing economies.

Notes

1. CRP Member countries are: Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Japan, Korea, Netherland, New Zealand, Norway, Poland, Portugal, Slovak Republic, Spain, Sweden, Switzerland, United Kingdom, United States.

2. On 1 January 2010, the Management Committee officially became the Scientific Advisory Body to reflect its mandate better.

Report from the CRP Reflection Group meeting on "Vision for the Future"

Budapest 7-8 April 2008

Introduction

On 7 and 8 April 2008 the Management Committee of the Co-operative Research Programme: Biological Resource Management of Sustainable Agricultural Systems (CRP), upon the request of the Governing Body, met in Budapest to consider a "Vision for the Future" for the CRP programme, with a view to contributing to the preparation of the CRP's mandate for 2010-2014. In addition to members of the Management Committee, Tony Burne (former Chair of the Governing Body), Yvon Martel (Vice-Chair of the GB), Peter Keet (GB) and Jim Lynch (former Chair of the Management Committee) participated in the deliberations.

The Reflection Group noted the appropriate timing of the meeting which offered the opportunity to provide input into the on-going in-depth evaluation of the CRP (and the Committee for Agriculture) in fulfilling its role in working towards sustainable agriculture.

The meeting discussed various issues related to the CRP. The present report is designed to provide the GB, the Mandate Steering Group (Messrs. Dodet, Burne, Fitt and Balázs) and the in-depth evaluators, with ideas for how the future mandate of the CRP might look. It is an input into a broader discussion and agreement by the GB and the COAG of a draft mandate that will precede the next mandate finally being adopted by the Council of the OECD in October 2009.

This report first reflects on the multiple roles of agriculture in the provision of public goods and services. The report then reflects on the CRP's present themes and suggests some specific priority research areas for future work. The report then considers the governance structure of the CRP and in particular the respective roles of the GB and the MC and the links between the CRP and the Committee for Agriculture. The Reflection Group finally found it appropriate also to include some suggestions for a communications strategy that might help in adding visibility to the Programme.

Role of the CRP

The primary role of the CRP is to enhance global networks focussed on globally relevant research issues, while contributing significantly at the boundaries between policy and research. The CRP seeks to be complementary and to add value to work on agriculture, fisheries and food, and to support the overall OECD-wide agenda.

The CRP delivers these outcomes through fellowships, conferences and workshops which meet agreed criteria.

Multiple roles of agriculture, forestry, fisheries and food systems

Besides providing food and fibre, agriculture plays several roles and contributes significantly to societal welfare in a range of ways. As such, agriculture contributes significantly to both private and public goods. Chief among these are in energy, medicine, landscape amenity and design, land management through preventing erosion and off-site impacts, migration of people, containment of disease, habitat for biodiversity, healthcare, recreation and leisure. An increasingly important contribution of agriculture is in its interface with climate change through carbon sequestration. In this domain forestry (in a wider definition of agriculture) is also an important land use contributing to climate change mitigation. Finally, agriculture contributes to the development and resilience of rural economies and communities.

In considering the challenges faced by agricultural systems we also note that ocean ecosystems (*e.g.* fisheries, aquaculture and algae) reflect many parallels with agriculture in their need for sustainable management and can help relieve the stresses on terrestrial ecosystems.

These challenges are to be met against a background of decreasing agricultural resources as the quantum of arable land is finite and there are competing uses. Concurrently water is becoming more and more scarce and here also agriculture is in competition with other uses. These facts all point to the need for innovative strategies if we are to feed an increasing population. The only way to do this is to invest the necessary funds, efforts and energy into agriculture, forestry, food and fisheries research to achieve sustainable production outcomes. The need for international networking in agricultural and food research has never been more important.

The CRP themes

During the current mandate period, the CRP is addressing three main research areas, with a focus within them on renewable resources. Within the context of the sustainable use of agriculture and biological resources, these are:

- THEME 1: Securing the availability and managing the quality of natural resources for sustainable agricultural production systems
- THEME 2: Developing and adapting food, fibre and bio-energy enterprises, both modern and traditional, to contribute to the sustainability of natural resources
- THEME 3: Contributing to technological advances to sustain the global food and agriculture systems from input to final consumption

The Reflection Group considers that the three themes are relevant and will provide sufficient flexibility for the delivery of the Programme while encompassing the growing suite of priorities from both the policy and research communities and in the light of the overarching responsibility to respond to the challenges of climate change and policy coherence for development.

There are a number of issues that all have implications for agricultural research and which need to be mainstreamed into a substantive, multidisciplinary research agenda (taking into consideration the economic, social and environmental challenges of a given research project) to be able to respond to policy makers' needs.

Few now doubt the growing scientific evidence that human actions are changing the global climate through the emission of greenhouse gases. The International Panel on

Climate Change (IPCC) has projected that temperatures are highly likely to increase by 1.4-5.8 degrees C over the next 100 years. The result may be an increased frequency of extreme weather events and changing rainfall regimes with detrimental impacts on the natural world and on human society. Understanding these impacts is the first step to determining plans for action nationally and at global level. It is therefore imperative that science financed by the CRP automatically integrates climate change as an overarching challenge and addresses this in its work.

Developing countries are playing an ever increasing role in the food production system while, concurrently, their resource base is also under stress. For OECD countries it is therefore important to consider in their policy making, and hence in the research underpinning policy-making decisions, the interaction between the developing and developed world with a view to mitigate geographically negative economic, social and environment impacts policies may have. Coherence across agriculture and development policies can contribute to this, and research underpinning agriculture policy making should take policy coherence for development into account. The future alignment of developing economies in Asia and South America with the OECD and the CRP offers a unique opportunity to address this need.

Finally, the CRP also needs to be seen against the context of new and developing technologies.

Specific priority areas of agriculture and fisheries research

In discussing a range of issues that would be of particular relevance and priority to consider, the Reflection Group focused on the 12 areas of work described below. This is not exhaustive and as the CRP develops over 2010-2014, guidance from the Committee for Agriculture will periodically be sought with a view to prioritising the work and ensure the continued policy relevance of the Programme.

Landscape

Landscape is a useful conceptual principle which captures the integration of ecological processes and agricultural productivity at relevant spatial scales. Healthy functioning landscapes, with their links to the urban environment, have multiple roles and deliver a range of services to society some of which are non-economic and intangible in nature. This includes, but is not limited to, leisure, health, tourism and biodiversity conservation. Key services provided by landscapes include the stabilisation of water resources, significant buffering of climate through carbon sequestration of soil and the role of vegetation cover. Agriculture plays a key role in maintaining landscapes that deliver such services to society.

Spatial policy

Management of space and therefore ecosystems may be an important future challenge with implications for agriculture roles. Scale of impact, different uses of space, competitive claims from different user groups, and prices all affect the way agriculture is positioned in the policy mix being applied to terrestrial space. There are major competitive forces with respect to the agricultural *versus* non-agricultural uses of space. This includes urban and coastal encroachment. Mapping of different uses of space is an

important component in the policy makers' toolkits for addressing conflicting user claims and societal needs.

Invasive species and bio-security

With increasing global interactions across countries and continents, invasive species are increasingly a challenge and the importance of biosecurity preparedness and risk assessment is growing. Invasive pests and diseases threaten both agricultural productivity and biodiversity. From a human perspective, the emerging issues of pathogens transmitted from animals to humans (zoonotic diseases like SARS, avian "flu"), or directly to humans, animals and crops, can have devastating effects across the globe within a short time span. Understanding the spread of these pests and diseases, early detection and assessment to develop appropriate policy responses are crucial for modern societies. In addition, risk assessment is needed to gauge the importance of these challenges.

Water

Agriculture is a major user of water and in some regions and for some crops may be the primary user. Falling water tables means that water is increasingly being mined, and not replenished. Agriculture is a key driver in the water dynamics of catchments and its total water use may be seriously depleting water availability and impacting on quality. This nexus is becoming a widely recognised problem that needs to be underpinned with appropriate agriculture and food policy research.

Animal production

Growing demand for animal protein due to increasing living standards across the world has put pressure on the animal production systems. This has possible negative consequences for the environment with impacts on the use of feed and feed compounds, and water. In addition, there is competition for alternative uses of the same resources. There is an urgent need to reconsider present production systems with a view to reducing the externalities of animal husbandry including the identification of new and improved protein sources, animal production practices and animal movement. It is recalled that animal production is an important source of greenhouse gases, notably methane. The role of aquaculture to provide alternative sources of protein and more generally the use of the oceans have a potential to help reduce the stress on the terrestrial food production systems.

Forests

Forests, when sustainably managed, provide an important carbon sequestration service to society over and above social amenities, water retention, biodiversity and the environmental protection of land. Nevertheless the continued deforestation and certain forest practices make this a key research area, most notably in countries not members of the OECD. In this respect, deforestation in the developing countries is a major policy coherence for development issue.

Bio-products and bio-processes

There is a growing demand for bio-products produced with biologically sound farming practices. While still relatively small in the overall food market, this has become a non-negligible part of the consumers' demand schedule. Further, there is a growing interest in bio-products and bio-processes on an industrial scale from the private sector. The interaction between these developments and traditional farming practices (*e.g.* food *versus* energy, pharmaceuticals, novel non-food uses for agricultural products) is prone to conflicts of interest and will take a growing space in the policy debate. Nevertheless, the science underpinning the possible externality effects of such production systems is underdeveloped and represents a significant opportunity.

Biodiversity

Biodiversity issues are increasingly coming to the forefront of the agriculture, forestry and fisheries policy debate. Modern management practices coupled with climate change and other human activities (*e.g.* urbanisation) consistently put pressures on biodiversity. The resultant loss of biodiversity not only threatens the functioning of terrestrial and marine ecosystems, but also the capacity of society to adapt to certain challenges (*e.g.* diseases). It is therefore important that management practices take into consideration the protection and enhancement of biodiversity and that policies are being brought to bear so as to define the limits of tolerable impacts. Two particular areas of concern with respect to biodiversity are "subsidies" for biodiversity and how to deal with property rights for genetic resources.

Waste (and by-products)

The policy and research challenges are to realise the potential and value of what might be regarded as waste. Recycling is an important objective for food production systems with a view to capturing the externalities. Animal husbandry is chief among the agriculture practices with major waste effects with impacts on the environment. Research in this area seeks to understand the potential of waste for alternative uses, improve the use of waste, for example, in energy production, including better sources of fertiliser and conditioners of soil.

Food security

Global food demand is undergoing major change in quantity and structure and will dramatically increase along with demographic changes. Globalisation of food production systems may add an additional food security risk. Both are likely to increase the uncertainty and vulnerability of the food production system. Research in this area can contribute to better identifying risks in food production chains through vulnerability, disease, outbreaks (biological and physical crises) and identify best practices among member countries in addressing such risks. The costs of inaction in this respect may add political risks and undermine the stability of societies.

Aquaculture and marine ecosystems

The marine ecosystem can also be an important provider of food and bio-energy products. Given pressures on terrestrial ecosystems it would be advisable to increasingly focus on the ability of the oceans to reduce the stress on the productive capacity of the

terrestrial ecosystem, while recognising that some marine ecosystems are already under pressure. Research in this area could include better aquaculture practices and the use of algae in bio-energy production.

Energy use in food production

Food production systems are also responsible for adding to climate change through the energy needed to grow crops and raise animals, transport, processing and distribution. Research in this area on life cycle analysis could contribute to identifying food production systems with greater energy efficiency.

Governance

The Reflection Group considers that the present governance structure is a useful and appropriate way of delivering the aims and objectives of the Programme. It would be useful for the Management Committee to receive more strategic direction from the GB (it is suggested after consultation with the Committee for Agriculture (COAG)) on the future key priorities so that the Management Committee can steer its choice of appropriate conferences, workshops and fellowships to be considered for finance.

The Reflection Group supports the two main vehicles for delivering the Programme *i.e.* sponsoring of workshops (conferences) and fellowships. In this respect, the Group noted that the longer term policy challenges are most likely to be dealt with by fellowships, while the immediate and medium term policy issues are best addressed by the sponsoring of workshops and conferences. The conferences are also a means to involve a broader range of stakeholders.

As to the function of the Governing Body, the Reflection Group agreed with the analysis of the Chair of the CRP, M. Michel Dodet, that there is, at present, an insufficient interaction between the GB, and hence the CRP as a whole, and the COAG. The means to achieve this is nested in more appropriate communication channels, including, for example: (i) by participation of the Chair of the GB in COAG meetings, (ii) OECD staff participation in conferences/workshops sponsored by the CRP with a view to giving the COAG a necessary feedback on outcomes, policy relevance etc., and (iii) through improving the reporting from conference evaluators and Theme Co-ordinators to COAG. Likewise, the MC should be able to suggest to the GB conferences they consider to be of particular research relevance.

As a result, a bottom-up, top-down approach is achieved, with respect to the prioritisation of deliverables. In this way, a demand-driven research agenda is likely to develop. It is suggested that the role of the CRP's GB will be, through its interaction with the COAG, to ensure that this is implemented so that the priorities of the COAG are continuously being considered by the Programme.

Communication strategy

The Reflection Group discussed and considered the communications of outcomes and intentions during the present mandate period and concluded that there is a need to revisit the way the CRP communicates both with the COAG and stakeholders at large. In particular, the Reflection Group suggests that, increasingly, recourse be taken to use (i) internet advertising (using the already existing CRP website), (ii) press releases as appropriate, (iii) reports of conferences (where some improvements have already been

taking place), and (iv) in the provision of an annual report to the COAG and external stakeholders.

While the primary responsibility for the production of such initiatives would be with the GB, it was suggested that the Management Committee should be taking the initiative to produce an annual activity report and Policy Briefs, when appropriate. In this respect the Reflection Group acknowledges the need to communicate in a language that is accessible to a broad range of stakeholders with interests in agriculture, forestry, food and fisheries research.

Part I

Coping with Pressures on Natural Resources (Water and Soil)

Summary of discussions

John Sadler, United States Department of Agriculture (USDA)-Agricultural Research Service (ARS) Cropping Systems and Water Quality, Columbia, United States

Research Unit

It takes only a cursory glance at per capita arable land and per capita fresh water supplies to recognise that global trends are not promising. Continued pressure both for land (housing, roads, and industrial uses plus degradation of producing lands), and for water (municipal, industrial, recreational, and environmental uses plus degraded water quality) combine to make global food production an increasingly worrisome issue. In recognition of the pressures on soil and water resources, four speakers were asked to provide summaries of the current state and trends of the soil and water resources, and to provide assessments of the resource trends on food production.

Charlotte de Fraiture, of the International Water Management Institute, in Accra, Ghana, presented "Balancing Global Agricultural Water Supply and Demand". Dr. de Fraiture outlined drivers for and disposition of the 7 100 km^3 per year of water depleted for food production globally, and emphasised how urbanisation, climate change, increasing energy prices, and evolution of human diets to include more meat all affect water use. She listed four particular challenges:

(i) increase productivity (both physical and economic productivity) of both rainfed and irrigated agriculture,

(ii) adapt irrigation to rapid changes in pressures on water resources,

(iii) transfer water-dependent production from water-scarce to water-rich areas through trade, and

(iv) reduce losses in the food chain to conserve water resources.

Claudia Ringler, International Food Policy Research Institute, Washington, D.C., USA, presented "Effect of Reduced Water Supplies on Food Production Economics". Dr. Ringler listed challenges including increasing intersectoral competition, degradation of water and land resources and the environment, growing water pollution, unsustainable groundwater use, water use for biofuel production, and climate change impacts on water for agriculture.

She outlined long-term projections assuming business as usual, decreased investment in agricultural research and development (R&D), increased investment in agricultural R&D, and the most optimistic possibility assuming investments in irrigation, drinking water, and access to female secondary education. Complementary investments in agricultural technologies (seeds, fertiliser), rural infrastructure (roads, telecommunications) and in complementary sectors (education, health) are needed to increase agricultural productivity sustainably to reduce growing agricultural water scarcity and agricultural production risk.

Rattan Lal, Ohio State University, Columbus, OH, USA, presented "Global Soil Resource Base: Degradation and Losses to other Uses". Dr. Lal outlined per capita arable land resources and trends, with projections toward 0.1 hectare (ha) per person and described types of degradation (erosion, salinisation, nutrient depletion, and chemical or physical degradation). Land use changes of concern included urbanisation, use for infrastructure, and the emerging conversion of land to plantations to provide biofuel feedstocks. Concentration of minerals into urbanised areas were pointed out as a significant problem. He defined the terms soil degradation, land degradation, land desertification, and vulnerability to desertification, and emphasised that science must standardise terminology to have credibility outside science. He also emphasised the need to increase understanding of nutrient mining in Sub-Saharan Africa. He outlined the basic principles of sustainable management of soils, the need to create positive carbon and nitrogen budgets, and the strategy of carbon sequestration in soil to mitigate climate change.

Pedro Sanchez, The Earth Institute at Columbia University, New York, NY, USA, presented "Effect of Shrinking Soil Resources on Food Production". Dr. Sanchez reviewed nutrient mining in poor countries and excessive nutrient loading in richer countries as causes of soil degradation. He listed and explained policy needs to reverse soil degradation. As a case study, he described the Millennium Village Project. The cost of providing mineral fertiliser and improved seeds to farmers who produced a tonne of maize was one-sixth that of the equivalent support through US food aid. He promoted the advantages of the global digital soil map as a way to catalog and quantify the soil resource base.

Discussion

Questions from the audience included issues regarding biotechnology (especially regarding drought resistance), soil biology, water pricing, and what were the new topics for research. Lal responded about types of improved germplasm that would help conserve water, produce high biomass, deep root systems to transfer carbon into the subsoil, and contain recalcitrant compounds so that biomass would not decompose rapidly. De Fraiture explained the successful implicit water pricing that already exists in areas where pumping costs provide the same incentive, but where water is provided via infrastructure that farmers cannot control, then water pricing policy is likely not possible. Lal and Sanchez discussed soil biology and microbiology implications to nutrient cycling, biological nitrogen fixation, and soil structure.

Speakers were provided an opportunity to offer their perspectives on promising new areas for research: Dr. Lal listed a) nanotechnology, particularly for slow-release fertilisers (including zeolites), b) water delivery methods (perhaps as vapour directly to roots, where it condenses), and subsurface drip irrigation, c) using carbon dioxide (CO_2) as a resource instead of as a waste product, as implied by geologic sequestration, to develop Bioeconomy, d) linking the carbon (C) deficit with the nitrogen (N) deficit, and the need to enhance both C and N in soil, and to improve its quality, e) soil biology, especially with regards to earthworms and soil microbial biomass, f) plants that emit molecular signals when under stress (drought, nutrient deficit) that can be detected by remote sensors and treated with targeted interventions.

Dr. Sanchez listed a) nanofertilisers, b) biotech plants for improved soil management – both water and nutrient efficiency, c) adaptation to climate change – both water and temperature, d) modern soil mapping.

Dr. De Fraiture listed a) the need for more research on adoption strategies of new technologies for poor smallholder farmers in developing countries, b) although not really new, the need for more research on groundwater recharge as response to climate variability, c) on-farm water storage – linings and other ways to reduce losses.

Dr. Ringler listed a) sustainable agricultural productivity increases to combat climate change, water quality effects, and reduce farmer risk, b) education needs, especially secondary female education.

Dr. Lal added a) finding ways to use human waste and recycle nutrients and water, b) Africa – soil knowledge (education), c) soil quality and malnourishment that affects 3.7 billion people, especially deficiency of micronutrients (iron (Fe), zinc (Zn), iodine (I), selenium (Se)), d) manage rhizosphere processes to create disease-suppressive soils, e) sse remote sensing (normalised difference vegetative index (NDVI)) to enhance nutrient use efficiency.

Session moderator Dr. John Sadler of the USDA-ARS Cropping Systems and Water Quality Research Unit, Columbia, MO, USA, added the following: a) extending the idea of on-farm storage into the general terms of retaining water as high in the watershed as possible, b) scaling issues – scaling up from point research to mixed landscapes, to multiple watersheds, to multiple political entities, c) stochastic analytical tools to quantify risk by primarily deterministic scientists, d) understanding lack of adoption of known solutions will require social sciences and probably base-level education.

The speakers collectively outlined the state and trends of soil and water resources and presented the numerous challenges these represent to global food production. This context set the stage for the discussions following in later sessions.

Chapter 1

Balancing Global Agricultural Water Supply and Demand

Charlotte de Fraiture

International Water Management Institute, Accra, Ghana

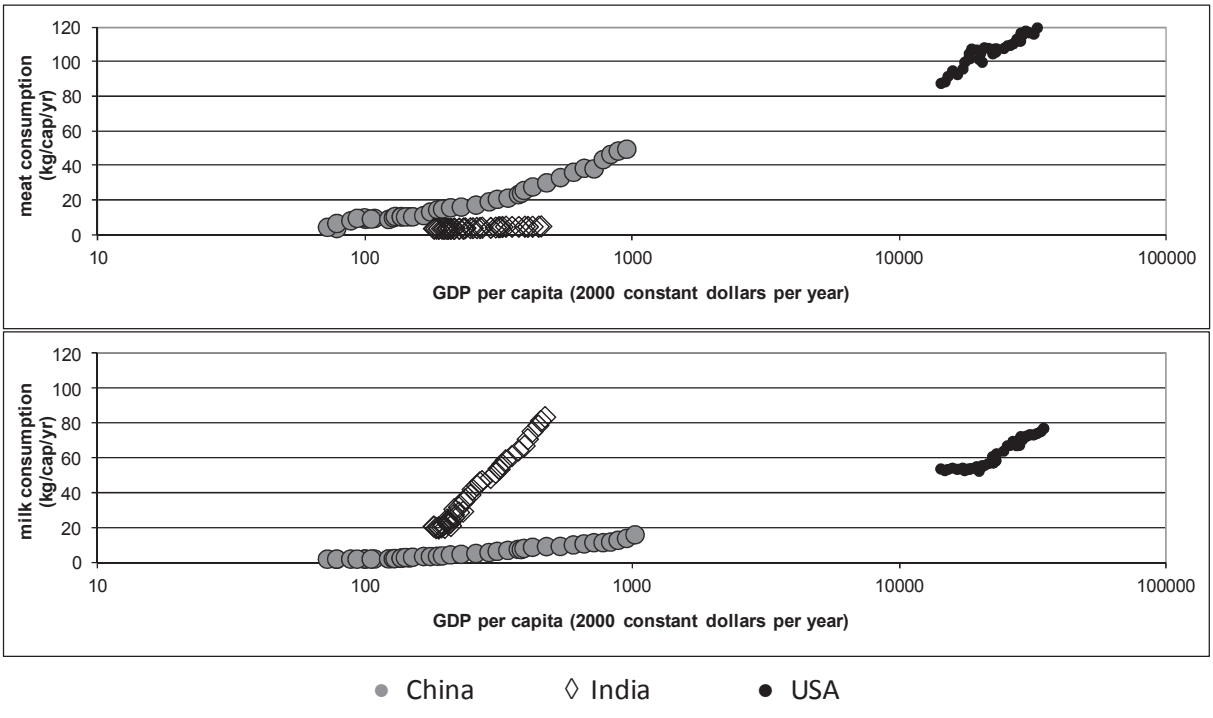
The recently completed Comprehensive Assessment of Water Management in Agriculture concluded that globally there are sufficient land and water resources to produce food for a growing population over the next 50 years. But it is probable that today's trends, if continued, will lead to water crises in many parts of the world. Yearly some 7 100 billion cubic meters (m^3) of water are evaporated by crops to meet global food demand, equivalent to more than 3 000 litres per person per day. With a growing population, rising incomes and changes in diets, food demand will increase rapidly. Demand for biomass for biofuels will further drive the demand for agricultural products and hence agricultural water. Some forecasts foresee a doubling of agricultural water demand in the coming 50 years. This is reason for concern as already 1.2 billion people live in areas where water is insufficient to meet all demands. Fortunately, there seems much scope to improve productive use of water and get more out of a unit of water. This paper explores forecasts of global agricultural water demand and scenarios to meet this. It concludes with challenges in future water supply.

"Globally there are sufficient land and water resources to produce food for a growing population over the next 50 years. But it is probable that today's food production and environmental trends, if continued, will lead to crises in many parts of the world. Only if we act to improve water use in agriculture will we meet the acute freshwater challenge facing humankind over the coming 50 years." (CA, 2007)

More food

As incomes rise, food habits change in favour of more nutritious and more diversified diets. Generally this leads to a shift in consumption patterns among cereal crops and away from cereals toward livestock products and high-value crops such as fruits, vegetables, sugar and edible oils (Rosegrant, 2002). For example in south-east Asia the per capita rice consumption peaked at around 120 kg per capita per year during the 1980s while per capita wheat consumption more than tripled between 1961 and 2002 and is still increasing. Meat consumption grew by a factor of seven from 6 to 40 kg per capita per year. Consumption of high-value crops – such as fruit, sugar and edible oils – also increased substantially (FAOstat, 2006). While the trends in diets follow similar patterns, regional and cultural differences are pronounced. For example, meat consumption in India rose much slower than in China considering the same increase in income, but consumption of milk product increased more rapidly. Figure 1.1 illustrates this for India, China and the United States (USA). The graph based on historic data from 1960 to 2000 shows a clear relation between per capita GDP and the per capita meat consumption in China. In India, a largely vegetarian country, meat consumption remains low despite increasing incomes. Milk consumption however shows a clear rising trend. In the USA where incomes are high meat and milk consumption are also high. The general message is clear: with increased income, consumption of livestock products increases.

Figure 1.1. Trends in meat and milk consumption and GDP per capita (1961-2000)

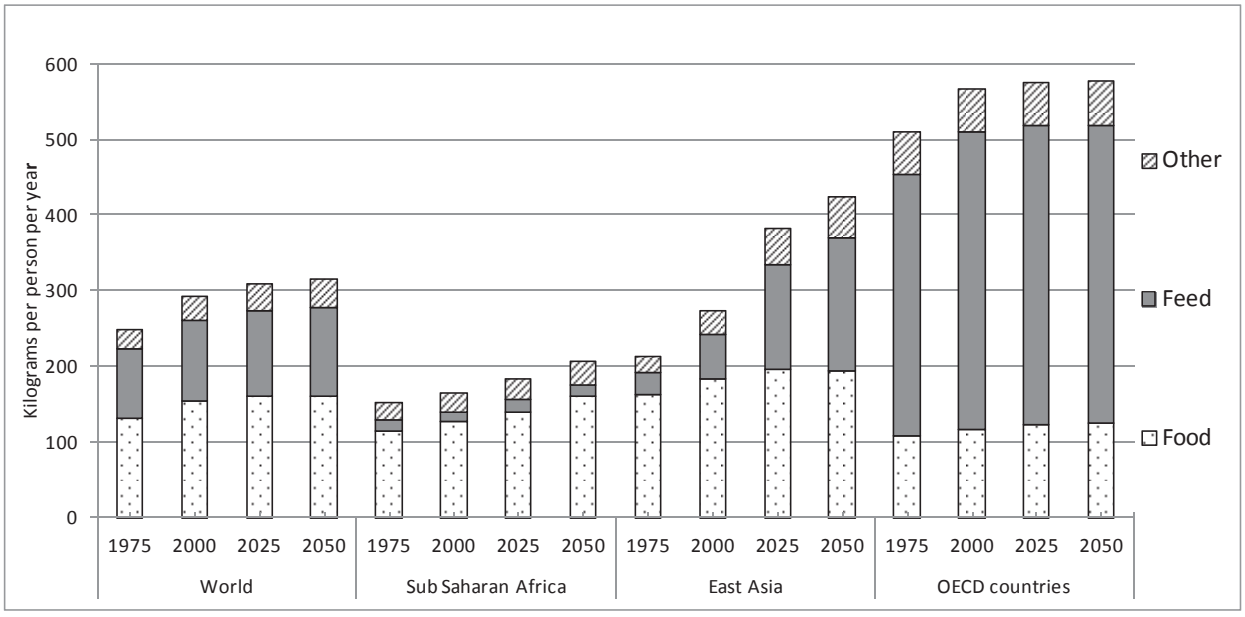


Source: GDP data from Worldbank WDI online; consumption data from FAOstat.

General trends toward more diversified and meat based diets are well documented (Pingali, 2004). But considerable uncertainties remain regarding some of the major

factors driving future food and feed demand. First, environmental concerns and emerging health problems related to obesity might generate new trends, particularly in high income countries. Outbreaks of diseases such as mad cow disease and, more recently, avian and swine flu might frighten consumers away from meat consumption. Second, much uncertainty relates to feed grain requirement per kg of meat, milk and eggs. Livestock are fed primarily by a combination of grazing, crop residuals, and feed stuffs (primarily grains). In OECD countries where cattle are raised largely on feed grains, two-thirds of average per capita grain consumption is devoted to feeding cattle. By contrast in sub-Saharan Africa and India where livestock are fed crop residuals, grazing lands and by-products, less than 10% of the grain supply is used for feed (Figure 1.2). The big question is how livestock will be fed in future. Third, though figures are sketchy and outdated, evidence points to substantial losses in the food chain (from field to fork) (Lundqvist *et al.*, 2008). Losses in the field (between planting and harvest) may be as high as 20% to 40% of the potential harvest in developing countries due to pests and pathogens. Losses in processing, transport and storage are conservatively estimated between 10% and 15% in quantity terms, but could amount to 25–50% of the total economic value because of reduced quality (Kader, 2005; Kantor *et al.*, 1992). During retail and consumption 10-25% of fresh fruit and vegetables are wasted. Most projections assume that losses remain large, but bigger awareness may lead to a greater effort to reduce post-harvest losses. Fourth, incomes that drive changes in diets are difficult to predict. For example, the difference between the most optimistic and most pessimistic income projections for 2050 made by the Millennium Ecosystem Assessment (MEA) differ by a factor 2.5 (MEA, 2005).

Figure 1.2. Per capita cereal consumption by region and by use



Source: For 1975 and 2000, FAOSTAT (2006); for 2025 and 2050, International Water Management Institute analysis done for the Comprehensive Assessment of Water Management in agriculture using the Watersim model.

Projections of future food demand reflect these uncertainties. Cereal demand projections range from 2 800 to 3 200 million tons (mt) by 2050, an increase of 55% to

80% from today (Fraiture *et al.*, 2007). A large part of the future increase will be fed to animals to meet future meat demand. Today some 650 mt of grains – or nearly 40% of the global production – is fed to livestock. This may increase to 1 100 mt by 2050. Meat demand projections vary between 375 and 570 mt by 2050, an increase of 70% to 160% compared to 2000. Sugar, oil, vegetable and fruit demand are projected to increase by 70% to 110%. But while the changes in diets as a result of income growth follow similar patterns, regional and cultural differences are pronounced – and are expected to remain so in the coming decades. For example, per capita consumption in India remains relatively low, projected at 15 kg per capita per year by 2050, while China is projected to consume six times more.

At present the role of biomass in meeting energy demand is modest. Only 7% of global energy needs is derived from biomass *i.e.* wood, crop residues, and dung. But regional variation is substantial: in sub-Saharan Africa, close to 60% of energy use comes from biomass (mainly firewood), while in OECD countries this portion is only 2% (Kemp-Benedict, 2006). The general expectation is that the role of firewood will decrease, while the role of biomass in transport fuels (*i.e.* biofuels) will expand due to rising energy prices, geopolitics and concerns over green house gas emissions.

Non-food crops (such as cotton) occupy only 3% of the cropped area, and 9% of the irrigated area. But the importance of non-food crops will become more important as demand for cotton is expected to more than double by 2050.

More water because of changing diets

Changes in diets towards more livestock products have enormous implications for water demand in agriculture. While estimates on water requirements of crops and livestock products widely vary, most studies agree on the main points (Fraiture *et al.*, 2007). Higher value crops such as sugar, vegetables and oil typically require more water than staple cereal crop. The production of meat and dairy products is more water intensive than vegetal products. For example, the quantity of water evaporated in the production of one kilogram of wheat varies between 500 and 4 000 litres (L) depending on climate, agricultural practices variety and length of growing season, and crop yields. But to produce a kilogram of meat takes anywhere between 5 000 to 20 000 litres per kilogram, mainly to grow feed. The water requirements of livestock products highly depend on how the cattle are fed. Meat derived from grazing cattle tends to require less water per kilogram produced than from cattle in industrial feedlots. Biofuels take 2 000 - 3 000 L to produce (Fraiture *et al.,* 2008)

Diets based on meat from grain-fed cattle may take two times more water than pure vegetarian ones (Renault 2004). Thus, the potential to reduce pressure on water resources by changes in food consumption patterns seems high. For example, in the four scenarios used by the MEA, the meat consumption varies from 41 to 70 kg per person per year, depending on income, price, and public perceptions about health and environment (MEA, 2005). Under the high meat scenario global agricultural water consumption is 15% (or 950 km^3) higher than under the high vegetable scenario.

Water evaporated by crops to meet today's food demand is estimated between 6 800 km^3 to 7 500 km^3 annually (Rockstrom *et al*., 1999; Postel, 1998; Chapagain 2006; CA, 2007), roughly 3 000 L per person per day or one litre per calorie. A large portion, an estimated 78% globally, comes directly from rainfall that infiltrates the soil to generate soil moisture. The other 22% (or 1 570 km^3) is met by irrigation withdrawn from surface

and groundwater sources and delivered to farm fields. Agriculture is the largest water user worldwide and the large quantities of water currently used for irrigation put a substantial strain on water resources, particularly in arid and semi-arid tropical areas. Already about 900 million people live in water-scarce river basins, while another 700 million live where the limit to water resources is fast approaching. Yet another 1 billion people live in basins where economic constraints limit the pace of much-needed investments in water management (Molden *et al*., 2007).

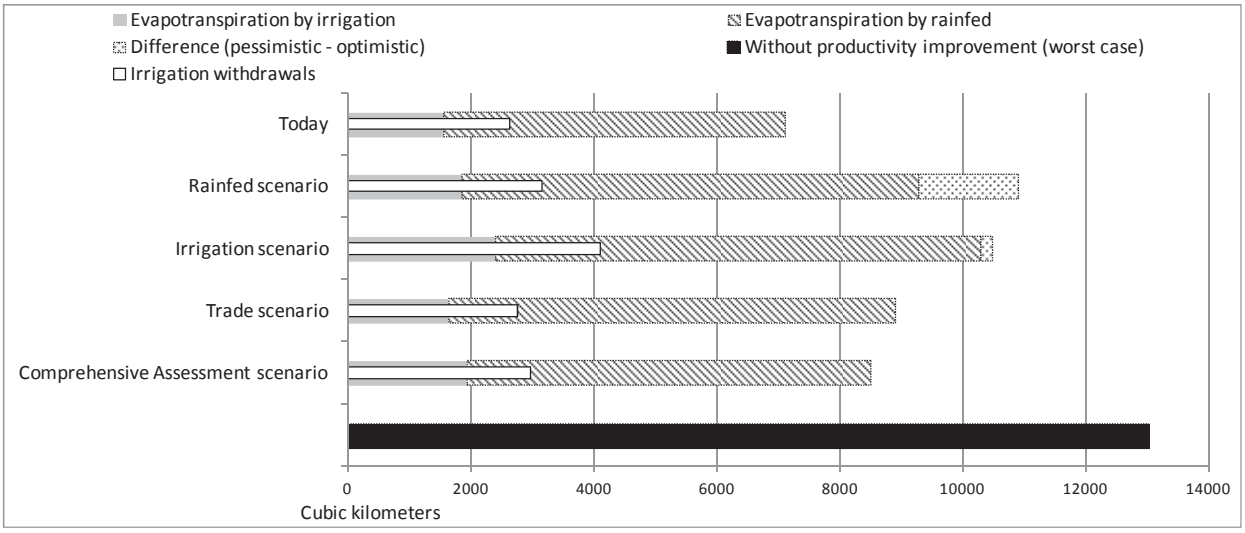
Increases in water for food and fuel affect ecosystems in several ways (Falkenmark *et al*., 2007). River depletion and changes in hydrologic regime by dam building disrupt downstream aquatic ecosystems. Groundwater over-exploitation damages groundwater dependent ecosystems. Overuse or unwise use of nutrients and agro-chemicals affects both aquatic and terrestrial ecosystems due to polluted return flow from crop lands. Drainage of wetlands for agricultural use leads to habitat loss of flora and fauna and reduces ecosystems services from wetlands such as fisheries, flood retention and groundwater recharge. Reduction in ecosystem services can have severe consequences for the poor who depend on ecosystems for their livelihoods. Signs of environmental degradation because of water scarcity, over-abstraction and water pollution are apparent in a growing number of places.

Quantities of water needed to produce the amount of food matter are enormous. But increasingly attention is drawn to water quality and timing issues – flow quantities, temporal patterns, overall flow variability, and water quality (Arthington *et al.*, 2006). There may be tradeoffs between water quantity and quality (Nangia *et al*., 2008). Where yields are low due to limited nutrient and water supply, water productivity can be enhanced through higher fertiliser gifts and improved water supply. This limits the amount of additional water needed to meet increased food demand, thus leaving more water in rivers to meet environmental requirements. But it also increases the amount of nutrient leaching, thus adversely affecting water quality of groundwater, rivers and lakes. Eutrophication of lakes and rivers due to polluted agricultural return flows degrades aquatic ecosystems, reducing fish stocks and increasing human health hazards (Diaz and Rosenberg, 2008).

Scenarios of future water for food demand

Future water demand projections vary enormously. Scenarios done for the Comprehensive Assessment indicate a range from 7 800 to 13 050 km^3 of total crop evapotranspiration and from 2 760 to 4 120 km^3 of irrigation withdrawals, an increase anywhere between 5% and 57% (Figure 1.3). Forecasts vary with assumptions regarding the potential of rain fed agriculture (bar labelled "rainfed scenario" in Figure 1.3), the potential of water productivity improvement in irrigated areas and the scope of irrigated area expansion (labelled "irrigated scenario") and agricultural trade (labelled "trade scenario". The upper bar in Figure 1.3 depicts the crop water requirements today (7 100 km^3); the bar at the bottom of the picture shows the amount if no improvements in water productivity would take place (13 050 km^3). The "comprehensive assessment scenario" combines the most optimistic assumptions depending on the region.

Figure 1.3. Future crop water requirements under different scenarios and assumptions



Source: Comprehensive Assessment of Water Management in Agriculture (CA), 2007.

Role of rainfed agriculture

Enhanced agricultural production from rainfed areas can offset the need for the development of additional water resources (Rosegrant *et al.*, 2002; Rockstrom *et al.*, 2003). But the potential of rainfed agriculture and the scope to improve water productivity in irrigated areas is debated (Seckler *et al.*, 2000; Kijne *et al.*, 2003). The "rainfed scenario" in Figure 1.3 reflects this uncertainty. An optimistic scenario assumes significant progress in upgrading rainfed systems while relying on minimal increases in irrigated production, by reaching 80% of the maximum obtainable rainfed yield. The solid grey-slashes bar ( ) under the rainfed scenario in Figure 1.3 shows that the optimistic scenario cuts the crop water requirements substantially compared by a scenario without productivity improvements (solid black bar). However, relying on rainfed agriculture as a major source of food production carries risks. Most water harvesting techniques are useful for bridging short dry spells but longer dry spells can lead to partial or total crop failure. Further, while numerous case studies document the benefits of upgrading rainfed agriculture, achieving such results more broadly, throughout one or more production regions remains challenging. If adoption rates of improved technologies are low and rainfed yield improvements do not materialise, the cropped area expansion required to meet rising food demand would be around 60%, and lead to 1 850 km^3 additional crop water requirements (dotted bar under the rainfed scenario).

Productivity improvements in irrigated areas

Under optimistic assumptions about water productivity gains, three-quarters of the additional food demand can be met by improving water productivity on existing irrigated lands (Fraiture *et al.*, 2007). In South Asia – where more than 50% of the cropped area is irrigated and productivity is low – additional food demand can be met by improving water productivity in irrigated agriculture rather than area expansion (solid grey-slashes bar under irrigated scenario in Figure 1.3). But in parts of China and Egypt and in developed countries, yields and water productivity are already quite high and the scope

for further improvements is limited. Investments in irrigated agriculture will help alleviate rural poverty (Castillo *et al*., 2007; Faures *et al.*, 2007). But irrigated area expansion may have serious consequences for the environment (Falkenmark *et al*., 2007). A scenario in which the irrigated area continues to expand at the historic rate would require added withdrawals of water to agriculture of more than 40% (dotted bar under the irrigation scenario in Figure 1.3), posing a threat to aquatic ecosystems in water stressed areas though in Sub-Saharan Africa where there is very little irrigation expansion seems warranted.

Trade

Trade can help mitigate water scarcity if water-short countries import food from water abundant countries (Hoekstra and Hung, 2005). By importing agricultural commodities, a country "saves" the amount of water it would have required to produce those commodities domestically. Thus food imports can be thought of as "virtual water." For example, Egypt, a highly water-stressed country, imported 8 million metric tons (mMT) of grains from the United States in 2000. Producing that grain in Egypt would have required about 8.5 billion cubic metres (bn m^3) of irrigation water – about one-sixth of Egypt's annual releases from Lake Nasser (Fraiture *et al.*, 2004). A well planned increase of international food trade could thus mitigate water scarcity and reduce environmental degradation. Instead of striving for food self-sufficiency, water-short countries would import food from water-abundant countries. The scenario analysis reveals, in theory, that world food demands can be satisfied through international trade, without worsening water scarcity or requiring additional irrigation infrastructure. But political and economic factors may limit its scope (Fraiture *et al*., 2004; Wichelns, 2004). For example, poor countries are reluctant to depend on imports to meet basic food needs because it could increase their vulnerability to global fluctuations in market prices, as well as to geopolitics. For many countries, food self-sufficiency remains an important policy goal, and, despite emerging water problems, many countries view the development of water resources as the best way to achieve food security and promote income growth, particularly in poor rural communities. The implication is that under the present global and national geopolitical situation, it is unlikely that food trade will solve water scarcity problems in the near term.

Challenges

Potential of productivity improvements

There is considerable scope for improving crop water productivity through water harvesting, supplemental irrigation, deficit irrigation, precision irrigation techniques and soil-water conservation practices (Molden *et al*., 2007b). There is also great scope for improving economic water productivity by increasing the values generated by water use and decreasing associated costs. But there are several reasons to be cautious about the scope and ease of increasing crop water productivity. First, crop water productivity is already quite high in highly productive regions. Second, reuse and recycling of water already may be high, and perceived losses and inefficiencies might be lower than generally assumed. Third, while improvements in crop genetics have notably improved water productivity in the past, such large gains are not easily foreseen in future. Lastly, the enabling conditions for farmers and water managers to enhance water productivity are

not in place. Priority areas for improving water productivity include areas where water is scarce, yields are low, and poverty is prevalent.

Adapt yesterday's irrigation to tomorrow's need

The days of rapid irrigated area expansion are over, though growth in areas with abundant water resources and little infrastructure, such as sub-Saharan Africa, is warranted (Faures *et al*., 2007). A major new task is adapting yesterday's irrigation systems to tomorrow's needs. Modernisation, a mix of technological and managerial upgrading to improve responsiveness to stakeholder needs, will enable more productive and sustainable irrigation. As part of the package irrigation needs to be better integrated with agricultural production systems to support higher value agriculture and to integrate livestock, fisheries, and forest management. There are compelling reasons to continue to invest in irrigation: to preserve the existing stock of irrigation infrastructure and the value of that investment; to assist the rural poor in gaining livelihoods that move them out of poverty; to adapt to and satisfy the changing food preferences of increasingly wealthy urban and rural populations; to improve irrigation performance; to adapt to the impacts of climate change; and to productively, safely and cheaply re-use the increasing volumes of urban wastewater that will be generated in the future.

Water storage to mitigate climate variability impacts

Climate change will likely increase rainfall variability, and hence variability in water available for agriculture. An obvious response to variability in supply is to store water when it is abundant for use during dry periods (Keller *et al.*, 2000). Water storage improves the ability of rural poor to cope with climate shocks by increasing agricultural productivity (and hence income) and by decreasing fluctuations (and hence risks). There are many proven ways to store water including off-stream reservoirs, natural surface cavities, on-farm ponds and networks of small reservoirs. Small reservoirs, providing water for domestic use, livestock watering and small-scale irrigation allow livelihoods of rural households to be diversified increasing social resilience (Liebe *et al.*, 2007). Geology allowing, groundwater storage can be enhanced by artificial recharge (Shah *et al.*, 2007). Water storage in the root zone can be boosted through a variety of water harvesting techniques and soil moisture conservation measures (Rockstrom *et al*., 2007). Water can also be 'stored' in stream channels and utilised via river pump irrigation, which makes *control* of water part of the "*storage continuum*". It can also be stored "virtually" – as food for the production of which the water was used. Many of these options are already being used but their potential remains largely unquantified and, most likely, underexploited.

There is a renewed interest in large scale water infrastructure in the developing world with significant investments in fast developing economies (such as China and India) and in sub-Saharan Africa, where there has been a general underinvestment in water related infrastructure (Faures *et al.*, 2007). But investments in large scale water infrastructure can be risky and controversial when silent stakeholders such as disadvantaged rural farmers, especially women, and the environment are insufficiently considered during design, implementation and operation. Conventional storage may not always be the most suitable option to decrease vulnerability to climate change induced variability in water supply and may result in maladaptation, when water storage designs create dependencies and expectations of reliability that cannot be met. Large scale storage without institutions and policies that safeguard benefits to rural poor may lead to increased inequity. It is

therefore essential to take a much broader perspective on "water storage" in the context of increased rainfall variability and adaptation to climate change.

Reduce losses in the food chain

While estimates are sketchy and rather outdated, available evidence points to a staggering amount of agricultural produce lost in the food chain, *i.e.* from field to fork. There are several stages in the food chain where substantial losses occur. Losses in the field (between planting and harvest) may be as high as 20% to 40% of the potential harvest in developing countries due to pests and pathogens. Losses in processing, transport and storage are conservatively estimated between 10% and 15% in quantity terms, but could amount to 25–50% of the total economic value because of reduced quality (Kader, 2005; Kantor, 1997). Lastly, substantial losses occur during retail and consumption, due to discarding excess perishable products, product deterioration and food not consumed (so called plate waste). In the USA around 25% of fresh fruit and vegetables are not consumed by humans (though part of it may be used as animal food) during retail and consumption. In developing countries this is estimated at around 10%.

These numbers suggest considerable inefficiencies in the food chain and therefore large scope to reduce gross food and thus water demand. But this is by no means easy. There are many steps and many actors from field to fork, such as farmers, agricultural workers, truck drivers, shopkeepers, government officials and consumers. Individually they have little incentive to improve efficiency because the waste in each step is small and costs or efforts may outweigh benefits (Lundqvist *et al*., 2008). Hence public programmes and incentives might be needed to motivate socially desirable reductions in crop losses and food waste.

Bibliography

Arthington, A.H., *et al.* (2006), "The Challenge of Providing Environmental Flow Rules to Sustain River Ecosystems", *Ecological Applications*, Ecological Society of America, Washington, D.C., Vol. 16, No. 4, pp. 1311-1318.

Castillo, G., *et al*. (2007), "Reversing the Flow: Agricultural Water Management Pathways for Poverty Reduction", Chapter 4 in *Water for Food, Water for Life: A Comprehensive Assessment of Water Management in Agriculture*, Earthscan, London, and International Water Management Institute, Colombo.

Chapagain, A. (2006), "Globalization of Water, Opportunities and Threats of Virtual Water Trade", PhD thesis, IHE-Unesco.

Comprehensive Assessment of Water Management in Agriculture (CA) (2007), *Water for Food, Water for Life: A Comprehensive Assessment of Water Management in Agriculture*, Earthscan London and International Water Management Institute, Colombo.

Diaz, R.J., and R. Rosenberg (2008), "Spreading Dead Zones and Consequences for Marine Ecosystems", *Science*, Vol. 321, No. 5891, pp. 926-929.

Falkenmark, M., M. Finlayson and L. Gordon (2007), "Agriculture, Water and Ecosystems: Avoiding the Costs of Going too Far", Chapter 9 in *Water for Food, Water for Life: A Comprehensive Assessment of Water Management in Agriculture*, Earthscan, London, and International Water Management Institute, Colombo.

FAOSTAT (Food and Agriculture Organization of the United Nations) (2006), Statistical database. Accessed December 2006, *http://faostat.fao.org/*.

Faures, J., M. Svendsen and H. Turral (2007), "Reinventing Irrigation", Chapter 9 in *Water for Food, Water for Life: A Comprehensive Assessment of Water Management in Agriculture*, Earthscan, London and International Water Management Institute, Colombo.

Fraiture, C. de, *et al.* (2007), "Looking ahead to 2050: Scenarios of Alternative Investment Approaches", In: Molden, D. (ed.), *Water for Food, Water for Life: A Comprehensive Assessment of Water Management in Agriculture*, Earthscan, London, and International Water Management Institute, Colombo.

Fraiture, C. de, M. Giordano and Y. Liao (2008), "Biofuels and Implications for Agricultural Water Uses: Blue Impacts of Green Energy", *Water Policy*, Vol. 10, No. S1, pp. 67-81.

Fraiture, C. de, X. Cai, U. Amarasinghe, M. Rosegrant and D. Molden (2004), "Does International Cereal Trade Save Water? The Impact of Virtual Water Trade on Global Water Use", *Comprehensive Assessment of Water Management in Agriculture*, International Water Management Institute, Colombo.

Hoekstra, A.Y., and P.Q. Hung (2005), "Globalisation of Water Resources: International Virtual Water Flows in Relation to Crop Trade", *Global Environmental Change*, Vol. 15, No. 1 pp. 45-56.

Kader, A.A. (2005), "Increasing Food Availability by Reducing Postharvest Losses of Fresh Produce", *Proceedings of the 5th International Postharvest Symposium*, Mencarelli, F. and Tonutti P. (eds.), International Society for Horticultural Science *Acta Horticulturae* 682, Verona, Italy, Vol. 3 No. 682.

Kantor, L., *et al*. (1997), "Estimating and Addressing America's Food Losses", *Food Review*, Jan.-Apr. pp. 2-12.

Keller, A., R. Sakthivadivel and D. Seckler (2000), Water Scarcity and the Role of Storage in Development, *IWMI Research Report* 39, International Water Management Institute, Colombo.

Kemp-Benedict, E. (2006), "Background Technical Reports for the Comprehensive Assessment: 1) Land for Livestock Scenario Notes. 2) Water for Biomass in the Baseline CA Scenario. 3) Energy Scenario Notes", Stockholm Environmental Institute (SEI).

Kijne, J., R. Barker and D. Molden (2003), *Water Productivity in Agriculture: Limits and Opportunities for Improvement*, CAB International, Wallingford, United Kingdom.

Liebe, J., *et al*. (2007), "The Small Reservoirs Project: Research to Improve Water Availability and Economic Development in Rural Semi-Arid Areas", In: Kittisou, M., M. Ndulo, M. Nagel, and M. Grieco (eds), *The Hydropolitics of Africa: A Contemporary Challenge*, Cambridge Scholars Publishing, Cambridge, United Kingdom.

Lundqvist, J., *et al.* (2008), "Saving Water: From Field to Fork - Curbing Losses and Wastage in the Food Chain", *SIWI Policy Brief*, Swedish International Water Institute, Stockholm, Sweden.

MEA (Millennium Ecosystem Assessment) (2005), *Ecosystems and Human Well-Being: Synthesis*, Island Press, Washington D.C.

Molden, D., *et al.*, "Trends in water and agricultural development", In: Molden, D. (ed.), *Water for Food, Water for Life: A Comprehensive Assessment of Water management in Agriculture*, Earthscan, London and International Water Management Institute, Colombo.

Molden, D., *et al.* (2007b), "Pathways for Increasing Agricultural Water Productivity", Chapter 7 in *Water for Food, Water for Life: A Comprehensive Assessment of Water Management in Agriculture*, Earthscan, London and International Water Management Institute, Colombo.

Nangia, V., C. de Fraiture, H. Turral and D. Molden (2008), Water Quality Implications of Raising Crop Water Productivity, *Agricultural Water Management*, Vol. 95, No. 7, pp. 825-835.

Pingali, P. (2004), "Westernization of Asian Diets and the Transformation of Food Systems: Implications for Research and Policy", *ESA Working Paper*, No. 04-17, Agricultural and Development Economics Division of the Food and Agriculture Organization of the United Nations, Rome, Italy.

Postel, S.L. (1998), "Water for Food Production: Will there be Enough in 2025?", *Bioscience*, Vol. 48, No. 8, pp. 629-637.

Renault, D. and W.W. Wallender (2000), "Nutritional Water Productivity and Diets", *Agricultural Water Management*, Vol. 45, No. 3, pp. 275–96.

Rockström, J. (2003), "Water for Food and Nature in Drought-Prone Tropics: Vapour Shift in Rain-Fed Agriculture", *The Royal Society*, Vol. 358, pp. 1997–2009.

Rockström, J., *et al.* (1999), "Linkages Among Water Vapor Flows, Food Production and Terrestrial Services", *Conservation Ecology*, Vol. 3, No. 2, p. 5, *www.consecol.org/vol3/iss2/art5*

Rosegrant, M., X. Cai, and S. Cline (2002), *World Water and Food to 2025: Dealing with Scarcity*, International Food Policy Research Institute, Washington D.C.

Seckler, D., D. Molden, U. Amarasinghe and C. de Fraiture (2000), "Water Issues for 2025: A Research Perspective", IWMI's contribution to the 2nd World Water Forum, International Water Management Institute, Colombo, Sri Lanka.

Shah, T., J. Burke and K. Villholth (2007), "Groundwater: a Global Assessment of Scale and Significance", in Molden, D. (ed.), *Water for Food, Water for Life: A Comprehensive Assessment of Water Management in Agriculture*, Earthscan, London and International Water Management Institute, Colombo.

Wichelns, D. (2004), "The Policy Relevance of Virtual Water can be Enhanced by Considering Comparative Advantages", *Agricultural Water Management*, Vol. 66 No. 1 pp. 49-63.

Chapter 2

Effect of Reduced Water Supplies on Food Production Economies

Claudia Ringler

International Food Policy Research Institute, Washington, D.C., United States

This paper describes the challenges facing irrigated agriculture today and in the future, with a focus on recent challenges, including rapid increases in non-irrigation water demands, growing water pollution, competition from biofuels, and growing impact from climate variability and change. Increased agricultural productivity is suggested as a key investment to counteract growing water shortages for food production and food security.

Drivers for water scarcity

The world has to brace itself for a series of old and new challenges in water management. Old, but nevertheless crucial challenges include:

- continued need to increase food supplies, with a gradual change to more water-intensive diets as a result of economic growth and urbanisation in much of the developing world;
- slow increase in water investments and escalating costs;
- deterioration of the (irrigated) land base, and (coastal) ecosystems;
- subsidies and distorted incentives in the water sector leading to high levels of wastage; and
- unsustainable dependence on groundwater resources.

New challenges facing water management that have arisen in the last several years will make it more difficult to meet traditional water challenges and include:

- new and sharply increasing demands on water resources – from industries, household uses, the environment, and fisheries;
- rapidly growing water quality problems;
- new competition for water from biofuel production (for example, for sugarcane or corn) an increased demand for energy production from hydropower;
- growing impact of climate variability and climate change, including both more extreme events, higher temperatures, and increased demands on water resources.

Importance of "new" challenges for agricultural water availability

Growing intersectoral competition

Sharp increases in non-irrigation water demands are expected over the next 50 years, with increases concentrated in the group of developing countries. By 2050, non-irrigation water consumption is expected to more than double, approaching more than 700 km^3 per year. Developing countries are projected to contribute most of the increase in demand, while total non-irrigation water consumption in developed countries is expected to increase only moderately.

Given that water supply growth is limited but domestic, and industrial, and livestock water demand are growing rapidly, a significant share of the additional water for these other domestic and industrial uses will come from the irrigation sector. This transfer will lead to a substantial increase in water scarcity in terms of the amount of water available for irrigation compared to water demand for irrigation, as the projected decline in irrigation water use for China and some countries in the Middle East and North Africa shows.

Growing water pollution

Water pollution affects human health, economic development, and the environment. Water quality impairments can lead to increased competition among water users for the shrinking supplies of unpolluted water. Pollutants can include both human-induced pollution such as salinisation, microbiological contamination, eutrophication and excess nutrients, acidification, metal pollutants, toxic wastes, saltwater contamination, thermal pollution, and increases in total suspended solids, as well as natural pollutants such as arsenic and fluoride. Poor water quality increasingly constrains agricultural and economic development in densely populated regions that experience water scarcity and are plagued by poor wastewater treatment, particularly in densely populated Asia. Water pollution reduces agricultural production, threatens fish and other aquatic life and human health. Salinity is one of the largest water quality problems facing the agricultural sector. Freshwater biodiversity and associated fisheries are on a decline in almost all developing countries with negative impacts on protein availability for the poor.

The role of biofuels

The production of biofuels affects water resources in two ways: directly through water withdrawals for irrigation and the industrial processes of feedstock conversion; and indirectly by increasing water loss through evapotranspiration that would otherwise be available as runoff and groundwater recharge (Berndes *et al*., 2003). Biofuel production can also affect water quality by increasing nutrient loads in rivers and lakes. Even though globally the amount of water withdrawn for the production of biofuels is modest, local water scarcity problems may worsen due to irrigation of feedstocks (Rosegrant *et al.*, 2008). In many countries, there is little land and water available for biofuel expansion – the use of water for biofuel production in these areas is likely to affect existing water allocation both across sectors as well as within agriculture and involve serious tradeoffs between energy, environment, food security, and livelihood protection (McCornick *et al.,* 2008; Muller *et al.*, 2008). Comparing actual and projected land and water use for food production with and without additional demand for biofuels, De Fraiture *et al.* (2008) also find that while biofuels are of lesser concern at the global level, local and regional impact could be substantial. They argue that the strain on water resources in China and India makes it unlikely that policy makers will pursue biofuel options, at least those based on traditional field crops.

However, the negative impacts can be minimised by careful land and water use planning focusing on rainfed or marginal water using feedstocks such as sweet sorghum and jatropha (McCornick *et al.*, 2008); and by developing new technologies for generating biofuels from cellulosic substances. Development of second-generation biofuels has been cited as another important avenue to achieve energy and greenhouse gases (GHG) mitigation goals while preserving environmental and food security objectives. However, second-generation biofuels will still require water resources that may prohibit their sustainable production in arid regions.

Impact of climate change

The principal water-related climate changes include changes in the volume, intensity, and variability of precipitation and higher crop water evapotranspiration needs as a result of higher temperature. Finally, the CO_2 fertilisation effect resulting from global warming might benefit some crops if the crop is not stressed otherwise. While there is a high

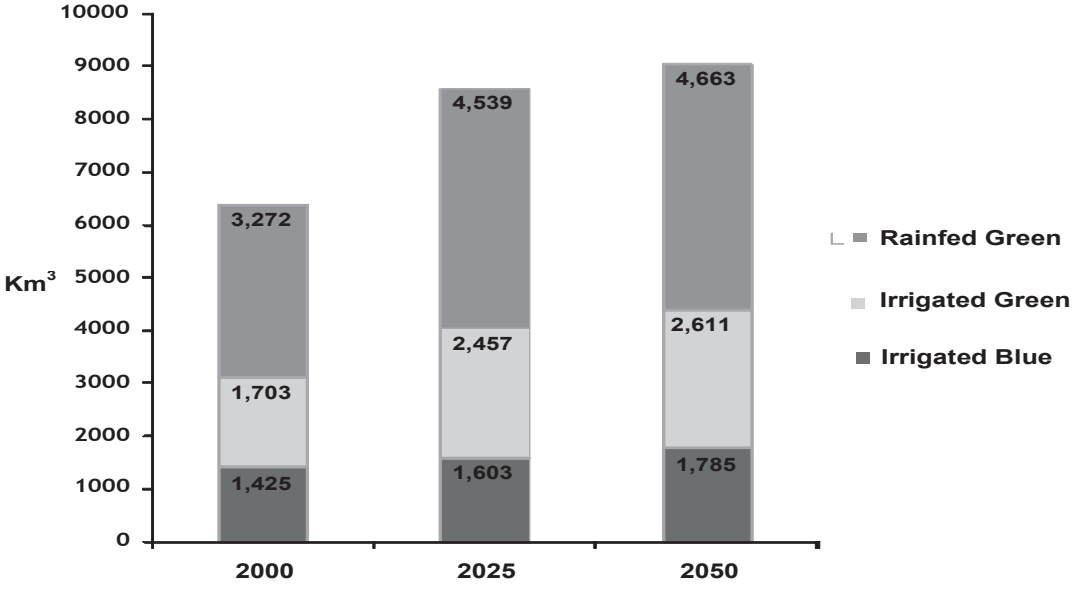
degree of uncertainty in predictions of future precipitation, increases in precipitation are mainly expected in high latitudes while decreases are expected in sub-tropical and lower latitude regions (Bates *et al.*, 2008). Furthermore, rising temperatures will increase the rate of snow cap and glacier melt affecting agricultural production in river basins fed by mountain ranges. Of key concern are the Himalayas feeding Asia's bread bowls in China, India, and Pakistan. Sea-level rise due to the thermal expansion of seawater and the melting of continental glaciers will lead to inundation of low-lying coastal areas, with significant adverse effects including salinisation of coastal agricultural lands, damage to infrastructure, and tidal incursions into coastal rivers and aquifers. Here Bangladesh and Vietnam's rice bowls are threatened (Kundzewicz *et al.*, 2007).

Analyses of multiple climate change scenarios indicates that climate change will likely have a slight to moderate negative effect on crop yields (Parry *et al.,* 2004; Cline, 2007), but crop irrigation requirements would increase (Frederick and Major, 1997; Döll, 2002; Fischer *et al.*, 2006), as would overall water stress in many areas dependent on irrigation (Arnell, 1999; Fischer *et al.*, 2006).

Impact of growing water scarcity on agricultural water use and food production

Given the high demand on water resources from non-irrigation uses, irrigated harvested area and irrigation demand are expected to increase only slowly over the next 40 years. Irrigated harvested area – taking multiple cropping into account – is expected to increase from 421 million hectares (Mha) in 2000 to 473 Mha by 2050 at 0.23% per year. Irrigation water use ("irrigated blue water") is projected to increase from 1 425 km^3 in 2000 to 1 603 km^3 in 2025 and 1 785 km^3 by 2050, or 0.45% per year. At the same time, precipitation falling on both irrigated ("irrigated green water") and rainfed ("rainfed green water") areas is expected to increase from 4 975 km^3 to 7 274 km^3, at 0.76% per year (Figure 2.1).

Figure 2.1. Projected changes in total agricultural water use, global (2000-2050)

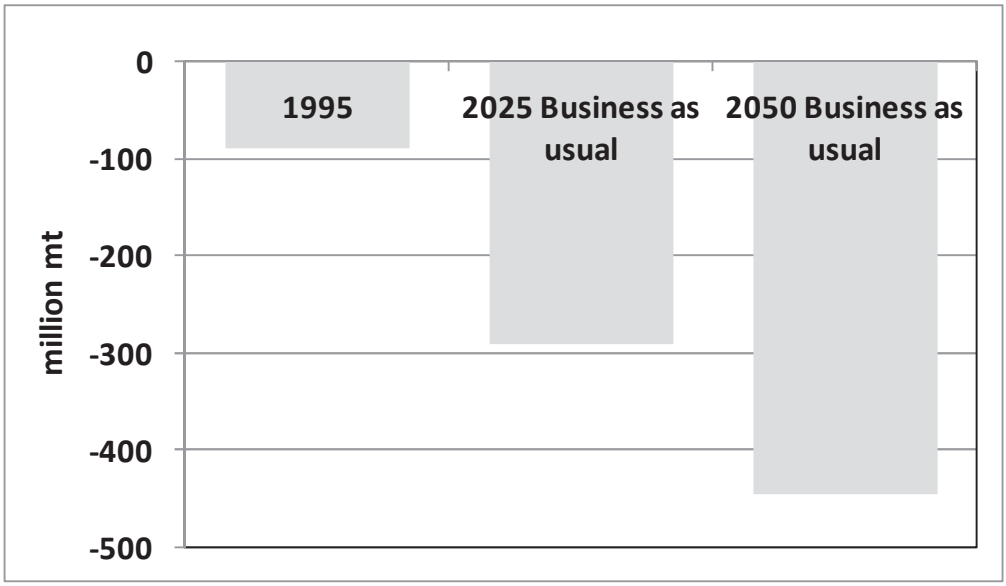


Source: IMPACT simulations (2009).

As a result of growing water shortages, the irrigation water supply reliability index (IWSR), which measures the availability of water relative to full water demand for irrigation, declines from 0.71 globally in 2000 to 0.66 by 2050; the decline will be steeper in water-scarce basins. As water supply reliability declines, irrigators are hurt not only on average, but because water availability becomes more susceptible to downside risk in low rainfall years. The problem will be compounded by increasing variability in rainfall, with significant increases in the number and severity of drought in much of the world due to climate change (Meehl *et al.*, 2007).

What are the implications of growing water scarcity for food production? Rosegrant *et al.,* (2002) estimated loss of cereal production potential from growing water scarcity over time (Figure 2.2). While in 1995 about 5% of developing country grain production potential was lost as a result of lack of water alone, by 2025 this share is expected to increase to 11% and by 2050 to 14% of global cereal production potential.

Figure 2.2. Loss of grain production potential due to water scarcity, developing countries



Sources: Rosegrant *et al*. (2002); International Food Policy Research Institute (IFPRI) IMPACT simulations (2008).

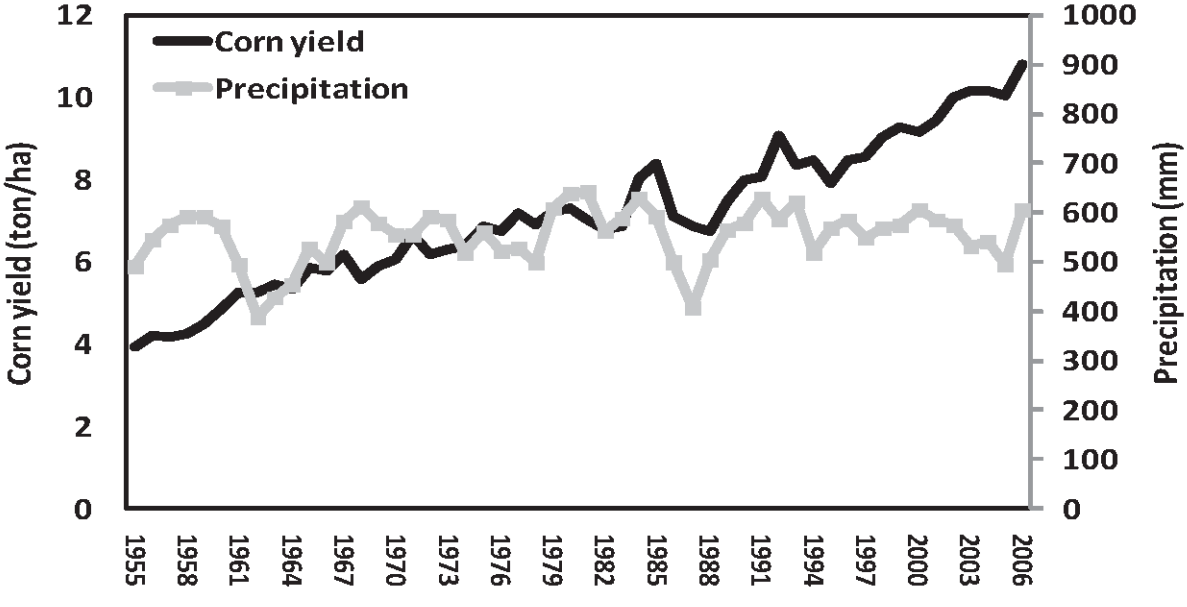
Role of agricultural productivity

While there is considerable scope for improved performance, water savings, and economic gains through direct investments and policy reform in the water sector, ranging from water-saving irrigation technologies to water pricing reform and enhanced co-ordination among agencies charged with governance over water resources, larger gains are likely to be achieved through a direct focus on agricultural productivity enhancements.

Increasing crop yields, for example, through closing the yield gap between developed and developing regions and between rainfed and irrigated crops can save significant water

resources and help conserve ecosystems and remaining forest areas in the developing world. Figure 2.3 presents changes in rainfed corn yield and annual precipitation for Central Illinois over time. As the graph shows, yields increased continually during 1955 to 2008 while precipitation levels show no long-term upward or downward trends. If agricultural research investments can be sustained, the continued application of conventional breeding and the recent developments in non-conventional breeding offer considerable potential for improving cereal yield growth, particularly in rainfed environments. Three major breeding strategies include research to increase harvest index, to increase plant biomass, and to increase stress tolerance (particularly drought resistance). The first two methods increase yields by altering the plant architecture, while the third focuses on increasing the ability of plants to survive stressful environments (Rosegrant *et al.*, 2002). The first of these may have only limited potential for generating further yield growth due to physical limitations, but there is considerable potential from the latter two (Cassman, 1999; Evans, 1998). For example, the "New Rice for Africa", a hybrid between Asian and African species, was bred to fit the rainfed upland rice environment in West Africa. It produces over 50% more grain than current varieties when cultivated in traditional rainfed systems without fertiliser. In addition to higher yields, these varieties mature 30 to 50 days earlier than current varieties and are far more disease and drought tolerant than previous varieties (WARDA, 2000).

Figure 2.3. Changes in crop yields versus changes in precipitation
Example of rainfed corn in Illinois, 1955-2008



Sources: Corn yield: USDA-National Agricultural Statistics Service (NASS); Precipitation: National Climatic Data Center (NCDC): daily observations of precipitations from six weather stations (Freeport in northern Illinois, Carbondale and Du Quoin in southern Illinois, and Rantoul, Peoria and Bloomington in central Illinois) are aggregated and averaged to compute annual precipitation.

Conclusions

Irrigation is, and will remain, the largest single user of water, but its share of world water consumption is projected to decline. Growing scarcities of water and land are projected to progressively constrain food production growth, slowing progress toward food security and human well-being goals. Moreover, significant water scarcity impacts on food production can easily be aggravated by the thin markets for some of the key staple crops, like rice, and protectionist measures taken up by governments in times of food price spikes, as was evidenced (again) by the 2007/2008 food crisis.

Increasing water scarcity for agriculture not only limits crop area expansion but also slows irrigated cereal yield growth in developing countries. Despite recent commitments to increase investment in irrigation, particularly in Sub-Saharan Africa, projected irrigation expansion will be insufficient to reduce rapidly growing levels of net food imports in the developing world. Moreover, given that water supply growth is limited but domestic and industrial water demand are growing rapidly, a significant share of the additional water for domestic and industrial uses will come from the irrigation sector. This transfer will lead to a substantial increase in water scarcity for irrigation, giving rise to more conflicts, in the future, between water for food and water for other uses in many parts of the world.

Water scarcity could severely – and easily – worsen if policy and investment commitments from national governments and international donors and development banks weaken further. Policy reform including agricultural research and management in rainfed areas and changes in the management of irrigation and water supplies are therefore urgently needed to ensure sustainable water access and affordable food prices. Productivity enhancement in rainfed and irrigated agriculture are key proven investments needed to offset growing impacts of water scarcity on the environment and risks to farmers. Thus, for agricultural water use to fulfil its full potential, complementary investments in agricultural technologies, such as seeds and fertilisers, as well as in rural infrastructure, including roads and telecommunications, and in complementary sectors, particularly education and health are needed.

Bibliography

Arnell, N.W. (1999), "Climate Change and Global Water Resources", *Global Environmental Change*, Vol. 9/1, pp. S31-S49, Elsevier B.V., Amsterdam, Netherlands.

Bates, B.C., *et al.* (2008), "Climate Change and Water", *Technical Paper VI of the Intergovernmental Panel on Climate Change*, IPCC Secretariat, Geneva, pp. 210.

Berndes, G., M. Hoogwijk and R. van den Broek (2003), "The Contribution of Biomass in the Future Global Energy Supply: A Review of 17 Studies", *Biomass and Bioenergy*, Vol. 25 pp. 1–28.

Cassman, K.G. (1999), "Ecological Intensification of Cereal Production Systems: Yield Potential, Soil Quality, and Precision Agriculture", *Proceedings of the National Academy of Sciences of the United States of America*, Vol. 96 No. 11, pp. 5952-5959.

Cline, W.R. (2007), *Global Warming and Agriculture: Impact Estimates by Country*, Washington, D.C, Center for Global Development.

Döll, P., (2002), "Impact of Climate Change and Variability on Irrigation Requirements: a Global Perspective", *Climatic Change*, Vol. 54 pp. 269-293.

Evans, L. T. (1998), *Feeding the Ten Billion: Plants and Population Growth*, Cambridge University Press, Cambridge, University Press.

Fischer, G., *et al.* (2006), "Climate Change Impacts on Irrigation Water Requirements: Global and Regional Effects of Mitigation", *1990-2080 Technology Forecasting Social Change*, Vol. 74/7 pp. 1083-1107.

Fraiture, C. de, M. Giordano and L. Yongsong (2008), "Biofuels and Implications for Agricultural Water Use: Blue Impacts of Green Energy", *Water Policy*, Vol. 108/1 pp. 67-81.

Frederick, K.D. and D.C. Major (1997), "Climate Change and Water Resources", *Climatic Change,* Vol. 37, pp. 7-23.

Kundzewicz, Z.W., *et al.* (2007), *Freshwater resources and their management, Climate Change 2007: Impacts, Adaptation, and Vulnerability*, Contribution of Working Group II to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change, M.L. Parry, O.F. Canziani, J.P. Palutikof, P.J. van der Linden, C.E. Hanson (eds.), Cambridge University Press, Cambridge, United Kingdom, pp. 173-210.

McCornick, P.G., S.B. Awulachew and M. Abebe (2008), "Water-Food-Energy-Environment Synergies and Tradeoffs: Major Issues and Case Studies", *Water Policy*, Vol. 10/1 pp. 23-36.

Meehl, G.A., *et al. (*2007), *Global Climate Projections, Climate Change 2007: The Physical Science Basis*, Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change, Q.D. Solomon *et al.* (eds.) Cambridge, UK, Cambridge University Press, Chapter 10.

Muller, A., *et al.* (2008), "Some Insights in the Effect of Growing Bio-energy Demand on Global Food Security and Natural Resources", *Water Policy*, Vol. 10/1.

Parry, M.L., *et al.* (2004), "Effects of Climate Change on Global Food Production Under SRES Emissions and Socio-economic Scenarios", *Global Environmental Change*, Vol. 14 pp. 53-67.

Rosegrant, M.W., X. Cai and S.A. Cline (2002), *World Water and Food to 2025: Dealing with Scarcity*, Joint Publication of IFPRI, Washington D.C., USA and International Water Management Institute (IWMI), Sri Lanka.

Rosegrant, M.W., T. Zhu, S. Msangi and T. Sulser (2008), "Global Scenarios for Biofuels: Impacts and Implications", *Review of Agricultural Economics*, Vol. 30/3 pp. 495-505.

WARDA (West Africa Rice Development Association) (2000), Consortium Formed to Rapidly Disseminate New Rice for Africa, *http://www.warda.cgiar.org/News/NERICAConsortium.htm.*

Chapter 3

Global Soil Resource Base: Degradation and Loss to Other Uses

R. Lal

Carbon Management and Sequestration Center,
Ohio State University, Columbus, Ohio, USA

Rapid increase in world population during the 20th century, along with the conversion of land to non-agricultural uses, have drastically decreased the availability of finite soil resources for agricultural use. Per capita soil area for agricultural use is also decreasing because of soil degradation. Four related but different terms, often used interchangeably with erroneous and confusing interpretations, are soil degradation, land degradation, desertification and vulnerability to desertification. Global area subject to different degradation processes is estimated at 1 965 Mha by soil degradation, 3 506 Mha by land degradation, 3 592 Mha by land desertification of which 1 137 Mha is soil desertification, and 4 324 Mha by vulnerability to land desertification. Urbanisation and conversion to industrial land uses and development of infrastructure are also competing land uses. In 2005, 3.16 billion people lived in urban centres over a globally urbanised land area of 351 Mha. In the United States, 79% of the total population of about 300 million lives in urban centres over a land area of 18.6 Mha, or 2% of the total US land area. In rapidly urbanising China, India and other Asian countries, brick making uses topsoil to 1-m depth equivalent to 0.5%-0.7% of cropland area per year in some regions. Policy interventions are needed to limit conversion of prime farmland to non-agricultural uses.

Introduction

Soil resources of the world are finite, unequally distributed among geographic regions, prone to degradation by land misuse and soil mismanagement, and under pressure for conversion to other land uses (Lal, 2009). There exists an inverse relationship between the human population and availability of high quality soil resources. As the world population increases, per capita soil resource base decreases. For example, the per capita grain land area declined from 0.27 ha in 1950 to 0.11 ha in 2000, and may be <0.07 ha by 2050 (Brown, 2004). The per capita grain land area is declining rapidly, because of three factors: (i) increase in world population by about 70 million per year with a total projection of increase from 6.7 billion in 2009 to 7.5 billion by 2030, 9.2 billion by 2050, and 10 billion by 2100, (ii) degradation of soil resources resulting in decline in its capacity to produce economic and environmental goods and services, and (iii) conversion of prime quality soils to non-agricultural uses. This paper reviews interaction among these three factors in terms of the global availability of soil resources for meeting the ever increasing demands of humanity for food, feed, fibre, fuel and other needs of increasingly affluent societies.

World population and soil resources

Domestication of plants and animals, about 10 000 years ago, has been the principal cause of increase in human population. It was the spread of agriculture that caused the increase in the world population of merely 4 million, doubling every 1 000 years, to 50 million by 1000 BCE (Ponting, 2007). It reached 250 million by 250 AD, 700 million by 1780, 900 million by 1825, and 1.6 billion by 1900. The population increased to 2 billion by 1930, 4 billion by 1975 and will double to 8 billion before 2025 (Bartlett, 2004). The world population will never double again after 2025. However, there are several critical features of the future increase in human population. (i) Almost all the future increase in population, 3.5 billion between 2009 and 2050, will occur in developing countries where soil, water, and other natural resources are already under great stress. (ii) The magnitude of absolute increase in population (3.5 billion) over a short period of 3 to 4 decades is unprecedented in human history. (iii) All the human demands for basic necessities must to be met from the ever decreasing per-capita soil resource. (iv) Over and above the basic necessities, there are also strong aspirations and expectations of increase in affluence and standards of living. For example, the per capita C emission (based on the use of fossil fuel energy use in 2005) was 5.32 Mg C per person per year in USA, 1.16 in China (22% of USA), 0.35 in India (7% of USA), and 0.01 in Burundi (0.2% of USA) (Marland *et al.*, 2001). If the use of goods and services in developing countries, based on fossil fuel energy, increases to the same level as that in North America and other industrialised nations, the demand on natural resources would increase exponentially. Some argue that humans have lost control on the world population dynamics, and the major determinants of future growth in human population are natural causes. Such a trend would have drastic consequences on availability and quality of soil and other natural resources.

Soil degradation, land degradation and desertification

The term degradation refers to decline in quality and productive capacity. Therefore, the term soil degradation implies decline in soil quality and reduction in its capacity to produce economic goods and ecosystem services. For the entire biosphere, total ecosystem services are worth USD 16-54 trillion per year (Costanza *et al.*, 1997). In this context, soil quality refers to its capacity to produce economic goods and perform other ecosystem services (Lal, 1997; Doran and Jones, 1996; Gregorich and Carter, 1997). Soil degradation can happen due to natural and human-induced causes. Natural causes generally operate at a longer (often geological) time scale. However, human-induced or anthropogenic factors are rapid and operate at decadal or generational scale. There are two other related but subtly different terms: land degradation and desertification. The term land encompasses all terrestrial/natural resources including climate, vegetation, soil, terrain, hydrology, biodiversity, people, animals, etc. In this context, soil is one of the components of land. Thus, the term "land degradation" is much broader in scope and encompasses decline in quality of climate, water, terrain, vegetation, soil and other components. The term "soil degradation" is very specific and must not be confused with "land degradation", and these terms must not be used interchangeably. Similarly, the term "desertification" refers to land degradation (decline in quality of soil, vegetation, water, climate etc.) in dry climates (UNEP, 1991 and 1992; Dregne and Chou, 1992; Lal, 2001). Because of their broader scope, both terms (land degradation and desertification) are often used vaguely, qualitatively and subjectively leading to confusion, misunderstanding and erroneous interpretations.

Determinants of soil degradation

Processes of soil degradation involve mechanisms responsible for decline in soil quality. Factors of soil degradation are environmental parameters which moderate the rate of soil degradation by specific processes. Causes of soil degradation refer to human activities which alter the impact of both processes and factors. Increase in human population, and the attendant human dimensions (*e.g.* economics, policy, social, ethnic and cultural factors) are the predominant drivers of the biophysical processes and physiogeographic factors of soil degradation. Some examples of processes, causes and factors are outlined in Table 3.1. The extent and severity of soil degradation depends on the strong interaction among processes, causes and factors of soil degradation.

Table 3.1. Processes, factors and causes of soil degradation

Processes	Factors	Causes
1. Physical: Crusting compaction, Anaerobiosis, Erosion, Sedimentation	1. Climate: Precipitation, Temperature, Aridity Index, Frequency of extreme events	1. Land Use Change: Conversion of natural to agricultural and other managed ecosystems
2. Chemical: Acidification, Salinisation, Nutrients depletion, Elemental toxicity (Al, Fe, Mn)	2. Terrain: Slope (Gradient, Length, Aspect, Shape), Drainage, Landscape position	2. Vegetation Cover: Deforestation, Afforestation, Reforestation, Fire
3. Biological: Depletion of soil organic matter, Reduction in activity of soil biota, Build up of soil pathogens, Methanogenesis, Denitrification.	3. Vegetation: Species composition, NPP, Biomass partitioning	3. Water Management: Drainage (of wetlands), Irrigation, Water harvesting and recycling
	4. Biodiversity: Fauna and Flora	4. Soil Management: Ploughing use of fertilisers and amendments, crop residue management, etc.
	5. Natural Perturbations: Seismic activity, Tsunami	5. Farming System: Arable, Silviculture, Pastoral, Agrisilviculture, Silvopastrol

Source: Author's own work.

Processes of soil degradation

Interactive effects of physical, chemical, biological (and agronomic) processes on the extent and severity of soil degradation are outlined in Figure 3.1. The complexity of the degradation process is further accentuated by the continuity and overlap of different processes (physical, chemical, biological), with positive feedback, which exacerbate the net impact. For example, accelerated erosion and nutrient depletion reinforce one another (Eq. 1 and 2):

Nutrient depletion→poor plant growth→accelerated erosion→severe nutrient depletion..... Eq. 1

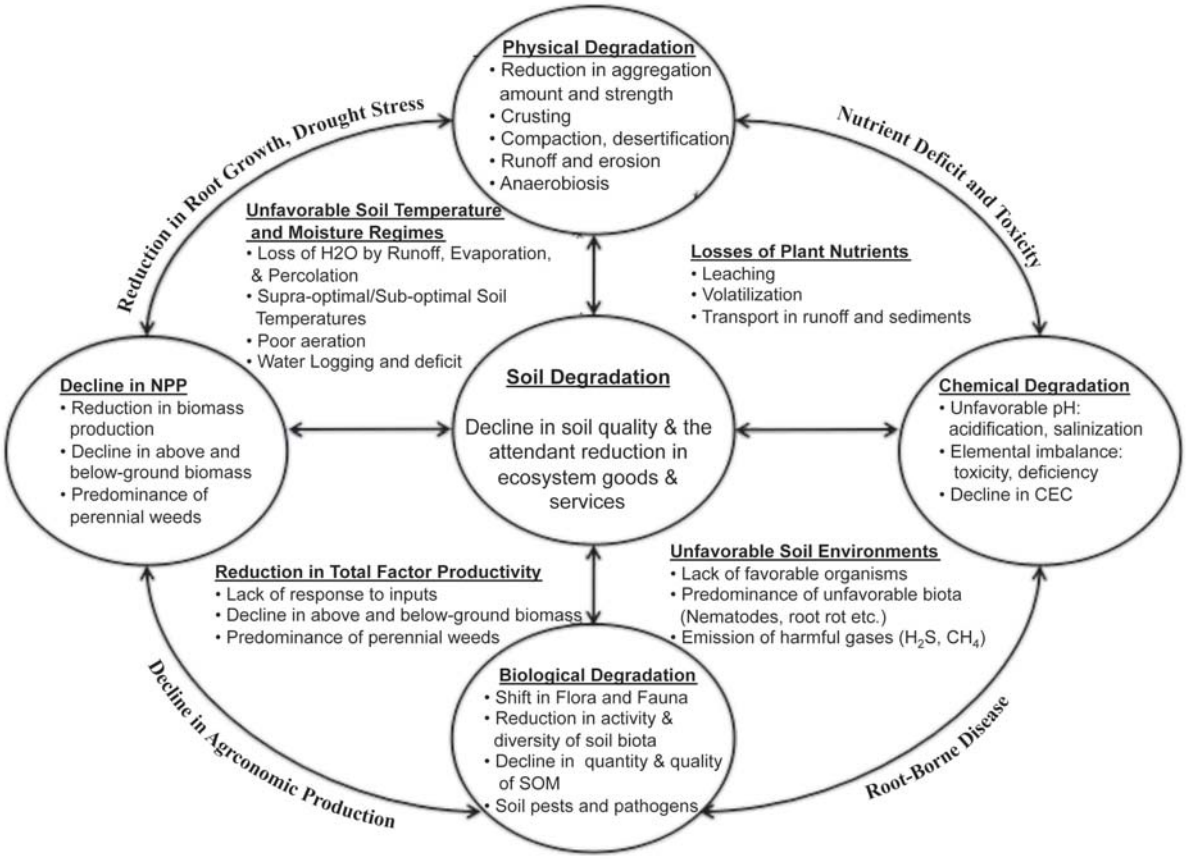
Accelerated erosion→nutrient depletion→poor plant growth→more severe erosion..... Eq. 2

Similar mutually reinforcing effects are observed between soil structural degradation and accelerated erosion (Eq. 3 and 4):

Decline in soil structure→crusting→compaction→high runoff→severe erosion..... Eq. 3

Severe erosion→crusting→compaction→more runoff→severe decline in soil structure..... Eq. 4

Figure 3.1. Types of soil degradation and contamination



Source: Author's own work.

Once initiated, positive feedbacks exacerbate the entire degradation process through strong interaction among physical, chemical, and biological processes (Figure 3.1). The strong interaction among processes, and with factors and causes, makes it difficult to break the vicious cycle. Therefore, preventative measures which limit the onset of degradation processes are more effective than adoption of the restorative techniques after the process has been set in motion.

Cause of soil degradation

Principal causes of soil degradation are anthropogenic activities. Increase in human population, along with increasing aspirations for a high standard of living, cause soil degradation through a range of activities. Important among these are: deforestation, biomass burning, draining of wetlands, soil cultivation including mouldboard ploughing, extractive farming practices, uncontrolled grazing etc. In addition, soil resources are also being depleted by conversion to other land uses through urban encroachment, development of infra-structure and industrial complexes. Waste disposal and land application of industrial and urban effluents are also important to soil contamination and pollution.

Assessment of soil degradation, land degradation and desertification

The available statistics on soil degradation are highly variable, qualitative, subjective, and often full of emotions and rhetoric rather than credible and verifiable facts. Reading the popular literature often gives the impression that there are vast tracks of degraded and desertified soils throughout the world. Among numerous reports on the extent, severity and impact of soil degradation, there are four reports which adopt different but relatively quantitative approaches to the assessment of soil and land degradation. These approaches are as follows:

- Global Assessment of Soil Degradation (Glasod): The project, undertaken by ISRIC in Wageningen, Netherlands, was sponsored by FAO/UNEP/UNESCO (1979). It adopted the following definition: "soil degradation is a process that describes human-induced phenomena which lowers the current and/or future capacity of the soil to support human life". The project assessed two distinct parameters: (i) the type of soil degradation in relation to the specific process that causes degradation (*e.g.* physical, chemical, biological; Figure 3.1), and (ii) the degree of degradation (*e.g.* light, moderate, severe and extreme). The data shown in Table 3.2 indicate that globally about 1 965 Mha of soil have been degraded to some degree. Of this, 1 094 Mha (56%) is by water erosion, 549 Mha (28%) by wind erosion, 240 Mha (12%) by chemical degradation, and 83 Mha (4%) by physical degradation. Thus, accelerated erosion is the most predominant process of soil degradation (Table 3.2). Distribution of soil degradation on a continental basis is shown by the data in Table 3.3. The extent of soil degradation is more severe in Asia, with high population density and predominately resource-poor farmers, than in other regions. Of the total degraded areas of 1 965 Mha, 494 Mha (25%) is in Africa, 749 Mha (39%) in Asia, 243 Mha (12%) in South America, 63 Mha (3%) in Central America, 96 Mha (5%) in North America, 218 Mha (11%) in Europe, and 102 Mha (5%) in Oceania (Table 3.3). This is the only study dealing strictly with soil in the quantitative assessment of degradation.

Table 3.2. Estimates of soil degradation by Glasod methodology

Degradation Process	Area Affected (10^6 ha)			
	Light	Moderate	Strong + Extreme	Total
Water Erosion	343	527	224	1 094
Wind Erosion	268	254	26	548
Chemical degradation	93	104	43	240
Loss of nutrients	52	63	20	135
Salinisation	35	20	21	76
Pollution	4	17	1	22
Acidification	2	3	1	6
Physical degradation	44	27	12	83
Total	749	911	305	1 965

Source: Oldeman (1994).

Table 3.3. Continental distribution of soil degradation by Glasod methodology

Region	Area Affected (10^6 ha)				
	Water Erosion	Wind Erosion	Chemical degradation	Physical degradation	Total
Africa	227	186	62	19	494
Asia	441	222	74	12	749
South America	123	42	70	8	243
Central America	46	5	7	5	63
North America	60	35	-	1	96
Europe	114	42	26	36	218
Oceania	83	16	1	2	102
Total	1 094	548	240	83	1 965

Source: Oldeman (1994).

- Desertification: A similar approach had been previously adopted to assess land area affected by desertification (Dregne and Chou, 1952; UNEP, 1992, Dregne, 1998). However, the approach to assess desertification is more qualitative than the Glasod methodology to assess soil degradation. The data in Table 3.4 list estimates of desertification by using Dregne's methodology with that by the Glasod technique adopted by Oldeman and Van Lynden (1998). The data are not comparable because of the differences in criteria used and whether or not the degradation of vegetation assessment is included. Such differences in criteria used to define soil or land cause confusion and misunderstanding. With degradation of vegetation included, Dregne's estimates show that total land area affected by desertification is 35.92 x 10^6 km^2 (69.5% of the total dry land area) (UNEP, 1991). Of this, the area affected by soil degradation is < 7.6 x 10^6 km^2. In comparison, Oldeman and Van Lynden (1998) estimated soil degradation in dry lands at 11.37 x 10^6 km^2. Both estimates are different, and not comparable.

Table 3.4. Comparison between Glasod estimates of desertification in dry areas with that of UNEP methodology

UNEP (1991)	Area (10^6 km^2)	Oldeman and Van Lynden (1998)	Area (10^6 km^2)
Degraded irrigated land	0.43	Water erosion	4.78
Degraded rainfed cropland	2.16	Wind erosion	5.13
Degraded rangeland (Soil and vegetation)	7.57	Chemical degradation	1.11
		Physical degradation	0.35
Sub-total	10.16		
Degraded rangeland (vegetation only)	25.76	Total	11.37
Grand total	35.92	Light	4.89
Total arid land area	51.72	Moderate	5.09
% degraded	69.5	Severe and extreme	1.39
		Total	11.37
		These estimates refer to soil degradation only	

Source: Lal, Hassan and Dumanksi (1999).

- Global Desertification Tension Zones: Rather than assessing the current extent and severity of soil degradation, Eswaran *et al.*, (2001) and Reich and Eswaran (1998) estimated desertification tension zones based on the land quality class and the population that it supports, soil-related constraints and vulnerability to desertification. This approach indicates the land area belonging to vulnerability classes and the corresponding number of impacted population. It is an assessment of the risk of human-induced land desertification (Tables 3.5 and 3.6). The area vulnerable to desertification is estimated at 43.2 x 10^6 km^2 (33%) and the total population impacted at 2.6 billion (46%) (Table 3.5). Of this, 11.7 x 10^6 km^2 lies in regions of high population density of > 41 persons/km^2 (Table 3.6).

Table 3.5. Estimates of land area under different vulnerability classes of desertification and the number of impacted population

Vulnerability Class	Area Affected		Population	
	10^6 km^2	% of Global Land Area	10^6 People	% of Global Population
Low	14.60	11.2	1 085	18.9
Moderate	13.61	10.5	915	15.9
High	7.12	5.5	393	6.8
Very High	7.91	6.1	255	4.4
Total	43.24	33.3	2 648	46.0

Source: Eswaran *et al.* (2001).

Table 3.6. Estimates of land area in human-induced desertification risk classes

Vulnerability Class	Population Density (persons/km^2)			
	<10	11-40	>41	Total
	----------$10^6$$km^2$----------			
Low	7.1	3.2	4.3	14.6
Moderate	5.4	4.0	4.2	13.6
High/Very High	7.4	4.4	3.2	15.0
Total	19.9	11.6	11.7	43.2

Source: Eswaran *et al.* (2001).

- Land Degradation Assessment in Drylands (LADA): Bai *et al.,* (2008) defined land degradation as "long term loss of ecosystem functions and productivity caused by disturbance from which land cannot recover unaided". They measured land (not soil) degradation by measuring change in net primary productivity (NPP) with deviation from the norm taken as an indication of land improvement or degradation. It is based on the normalised difference vegetation index (NDVI) as derived from remotely sensed imagery. The data in Table 3.7 show that land degradation affects 35 x 10^6 km^2 (23.5% of the land area), and impacts 1.5 billion people (23.9%). Bai and colleagues claim that LADA data is more quantitative and consistent than the Glasod methodology. Yet, it deals with land (encompassing all factors similar to the assessment of desertification) rather than soil.

Table 3.7. Estimates of area affected by land degradation

Parameter	Value
Area affected ($10^6 km^2$)	35.06
Percent of the land area	23.54
Total NPP Loss (Tg C/y)	955
Percent of Total Population Affected	23.9
Total Population Affected (billion)	1.54

Source: Bai *et al*. (2008).

The data from these four approaches are not comparable, and add to the confusion and misunderstanding. There is a strong need for standardisation of methodology and criteria used.

Soil degradation by land misuse and soil mismanagement

The principal processes of human-induced degradation of agricultural soils are: (i) accelerated erosion caused by excessive and inappropriate ploughing in conjunction with removal of crop residues and excessive or uncontrolled grazing, (ii) depletion of soil organic matter (SOM) by perpetual/long-term use of farming practices which create a negative soil ecosystem C budget, (iii) nutrient depletion resulting in negative elemental (N, phosphorus (P), potassium (K)) budget of 20-40 kg per ha per year such as vast scale soil exhaustion observed in Africa (Anonymous, 2006), (iv) secondary salinisation of irrigated land (Table 3.8) especially in South Asia, and (v) conversion of prime farmland to other uses. Among these processes, soil salinisation and conversion to non-agricultural uses needs further discussion. Globally, secondary salinisation of land affects 76 Mha (Table 3.2). Of this, 15 Mha (20%) occurs in Africa, 53 Mha (70%) in Asia, 4 Mha (4.5%) in North America, 4 Mha (4.5%) in South and Central America, and 1 Mha (1%) in Oceania (Oldeman, 1994). Inappropriate irrigation methods (*e.g.* excessive irrigation by flooding with poor quality water and lack of proper drainage) are the principal causes of secondary salinisation. The data in Table 3.8 show estimates of salinisation of irrigated land of 50% in Iran, 25–30% in Pakistan, 32–40% in Australia, 28% in Bangladesh, 13% in India, 12% in China and 9% in Egypt. Improving irrigation systems is important to decreasing risks of soil salinisation.

Table 3.8. Estimate of secondary salinisation of irrigated lands in some countries

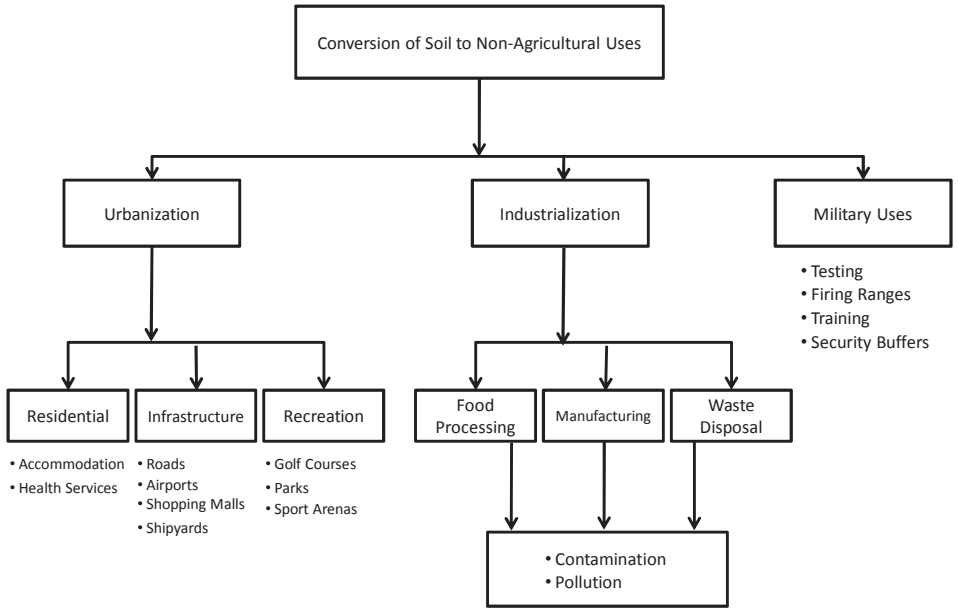
Country	Area (10^6 ha)		% Salinised
	Irrigated	Salinised	
Australia	2.5	0.8-1.0	32-40
Bangladesh	4.7	1.3	28
China	55.0	6.7	12
Egypt	3.4	0.3	9
India	55.8	10.0	18
Iran	8.1	4.05	50
Pakistan	18.2	4.5-6.0	25-33
USA	22.4	0.6	3

Sources: FAO (1994); Aquastat, (2008); ICID (2002); Qureshi *et al.* (2008); Mishra and Sharma (2003); Farrington and Salma (1996); Qadir *et al*. (2008).

Conversion to other land uses

Increase in human population is exacerbating the competition for soil and water resources for other uses such as urbanisation, infrastructure development, and industrial uses (Figure 3.2). Farmlands in developed and developing countries are rapidly being converted to urban land use and building shopping malls. The data in Table 3.9 show urban land use of 351 Mha or 3% of total land area on Earth. World population living in urban areas is increasing very rapidly, and more than 50% of the population already lives in urban centres (Figure 3.3). The world's urban population (billions) was 0.74 in 1950, 1.0 in 1960, 1.33 in 1970, 1.74 in 1980, 2.27 in 1990, 2.85 in 2000 and 3.16 in 2005 (UN-ESA, 2008). The urban population is projected (billions) to be 3.49 in 2010, 4.21 in 2020, 4.97 in 2030, 5.71 in 2040 and 6.40 in 2050 (Figure 3.3). In the USA, the urban population is 192 million covering an urban land area of 186 600 km^2 or 18.6 Mha. Of the total land area of 936 Mha, land area under urban use in the USA is 2% of the total area (Table 3.10). The urban population in Ohio (large and small cities) was 6.20 million (64.2%) in 1960, 6.75 million (63.6%) in 1970, 6.45 million (59.8%) in 1980, 6.35 million (58.8%) in 1990, 6.63 million (58.4%) in 2000 and 6.60 million (57.5%) in 2005 (Partridge *et al.*, 2007). Urban encroachment depletes soil resources in two related but different manners. (i) Large areas of topsoil are used for brick making especially in South Asia and China. As much as 1-m of topsoil is removed annually from 0.5% to 0.7% of the cropland area and used for brick manufacture. The exposed sub-soil, although used for crop production, is of poor quality and often deficient in macro (N, P, K) and micronutrients (Zn, Fe, I, molybdenum (Mo), etc). (ii) Prime farmland soil is also suitable for building houses, roads and airports, and industrial complexes. Urban encroachment is an important factor depleting the world's prime soil resources.

Figure 3.2. Reduction in soil resources base through conversion to non-agricultural uses



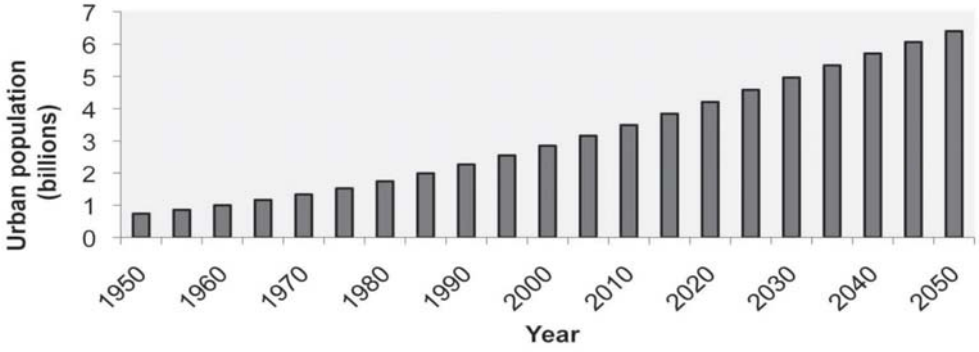
Source: Author's own work.

Table 3.9. Extent of urbanisation among other land uses in 2005

Land use	Area (10^6 ha)
Total	12 980
Urban	351
Arable	1 402
Pasture	3 442
Forest	3 539
Wooded	492
Plantations	142
Others	3 612

Source: FAO (2005).

Figure 3.3. Temporal changes in global urban population



Source: *http://esa.un.org/unup/.*

Table 3.10. Urbanisation in the USA

Parameter	Quantity	
Total US population (millions)	285	
Population in urban areas (millions)	226	(79% of the total)
Number of urban areas	3 629	
Land areas in urban centres (Mha)	18.6	(2% of the total)
Total land area (Mha)	936	

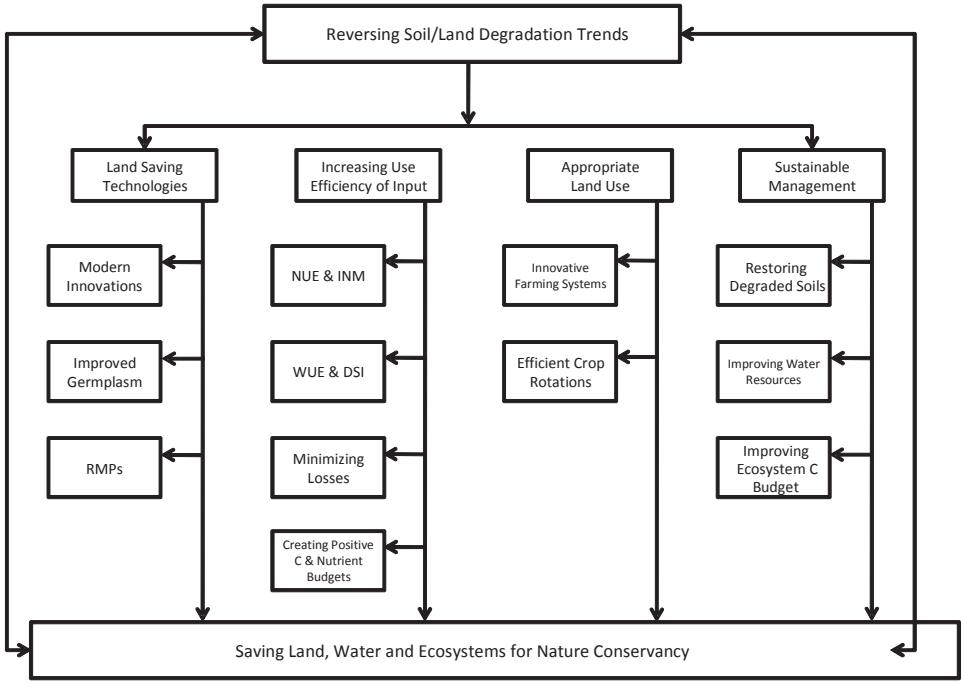
Source: US Census (2000).

Strategies to reverse soil and land degradation trends

In the context of the severe problems of soil degradation and land desertification, business as usual (BAU) is not an option because of the finite soil resources and ever increasing demands of increasing population with the rising aspirations and the high standards of living. Not only the degraded soils must be restored, but the risks of new soil degradation and desertification must also be minimised. Some strategies to reverse degradation trends outlined in Figure 3.4 indicate four options: (i) land saving technologies, (ii) increasing use efficiency of inputs, (iii) choice of appropriate land uses, and (iv) adoption of sustainable management techniques. With ever decreasing per capita cropland area, low-output and extractive farming practices widely practised in developing countries (Sub-Saharan Africa, South Asia, Central America, Caribbean) must be

replaced by modern innovations of soil and crop management and other recommended practices. Crop yields in Sub-Saharan Africa and elsewhere can be increased by a factor of 2 to 4 through adoption of Recommended Management Practices (RMPs). Similarly, improving use efficiency of inputs (fertiliser, water, energy) is essential. The goal is to minimise losses by erosion, runoff, leaching and volatilisation, and create positive C and nutrient budgets. In this context, the importance of appropriate land use, farming systems, crop combinations and rotation systems, mixed farming and agroforestry systems cannot be over-emphasised. The objective is to adopt sustainable soil use and management systems which restore, improve and enhance ecosystem services from the soil resources already allocated to agricultural production. Recent innovations in soil and water management include: (i) nano-enhanced fertilisers including zeolites, (ii) use of soil conditioners to improve soil structure, (iii) improved techniques of biological nitrogen fixation and uptake of P, (iv) innovative methods of irrigation including drip sub-irrigation, (v) disease-suppressive soils, (vi) genetically modified (GM) crops which emit molecular signals for detection by remote sensing and targeted intervention, (vii) assessing soil quality by remote sensing techniques, (viii) C sequestration in soil and terrestrial ecosystems to improve soil quality and agronomic productivity, (ix) trade credits of C sequestered in soils and trees, and (x) use innovative soil/agronomic systems to enhance production of GM crops (NRC, 2008).

Figure 3.4. Strategies for reversing soil degradation trends



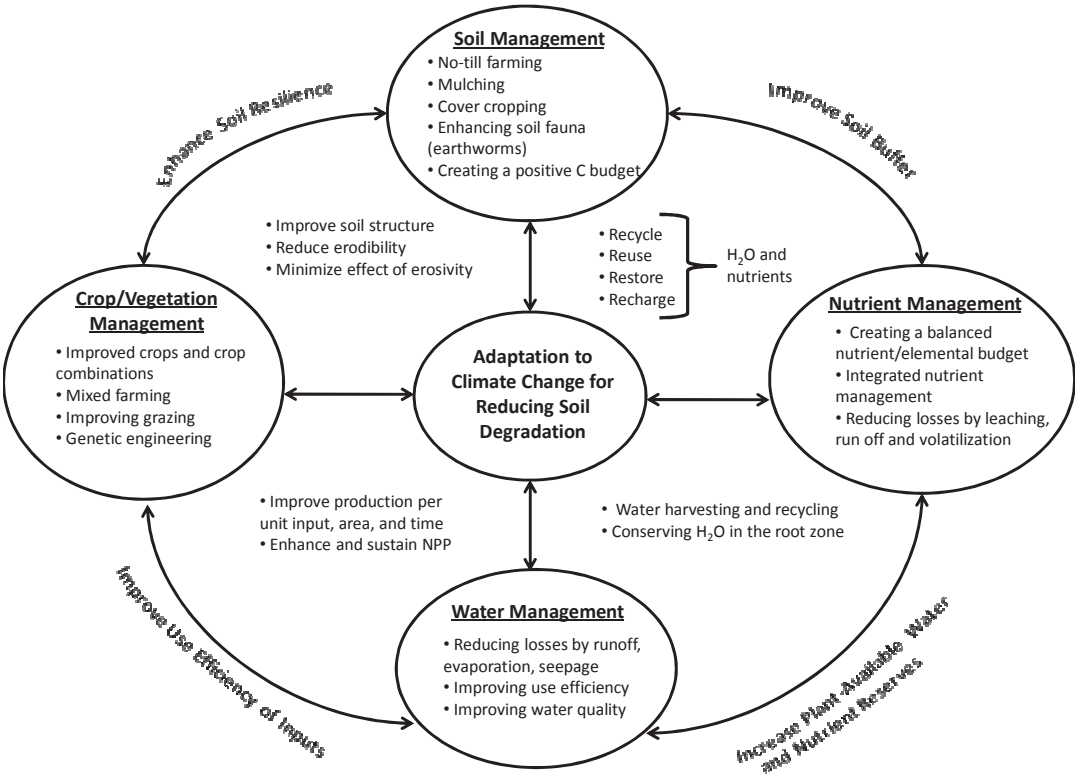
Notes: NUE = Nutrient use efficiency; INM = Integrated nutrient management; WUE = Water use efficiency; DSI = Drip subsurface irrigation; RMPs = Recommended management practices.

Source: Author's own work.

Sustainable soil management also implies adaptation to climate change. While mitigation strategies are important, adaptation to changing climate is extremely relevant to enhancing and sustaining agricultural production. Technological options for adaptation

to climate change include innovative systems of soil management, nutrient management, water management, and crop/vegetation management (Figure 3.5). The choice of soil-specific management must be aimed at: (i) enhancing soil resilience, (ii) improving soil buffering capacity against extreme events and related vagaries of changing climate, (iii) increasing plant-available water and nutrient reserves, and (iv) improving productivity per unit area, time and input of non-renewable resources. There are numerous RMPs (Figure 3.5), and the choice of soil-specific technologies depends on a range of biophysical and socio-economic factors. Reversing soil degradation trends implies adoption of modern innovations and adaptation to changing climate.

Figure 3.5. Technological options for adaptation to climate change



Source: Author's own work.

Conclusion

Soil degradation, an important issue of global significance, is a biophysical process but driven by social, economic, cultural and other issues related to human dimensions. Rapid increase in human population since 1800 but especially during the 19th century, and increase in human demands and aspirations, have aggravated the exploitation of soil and water resources, and exacerbated the problem of soil and environmental degradation. Processes of physical, chemical and biological degradation are accentuated by physiographic, climate, and terrain factors such as intensity and frequency of extreme climatic events, steep gradient and long slopes, and fragile soils in harsh climates. Over

and above the natural factors, soil degradation is exacerbated by several causes related to human activities. Important among these causes are deforestation, biomass burning, excessive ploughing, inappropriate irrigation, extractive farming etc. Given the magnitude of the problem, and the fact that is it likely to be aggravated because of the increase in human population and the projected climate change, it is important to identify strategies to reverse the degradation trends. Adoption of land saving and soil restorative technologies which enhance production while creating positive C and elemental budgets is a win-win option. In addition, it is equally important to identify techniques to adapt to climate change. Adoption of adaptive measures is especially important in developing countries with predominately resource-poor farmers.

In this context, there are several questions which need to be addressed through appropriate research at the ecoregional level. Important among these are the following:

- What are the credible and reliable estimates of the extent and severity of soil degradation?
- What are the principal processes of soil degradation, and how do factors and causes impact these processes in public ecoregions because of differences in the biophysical and the human dimension factors?
- What is the impact of soil degradation by different processes on agronomic productivity and other ecosystem services?
- How can degraded soil be restored?
- What are the soil-specific land use systems which can minimise risks/vulnerability of soil degradation and desertification?
- What are the impacts of soil degradation on food security and human nutrition?
- What are the policy interventions that can reduce urban encroachment and minimise the conversion of prime farmlands to other uses?
- What are the land use and management systems that enhance soil resilience?
- How can communication about soil degradation be strengthened among all stakeholders (policy makers, land managers, researchers, and the public at large)?
- How and where can a central data bank be established that collates credible information on the extent and severity of soil degradation by different processes?

Bibliography

Anonymous (2006), "African Soil Exhaustion", *Science,* Vol. 312, No. 31.

Bai, Z.G., *et al.* (2008), "Proxy Global Assessment of Land Degradation", *Soil Use and Management*, Vol. 24 pp. 223-234.

Bartlett, A.A. (2004), *The Essential Exponential: for the Future of our Planet, University of Nebraska*, Lincoln, Nebraska, USA, p. 291.

Brown, L.R. (2004), *Outgrowing the Earth*, Earth Policy Institute, W.W. Norton and Co. (ed.), New York, USA, p. 239.

Costanz, R. *et al.* (1997), "The Value of the World's Ecosystem Services and Natural Capital", *Nature*, Vol. 387 pp. 253-260.

Dregne, H.E. (1998), "Desertification Assessment", In R. Lal, W.H. Blum, C. Valentine, B.A. Stewart (eds.) *Methods for Assessment of Soil Degradation*, CRC, Boca Raton, Florida, USA, pp. 441-458.

Dregne, H.E. and N.T. Chou (1992), "Global Desertification Dimensions and Costs", In H.E. Dregne (eds.) *Degradation and Restoration of Arid Lands*, Texas Tech., Lubbock, Texas, USA, pp. 242-252.

Doran, J.W. and A.J. Jones (eds.) (1996), *Methods of Assessing Soil Quality*, SSSA Special Publ. # 49, Madison, Wisconsin, USA, pp. 410.

Eswaran, H., P. Reich, and F. Beinroth (2001), "Global Desertification Tension Zones", In D.E. Scott, R.H. Mohtar, G.C. Steinhardt (eds.) *Sustaining the Global Farm*, ISCO, Thailand, pp. 24-28.

FAO/UNEP/UNESCO (1979), *A Provisional Methodology for Soil Degradation Assessment*, FAO, Rome, Italy, pp. 84.

Farrington, R. and R.B. Salma (1996), "Controlling Dryland Salinity by Planting Trees in the Best Hydrological Settings", *Land Degradation & Development* Vol. 7 pp. 183-204.

Food and Agriculture Organization of the United Nations (2008), *Global Forest Resources Assessment 2005*, *www.fao.org/forestry/fra2005/en/.*

Gregorich, E.G. and M.R. Carter (eds.) (1997), *Soil Quality Foe Crop Production and Ecosystem Health*, Elsevier, Amsterdam, pp. 448.

ICID (International Commission on Irrigation and Drainage) (2002), *Irrigation and Food Production Information about ICID Network Countries*, *http://www.icid.org/index.e.html*.

Kaiser, J. (2004), "Wounding Earths Fragile Skin", *Science*, Vol. 304 pp. 1616-1618.

Lal, R. (1994), "Methods and Guidelines of Assessing Sustainable Use of Soil and Water Resources in the Tropics", *SMSS Technical Bulletin* #21, NRCS, Washington, D.C.

Lal, R. (1997), "Degradation and Resilience of Soils", *Philosophical Transactions of the Royal Society B: Biological Sciences*, The Royal Society, Great Britton, Vol. 352 pp. 997-1010.

Lal, R. (2001), "Potential of Desertification Control to Sequester Carbon and Nitrate the Green House Effect," *Climactic Change*, Vol. 15 pp. 35-72.

Lal, R. (2009), "Laws of Sustainable Soil Management", *Agronomy for Sustainable Development*, Vol. 29 pp. 7-9.

Lal, R., G.F. Hall and F.P. Miller (1989), "Soil Degradation: I. Basic Processes", *Land Degradation and Rehabilitation*, Vol. 1 pp. 51-69.

Lal, R., H.M. Hassan and J. Dumanski (1999), "Desertification Control to Sequester C and Mitigate the Greenhouse Effect", In N.J. Rosenberg, R. Vesar Izaurralde, and E.L. Malone (eds.) *Carbon Sequestration in Soils: Science, Monitoring and Beyond*, Batelle Press, Columbus, Ohio, pp. 83-149.

Marland, G., T. Boden and R. Andres (2001), *National CO_2 Emissions from Fossil Fuel Burning, Cement Manufacture and Gas Flaring*, Carbon Dioxide Information Analysis Center, Oakridge National Laboratory, Oakridge, Tennessee, USA.

Mishra, A. and S.D. Sharma (2003), "Leguminous Trees for the Restoration of Degraded Sodic Wasteland in Eastern U.P., India", *Land Degradation and Development*, Vol. 14, pp. 245-261.

NRC (National Research Council) (2008), *Emerging Technologies to Benefit Farmers in Sub-Saharan Africa and South Asia*, National Research Council, Nation Academics of Sciences, Washington, D.C.

Oldeman, L.R. (1994), "Global Extent of Soil Degradation", In D.J. Greenland and I. Szaboles (eds.) *Soil Resilience and Sustainable Land Use,* CAB International, Wellingford, United Kingdom.

Oldeman, L.R. and G.W.J. van Lynden (1998), "Revisiting the Glasod Methodology", In R. Lal, W.H. Blum, C. Valentine, B.A. Stewart (eds.) *Methods for Assessment of Soil Degradation*, CRC, Boca Raton, Florida, USA, pp. 423-427.

Partridge, M.D., J.S. Sharp and J.K. Clark (2007), *Growth and Change, Population Change in Ohio and its Rural/Urban Interface*, OARD-Extension, Columbus, Ohio, USA.

Ponting, C. (2007), *A New Green History of the World: the Environment and Collapse of Great Civilizations*, Vintage, London, Second Edition, pp. 452.

Qudir, M., A.S. Qureshi and S.A.M. Cheraghi (2008), "Extent and Characterization of Salt-Affected Soils in Iran, and Strategies for their Amelioration and Management", *Land Degradation and Development*, Vol. 19 pp. 214-227.

Qureshi, A.S., P.G. McCornick, M. Qadir and Z. Aslam (2008), "Managing Salinity and Waterlogging in the Indus Basin of Pakistan", *Agriculture Water Management*, Vol. 95 pp. 1-10, Elsevier Science, Amsterdam.

Reich, P. and H. Eswaran (1998), *Desertification: a Global Assessment and Risks to Sustainability*, Proc. XVI. Int. Cong. Soil Sci., Montpellier, France.

UNEP (1991), *Status of Desertification and Implementation of the U.N. Plan of Action to Combat Desertification*, UNEP, Nairobi, Kenya.

UNEP (1992), *World Atlas of Desertification*, N.J. Middleton and D.S.G. Thomas (ed.), Edward Asnold, London, pp. 69.

UN-ESA (2008), *Population Data of the UN Economic and Social Affair*, *(http://esa.un.org/unup/).*

UN, *World Urbanization Prospects: the 2007 Revision*, Department of Economic and Social Affairs, *www.un.org/esa/population/publications/wup2007/2007wup.htm.*

Chapter 4

Soil Resources: Science-Based Sustainability

Pedro A. Sanchez

The Earth Institute at Columbia University, New York, United States

Soil resources are being degraded primarily by nutrient mining in poor countries and by nutrient loading and other excesses in rich counties. Both are reversible, by applying science-based policies to counteract them. Food production can drastically increase in Africa with the proper use of donor funding, limiting food aid to starvation situations, and enabling chronically hungry small farm households in Africa to have access to improved hybrid seeds and appropriate mineral fertilisers. The fertiliser and improved seed required to produce an additional tonne of maize grain by Millennium Village farmers cost six times less than the same tonne of US food aid.

I am lucky to work at the interface between science and policy, which is the *raison d'être* of the Tropical Agriculture of the Earth Institute at Columbia University. My first paper of the conference focuses on soils issues, while the second (see Chapter 7) focuses on broader sustainability issues.

Soils provide critical ecosystem services to humankind. Provisioning services consist of food, livestock feed, textiles, wood and biomass for fuel. Regulating services include climate regulation, hydrological cycles, nutrient cycles, biodiversity conservation and waste removal (Palm *et al.*, 2007). Supporting services include soil formation, support to plants and primary production. I focus on debunking four common misconceptions: agriculture should mimic natural systems; mineral fertilisers are bad; organic farming is the answer and can be done anywhere, and we know the effect of soil use on food production, environmental degradation and climate change.

Myth 1: Agriculture should mimic natural systems

Agriculture is different from natural forests or grassland ecosystems. Natural systems have virtually closed nutrient cycles. Very little is added from atmospheric deposition, and very little is lost from leaching, runoff and erosion. Agriculture involves major nutrient withdrawals from the soil, which must be returned in the form of mineral or organic fertilisers. Maintaining a balance between inputs and outputs is a key to sustainable agriculture. When this does not happen, as is the case in most of Africa, the result is nutrient mining, depleting the soil of its nutrient reserves. This soil fertility depletion is the fundamental biophysical root cause for hunger in Africa (Sanchez *et al.*, 2002). When inputs far exceed outputs, nitrate pollution and eutrophication of waterways occurs, resulting in anoxic dead zones in coastal waters. Nutrient pollution was excessive in the USA and Europe in the last two decades, but effective policies are resulting in dramatic reductions and environmental enhancement. The main agricultural nutrient polluter is now China, where extremely high fertiliser applications are causing major nutrient loading (Vitousek *et al.*, 2009).

Myth 2: Mineral fertilisers are bad

The plant does not care whether the nitrate or phosphate ions they absorb come from a bag of fertiliser, a piece of manure or a decomposing leaf. It is a matter of nutrient balances. There is nothing wrong with mineral fertilisers when properly applied. If the world were to go totally dependent on organic fertilisers, it would be able to feed only about two billion people, a third of our present population. The main reasons are the differences in concentration and related transport costs. A bag of urea has 46% nitrogen dry weight while animal manures and leaves of leguminous plants have 2–4% nitrogen dry weight and a lot of water. I am not aware of any conventional agriculture system in rich countries that do not combine mineral and organic fertilisers because organic fertilisers also provide carbon, the substrate for micro-organisms that enable them to improve ecosystem functions such as nutrient and hydrological cycling.

Myth 3: Organic farming can be done anywhere

Organic farming is feasible in soils with high nutrient capital as a product of decades of mineral fertilisation or in soils high in natural fertility. Organic farming is definitely

not feasible in nutrient-depleted soils because the transition from conventional to organic farming involves drawing down soil nutrient capital. This is what happens in most of African smallholder farms' soils. Furthermore the high transport costs of organic inputs as well as the large quantities involved make it very difficult and costly to provide organic inputs in Africa. Organic farming in rich countries often bypasses this difficulty by growing nitrogen fixing legumes in the farms, something that is possible but not widespread in Africa. Organic farming is currently heavily promoted in Africa by well-meaning NGOs and even the United Nations Environment Program. This will result in failures when applied to nutrient-depleted African soils. The love for going organic must be tempered by scientific realities.

Myth 4: We know quantitatively the effects of soil use on food production, environmental degradation and climate change

Communicating soils information to diverse audiences is challenging because of technical jargon, outdated methods and pre-computer logic. Other Earth-system sciences (climatology, plant ecology, geology) have become quantitative and have taken full advantage of the digital revolution. Conventional soil maps, the main vehicle for conveying geographical information, are composed of polygons (mapping units) delineated according to mostly qualitative and static criteria. In most parts of the world, the spatial resolution is too broad to help with practical land management and the often complex conceptual model (each polygon including small areas of unmapped soil types) is difficult for users to understand and apply. At this point, soil scientists cannot provide quantitative answers to questions often asked by policymakers, such as: How much carbon is sequestered or emitted by soils of a particular country? What is its impact on biomass production and human health? The digital solution is clear – produce a fine-resolution and three-dimensional grid of the functional properties of soils relevant to land management. GlobalSoilMap.net, a new consortium, was launched in February 2009 to produce a digital soil map of the world at 90 metre resolution and an accompanying information service to provide such answers (IUSS *et al.*, 2009).

Bibliography

IUSS (International Union of Soil Sciences) (2009), Global Soil Map website, *www.GlobalSoilMap.net*, accessed May 2009.

Palm, C.A., P.A. Sanchez, S. Ahamed and A. Awiti (2007), "Soils: A Contemporary Perspective", *Annual Review of Environment and Resources*, Vol. 32 pp. 99-121.

Sanchez, P.A. (2002), "Soil Fertility and Hunger in Africa", *Science*, Vol. 295 pp. 2019-2020.

Vitousek, P., *et al.* (2009), "Nutrient Balances in Agricultural Development", *Science* 324(5934): 1519-1520.

Part II

Delivering Agriculture for Food and the Environment

Summary of discussions

Gary Fitt, CSIRO, Australia

Issues of food security, climate change and population growth all conspire to put increasing pressure on the global environment. In this session, four expert speakers discussed key issues relevant to the significant challenges of achieving a balance between the productivity of agricultural systems and the societal expectations for a healthy biodiverse environment.

What is clear from the presentations is that the growing imperative to achieve food security for a growing world population – a doubling of food production by 2050 – while at the same time deal with the challenges of climate change, limitations on water and land availability, soil degradation and limited options for landuse change may all compromise the opportunity to enhance the sustainability profile of agricultural production systems.

Dr. Les Firbank, North Wyke Research, UK, discussed options for Managing Agricultural Landscapes for Production and Biodiversity Outcomes. He highlighted the trends in habitat modification and biodiversity loss associated with agriculture globally, but particularly in temperate regions where forest loss has been extensive. Biodiversity losses associated with these habitat modifications and the off site impacts of agricultural contaminants are well quantified and concerning. Firbank outlined several future scenarios and their consequences:

- Business as Usual *will continue trends of biodiversity losses;*
- Extensive agriculture *or organics will not provide sufficient productivity;*
- Land sharing *with balanced production and biodiversity conservation is feasible in rich economies – "when land, food and money are plentiful";*
- Eco-agriculture *allows full accounting of costs and benefits, can enhance resilience and complexity and thus sustain biodiversity with productivity.*

He argued that what is needed is a "new narrative for agriculture and biodiversity" which leads to integrated land uses which are productive, resilient and adaptable and appropriately values natural resources and biodiversity. Easy to say but the ongoing need for integrated science to achieve these landscape scale changes is very real.

Firbank concluded that future changes in agricultural landscapes must be based on comprehensive knowledge of local ecosystems and will always be site specific – "sensitive to place".

Dr. David Kendra, from USDA ARS dealt with a major issue in food quality by dealing with the Impact of Crop, Pest and Agricultural Management Practices on Mycotoxin Contamination of Field Crops.[1] Extensive evidence shows how vulnerable significant grain production systems are to infection with several fungal pathogens which produce mycotoxins and Kendra outlined the significant challenge this poses to human and livestock health in food supply chains. Mycotoxins cannot be eliminated from food or feed supplies; however, their levels can be substantially reduced using good agricultural and management practices. Of most importance is the management of crop rotations and crop residues, the timing of harvest and then the appropriate storage of the grain after harvest to minimise mycotoxin contamination. Achieving efficient systems which achieve low mycotoxin levels is an ongoing challenge consistent with the needs for sustainable production.

Genetically modified crops will undoubtedly play a key role in future production systems as areas continue to grow globally. In 2008, GM crop area reached 125 Mha in some 25 countries. Dr. Franz Bigler, Agroscope, Switzerland addressed the question of whether genetically modified plants can play a role in sustainable crop protection? He highlighted the magnitude of crop losses to insect pests (20–40%) and the potential role of GM crops in addressing these losses. He argued convincingly that GM crop adoption can be consistent with Integrated Pest Management as one new tool in a toolbox for sustainable production which reduces reliance on interventions with synthetic pesticides. Evidence from some currently deployed GM crops indicate significant environmental benefits from reduced pesticide use (up to 85% reduction). After more than a decade of commercial use there are no negative environmental impacts attributed to GM crops. With the EU adopting a directive to mandate the adoption of IPM by EU farmers by 2014 there will be increasing pressures to consider GM crops as part of an IPM response as policy agendas evolve. Greater understanding of public perceptions is needed to ensure GM crops are able to contribute in systems where they can bring real benefits.

Finally Dr. Pedro Sanchez (The Earth Institute, Columbia University) discussed the significant challenge of Making Sustainability Happen on the Ground. In doing so he dismissed many widespread misconceptions about agricultural production in developed countries. Western populations have little understanding of where food comes from, and which production practices are most acceptable or sustainable. Many of these misconceptions emphasise the disconnect of urban populations from agriculture and food production. Sanchez highlighted the overall trend of declining prices for agricultural products, despite the recent spike which followed the food security crisis. He then dealt with some initiatives in developing countries such as the Millennium Villages project which attempt to enhance productivity through the provision of science to a community lead initiative. Appropriately targeted input subsidies and input credit schemes can all act as legitimate and effective vehicles for impact on food security in developing countries. Sanchez also highlighted the magnitude of post harvest losses of grain in storage, particularly across Africa, and the real opportunities in this area for improvements in food availability. Finally, he argued that helping Africa to achieve sustainable food production will have much greater benefits than continually providing short term food aid.

Collectively the four papers touched on the key challenges for agriculture in a changing world and highlighted the need for confluence of science and policy to ensure food security, sustainable landscapes and biodiversity values.

Note

1. Insofar as this paper is concerned, it was not submitted in time for this publication.

Chapter 5

Managing Agricultural Landscapes for Production and Biodiversity Outcomes

Les Firbank

Faculty of Biological Sciences, University of Leeds, Leeds, United Kingdom

Pressure is increasing globally to increase agricultural production (including bioenergy) per unit area, provide ecosystem services such as carbon sequestration, flood control etc., and maintain cultural and biodiverse landscapes. These functions should not be totally separated; rather, we need to develop agricultural systems and landscapes that also provide these services, though the balance between them will vary from place to place. Such systems must be productive, resilient and profitable, raising the issue of how the public benefits of ecosystem services are valued and captured. While many agricultural landscapes will change, there is real scope to develop systems that are both productive and biodiverse – but these need to be well thought through, they will not happen by chance.

Introduction

Agriculture is the major process by which species and ecosystems are manipulated to deliver food, fibre, energy and other products for human needs. Through agriculture, an astonishing 24% of terrestrial primary production is estimated to be appropriated by people, either by harvest or land use change (Aberl *et al.*, 2007). Given forecasts of population increase and the requirements for greater use of renewable energy and materials, there is every likelihood that this proportion will increase substantially during the present century. Virtually all species, human and non-human, derive their energy from photosynthesis, and so the more that is appropriated by humanity, the less is available for all other taxa. Less energy means fewer organisms, with risks of extinctions at higher trophic levels. Given the confounding factors of climate change, human consumption, land use change and sea level rise, the prospects for global biodiversity (defined here to encompass the global range of genetic, species and ecosystem diversity) are very poor.

Erhlich and Pringle (2008) put the situation simply and starkly:

"Although there are many uncertainties about the trajectories of individual populations and species, we know where biodiversity will go from here in the absence of a rapid, transformative intervention: up in smoke; toward the poles and under water; into crops and livestock; onto the table and into yet more human biomass; into fuel tanks; into furniture, pet stores, and home remedies for impotence; out of the way of more cities and suburbs; into distant memory and history books. As biodiversity recedes, we also lose the stories that go with it and many ways of relating to the world in which we evolved."

It is not just stories that could be lost, to be replayed through endless repeats of ageing documentaries. The loss of biodiversity also represents a loss of agricultural function and resilience. As the new International Assessment of Agricultural Science and Technology for Development points out: "During the last 50 years, the physical and functional availability of natural resources has shrunk faster than at any other time in history due to increased demand and/or degradation at the global level." (MacIntyre *et al.*, 2009).

In the past, such loss of natural resources has sometimes led to catastrophic declines in human wellbeing. But not always; resource loss can be managed in ways that slow and even reverse the declines to lead to more sustainable outcomes (Diamond, 2005).

Most scientific literature of interactions between productive agriculture and biodiversity document the negative impacts of the former on the latter, and discuss how they can be mitigated; turning win-lose scenarios into win-draw outcomes. Here I argue that this approach may not prove sufficient; that instead of regarding biodiversity conservation as competing with agriculture, I will suggest that we ought to consider them as two sides of the same coin, and that our approach should be joint development of agriculture, natural resource and biodiversity management. First I will review the major trends in agriculture/biodiversity interactions during the late 20th century. I will then discuss some of the ideas about how agriculture can co-exist alongside biodiversity, to suggest how one could try at least a measure of sustainable integration of agricultural systems and biodiversity. While I will be addressing global issues, I will draw most heavily on my experience as a scientist working in the United Kingdom and Western Europe.

The ongoing declines in biodiversity

While losses in biodiversity from human action are nothing new, they are accelerating rapidly at the global level (MEA, 2005; Secretariat for the Convention on Biological Diversity, 2006). Agriculture has contributed to this expansion in three major ways: transformation between agriculture and non-agricultural habitats; transformation of agricultural landscapes; and changes to crop management (Firbank *et al.*, 2008). In western Europe, these changes were first manifest through the historic clearing of forests to make way for farming, along with hunting of the large herbivores and predators that are now restricted to tiny fragments of their original geographic ranges, while the rest of the land surface became dominated by agriculture and forestry, with increasing urbanisation and the creation of protected areas (Foley *et al.*, 2005). More recent declines in British birds (Baillie *et al.*, 2007) and plants (Pearman and Preston, 1996) can be traced to reductions in landscape diversity, as complex mixed arable/grass/ woodland landscapes were partially replaced by larger fields on more specialised units (Benton, Vickery and Wilson, 2003; Haines-Young *et al.*, 2003), and to changing rotations, use of herbicides and increased inputs of nitrogen (Krebs *et al.*, 1999; Smart *et al.*, 2003a and 2003b; Chamberlain *et al.*, 2000; Stoate, 1995). Not only did plant communities become more species poor at the local scale, they became more similar over larger scales, as increasing levels of nitrogen and phosphorus encouraged more competitive species to thrive (Smart *et al.*, 2006), while bird communities in France have become more dominated by generalists able to cope with disturbed and fragmented landscapes (Devictor *et al.*, 2008).

The greatest declines in breeding bird numbers were associated with an increase in agricultural intensification in the 1970s, expressed by changes from spring to winter crop rotations and increased inputs (Chamberlain *et al.*, 2000; Donald, Green and Heath, 2001). By the mid-1990s, the policy emphasis on food production was replaced by a greater concern to promote environmental quality in agricultural landscapes, creating new habitats (including on set-aside land) and supporting more environmentally sensitive management of features. There have been clear benefits to different species under some situations (Firbank *et al.*, 2003; Roth *et al.*, 2008), notably to plant species richness in lowland enclosed grassland (Carey *et al.*, 2008; Kleijn *et al.*, 2006). Nevertheless, the responses of species overall has been mixed (Baillie *et al.*, 2007), with declines in bird numbers slowing in the United Kingdom (Baillie *et al.*, 2007), and continuing to decline in Europe as a whole, where the situation has been complicated by the tendency for extensive, species-rich agriculture to be replaced by intensively managed or abandoned land (Petit and Elbersen, 2006).

The renewed emphasis on agricultural production (for food, bioenergy, fibre and industrial feedstocks) clearly has the potential to continue these declines, whether by the widespread adoption of intensive crop management practices such as the use of herbicide tolerant crops (Firbank *et al.*, 2006) or homogenisation of landscapes through, for example, the switch of large areas of land to bioenergy monocultures (Firbank, 2008). Internationally, the potential impacts are even greater, with renewed pressure on transformation of the remaining great forests into agricultural land. In general terms, the loss of blocks of primary habitat threaten particularly those species that have large home ranges, in particular large mammals; the loss of landscape diversity disfavours those species with specialist requirements that are poor dispersers, while the effects of high nutrient loads favour generalist species that outcome others, reducing diversity at a site but also tending to make ecological communities more similar from one place to another.

Current approaches to managing interactions between agriculture and biodiversity

It is clear that an agricultural scenario of business as usual will be extremely damaging for biodiversity. If the industry continues to be driven mainly by economics and regulation for environmental protection, there may well be further concentration of crops into large monocultures, and increasing conversion of land to arable, not least to compensate for the risk of desertification (see Lal, Chapter 3). Thomas *et al.* (2004) estimate that as many as 15-20 of forest species could become globally extinct by 2050 through habitat loss to agriculture alone: the estimates become much higher if climate change effects are taken into account.

There are many ways of addressing interactions between agriculture and wildlife more proactively. Fundamentally, they vary according to the degree of separation and integration of cropped and non-cropped species.

Minimising negative environmental impacts of agriculture

It is argued that increased crop production per unit area, and on degraded and marginal land, benefits biodiversity by reducing pressure on other elements of the landscape (Green *et al.*, 2005). Moreover, it is suggested that the major environmental problems associated with intensive agriculture are potentially avoidable by the more efficient use of inputs and by controlling the potential impacts of pollution through use of improved technology (Royal Society, 2009). Certainly, intensive agriculture can be much more environmentally benign than in the past, as evidenced from the bans on dichlorodiphenyltrichloroethane (DDT), the adoption of integrated pest management, and the use of sensing to inform precision application of fertilisers. *Bt*, drought tolerant and nitrogen fixing crops should improve the resource efficiency of agriculture. Such practices could reduce the impacts of crop management, not least by reducing levels of eutrophication and slowing down the process of homogenisation of ecological communities. However, they do not in themselves reduce the potential for land transformation and landscape change. Moreover, there are limits to resource efficiency in current farming systems, though there is the potential for new cropping systems and varieties to improve efficiency of water and nutrient use.

Separation of agriculture from wild nature

The stronger argument that intensive agriculture can be beneficial to biodiversity asserts that, by increasing production in some areas, there is reduced pressure on the rest of the landscape, which can therefore be left for biodiversity (Green *et al.*, 2005). Various techniques exist to allow biodiversity to coexist with modern, intensive practices right down to within-field scales. These range from creating patches within or adjacent to crops (Pidgeon *et al.*, 2007; MacLeod *et al.*, 2004; Sotherton, 1998) to sowing crops for bird food (Parish and Sotherton, 2004) and managing field boundaries for invertebrates (Sotherton, 1991). Set-aside and agri-environmental schemes were European policy responses to over-production and concern about the environmental quality, and have both benefited a range of taxa (Firbank *et al.*, 2003; Carey *et al.*, 2002).

The argument for land sharing loses its force if agricultural intensification is insufficient to reduce food security. Thus in Europe, farmers are no longer obliged to set aside land to obtain subsidies. Further afield, tropical forests continue to be exploited for bushmeat and converted to farmland. Legal and illegal encroachment into nature reserves

is leading to increasing confrontation between villagers and large mammals, including tigers and elephants, to the benefit of neither (Sillero-Zubiri, Sukumar and Treves, 2007).

Extensive farming

During the 1990s, there was a lot of interest in the potential benefits to biodiversity of extensive and organic farming, in Europe especially. This came from two directions: the first was recognition that the high biodiversity value of traditional farming systems was under threat of intensification or abandonment (Petit *et al.*, 2001; McCraken, Bignal and Wenlock, 1995; Pain and Pienkowski, 1997; Woodhouse *et al.*, 2005) and second, observations that a wide range of taxa were more abundant and diverse under organic farming systems (Fuller *et al.*, 2005; Hole *et al.*, 2004). At a time when there were both policy and consumer-led moves for more environmentally friendly production, in a continent largely depleted of large areas of unmanaged land, extensive agriculture is now supported through localised or high quality markets (Ilbery *et al.*, 2005), others through agri-environment schemes (*e.g.* Roth *et al.*, 2008; Kleijn *et al.*, 2006).

Extensive agriculture tends to be beneficial for different taxa for several reasons: soil fertility levels are often low; habitats and landscapes tend to be more varied; less competitive crops are grown; and there has been a continuity of land management that has retained rich species pools. The species that benefit are typically those associated with traditional farmland, as opposed to those of forest and other habitats. However, the increases in numbers of both species and individual organisms when comparing organic and conventional farmland disappear if they are measured per unit of produce, rather than per unit area. There is no realistic scenario that extensive agriculture will feed the growing global population, and so it cannot be the only way of integrating agriculture and biodiversity. However, it certainly has a role in particular locations, conserving particular taxa and serving particular consumer and policy needs.

Integration of agricultural production and ecosystem service delivery

The previous scenarios tend to consider the balance between agriculture and biodiversity as a zero-sum game; the higher agricultural production, the less biodiversity. Another approach is to increase the total amount of agricultural productivity that reaches the consumer and also to increase productivity of other ecosystem services such as flood control and carbon sequestration. Emphasis is placed on the long-term sustainability of natural resources, reducing the risk of erosion and degradation. There are many flavours of such systems that aspire to be productive and multifunctional, ranging from permaculture and agroforestry, through enhanced natural resource management (Pretty *et al.*, 2006; Sanchez, Chapter 4), to the complex, integrated landscapes described as ecoagriculture (Scherr and McNeely, 2008). It is also important to reduce the 50% losses between the crop plant and human consumption (See de Fraiture, chapter 1).

Such systems work best when the non-agricultural products are appropriately valued, whether by the farming community itself, or through appropriate pricing and regulation mechanisms. These are not necessarily designed with the interests of biodiversity in mind, except for pollinators and predators that have a direct function supporting agriculture. However, such landscapes will tend to create their own distinct habitats and niches available to those species that are in the vicinity and are pre-adapted to take advantage of them. This is exactly how cultural landscapes developed in the past; they will tend not to suit rare species, or those with stringent habitat requirements, and the

species assemblages may be new. But in time they could develop their own character and value.

Conclusion

The ideal way to benefit biodiversity is to conserve large areas of natural habitat intact, to maintain and enhance the complexity of agricultural landscapes by managing them for ecosystem services as well as agricultural production, and to minimise the negative impacts of crop and livestock management. But this is unrealistic unless food security is also addressed for the growing population.

Extensive agriculture alone is not a realistic scenario. Forest conservation is not simply a matter of reducing pressure on agriculture, though that will help. However, it is possible to achieve sustainable, multifunctional agriculture provided there is investment in the people that live there (Sanchez, Chapter 4). We need to design landscapes that can integrate productivity of agriculture, ecosystem services and biodiversity if we are to deliver food security and thriving biodiversity into the future.

Bibliography

Baillie, S.R., *et al.* (2007), "Breeding Birds in the Wider Countryside: their Conservation Status 2007", in *BTO Research Report No. 487*, BTO: Thetford.

Benton, T.G., J.A. Vickery and J.D. Wilson (2003), "Farmland Biodiversity: is Habitat Heterogeneity the Key?", *Trends in Ecology and Evolution*, 18: pp. 182-188.

Carey, P.D., *et al.* (2002), "A Comparison of the Ecological Quality of Land Between an English Agri-Environment Scheme and the Countryside as a Whole", *Biological Conservation*, 108: pp. 183-198.

Carey, P.D., *et al.* (2008), *Countryside Survey: UK Results from 2007*, NERC/Centre for Ecology and Hydrology.

Chamberlain, D.E., *et al.* (2000), "Changes in the Abundance of Farmland Birds in Relation to the Timing of Agricultural Intensification in England and Wales", *Journal of Applied Ecology*, 37: pp. 771-788.

Devictor, V., *et al.* (2008), "Functional Biotic Homogenization of Bird Communities in Disturbed Landscapes", *Global Ecology and Biogeography*, 17(2): pp. 252-261.

Diamond, J. (2005), *Collapse: How Societies Choose to Fail or Survive*, Viking Penguin.

Donald, P.F., R.E. Green and M.F. Heath (2001), *Agricultural Intensification and the Collapse of Europe's Farmland Bird Populations*, Proceedings of the Royal Society of London Series B-Biological Sciences, 268 (1462): pp. 25-29.

Ehrlich, P.R. and R.M. Pringle (2008), *Where Does Biodiversity Go from Here? A Grim Business-As-Usual Forecast and a Hopeful Portfolio of Partial Solutions,* Proceedings of the National Academy of Sciences of the United States of America, 105: pp. 11579-11586.

Firbank, L.G. (2008), "Assessing the Ecological Impacts of Bioenergy Projects", *Bio-Energy Research* 1 (1): pp. 12-19.

Firbank, L.G., *et al.* (2003), "Agronomic and Ecological Costs and Benefits of Set-Aside in England", *Agriculture Ecosystems and Environment*, 95: pp. 73-85.

Firbank, L.G., *et al.* (2006), "Effects of Genetically Modified Herbicide-Tolerant Cropping Systems on Weed Seedbanks in Following Years", *Biology Letters*, 2(140-143).

Firbank, L.G., *et al.* (2008), "Assessing the Impacts of Agricultural Intensification on Biodiversity: a British Perspective", *Philosophical Transactions of the Royal Society B-Biological Sciences*, 363 (1492): pp. 777-787.

Foley, J.A., *et al.* (2005), "Global Consequences of Land Use", *Science*, 309 (5734): pp. 570-574.

Fuller, R.J., *et al.*(2005), "Benefits of Organic Farming Vary Among Taxa", *Biology Letters*, 1: pp. 431-434.

Green, R.E., *et al.* (2005), "Farming and the Fate of Wild Nature", *Science*, 307: pp. 550-555.

Haberl, H., *et al.* (2007), *Quantifying and Mapping the Human Appropriation of Net Primary Production in Earth's Terrestrial Ecosystems*, Proceedings of the National Academy of Sciences of the United States of America, 104 (31): pp. 12942-12945.

Haines-Young, R., *et al.* (2003), "Changing Landscapes, Habitats and Vegetation Diversity across Great Britain", *Journal of Environmental Management*, 67: pp. 267-281.

Hole, D.G., *et al.* (2004), "Does Organic Farming Benefit Biodiversity?", *Biological Conservation*, 122: pp. 113-130.

Ilbery, B., *et al.* (2005), "Product, Process and Place - An Examination of Food Marketing and Labelling Schemes in Europe and North America", *European Urban and Regional Studies*, 12 (2): pp. 116-132.

Kleijn, D., *et al.* (2006), "Mixed Biodiversity Benefits of Agri-Environment Schemes in Five European Countries", *Ecology Letters*, 9 (3): pp. 243-254.

Krebs, J.R., *et al.* (1999), "The Second Silent Spring?", *Nature,* 400: pp. 611-612.

MacIntyre, B.D., *et al.* (eds) (2009), *Agriculture at a Crossroads: International Assessment of Agricultural Science and Technology for Development Global Report*, Island Press: Washington, 590.

MacLeod, A., *et al.* (2004), "'Beetle Banks' as Refuges for Beneficial Arthropods in Farmland: Long-Term Changes in Predator Communities and Habitat", *Agricultural and Forest Entomology*, 6 (2): pp. 147-154.

McCraken, D.I.B., E.M. Bignal and S.E. Wenlock (1995), "Farming on the Edge: the Nature of Traditional Farmland in Europe", Fourth European Forum on Nature Conservation and Pastoralism, Trujillo, Spain: JNCC.

MEA (Millennium Ecosystem Assessment) (2005), *Ecosystems and Human Well-being: Biodiversity synthesis*, World Resources Institute, Washington, D.C.

Pain, D.J.P. and M.W. Pienkowski (1997), *Farming and Birds in Europe: the Common Agricultural Policy and its Implications for Bird Vonservation*, Academic Press, 436p.

Parish, D. and N. Sotherton (2004), "Game Crops and Threatened Farmland Songbirds in Scotland: a Step Towards Halting Population Declines?", *Bird Study*, 57: pp. 107-112.

Pearman, D.A. and C.D. Preston (1996), "Atlas 2000 - a New Atlas of Flowering Plants and Ferns", *British Wildlife*, 7: pp. 305-308.

Petit, S. and B. Elbersen (2006), "Assessing the Risk of Impact of Farming Intensification on Calcareous Grasslands in Europe: a Quantitative Implementation of the MIRABEL Framework", *Ambio*, 35 (6): pp. 297-303.

Petit, S., *et al.* (2001), "MIRABEL: Models for Integrated Review and Assessment of Biodiversity in European Landscapes", *Ambio*, 30: pp. 81-88.

Pidgeon, J.D., *et al.* (2007), *Mitigation of Indirect Environmental Effects of GM Crops*, Proceedings of the Royal Society B-Biological Sciences, 274 (1617): pp. 1475-1479.

Pretty, J.N., *et al.* (2006), "Resource-Conserving Agriculture Increases Yields in Developing Countries", *Environmental Science and Technology*, 40 (4): pp. 1114-1119.

Roth, T., *et al.* (2008), "A Swiss Agri-Environment Scheme Effectively Enhances Species Richness For some Taxa over Time", *Agriculture Ecosystems and Environment*, 125 (1-4): pp. 167-172.

Royal Society (2009), *Reaping the Benefits: Science and the Sustainable Intensification of Global Agriculture*, Royal Society, London, p. 72.

Scherr, S.J. and J.A. McNeely (2008), "Biodiversity Conservation and Agricultural Sustainability: Towards a New Paradigm of 'Ecoagriculture' Landscapes", *Philosophical Transactions of the Royal Society B-Biological Sciences*, 363 (1491): pp. 477-494.

Secretariat for the Convention on Biological Diversity (2006), *Global Biodiversity Outlook 2*, Montreal.

Sillero-Zubiri, C., R. Sukumar and A. Treves (2007), *Living with Wildlife: the Roots of Conflict and the Solutions, in Key Topics in Conservation Biology*, D. Macdonald and K. Service (Eds), Blackwell: Maiden, pp. 253-270.

Smart, S.M., *et al.* (2003a), "Locating Eutrophication Effects Across British Vegetation Between 1990 and 1998", *Global Change Biology*, 9: pp. 1763-1774.

Smart, S.M., *et al.* (2003b), "National-Scale Vegetation Change Across Britain; an Analysis of Sample-Based Surveillance Data from the Countryside Surveys of 1990 and 1998", *Journal of Environmental Management*, 67: pp. 239-254.

Smart, S.M., *et al.* (2006), *Biotic Homogenization and Changes in Species Diversity across Human-Modified Ecosystems*, Proceedings of the Royal Society B-Biological Sciences, 273 (1601): pp. 2659-2665.

Sotherton, N.W. (1991), "Conservation Headlands: a Practical Combination of Intensive Cereal Farming and Conservation", in *The Ecology of Temperate Cereal Fields*, L.G. Firbank *et al.*, (eds), Blackwell Scientific Publications, Oxford, pp. 373-397.

Sotherton, N.W. (1998), "Land Use Changes and the Decline of Farmland Wildlife: an Appraisal of the Set-Aside Approach", *Biological Conservation*, 83 (3): pp. 259-268.

Stoate, C. (1995), "The Changing Face of Lowland Farming and Wildlife, Part 2 1945-1995", *British Wildlife*, 7: pp. 162-172.

Thomas, C.D., *et al.* (2004), "Extinction Risk From Climate Change", *Nature*, 427: pp.145-148.

Woodhouse, S.P., *et al.* (2005), "Effects of Land-Use and Agricultural Management on Birds of Marginal Farmland: a Case Study in the Llyn Peninsula, Wales", *Agriculture Ecosystems and Environment*, 107 (4): pp. 331-340.

Chapter 6

The Role of Genetically Modified Plants in Sustainable Crop Protection

Franz Bigler and Jörg Romeis

Agroscope Reckenholz-Tänikon Research Station ART, Zurich, Switzerland

*Potential yield loss (*i.e. *production without crop protection) of major crops is estimated at 50% to 80% worldwide, whereas actual yield loss (*i.e. *loss despite crop protection) ranges from 25% to 40% on average of crops. These figures show that crop protection plays a crucial role in safeguarding crop productivity against competition from pests (weeds, animals, pathogens and viruses) and in preventing pre- and post-harvest loss of food, feed and fibres. Sustainable crop protection should utilise all suitable techniques and methods which are compatible with economic, ecological and social requirements. Integrated Pest Management (IPM) is considered to fulfil the conditions of sustainability, and IPM is thus a strategy that can contribute most efficiently to food security. IPM is one of the most effective strategies to contribute to crop productivity per harvested area which reflects in sustainable production systems the desire to increase land use efficiency and income by minimising adverse environmental and social impacts.*

Genetically modified plants (GMP) with resistance against insects and tolerance against herbicides were harvested in 2008 worldwide on approximately 8% of the total land managed for food and feed production. It is projected that this trend will continue and reach about 15% by the year 2015. Do GMP contribute to sustainable solutions of crop production and what is the experience so far in IPM? To what extent do insect resistant plants contribute to reduce crop loss, increase income and economic stability? Under what production conditions are pesticide applications with adverse effects on natural resources reduced? The contribution discusses landscape effects of GMP and impacts on and compatibility with conservation biological control. Finally it approaches socio-ethical issues related to reduced pesticide applications due to GM crops in third world countries.

Human population is projected to grow to approximately 9 billion by 2050 (Anonymous, 2007). The increased population coupled with changes in dietary habits, particularly in developing countries, towards more and higher quality food (*e.g.* higher consumption of animal products), preference of wheat and rice as staple food over other cereals, increasing use of grains for livestock feed and the much debated production of energy plants, will boost the demand for agricultural land. Suitable land for agricultural production is limited and most fertile land is already under cultivation and in some regions depleted. Given these limitations, higher productivity of crops per unit land will be needed, particularly in developing countries. Improved plant genetic resources coupled with better management practices (*e.g.* irrigation, nutrient supply, crop protection) and combined with high education and training levels of farmers are the major sources to increase food security. The combined effect of these factors allowed world food production to double in the past 40 years (Gruissem and Baettig-Frey, 2009; Oerke and Dehne, 2004). The challenge of future food production will be to increase productivity on the existing agricultural land and the careful use of natural resources such as soil, water, nutrients and biodiversity with the ultimate goal to lower adverse impacts to the environment. To meet these needs, improved production systems, making use of all appropriate technologies that contribute to sustainability, should be adopted and adapted to local conditions. Increased production requires more efficient protection of crops during growth and at subsequent storage of foods to safeguard added values of novel production systems for food security.

We discuss in this article the role of genetically modified (GM) insect-resistant plants in sustainable crop protection, whether or not they fit into integrated pest management systems, how they impact conservation of natural enemies and in what respect farmers' economy and social life is affected.

Crop losses by pests and food security

Yield and quality of cultivated plants are threatened by competition of weeds and destruction by animals (insects, mites, nematodes, rodents, slugs, etc.) and pathogens (fungi, bacteria, viruses) that may damage crops in the field (pre-harvest) and during storage as food and feed (post-harvest). High yields are often associated with higher risks of crop loss due to higher pest populations favoured by high plant densities, high nutrient supply and irrigation, making plants more sensitive to pathogens and animal pests. The use of varieties with high yield potential has favoured large-scale cropping of uniform cultivars, reduced crop rotation and reduced tillage cultivation, offering better conditions to development of pest organisms. The increased threat of higher crop losses to pests must be counteracted by improved crop protection that renders the production systems more efficient and sustainable. An intensification of crop production without adequate protection from pest damage is irresponsible because it would lower yields and thus reduce resource efficiency of fertiliser, water and energy (Oerke, 2006). In order to safeguard or reach high productivity levels that are able to satisfy increasing demands for food and feed, it is absolutely necessary to develop and implement sustainable crop protection strategies in regions where demands are high.

Average crop losses due to pests (weeds, animals, diseases) are estimated by FAO (*http://faostat.fao.org/faostat/collections?/subset=agriculture*) to range on average from 20% to 40% worldwide depending on the crop. Oerke and Dehne (2004) estimated potential crop losses (without crop protection) by pests of eight major crops from 48% to 83%, and actual losses (despite current crop protection applied) from 27% to 42% which

confirm FAO estimates. The differences between potential and actual losses correspond to the efficacy of pest control which ranges from roughly 20% to 50% for the eight crops considered by Oerke and Dehne (2004). The significance of weeds, animal pests and diseases differ from region to region and among crops. Weeds and diseases have in general a higher impact in temperate climates whereas arthropod pests are more important in sub-tropical and tropical regions. Oerke and Dehne (2004), estimate that 14% of wheat is lost to pests in Western Europe whereas in Central Africa and Southeast Asia losses lie above 35%. In rice, the total loss potential by pests accounts for 65–80% of attainable yield. The variation of total actual loss ranges from 23% in Oceania to 52% in Central Africa, indicating significant differences in the efficacy of crop protection practices. About one third of potential maize yield worldwide is still lost to pests, with highest damage (pre- and post-harvest) of over 50% in Africa where this important staple food is most needed for better food security. Demographic trends in Africa show the urgent need for increased agricultural productivity, including improved pest management to safeguard production, on a steadily decreasing amount of agricultural land per rural inhabitant (Neuenschwander *et al.*, 2003). According to Oerke (2006), the overall proportion of crop losses has increased in the past 40 years despite a 15-20 fold increase of the amount of pesticides used. Obviously, increased pesticide use has not resulted in a decrease of crop losses; however, in many regions pesticides have enabled farmers to increase productivity and economic benefits per unit land area considerably. Despite the fact that crop protection has substantially contributed to high and stable yields in many regions, overall losses are still far too high to be acceptable in view of the burning problems of food security.

Sustainable crop protection: the concept of IPM

Integrated pest management (IPM) roots back to the late 1950s when the first insect resistance problems with synthetic insecticides were recorded and entomologists became aware of the limitations of applying pesticides as the sole crop protection method (Freier and Boller, 2009). Theory and practice of IPM were developed from the 1960s onward (FAO, 1965; IOBC/WPRS, 1961). Inspired by pioneering work in the USA, Canada and Europe, IPM evolved in the 1970s and 1980s to an accepted sustainable crop protection strategy (Brader, Buyckx and Smith, 1980; Brookes and Barfoot, 2008; Glass, 1975; Huffaker and Smith, 1980; IOBC, 1980). The multitude of similar definitions of IPM as a concept can be summarised as "…being the crop protection strategy utilising all suitable and innovative methods and techniques that are compatible with economic, ecological and social requirements to keep damaging organisms below economic injury levels". The essence of IPM is that all appropriate control methods and techniques can be applied singly or in combination to maintain pest infestations below economic levels by encouraging methods which are economically and environmentally sound and socially acceptable, such as biological control, resistant plant varieties, cultural control techniques, habitat management and pesticides as the last resort. In the past, implementation of IPM concepts into agricultural practice proved to be difficult because of its demanding requirements to the farmer and the lack of short-term economic incentives. Despite these obstacles, IPM has become a unique concept which has been adopted across the crops and has proved to work in all geographic regions.

More recently, the Council of the European Union (EU) has adopted a new directive in which the concept of IPM is intended to become current agricultural practice in all member states of the EU (EC, 2009). The directive states that member states shall support

the establishment of necessary conditions for the implementation of IPM. In particular, they shall ensure that professional users have at their disposal information and tools for pest monitoring and decision making, as well as advisory services on integrated pest management. Member states shall describe in their national action plans how they ensure that the general principles of IPM are implemented by all professional users. The new directive declares IPM as being the official crop protection concept in the EU by January 2014, *i.e.* that the general principles of IPM must be developed, implemented and adopted by EU farmers to site- and crop- specific conditions. This will be a big challenge for science, advisors, industry and farmers and can be met satisfactorily only if farmers get support for implementing IPM and adopting alternative tools and methods and if training is intensified. Never in the past, has IPM got a better chance to be propelled on this level and to become current practice for so many farmers and to contribute to sustainable agriculture and food security.

Pest-resistant plants and sustainable crop protection

Insect pest-resistant cultivars developed through conventional plant breeding methods have been used in the past with great success against important pests in numerous crops (Adkisson and Dyck, 1980; Painter, 1951; Smith, 2005). Insect-resistant varieties, used within the IPM context, offer a number of advantages. They are safe for the environment and users, easy to deploy, requiring only sowing seeds of adapted, resistant varieties that meet the needs of farmers and markets. The reduction in pest numbers achieved through resistance is cumulative with other control strategies and practically without additional costs to the farmer. The reduction in pest populations by resistance makes control by other methods superfluous or easier (Adkisson and Dyck, 1980). Pest-resistant plants are self-sustaining, require little management, and are generally compatible with other pest management tactics (Romeis *et al.*, 2008a). Economically, plant resistance can often yield higher returns on investment than insecticide development (Smith, 2005). The development of commercially viable resistant cultivars using conventional breeding is a complex process that can take many years. The sources of resistant genes are generally limited to plants that can be crossed with the crop plant and thus naturally occurring resistance is limited.

Despite the many advantages of host-plant resistance as an IPM tool, the widespread adoption of non-transgenic, insect-resistant crops has been constrained by the limited availability of cultivars possessing high level of resistance to key pest species (Kennedy, 2008). Recombinant DNA technology greatly increases the potential array of available resistance traits that can be used to obtain insect-resistant crops (Gatehouse, 2008; Malone, Gatehouse and Barratt, 2008) and it reduces the time required to produce commercial cultivars with the desirable traits.

The majority of insect-resistant GM crops grown today express *cry* genes derived from the soil bacterium *Bacillus thuringiensis* (*Bt*). The first so-called *Bt* crop was commercialised in 1996. In 2008, *Bt*-transgenic maize and cotton cultivars were grown on a total of 46 Mha worldwide (James, 2008). While the first products expressed single toxins, the more recent ones express multiple genes to control the same pest complex (pyramids) or different pests (stacks). Besides expanding the spectrum of pest species controlled, plants expressing multiple insecticidal genes also help to delay the development of pest resistance to *Bt* toxins (Ferré, Van Rie and Macintosh, 2008; Hellmich *et al.*, 2008; Naranjo *et al.*, 2008). Besides new *Bt* maize and cotton varieties, other plants likely to be released in the foreseeable future include *Bt* rice

(Cohen *et al.*, 2008) and vegetables (Shelton, Fuchs and Shotkoski, 2008). Other non-*Bt* based insecticidal traits, presently in the early stage of development, such as protease inhibitors, lectins, chitinases, etc. may open new avenues to commercial crops that may be used in a similar manner as *Bt* crops to control non-lepidopteran pests (Gatehouse, 2008; Malone, Gatehouse and Barratt, 2008).

Pest-resistant plants in an IPM perspective

Pest-resistant plants are considered in IPM concepts as being one control tactic among an array of other methods. The level of resistance or tolerance can result in partial or complete defence or tolerance which entails different applications and implementations into site-specific IPM systems. Painter (1951) already stressed that resistant varieties are not a panacea for all pest problems. To be most effective, they must be carefully fitted into full pest control programmes designed for a crop with its specific management requirements.

Control of key pests with high efficacy

Ideally, pest-resistant varieties should provide complete and permanent control of the major crop pests. However, only a few cases of complete and permanent pest control are known from resistant plants bred with conventional methods (Adkisson and Dyck, 1980). Cultivars with low or moderate levels of resistance can still be used with great advantages for pest suppression because the key of success lies in the well designed incorporation into IPM systems. The systems adopting resistant plants should suppress and delay build-up of pest numbers, conserve natural enemies and their biological control function and consequently allow the use of more selective insecticides at lower frequency.

The only commercial insect-resistant GM crops grown today on large areas are *Bt* maize and *Bt* cotton. Both crops harbour a number of key pest insects depending on the geographic region. Hellmich (Hellmich *et al.*, 2008) and Naranjo (Naranjo *et al.*, 2008) have listed the key pests for maize and cotton, respectively, and gave information on the sensitivity to *Bt* toxins as deployed in GM plants. Hellmich (Hellmich *et al.*, 2008) concludes that out of 15 lepidopteran pest species in maize, five stemborers show excellent control with *Bt* maize and two have good control. Out of eight other lepidopteran pest insects, three are well controlled, four show some control and one species is not affected by the *Bt* toxin. Other arthropod pests in maize such as *Hemiptera*, *Coleoptera*, *Diptera* and *Thysanoptera* are not affected. Naranjo (Naranjo *et al.*, 2008) has identified 28 lepidopteran pest species for cotton worldwide of which nine get full control, 13 good control, five some control and one no control. There is no control of non-lepidopteran pests by *Bt* toxin in cotton. These figures show that single and double gene *Bt* Crys provide good control to a number of key pests; however, some economically important pests remain uncontrolled. In the future, more multiple *Bt* Crys pyramided or stacked in one plant will reach the market and improve the current lack of efficacy against some key pests.

Conservation of natural enemies and biological control

The preservation of natural enemy species and the biological control function they provide is a central requirement of IPM systems in almost any crop. Pest control by conservation and enhancement of natural enemies can be a successful strategy in IPM;

however, its success is often limited by the use of broad-spectrum pesticides and other management tactics that may have negative impacts on natural enemies. There have been several reviews of plant resistance and natural enemy interactions (Bottrell, Barbosa and Gould, 1998; Boethel and Eikenbary, 1986; Hare, 2002; Kennedy and Gould, 2007). These reviews give a number of examples of conventionally bred insect-resistant plants that negatively affect different important life-table parameters of natural enemies. Conversely, there are studies that have provided examples of positive effects or enhancement of natural enemy activity on insect-resistant plants, and some plants with pest resistance that appear to have no impact on biological control agents.

For the insecticidal proteins of insect-resistant GM plants to directly affect an individual natural enemy, the organism has to be exposed to the toxin and be susceptible to it. Consequently, an organism is not affected by the GM plant when either exposure or sensitivity (hazard) does not occur. For an effect to be of ecological relevance it must result in changes in populations or community processes. Similarly, direct or indirect effects of the GM plant on individuals of natural enemy species or guilds thereof will not lead to decreased biological control functions (Naranjo, 2005a and 2005b). Those principles are the same as for insect-resistant plants that are bred by conventional techniques. In contrast to chemical insecticides with contact toxicity, insecticidal proteins expressed by GM plants have to be ingested to affect arthropods. This reduces the number of non-target species in a crop that are exposed to the toxin.

Bt Cry proteins are known for their specificity, being active only against a narrow range of organisms. This host range limitation is due to the mode of action of these toxins (Schnepf *et al.*, 1998). The Cry proteins expressed in today's *Bt*-transgenic maize and cotton varieties are known to be specific to *Lepidoptera* or *Coleoptera*.

Recent review articles have summarised the available knowledge on the effects of *Bt* crops on natural enemies (Chu *et al.*, 2006; Romeis, Meissle and Bigler, 2006). In addition, Marvier (Marvier *et al.*, 2007), Wolfenbarger (Wolfenbarger *et al.*, 2008), and Naranjo (Naranjo, 2009), conducted a number of meta-analyses of the published field studies on non-target effects of *Bt* crops. Overall, the available field results from *Bt* crops confirm the findings of the studies conducted under confined conditions: *Bt* plants provide good protection against the target pests and have no or only negligible impacts on natural enemies. An exception are specific parasitoids of the target pests that are significantly reduced in the field due to the fact that their hosts are so efficiently controlled by *Bt* plants. However, such effects are a well known and inevitable phenomenon in efficient crop protection, and this is not a specific feature of *Bt* plants (Romeis, Meissle and Bigler, 2006).

Resurgence of target pests

A quick return of pests to damaging levels sometimes follows the routine use of broad-spectrum insecticides. This phenomenon of pest resurgence occurs because natural enemies are often more sensitive to insecticides than are the pests themselves (Croft, 1990). If the parasitoids and predators that normally attack a pest are destroyed, those pests that are still alive after insecticide residues dissipate will live in an environment with fewer natural enemies, leading to higher reproduction and populations. Pest resurgence caused by pesticides has been observed in diverse crops, for many kinds of pests (Buschman and DePew, 1990; Gerson and Cohen, 1989; Heinrichs *et al.*, 1982; Holt, Wareing and Norton, 1992; Talhouk, 1991).

For insect resurgence to happen, several conditions must be met. First the pest-suppressing toxic residue or other suppressive factors must be temporary. With insecticides, toxic residues are present immediately after application, but later dissipate. This is not the case with *Bt* plants, which continue to produce the toxin throughout the crop cycle. Second, the suppressing force must reduce populations of the pest's natural enemies more than the pest. With insecticides, this often happens because most conventional insecticides are broad-spectrum contact poisons that readily kill parasitoids and predators foraging on crop foliage at rates equal to or greater than the pest's mortality. In contrast, for *Bt* crops the suppressing force, the *Bt* toxins in the plant, is not a contact poison but a highly selective stomach poison (Schnepf *et al.*, 1998). Since natural enemies are in general both less exposed and less susceptible to the *Bt* toxins than their herbivorous hosts/prey, *i.e.* the target pests, *Bt* plants should either be harmless to the pest's natural enemies or kill them at a lower rate than the pest, thus preserving a favourable pest/natural enemy ratio. Consequently, *Bt* crops are unlikely to induce resurgence of target pests and there is no indication to date that this has happened (Romeis *et al.,* 2008a).

Secondary pest outbreaks

Broad-spectrum insecticides are well known to induce outbreaks of herbivores that are not normally pests. Secondary outbreaks occur because pesticides applied for key pests kill the natural enemies of other herbivores and release them from regulation. Prominent examples are outbreaks of spider mites, scales (Luck and Dahlsten, 1975), brown planthopper in rice (Gallagher, Kenmore and Sogawa, 1994), and sap-sucking pests in cotton (Naranjo *et al.*, 2008). As new herbivores reach pest status, the crop's IPM system has to be altered to include control for these "new pests".

In the case of insect-resistant GM plants, there would be little chance of induced outbreaks of secondary herbivores unless their natural enemies were able to consume plant tissues and were sensitive to the ingested insecticidal protein. Some groups such as predatory bugs feed on plant tissues to sustain themselves when prey are scarce and many predator groups feed on pollen, which may contain the insecticidal protein. Thus, direct exposure to plant-expressed toxins is possible. However, even if exposure and toxicity occur, enough predators would have to be killed to lower their population density in order to cause secondary pest outbreaks. For the currently available *Bt* crops such an effect has, however, not been observed (Romeis *et al.,* 2008a).

GM crops with insecticidal traits specific for the crop's key pests, such as *Bt* crops that control larvae of key *Lepidoptera* and *Coleoptera* species, are sometimes reported to carry higher populations of other herbivores. While this may appear to be secondary pest outbreaks, typically they are not. Rather, as GM crops are left less treated or untreated with conventional insecticides, other herbivores that are not susceptible to the GM trait, will no longer be chemically controlled by broad-spectrum insecticides. Some such herbivores will continue to remain rare because they are under natural biological control by local natural enemies. However, some herbivores among those not affected by the insecticidal trait of the GM crop may lack local effective natural enemies. Such species can become pests in GM crops. Good examples are the occasionally observed outbreaks of mirid plant bugs in *Bt* cotton (Men *et al.*, 2005; Wu *et al.*, 2002). This phenomenon may also occur when more specific conventional insecticides replace broad-spectrum ones in crops with multi-pest complexes.

Insecticide use and insect-resistant GM plants

The currently available data show that the adoption of *Bt*-transgenic crops has led to substantial reductions in the use of chemical insecticides (Fitt, 2008; Qaim, Pray and Zilberman, 2008). Large per acre reductions in conventional insecticide use and large areas planted to *Bt* crops means that these varieties are reducing agricultural insecticide use on a scale that outstrips all other IPM efforts.

For the period from 1996 to 2005, use of *Bt* cotton caused a 19.4% reduction in the total volume of insecticide active ingredient in global cotton production (Buschman and DePew, 1990). Data from many countries that grow *Bt* cotton show that the average insecticide use in *Bt* cotton was reduced by 25–80% when compared to non-*Bt* cotton (Fitt, 2008). In particular, significant reductions in insecticide use have been recorded in developing countries where the use of insecticides is often accompanied by serious health effects on farm workers (Brookes and Barfoot, 2008; Qaim, Pray and Zilberman, 2008; Raney, 2006). Novel double gene (pyramid) varieties require even less insecticide. Data from four seasons in Australia showed an average reduction in insecticides for Lepidoptera control of 65–75% in Cry1Ac/Cry2Ab cotton fields (Fitt, 2008). The potential for insecticide reduction depends on a number of factors including the targeted pest complex, the intensity of infestation and the general level of insecticide application before the introduction of *Bt* cotton.

In contrast, the use of *Bt* maize has caused a decline of only 4.1% in insecticide active ingredient, estimated for the period 1996-2005 for maize on a global scale (Buschman and DePew, 1990)). Similar to cotton, the deployment of insect-resistant *Bt* rice or vegetables such as eggplant or crucifers will likely lead to significant reductions in insecticide use (Cohen *et al.*, 2008; Shelton, Fuchs and Shotkoski, 2008). An experimental field study with *Bt* rice in China for control of stemborers has already shown a great potential for insecticide reductions (Huang *et al.*, 2005 and 2008).

Insecticide resistance in target pests

Resistance of pests against chemical pesticides is a widespread phenomenon. More than 7 747 cases of resistance with more than 331 insecticidal compounds involved are registered (Whalon, Mota-Sanchez and Hollingworth, 2008). From the estimated 10 000 arthropod pests worldwide, 553 species are reported with resistance to one or more insecticides. The occurrence of pesticide resistance frequently leads to the increased use, overuse and even misuse of pesticides that pose a risk to the environment, market access, global trade and human health (Mota-Sanchez, Whalon and Hollingworth, 2008). Farmers, industry and advisors are constantly challenged by new resistance of pest insects particularly in situations with high pest pressure and intensive production.

Resistance management for *Bt* plants remains a serious concern similar to pesticides (Bates *et al.*, 2005; Ferré, Van Rie and Macintosh, 2008; Shelton, Zhao and Roush, 2002). Keys to resistance management in *Bt* plants are: first, the use of non-*Bt* refuges in close vicinity to the *Bt* crops to conserve susceptible individuals within the pest population. Second, to incorporate high doses of *Bt* toxin into *Bt* plants to ensure that all heterozygote individuals with low and moderate levels of resistance are killed (Ferré, Van Rie and Macintosh, 2008). Third, resistance can be delayed by combining in the same plant two or more *Bt* Cry proteins that are effective against the same pest. The chance to find individuals which are simultaneously resistant to two or more proteins is almost negligible. For more than ten years, the sustained efficacy of the first generation

Bt crops (expressing a single *Bt* Cry toxin) against nearly all targeted pests has exceeded the expectations of many (Tabashnik *et al.*, 2008). Only recently, Tabashnik *et al.*, report putative Cry1Ac field-evolved resistant populations of *Helicoverpa zea,* an important pest insect in the USA in cotton. Moar *et al.* (2008) challenge these findings and conclude, after having examined other data sets, that the large genetic variation has always been present in *H. zea* populations, and there is no evidence for these authors to suggest a significant shift of susceptibility to *Bt* toxin Cry 1Ac since the introduction of *Bt* cotton. Two other cases of field resistance include *Busseola fusca* with resistance to Cry1Ab-expressing maize in South Africa (Van Rensburg, 2007), and *Spodoptera frugiperda* with resistance to Cry1F-expressing maize in Puerto Rico (Matten, Head and Quemada, 2008). For other important pest insects there is obviously no report suggesting decreased susceptibility to *Bt* toxins expressed in crops (Ferré, Van Rie and Macintosh, 2008; Tabashnik *et al.*, 2008).

The high-dose/refuge strategy coupled with the increasing trend to commercialise *Bt* plants with two or more Cry toxins incorporated in the same plant may reduce the risk of resistant populations. On the other hand, increasing use of the same *Bt* toxins expressed in different plants grown in vicinity and on large areas with no or insufficient crop rotation may increase the risk of resistance. The obvious ease of using *Bt* plants for solving key pest problems may dissuade farmers from principles of IPM such as crop rotation, cultural and biological control measures and, as a last resort, using pesticides in well-directed and selective ways to keep pests below economic injury levels and to prevent pest resurgence and secondary pest outbreaks.

The potential of resistance build-up of target pests on *Bt* crops is also a question on landscape scale effects. Extensive use of *Bt* crops in a landscape will impose selection pressure across significant components of pest populations and hence management strategies proposed to avoid resistance must be applied in a co-ordinated way across whole regions (Fitt, 2008).

Insect resistant plants in IPM and landscape effects

Agricultural crops and managed grass lands dominate large parts of terrestrial ecosystems and landscapes. Such anthropospheres are subject to constant and sometimes rapid changes with unprecedented and unexpected implications on ecological functions and ecosystem services provided by insects which are crucial to sustainable agriculture such as pollination of crops and wild plants, dung burring of grazing livestock, biological control of pests and decomposition of organic material in the soil. Economic values of such ecosystem services delivered by insects are estimated to over USD 57 billion per year in the USA alone (Losey and Vaughan, 2006). A more detailed study of the economic effects of increased maize areas for biofuel production in four US states (Minnesota, Wisconsin, Michigan and Iowa) results in lower landscape diversity, altering the supply of aphid natural enemies to soybean fields and reducing biocontrol services by 24% on average. This loss of biocontrol services cost soybean producers in these states an estimated USD 58 million per year in reduced yield and increased pesticide use (Landis *et al.*, 2008). For producers who rely solely on biological control, the value of lost services is much greater.

Diverse, small-scale agricultural landscapes with a high proportion of non-crop habitats frequently support a greater abundance of natural enemies and lower pest populations than large-scale monoculture landscapes with little non-crop habitats (Bianchi, Booij and Tscharntke, 2006). Simple agricultural landscapes had lower

abundance of natural enemies (76% of the studies) and increased pest pressure (45% of the studies).

In major farming regions, much of the landscape can be occupied by a few crops. In these settings, patterns of crop placements, size of the farms and single plots and crop management are major factors that determine population dynamics and levels of pest species at local and landscape scale (Kennedy, 2008). *Bt* maize and *Bt* cotton are now extensively planted in several countries and in 2008 *Bt* cotton represented 82%, 77% and 68% of the total production area under cotton in India, the USA and China, respectively (James, 2008). It may be expected that the economic incentives of growing *Bt* crops will drive farmers to even higher adoption rates, and increased proportion of these crops at the expense of other crops may result in monocultures of *Bt* crops in some landscapes. The most direct landscape-level effects of growing *Bt* crops in such settings would be expected to be observed for the targeted pest species that are sensitive to the *Bt* toxins, consume the crop as their primary or sole food source, and move across the landscape (Storer, Dively and Herman, 2008). Carrière *et al.* (2003) suggest that limited reproductive capacity and high mobility also tend to favour long-term population suppression. The best documented example of landscape-level effects of *Bt* cotton is that of the pink bollworm, *Pectinophora gossypiella*, in parts of the USA where the pest populations have become significantly reduced (Carrière *et al.*, 2003; Chu *et al.*, 2006). There is also evidence that populations of the cotton bollworm *Helicoverpa armigera* have declined as a consequence of continuous large-scale planting of *Bt* cotton (Wu *et al.*, 2008). Other studies suggest that populations of *O. nubilalis* have been suppressed at the landscape level after increased *Bt* maize adoption rates in some regions of the USA, and such reductions will have implications for control of this pest in other crops (Storer, Dively and Herman, 2008).

It is likely that the large scale adoption of *Bt* crops will also affect natural enemies. Food specialists might suffer from an area-wide reduction in their hosts or prey. This is especially likely for parasitoids of pests that do not occur on wild host plants in the region, such as *P. gossypiella* in Arizona. However, a landscape planted with *Bt* crops will still contain some hosts, for a number of reasons: (i) the *Bt* crops may not provide total control of the target pest(s), (ii) hosts may occur in non-*Bt* refuges of the same crop, and (iii) hosts or alternative hosts may occur on other crops or wild plants in the landscape. Therefore, the impact on a given parasitoid will also depend on its response to low host densities. For example, studies by White and Andow (2005), documented continued parasitism, albeit at a lower rate, of *O. nubilalis* larvae by *Macrocentrus grandii* at low host densities.

On the other hand there is growing evidence that biological control *per se* benefits drastically from substantial reductions in insecticide applications often associated with adoption of *Bt* crops (Fitt, 2008; Naranjo *et al.*, 2008). Thus, it is likely that biological control at the landscape level will be enhanced by planting of *Bt* crops, with potential benefits for other crops in the landscape.

Economic benefits of insect resistant GM plants to farmers

Since *Bt* cotton and *Bt* maize have been grown commercially in many countries and over several years, there is an increasing number of economic impact studies available for these two crops. Qaim, Pray and Zilberman (2008) have summarised yields of *Bt* cotton and *Bt* maize (in comparison to conventional cotton and maize) from published literature concluding that average yield increase in *Bt* cotton ranges from 9% in Mexico to 34% in

India. For *Bt* maize, mean yield increase in the USA reaches 5% and in South Africa 11%. Data on *Bt* cotton yields in some countries given by Fitt (2008) reflect different farmers' situations in industrialised countries like Australia and the USA and in developing countries like India, China, Mexico and South Africa. The percent yield increase in *Bt* cotton grown in Australia and the USA reaching 0–9% is relatively low compared to developing countries with increases ranging roughly from 10–80%, in exceptional cases up to 200%. Figures of both publications indicate a much higher yield increase in situations of developing countries where pest control before the introduction of *Bt*-transgenic varieties was insufficient.

In general, yield loss is a function of pest damage severity, and thus crops in areas with high pest pressure have a higher potential to prevent losses by applying GM technology. High yields of improved seeds can best be achieved if other important production factors, such as locally adapted varieties, water availability (irrigation), nutrient supply, control of other pests (weeds, diseases, viruses) and appropriate soil management, are optimally combined to provide the crop the best growth conditions. Variability of crop yields can be explained by the fluctuation of these factors, access of farmers to resources to cope with the problems and the level of training and education of farmers. For example, the use of non-adapted varieties has been identified as the main reason for *Bt* cotton failures in the Indian state of Andhra Pradesh (Qaim *et al.*, 2006). Small and resource-poor farmers may be more vulnerable to situations of adverse conditions and may not be able to compensate higher seed costs with higher yields and lower pesticide use (Bennet *et al.*, 2006). However, with a few exceptions, farmers in developing countries have relatively higher economic gains from *Bt* crops, in particular from *Bt* cotton, than farmers in industrialised countries, as evidenced by the increasing body of data published over the last few years (Anderson, Valenzuela, and Jackson, 2006; Bennet *et al.*, 2006; Gregory, Stewart and Stavrou, 2002; Morse, Bennet and Ismael, 2005; Pray *et al.*, 2002; Qaim, Pray and Zilberman, 2008; Raney, 2006). On a global scale, the great majority of farmers (> 90% of all farmers adopting GM technology) live in developing countries and are resource-poor and small farm holders (James, 2008), that have got a chance to improve livelihood with *Bt* crops.

Farmers' health

Direct health benefits of *Bt* crops accrue to farmers and farm labourers due to less insecticide exposure during spraying operations (Qaim, Pray and Zilberman, 2008). Problems of health hazards to farmers and farm workers are in general greater in developing countries than in developed countries, because environmental and health regulations are less severe, pesticides are mostly applied manually bringing farm workers in intimate contact with them, spray equipment is often defective and farmers are less educated and less informed about negative side effects of pesticides. Due to these factors, poisoning of farmers and labourers is a serious problem in developing countries, especially when crops like cotton and vegetables are grown, which receive high insecticide amounts. As discussed above, pesticide savings are particularly significant in *Bt* cotton. Hossain *et al.* (2004) have performed a survey on pesticide use in cotton and poisoning of farmers in some provinces of China. The data show that pesticide quantity used in non-*Bt* cotton was 46 kg/ha versus 18kg/ha in *Bt* cotton and acute poisonings with symptoms like breathing problems, skin and eye irritations, headache, nausea, were greatly reduced for farmers with *Bt* cotton. The authors were able to demonstrate a significant relationship between reduction in insecticide quantities and decrease of poisonings.

Conclusions

Bt-transgenic varieties have become a primary tool for managing key pests in cotton and maize. Significant reductions of insecticides, especially in cotton, have been experienced, and current practice continues to demonstrate positive effects on conservation of natural enemies with benefits for biological control. *Bt* crops are compatible with other pest control strategies and perfectly fulfil most sustainability criteria within the concept of IPM, contributing to improved food security. The attractiveness of insect-resistant *Bt* cotton and maize is their high effectiveness against key pests, the low hazard to natural enemies preserving biological control, often higher economic benefits and reduced health hazards to farmers, in particular in developing countries. In addition to these advantages it is crucial to most farmers that crop protection does not require highly sophisticated technology and resources. Growers in general are reluctant to adopt and implement complicated management systems that require additional financial investment, use of labour, water and other inputs. For this reason, adoption of *Bt* crops is rapid where pressing solutions against key pests are needed and efficient regulatory systems are in place. An increasing number of data evidence that *Bt* crops are deployed in a manner that improves economic, environmental and social sustainability of large- and small-holder farmers and their families. Similar to maize and cotton, it is expected that *Bt*-transgenic rice and vegetables will soon be commercialised and open new avenues for improved IPM programmes in these crops (Cohen *et al.*, 2008; Shelton, Fuchs, Shotkoski, 2008). Again, *Bt* varieties do have the potential to substantially reduce insecticides with major positive effects to the environment and human health and hence to contribute to sustainable crop protection and food security.

Challenges to use GM plants in sustainable crop protection

Current challenges for insect-resistant GM crops is the perception that these plants may be considered by farmers and advisory bodies as an alone-standing tool solving key pest problems without the need of integration into IPM programmes. Reduced use of IPM practices could lead to secondary pest outbreaks which are normally suppressed by crop rotation and other cultural management practices (Hellmich *et al.*, 2008). Due to easy deployment of *Bt* crops, fundamentally important principles of IPM may be disregarded leading to misuse and failures, such as planting *Bt* crops even if pests are not expected to reach damaging levels, or deploying *Bt* crops against pests that are not particularly sensitive to the insecticidal trait which could increase the risk of resistance build-up. Solutions to the problem of non-sensitive species will be given by stacked *Bt* Cry's making the crop resistant against a number of pests. In more complex pest situations, farmers need to know each single pest species to deploy the most efficient stack. This is not a problem for well trained farmers backed up by advisory services, however, this could pose serious questions for small farm holders in resource-poor countries where education and advisory services are not or less available. Increasing sophistication in GM crop deployment will demand better knowledge and training of farmers and extension services and ask farmers to adhere to the principles of IPM. Hence, a major challenge will be to develop innovative cropping systems in which *Bt* crops are implemented in sustainable ways in developed and developing countries.

A critical step in the application of GM crops is the regulatory approvals that must be obtained before they can be used, based on appropriate risk assessments by regulatory authorities. Therefore, a sound and functional regulatory system must be in place and

capable of making necessary scientific evaluations in order to arrive at a science-based decision. This is not the case everywhere, and missing or non-functional regulatory systems can be a major reason for GM crops not reaching the market (Matten, Head and Quemada, 2008). Absence of functional regulation of GM technology is a serious problem in many developing countries, over-regulation of GM plants, and dissent between regulatory authorities and countries, on the other hand, is a major constraint of *Bt* crops reaching the market in industrialised regions like western Europe. Harmonisation of regulatory systems and adoption of common principles of risk assessment in industrialised countries would facilitate and speed up (Romeis *et al.*, 2008b). Capacity building in risk assessment and expert training would be a key to improve regulation in resource-poor regions where governments lack the capacity to establish science-based regulation of GM technology.

The task of risk assessors in government regulatory agencies is to evaluate the risks posed by GM crops to the environment, and thus the focus lies on environmental safety such as adverse effects on non-target organisms and their ecological functions (*e.g.* biological control, pollination, soil processes), gene transfer to wild relatives and invasiveness. Once environmental risks are identified and valued, the regulatory agency should proceed further and compare risks of GM crops with observed impacts of alternative pest control technologies that farmers may currently use. For *Bt* crops, these alternatives are usually conventional insecticides. The assessment of relative risks of new and current pest control ensure that new technologies which are better or at least equal to current technologies reach the market and contribute to an agriculture that is more respectful of environmental issues. In doing so, regulatory agencies could ensure that environmental criteria coincide largely with sustainable agriculture and that GM plants fit well into IPM programs. Decisions for approval or rejection of GM plant applications are unfortunately still often based exclusively on risks of GM plants and no comparison with risks of current pest control technologies is made. By applying these principles, regulatory agencies may hold off environmentally friendly pest control methods from the market which could contribute extensively to improving sustainable pest control.

Bibliography

Adkisson, P.L. and V.A. Dyck (1980), "Resistant Varieties in Pest Management Systems", in *Breeding Plants Resistant to Insects,* Maxwell F.G., Jennings P. R. (eds.), John Wiley and Sons, New York, pp. 233-251.

Anderson, K., E. Valenzuela and L.A. Jackson (2006), *Recent and Prospective Adoption of Genetically Modified Cotton: A Global DGE Analysis of Economic Impacts*, World Bank/World Trade Organization, World Bank Policy Research Working Paper 3917.

Anonymous, (2007), *United Nations World Populations Prospects – The 2006 revision*, *www.un.org/esa/population/publications/wpp2006/WPP2006_Highlights_rev.pdf.*

Bates, S.L. *et al.* (2005), "Insect Resistance Management in GM Crops: Past, Present and Future", *Nat. Biotech.* 23: 57-62.

Bennet, R. *et al.* (2006), "Farm-level Economic Performance of Genetically Modified Cotton in Maharashatra, India", *Rev. Agric. Econ.* 28: 59-71.

Bianchi, F.J.J.A., C.J.H. Booij and T. Tscharntke (2006), "Sustainable Pest Regulation in Agricultural Landscapes - a Review on Landscape Composition, Biodiversity and Natural Pest Control", *Proc. R. Soc. London Ser.* B 273: 1715-1727.

Boethel, D.J. and R.D. Eikenbary (1986), *Interactions of Plant Resistance and Parasitoids and Predators of Insects*, Wiley, New York.

Bottrell, D.G., P. Barbosa and F. Gould (1998), "Manipulating Natural Enemies by Plant Variety Selection and Modification: a Realistic Strategy?", *Annu. Rev. Entomol.* 43: 347-367.

Brader, L. (1979), "Integrated Pest Control in the Developing World", *Ann. Rev. Entomol.* 24: 225-254.

Brader, L., E.J. Buyckx, and R.F. Smith (1980), "Past and Present Activities of the FAO/UNEP Panel of Experts on Integrated Pest Control", *Bull. Entomol. Soc. Am*. 26: 432-435.

Brookes, G. and P. Barfoot (2008), "Global Impact of Biotech Crops: Socio-economic and Environmental Effects 1996-2006", *AgBioForum* 11: 21-38.

Buschman, L.L. and L.J. DePew (1990), "Outbreaks of Banks Grass Mite (*Acari: Tetranychidae*) in Grain Sorghum Following Insecticide Application", *J. Econ. Ent.* 83: 1570-1574.

Carrière, Y. *et al.* (2003), "Long-Term Regional Suppression of Pink Bollworm by Bacillus Thuringiensis Cotton", *Proc. Nat. Acad. Sci. USA* 100: 1519-1523.

Chen, M. *et al.* (2006), "Impact of Insect-Resistant Transgenic Rice on Target Insect Pests and Non-Target Arthropods in China", *Insect Sci.* 13: 409-420.

Chu, C.C. *et al.* (2006), "Pink Bollworm Moth *(*Lepidoptera*: Gelechiidae)* Catches in the Imperial Valley, California from 1989 to 2003", *Insect Sci.* 13: 469-475.

Cohen, M.B. *et al.* (2008), "*Bt* Rice in Asia: Potential Benefits, Impact, and Sustainability", in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs*", J. Romeis, A.M. Shelton and G.G. Kennedy (eds.), Springer, Dordrecht: 223-248.

Croft, B.A. (1990), "Management of Pesticide Resistance in Arthropod Pests – Research and Policy Issues", *ACS Symposium Series*, Vol. 421: 149-168.

EC (2009), "Directive 2008/…/EC of the European Parliament and of the Council of Establishing a Framework for Community Action to Achieve the Sustainable Use of Pesticides", 6124/08, 31pp.

FAO (1965), "Report of the FAO Symposium on Integrated Pest Control", FAO Report PL/1965/15, Rome, Italy.

Ferré, J., J. Van Rie and S.C. Macintosh (2008), "Insecticidal Genetically Modified Crops and Insect Resistance Management (IRM)" in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs,* J. Romeis, A.M. Shelton and G.G. Kennedy (eds.), Springer, Dordrecht, pp. 41-85.

Fitt, G.P. (2008), "Have *Bt* crops led to changes in insecticide use patterns and impacted IPM?", *in Integration of Insect-Resistant Genetically Modified Crops within IPM Programs,* J. Romeis, A.M. Shelton, G.G. Kennedy (eds.), Springer, Dordrecht, pp. 303-328.

Freier, B. and E.F. Boller (2009), "Integrated Pest Management in Europe – History, Policy, Achievements and Implementation", in *Integrated Pest Management: Dissemination and Impact*, R. Peshin, A. K. Dhawan (eds.), Springer Science and Business Media B., V.: 435- 454.

Gallagher, K.D., P.E. Kenmore and K. Sogawa (1994), "Judicious Use of Insecticides Deter Planthopper Outbreaks and Extend the Life of Resistant Varieties in Southeast Asian Rice", in *Planthoppers: Their Ecology and Management*, R. F. Denno and J. T Perfect. (eds), Chapman and Hall, New York, pp. 599-614.

Gatehouse, J.A., *et al.* (2008), "Biotechnological Prospects for Engineering Insect-Resistant Plants", *Plant Phys.* 46: 881-887.

Gerson, U. and E. Cohen (1989), "Resurgences of Spider Mites (*Acari: Tetranychidae*) Induced by Synthetic Pyrethroids", *Exp. Appl. Acar.* 6: 29-46.

Glass, E.H. (1975), *Integrated Pest Management: Rationale, Potential, Needs and Implementation,* Entomological Society of America, Special Publication 75-2, 141pp.

Gregory, P., R. Stewart and S. Stavrou S. (2002), "Adoption of *Bt* Cotton by Small-Scale Farmers in South Africa", *Pesticide Outlook* 13: 31-34.

Gruissem, W. and P. Baettig-Frey (2009), "Magere Zeiten: Die Herausforderung der modernen Landwirtschaft", *BioFokus* 80: 3-16.

Hare, J.D. (2002), *Plant genetic variation in tritrophic interactions on Multitrophic Level Interactions*, T. Tscharntke and B. A. Hawkins (eds.), Cambridge University Press, Cambridge: 8-43.

Heinrichs, E.A. *et al.* (1982), "Resurgence of *Nilaparvata Lugens* (Stål) Populations as Influenced by Method and Timing of Insecticide Applications in Lowland Rice", *Environ. Entomol.* 11: 78-84.

Hellmich, R.L. *et al.* (2008), "The Present and Future Role of Insect-Resistant Genetically Modified Maize in IPM, in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs,* J. Romeis, A.M. Shelton and G.G. Kennedy (eds.), Springer, Dordrecht: 119-158.

Holt, J., D.R Wareing and G.A. Norton (1992), "Strategies of Insecticide Use to Avoid Resurgence of *Nilaparvata Lugens* (*Homoptera; Delphacidae*) in Tropical Rice: a Simulation Analysis", *J. Econ. Ent.* 85: 1979-1989.

Hossain, F. *et al.* (2004), "Genetically Modified Cotton and Farmers' Health in China", *Int. J. Occup. Environ. Health* 10: 296-303.

Huang, J. *et al.* (2005), "Insect-Resistant GM Rice in Farmers' Fields: Assessing Productivity and Health Effects in China", *Science* 308: 688-690.

Huang, J. *et al.* (2008), "Genetically Modified Rice, Yields, and Pesticides: Assessing Farm-Level Productivity Effects in China", *Econ. Dev. Cult. Change* 56: 241-264.

Huffaker, C.B. and R.F. Smith (1980), "Rationale, Organization and Development of a National Integrated Pest Management Project", in *New Technology of Pest Control*, C. B. Huffaker (ed.), Wiley-Interscience Publication, New York: 1-24.

IOBC (International Organization for Biological Control of Noxious Animals and Plants (1980), *Future Trends of Integrated Pest Management*, International Organization for Biological Control of Noxious Animals and Plants, IOBC Special Issue, Printed by Centre for Overseas Pest Research, London, 75pp.

IOBC/WPRS (International International Organization for Biological Control of Noxious Animals and Plants, West Palaearctic Regional Section) (1961), "Premier colloque sur la lutte intégrée dans les vergers", 5-9 Septembre 1961, Wageningen, *Entomophaga* VII 3: 965-293.

James, C. (2008), "Global Status of Commercialized Biotech/GM Crops: 2008", *ISAAA Brief* No. 39, International Service for the Acquisition of Agri-Biotech Applications, Ithaca, NY, United States.

Kennedy, G.G. (2008), "Integration of Insect-Resistant Genetically Modified Crops within IPM Programs, in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs,* J. Romeis, A.M. Shelton and G.G. Kennedy (eds.), Springer, Dordrecht: 1-26.

Kennedy, G.G. and F. Gould (2007), "Ecology of Natural Enemies and Genetically Engineered Host Plants", in *Perspectives in Ecological Theory and Integrated Pest Management*, M. Kogan and P. Jepson (eds.), Cambridge University Press, Cambridge: pp. 269-300.

Landis, D.A. *et al.* (2008), "Increasing Corn for Biofuel Production Reduces Biocontrol Services in Agricultural Landscapes", *Proc. Nat. Acad. Sci. USA* 105: 20552-20557.

Losey, J. and M. Vaughan (2006), "The Economic Value of Ecological Services Provided by Insects", *BioScience* 56: 311-323.

Luck, R.F. and D.L. Dahlsten (1975), "Natural Decline of a Pine Needle Scale (*Chionaspis pinifoliae* [Fitch])", outbreak at South Lake Tahoe, California, following cessation of adult mosquito control with malathion, *Ecology* 56: 893 – 904.

Malone, L.A., A.M.R. Gatehouse and B.I.P. Barratt (2008), "Beyond *Bt*: alternative strategies for insect-resistant genetically modified crops", in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs*, J. Romeis, A. M. Shelton and G. G. Kennedy (eds.), Springer, Dordrecht: 357-417.

Marvier, M. *et al.* (2007), "A Meta-Analysis of Effects of *Bt* cotton and Maize on Non-Target Invertebrates", S*cience* 316: 1475-477.

Matten, S.R., G.P. Head and H.D. Quemada (2008), "How Governmental Regulation Can Help or Hinder the Integration of *Bt* crops within IPM Programs", in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs*, J. Romeis, A.M. Shelton and G.G. Kennedy (eds.), Springer, Dordrecht: 27-39.

Men, X. *et al.* (2005), "The Influence of Pesticide Applications on *Helicoverpa Armigera Hubner* and Sucking Pests in Transgenic *Bt* Cotton and Non-Transgenic Cotton in China", *Crop Prot.* 24: 319-324.

Moar, W. *et al.* (2008), "Field-Evolved Resistance to *Bt* Toxins", *Nat. Biotech.* 26: 1072-1074.

Morse, S., R. Bennet and Y. Ismael (2005), "*Bt*-Cotton Boosts the Gross Margin of Small-Scale Cotton Producers in South Africa", *Int. J. Biotechnology* 7: 72-83.

Mota-Sanchez, D., M.E. Whalon and R.M. Hollingworth (2008), "Documentation of Pesticide Resistance in Arthropods", in *Global Pesticide Resistance in Arthropods*, M.E. Whalon, D. Mota-Sanchez and R.M. Hollingworth (eds.), CABI, Wallingford: 32-39.

Naranjo, S.E. (2005a), "Long-Term Assessment of the Effects of Transgenic *Bt* Cotton on the Abundance of Non-Target Arthropod Natural Enemies", *Environ. Entomol*. 34: 1193-1210.

Naranjo, S.E. (2005b), "Long-Term Assessment of the Effects of Transgenic *Bt* Cotton on the Function of the Natural Enemy Community", *Environ. Entomol.* 34: 1211-1223.

Naranjo, S.E. (2009), "Impacts of *Bt* crops on Non-Target Invertebrates and Insecticide Use Patterns", CAB Rev., *Perspect. Agr. Vet. Sci. Nutr. Nat. Resour.* 4: No.011. doi: 10.1079/PAVSNNR20094011.

Naranjo, S.E *et al.* (2008), "The Present and Future Role of Insect-Resistant Genetically Modified Cotton in IPM" in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs*, J. Romeis, A.M. Shelton and G.G. Kennedy (eds.), Springer, Dordrecht: 159-194.

Neuenschwander, P. *et al.* (2003), "Biological Control for Increased Agricultural Productivity, Poverty Reduction and Environmental Protection in Africa" in *Biological Control in IPM Systems in Africa*, P. Neuenschwander, C. Borgemeister, J. Langewald (eds.), CABI, Wallingford: 377-405.

Oerke, E.C. and H.W. Dehne (2004), "Safeguarding production – losses in major crops and the role of crop protection", *Crop Prot.* 23: 275-285.

Oerke, E.C. (2006), "Crop losses to pests", *J. Agric. Sci.* 144: 31-43.

Painter, R.H. (1951), *Insect Resistance in Crop Plants*, The Macmillan Company, New York: 520pp.

Pray, C.E. *et al.* (2002), "Five years of *Bt* Cotton in China - the Benefits Continue", *Plant J.* 31: 423-430.

Qaim, M. *et al.* (2006), "Adoption of *Bt* cotton and impact variability: Insights from India", *Rev. Agric. Econ. 28*: 48-58.

Qaim, M., C.E. Pray and D. Zilberman (2008), "Economic and social considerations in the adoption of *Bt* crops", in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs* J. Romeis, A.M. Shelton and G.G. Kennedy (eds.), Springer, Dordrecht: 357-417.

Raney, T. (2006), "Economic impact of transgenic crops in developing countries", *Curr. Opin. Biotech.* 17: 1-5.

Romeis, J., M. Meissle and F. Bigler (2006), "Transgenic Crops Expressing *Bacillus thuringiensis* Toxins and Biological Control", *Nat. Biotech.* 24: 63-71.

Romeis, J. *et al.* (2008a), "Insect-Resistant Transgenic Crops and Biological Control", in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs,* J. Romeis, A. M. Shelton and G. G. Kennedy (eds.), Springer, Dordrecht: 87-117.

Romeis, J. *et al*. (2008b), "Assessment of Risk of Insect-Resistant Transgenic Crops to Non-Target Arthropods", *Nat. Biotech.* 26: 203-208.

Schnepf, E. *et al.* (1998), "*Bacillus Thuringiensis* and its Pesticidal Crystal Proteins*"*, *Microb. Mol. Biol. Rev.* 62: 775-806.

Shelton, A.M., J. Z.Zhao and R.T. Roush (2002), "Economic, Ecological, Food Safety, and Social Consequences of the Deployment of *Bt* Transgenic Plants", *Annu. Rev. Entomol*. 47: 845-881.

Shelton, A. M., M. Fuchs and F.A. Shotkoski (2008), "Transgenic Vegetables and Fruits for Control of Insects and Insect-Vectored Pathogens" in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs,* J. Romeis, A.M. Shelton and G.G. Kennedy (eds.), Springer, Dordrecht: 249-271.

Smith, C.M. (2005), *Plant Resistance to Arthropods: Molecular and Conventional Approaches*, Springer Science and Business Media, Dordrecht.

Storer, N.P., G.P. Dively and R.A. Herman (2008), "Landscape Effects of Insect-Resistant Genetically Modified Crops in *Integration of Insect-Resistant Genetically Modified Crops within IPM Programs,* J. Romeis, A.M. Shelton and G.G. Kennedy (eds.), Springer, Dordrecht: 273-302.

Tabashnik, B.E. *et al.* (2008), "Insect Resistance to *Bt* Crops: Evidence Versus Theory", *Nat. Biotech.* 26: 199-202.

Talhouk, A.S. (1991), "On the Management of the Date Palm and its Arthropod Enemies in the Arabian Peninsula", *J. Appl. Entomol.* 111: 514-520.

Van Rensburg, J.B.J. (2007), "First Report of Field Resistance by Stem Borer, *Busseola Fusca* (Fuller) to *Bt*-transgenic Maize*"*, *S. Afr. J. Plant Soil* 24: 147-151.

Whalon, M.E., D. Mota-Sanchez and R.M. Hollingworth (2008), "Analysis of global pesticide resistance in arthropods" in *Global Pesticide Resistance in Arthropods*, M.E., M. Whalon, D. Mota-Sanchez and R.M. Hollingworth (eds.), CABI, Wallingford: 5-31.

White, J.A. and D.A. Andow (2005), "Host-Parasitoid Interactions in a Transgenic Landscape: Spatial Proximity Effects of Host Density", *Environ. Entomol.* 34: 1493-1500.

Wolfenbarger, L.L. (2008), *Bt Crops Effects on Functional Guilds of Non-Target Arthropods: A Meta-Analysis*,
PLoS ONE 3(5):e2118. doi/10.1371/journal.pone.0002118

Wu, K. *et al.* (2002), "Seasonal Abundance of the Mirids, *Lygus Lucorum* and *Adelphocoris* spp. *(Hemiptera: Miridae)* on *Bt* Cotton in Northern China", *Crop Protec*. 21: 997-1002.

Wu, K. *et al.* (2008), "Suppression of Cotton Bollworm in Multiple Crops in China in Areas with *Bt* Toxin-Containing Cotton", *Science* 321: 1676-1678.

Chapter 7

Science-Based Policy Issues to Enable Sustainability on the Ground

Pedro A. Sanchez

The Earth Institute at Columbia University, New York, USA

Using improved maize seed and appropriate mineral fertilisers in the 80 Millennium Villages, which comprise approximately 400 000 people in ten countries of sub-Saharan Africa, has drastically increased production of staple food crops, transforming food deficits into crop surpluses. Maize yields more than doubled at the village scale, from 1.7 to 4.1 tons ha^{-1}. In Malawi, because of a smart input subsidy programme implemented by the government, maize harvests have greatly surpassed those of previous years, turning that country from a recipient of food aid into a food exporter and food aid donor to neighbouring countries. Other countries are beginning to implement similar efforts. They will require novel financial mechanisms, but the way forward is clear.

Rich countries must stop their unsustainable practices that end up in severe nutrient loading, leading to pollution of rivers and dead zones in coastal waters. Also they should stop "horizon to horizon" sole cropping without rotations, and revert to practices that reduce soil erosion. Gradually eliminating farm subsidies will make agriculture more sustainable in rich countries. Sustainability concepts must be science-based. The use of appropriate genetically modified crops can help decrease insecticide use. Organic farming is only feasible in soils with high nutrient capital stocks, common in rich countries, but not in poor ones.

In Chapter 4 I focused on soils-policy issues, including fertilisers and organic farming. This paper focuses on some additional sustainability issues commonly misunderstood by the general public that are in need of science-based policy attention. Misconceptions about genetically modified organisms have been discussed by other participants.

Food comes from the supermarket

This is a common misconception among urban dwellers, particularly in those rich countries where the majority of the population no longer has agricultural roots. Education and public awareness are the policy options.

Food prices are too high

Historically this is not so. In constant dollar terms, food prices are one-quarter of what they were in 1975 (Masters). Food prices have been steadily decreasing since then largely due to increasing efficiency of farm production. The 25% increase in food prices that we have seen in the past two years is relatively small in comparison to the historical prices over the last 35 years. Nevertheless these increases are real and have posed strains to consumers. Higher food prices are, however, excellent for producers.

Purchasing seed every year is a conspiracy by multinational corporations

Seed companies marketing genetically modified crops have been accused of forcing farmers to buy seed every year. There are basically two types of improved seeds: hybrids and varieties. Hybrid seeds have been used by farmers worldwide since the 1940s. The hybrid vigour of the F_1 generation generally results in a 10-25% yield increase. If farmers plant an F_2 generation, the resulting crop is highly segregating, consisting of different plant types that together yield poorly.

Varieties, in turn, are not hybrids; they are stable generations (F_4 – F_8, depending on the crop) that have gone beyond the segregating phase. They lack the hybrid vigour and are therefore less productive than hybrids (in some crops), but the genetics are stable so it is perfectly acceptable to replant the seeds produced by farming.

Hybrids are appreciated by farmers everywhere. Even in Malawi, one of the world's poorest countries, when farmers were given the choice of purchasing at highly subsidised price either 3 kg of seed of improved maize varieties or 2 kg of hybrid maize seed, both well adapted to the local conditions, 76% of the farmers chose the hybrid maize (Denning *et al.*, 2009).

Rich country agriculture is extremely efficient and thus sustainable

The strong agricultural research tradition made agriculture in North America, Europe, Australia and Japan very efficient, one of the main reasons why food prices have steadily decreased from 1975 to 2005. But increases in farm size have reduced its sustainability. While being invited to talk at several US and Canadian universities and research centres, I require a consultancy fee – not cash but a visit to a farm – accompanied by extension specialists. Because of this, in the recent past, I have had quality visits to farms in

California, Florida, Illinois, Iowa, Indiana, Kansas, Missouri, Maryland, North Carolina, New York and Ontario, conventional and organic, large and small. While crop yields continue to climb, farmers are happy with the high food prices, very happy with the economic benefits of GMOs, but worry about the overall trends. Most farmers confess that they no longer know every square foot of their land, as they used to. Roadside to roadside cultivation, the elimination of buffer strips and many trees and visible erosion, particularly in Iowa, is very worrying. Cheap food prices provide a slim profit margin, forcing them to rely on government subsidies and ever larger machinery to take advantage of the narrow planting and harvesting windows when weather conditions are right. Cheap credit also spurred farmers to buy more exciting and complex farm machinery accumulating large debts that became a credit crisis when the value of their land began to drop. They are indeed efficient, but they live at the edge.

The excellent organic farms I have visited in California, New York and Ontario received decades – if not centuries – of mineral fertilisation, accumulating large nutrient capital stocks that farmers readily acknowledge are a main reason that they were able to convert into certified organic farms. The dairy cattle-based farms in New York and Ontario rely on nitrogen fixation through alfalfa or clover, which the cattle consumes, producing manure in large quantities that are used to fertilise cropping fields and the pastures themselves.

The smaller farms that I visited in North Carolina rely more on specialty crops, but the farmers show a strong interest in sustainability and have a wider margin of profitability. The trend away from large corporate farms to something in between – small specialty farms – is probably where the future lies.

Africa has no chance

This is a totally wrong statement. The African Green Revolution, called for by the former UN Secretary-General Kofi Annan, is starting to gain momentum, creating a sense of optimism about sub-Saharan Africa's ability to significantly and rapidly increase its agricultural productivity, a necessary condition for economic transformation. For 20 years, influential donors to Africa argued that markets alone would be sufficient to support Africa's agricultural transformation. That view is now changing, and a new policy activism is coming to the fore. Progress is happening on local, national and global scales.

The Millennium Villages Project, which reaches approximately 400 000 people in ten countries in sub-Saharan Africa, has drastically increased production of staple food crops, transforming food deficits into crop surpluses. Maize yields more than doubled at the village scale, with increases averaging 2.4 tons ha^{-1} and ranging from 1 to 5 tons ha^{-1} (Sanchez, Denning and Nziguheba, 2009). In Malawi, because of a smart-subsidy programme implemented by the government, maize harvests have greatly surpassed those in previous years, turning that country from a recipient of food aid into a food exporter donor to neighbouring countries (Denning *et al.*, 2009).

In 2006, the USA spent USD 1.2 billion in food aid for Africa, 20 times the USD 60 million spent for agricultural development in that continent (Chicago Council on Global Affairs, 2009). Delivering one metric ton of maize, as US food aid to a distribution point in Africa, cost USD 806 in December 2008. The fertiliser and improved seed required to produce an additional ton of maize grain by Millennium Village smallholder farmers cost an average of USD 135 at April 2008 prices, a six-fold

difference from food aid (Sanchez, 2009). Purchasing that same ton of maize locally – in an African country or a neighbouring one – now costs approximately USD 320. Selling that extra ton of maize makes a good profit, allowing farmers to generate cash, enter the market, and begin to exit the poverty trap.

There are approximately 100 million hectares of smallholder crop fields in sub-Saharan Africa. If these farmers raise their average cereal yields to three tons per hectare – the current average yield in tropical Asia and Latin America – from the current one ton per hectare level, the additional 200 million tons of cereal grain will more than compensate for the current food aid level, without putting additional land into crop production (Sanchez, 2009).

There is little question that sub-Saharan Africa can greatly improve food security with an ecologically sound African Green Revolution supported by science-based policies, community mobilisation and effective governance.

Bibliography

Chicago Council on Global Affairs (2009), *Renewing American Leadership in the Fight against Global Hunger and Poverty – the Chicago Initiative on Global Agricultural Development,* Chicago Council on Global Affairs, *www.thechigacocouncil.org/global development/pdf.*

Denning G., *et al.* (2009), "Input Subsidies to Improve Smallholder Maize Productivity in Malawi: Toward an African Green Revolution", *PLoS Biology* 7(1): e1000023 doi:10.1371/journal.pbio.1000023.

Masters W., Purdue University, personal communication.

Sanchez, P.A. (2009), "A Smarter Way to Combat Hunger", *Nature* 458: 148.

Sanchez, P.A., G.L. Denning and G. Nziguheba (2009), "The African Green Revolution Moves Forward, *Food Security* 1: 37-44.

Part III

Competition in Agriculture for Food, Fibre and Fuel

Summary of discussions

Dr. Kiyotaka Miyashito, Principal Research Director,
National Institute of Agro-Environmental Sciences, Tokyo, Japan

Demands for food and animal feed are increasing as a result of population growth and dietary changes in developing countries. The world's population, which currently exceeds 6.8 billion, is projected to increase by 50% by 2050. Biomaterials, including biofuels, are other factors that will boost demands on agriculture. Agriculture is expected to meet the increasing demands, which will have doubled by 2050. This must be achieved without adding any more strain on the environment. The title of Session 3 is "Competition in Agriculture for Food, Fibre and Fuel". There were four formal presentations, the topics of which covered: biofuel production, genetic improvement of wheat yield, genetic technology for sustainable animal production, and plant-derived feeds for aquaculture production.

The first topic was economic balance in competition for land between food and bioindustry, by Jozef Popp. He explained the outlook for world biofuel production. Altogether, 6%, 10%, and 10% of the global feed grain, of the global sugar production and of the global vegetable oil production, respectively, went to biofuel production in 2008. The renewable energy directive in the EU set the national target for renewable energy shares. These movements, together with other factors, brought about a spike in cereal and oilseed prices in 2008, resulting in a spread of concern throughout the world over food security. Although a sharp fall in food prices has occurred, agricultural prices are much more stable than the prices of other commodities. There will be more pressure on global markets and local ecosystems to supply food needs. Agriculture is being asked to increase yield, as land availability is limited and there are trade-offs between land expansion and ecosystem quality. For that purpose, the importance of technology uptake was stressed.

The second topic was genetic technology, sustainable animal agriculture and global climate change, by John Phillips. He showed state-of-the-art technology to reduce phosphorus contamination from pig production. Although the release of phosphorus into the environment from the animal industry causes serious water pollution, pig production will grow rapidly due to an increase in GDP per capita in developing countries. In order to reduce the environmental impact of pork production through enhanced dietary efficiency, transgenic pigs with a phytase gene, named Enviropigs™, were bred. The introduced gene was site-specifically expressed and salivary phytase activity was stably maintained. The results showed a reduction in the principal environmental pollutant from pig production of at least 50%. Phillips pointed out that regulatory approval is the next challenge.

The third topic was challenges and opportunities for further improvements in wheat yield, by Gustavo Slafer. He pointed out the importance of increasing wheat yield by breeding to meet growing demand. The yield of cereals has been significantly increased during the past half century, due to genetic improvements in both yield potential and in resistance to diseases as well as improvements in management. However, evidence of a slowdown in agricultural productivity growth has been clear in the past 15-20 years or so. In order to regain rates of yield gain compatible with the rates of growth in food demand, a substantial improvement in productivity (yield potential, water-use efficiency) is necessary. If the gains are to be compatible with environment safety and production sustainability, future gains must come more specifically from breeding. Slafer made the point that an understanding of the processes that matter at the crop level of organisation, and identification of genetic bases that might help rising crop yield, is necessary. He also emphasised the importance of funding agricultural research.

The fourth topic was plant ingredients as a replacement for fish meal in aquaculture diets, by Konrad Dabrowski. Aquatic organisms have advantages over terrestrial domesticated food animals in their low maintenance energy requirements, and the lack of necessity for detoxification of ammonia. As for the human health advantage resulting from seafood consumption, fish proteins have the highest value, and fish oils have a beneficial effect in decreasing coronary heart disease. In order to increase aquaculture production, a cost breakdown of the fish grower diet is anticipated as the cost of fish feed accounts for nearly half of the fish production. Replacement of fish meal by plant ingredients, such as soybean meal, soybean meal protein concentrate, corn gluten meal, cottonseed meal, distiller's dried grain-soluble and rice protein concentrate, is being pursued. Replacement of fish oils with plant oils, such as palm oil and soybean oil, is also being examined. Dabrowski pointed out the necessity of research to facilitate a wider, more large-scale use of plant ingredients in aquaculture, such as the interaction of protein in food, the food chain involved in the effects of a fish diet on the quality of fish meal, and the effect of plant specific substances such as appetite and growth promoters.

At the end of the formal presentations, there was an open discussion. The demands on agriculture are diversifying. In order to meet the growing demands on agriculture, the importance of agricultural research in many fields was affirmed.

Chapter 8

Economic Balance on Competition for Arable Land between Food and Biofuel: Global Responsibilities of Food, Energy and Environmental Security

Dr. József Popp

Research Institute for Agricultural Economics, Budapest, Hungary

Limited land is available globally to grow crops for food and fuel. There are direct and indirect pressures on forests and other lands to be converted from growing food for feedstock to be used for biofuel production. The balance of evidence indicates there will probably be sufficient appropriate land available to meet demands for both food and fuel, but this needs to be confirmed before the global supply of biofuel is allowed to increase significantly. There is a future for a sustainable biofuels industry, but feedstock production must avoid encroaching on agricultural land that would otherwise be used for food production. And while advanced technologies offer significant potential for higher greenhouse gas (GHG) savings through biofuels, these will be offset if feedstock production uses existing agricultural land and prevents land-use change. GHG savings can be achieved by using feedstock grown mainly on marginal land or that does not use land, such as wastes and residues (although this may compete with other uses of these materials). To ensure that biofuels deliver net GHG benefits, governments should amend, but not abandon, their biofuel policies in recognition of the dangers from indirect effects of land-use changes. Large areas of uncertainty remain in the overall impacts and benefits of biofuels. International action is needed in order to improve data, models and controls, and to understand and to manage effects.

Sustained economic growth worldwide during the last two decades has shown the benefits of globalisation. Although, it must be admitted, not for all. Much more could have been achieved if more progress had been made, notably on the Doha Development Agenda on trade. However, the current lower growth prospects worldwide associated with the high unemployment rate may trigger nationalism and protectionism. We need more responsibility in world trade in order to avoid globalisation allowing a few stakeholders to become rich by excluding many others from the benefit. Trade responsibility also means accepting special and differential treatment of developing countries under temporary trade protection in order to protect themselves from a food import surge.

The food crisis caught the world by surprise. Do we now expect a new policy paradigm from open markets to protectionism, from food security to self sufficiency, from imports to outsourcing (land acquisition) and from private to public market intervention? More recent transnational land deals are partly a consequence of the larger changing economic valuation of land and water. Higher agricultural prices generally result in higher land prices because the expected returns to land increase when profits per unit of land increase. Given that the food price crisis has increased competition for land and water resources for agriculture, it is not surprising that farmland prices have risen throughout the world in recent years.

An increasing number of countries are leasing and purchasing land abroad to sustain and secure their food production. Food-importing countries with land and water constraints but rich in capital are at the forefront of new investments in farmland abroad. Some agreements do not involve direct land acquisition, but seek to secure food supplies through contract farming and investment in rural and agricultural infrastructure, including irrigation systems and roads (Braun and Meinzen-Dick, 2009).

These include the acquisition of 690 000 ha of land in Sudan by South Korea, and around 320 000 ha of Pakistani land by the United Arab Emirates, as well as a pending Saudi request for 500 000 ha of Tanzanian land and Chinese attempts to secure more than one million hectares in the Philippines. A major evolution from past patterns is the transition from overseas profit oriented investments for tropical cash crops to farmland acquisition for growing basic staples, with an eye to bolstering a country's food security (Table 8.1).

Although additional investments in agriculture in developing countries by the private and the public sector should be welcome in principle, the scale, the terms and the speed of land acquisition have provoked opposition in some target countries (the Philippines, Madagascar). Well-documented examples on these developments are scarce. The lack of transparency limits the involvement of civil society in negotiating and implementing deals and the ability of local stakeholders to respond to new challenges and opportunities.

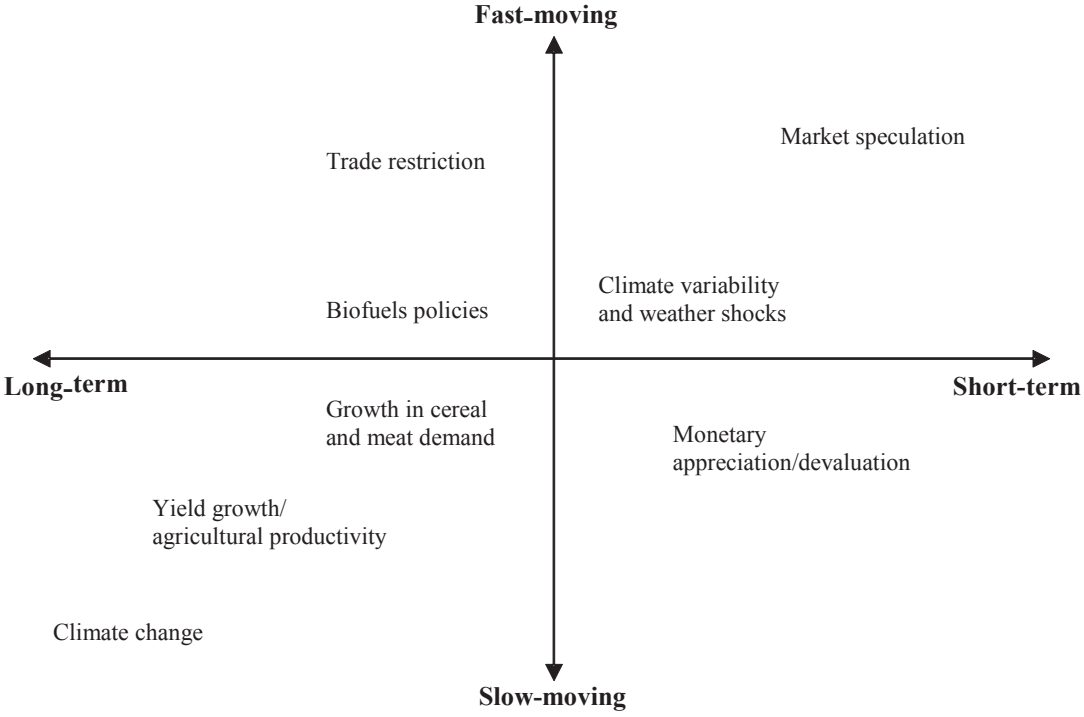
Table 8.1. Transnational land acquisition, 2006-2009

Country investor	Country	Plot size (hectares)
Bahrain	Philippines	10 000
China (with private entities)	Philippines	1 240 000
Jordan	Sudan	25 000
Libya	Ukraine	250 000
Qatar	Kenya	40 000
Saudi Arabia	Tanzania	500 000
South Korea (with private entities)	Sudan	690 000
United Arab Emirates (with private entities)	Pakistan	324 000

Source: Braun and Meinzen-Dick (2009). IFPRI has compiled this table from media reports. The responsibility for the accuracy of the information presented here, however, lies with the reporting media.

The main concerns today are the declining rate of food self-sufficiency and a growing sense of the potential for disruption to domestic food supplies in an uncertain world (climate change, energy security, safety concerns over imported food, geopolitical tensions and the food price spike in 2008). There are long and short term factors and fast and slow-moving drivers leading to food crisis (Figure 8.1). There will always be risks associated with food supply and thus a need to manage these risks. European consumers are well placed to cope with price risk and well-functioning markets can help to reduce this risk. Domestic food supplies are not less risky than imports (energy), but it is sensible to plan for systemic risks (such as nuclear fallout, port strikes, etc.). We experience food poverty due to a lack of entitlements, not lack of food availability.

Figure 8.1. Relationships between the long/short term factors and fast/slow-moving drivers



Source: Braun *et al.* (2008).

We face a future of food scarcity, with high, albeit very volatile prices both for inputs and outputs. Food scarcity is aggravated by managed trade and lack of finance and

eventually also by environmental degradation. The market has lost its magic. Recent events have shown that markets can fail as deregulation has backfired. But open trade and related financing depend on it so a new financial architecture is urgent. We also need greater responsibility in budgetary and financial affairs. However, increased government spending through stimulus packages poses a risk of plunging the world into a new crisis and sparking a return of inflation.

More responsibility is needed regarding food trade, and more responsibility in supporting a co-ordinated regulatory framework, as well as virtuous public and private behaviour fighting environmental degradation. We need greater responsibility in cutting GHG emissions to show greater respect for the environment and for the enlargement of the Kyoto protocol. If there is going to be enough food at affordable prices for the global population, we may also have to change our food habits and decrease food waste. Field losses amount to 20–40% due to pests and diseases. Food waste in the field pre-processing (broken grains, excessive dehulling), transport (spillage, leakage), storage (insects, bacteria) and processing and packaging (excessive peeling, trimming and inefficiency) goes up to 10–15% in quantity and 25–50% in value (quality). Marketing (retailing) and plate (by consumers and retailers) waste adds another 5–30% in developed and 2–20% in developing countries to the losses in the food chain (IWMI, 2007). We can save also water by reducing losses in the food chain.

World population growth is the biggest trend-making factor: 75 million more people a year, rising to 9 billion by 2050. Consequently, there is a rapidly growing demand for crop products, including feed with increasing meat consumption. Other major global trends are globalisation and urbanisation. With production moving to the most competitive regions, food trade is becoming more liberalised but also more concentrated. Growing energy demand and climate change will also influence food production, with agriculture contributing to emissions; agriculture will also suffer or benefit from changing climates depending on climatic zones. Additional challenges are increasing market volatility, resulting from yield and end stock fluctuations and consumer sensitivity to food quality, safety and price. There is uncertainty regarding the timing and application of innovations as regards biotechnology, nanotechnology, precision farming, carbon sequestration, and information technology.

Finally, there is the challenge of who will pay for agricultural public services provided by land managers that the market does not pay for, such as rural landscape maintenance, environmental protection, biodiversity and animal welfare. These challenges are aggravated by global irresponsibility, regarding food and energy security, water and environmental sustainability.

Food security

In 2008, the world's food import bill surged above USD 1 trillion, 23% more than in 2007, and 64% more than in 2006. Developing countries actually spent in 2008 about one-third of the world's food bill, or 35% more than in 2007 (FAO, 2008). There is good potential for new land cultivation in Latin America, Africa and Eastern Europe (Ukraine and Russia). However, new land is insufficient, and either inappropriate because of poor or polluted soils, or difficult to use for food production (due to doubtful property rights and/or poor finance and/or due to government mismanagement and lack of transportation infrastructure). Moreover, cultivated land is diminishing fast, not just because of expanding deserts, but also because much of it is being lost to

urbanisation. The addition of some 75 million people every year claims nearly 3 Mha for housing, roads, highways and parking lots. The main reasons why the world food supply is tightening are population growth and accelerated urbanisation,[1] changes in lifestyles, falling water tables and diversion of irrigated water towards the cities (The Earth Institute, 2005). All this leads to losses in soil availability, quality and use for food production.

By 2050, global food output must increase by about 70% due to higher food demand, changing diets and urbanisation. Urbanisation will double domestic and industrial water use, not to mention climate change and bioenergy production. Without water productivity gains, crop water consumption will double by 2050 (Table 8.2). The water "bubble" is unsustainable and fragile because 6.8 billion people at present have to share the same quantity as the 300 million global inhabitants of Roman times. About 80% of water for food production comes directly from rain, but an increasing part is met by irrigation (IWMI, 2007).

Table 8.2. Water security

Water use	Litres of water
Drinking water	2-5 litres per person per day
Household use	20-500 litres per person per day
Wheat	500-4 000 litres per kilo
Meat	5 000-15 000 litres per kilo
Biofuel	1 000-3 500 litres per litre
Cotton t-shirt	2 000-3 000 litres
Agriculture	3 000 litres per person per day 1 litre per calorie

Source: IWMI (2007) and Charlotte de Fraiture and David Molden, "Balancing global water supply and demand", Presentation: Challenges for Agricultural Research, OECD, 6-8 April 2009 Prague, Czech Republic.

Both the physical water productivity (more crop per drop) and economic water productivity (more value per drop) have to be increased by investing in rainfed agriculture and irrigation. Water productivity improvement is feasible, but farmers optimise land productivity rather than returns to water, particularly where water is subsidised. We do not know what the adequate incentives are, but farmers in the EU are fighting for a higher irrigation water subsidy without impact analysis of water productivity improvement. Promoting food trade from water rich, highly productive areas to water scarce areas contributes to global water productivity improvement.

To meet world demand the necessary production growth will, to a large extent, have to be met by a rise in the productivity of the land already being farmed today. However, this will be difficult to accomplish as global agricultural productivity growth has been in decline since the Green Revolution of the 1960s and 1970s. Global crop yield increases have plummeted from 4% per annum in the 1960s to 1980s to 2% in the 1990s, and to barely 1% in 2000 to 2010 forecasts (FAO, 2008). Yield increases have generally exceeded areal increases. While substantial yield increases in India, the USA, Russia and Ukraine are expected in the future, Europe's role and share as supplier of food to the world is diminishing. The net crop-trade position of the EU-27 can be expected to

deteriorate. The EU's capacity to help fight world starvation will be reduced at a time in which food production will decline predominantly in those countries which already have record increasing food import needs.

The discussion of the food crisis has faded into the background because it has been overshadowed by the global macroeconomic crisis and the financial crisis. The sharp rise in prices of basic foodstuffs created extreme difficulty for a large part of the world. The food crisis affected more people more severely than the macro crisis has done so far, because those who were most affected by the sharply rising food prices are those who spend a larger share of their income on food. One indication of it is the remarkable amount of civil unrest and political instability that happened in 2008 in dozens of countries (Ethiopia, Egypt, Mexico, Thailand etc.), as people were unable to afford basic nutrition (FAO, 2008).

There were also some extraordinary political responses. Much of the world's system of trade in foodstuffs broke down temporarily as food exporting countries moved to limit, or in some cases completely ban exports in an attempt to provide some protection to their domestic consumers. The severe economic slump striking the whole world has been quite clearly the worst downturn since the great depression. All of this has taken the attention away from the food crisis. The macro crisis has led to many people writing off the food – and more broadly the commodity price crisis of 2008 – as not fundamental. There is widespread belief that all that really happened was a speculative bubble, with too many people trading commodities, which drove commodity prices to unsustainable levels. Consequently all the concerns about ultimate supplies of food were misplaced (Krugman, 2009).

International trade in commodities futures has expanded enormously; food and commodity prices went up very sharply, and then fell significantly. It is not correct that it was a speculative bubble. The rise and fall of commodity prices affected not only commodities with large futures, but those without such as iron ore or oil. Trading commodity futures only affects the price to the extent that speculation leads to withdrawal of real supplies, which leads to hoarding. However, that was not the case with agricultural commodities, as food stocks were at record lows at that time. With an economic slump, the real price of commodities always falls and *vice versa*. The great depression showed a spectacular collapse of agricultural prices. The fall in prices in 2008 was the consequence of a global recession.

With the end of crisis, resource constraints plus bad policies are creating a major problem for the supply of food in the world. Despite the sharp fall in food prices since their peak in early 2008, prices of basic foodstuffs in real terms are still higher than the beginning of this decade. Aside from food prices being still on an upward trend, price volatility is a clear problem. People do not eat only in the long term, they eat every day. Should the high prices from 2008 re-occur, it would be a very serious problem, as people are very vulnerable to such high prices. For example, when a country imposes an export ban, the global economy is affected even if the domestic consumers are protected.

The poor have no access to ways of diversifying risk and they have no protection against high food prices. What can be done at this point? One thing is to invest in future food production and this includes both physical and R&D. We tend to think of agriculture as being an economics one on one – market producers and consumers getting the market right. This is true only up to a point. Agricultural production and progress in production depends heavily on public goods, especially R&D. There has been much less emphasis on this research and physical infrastructure for agriculture in recent years largely because

people thought these problems were solved. It looks like we have seriously underinvested and need to play catch up (Krugman, 2009).

With the end of recession, we are back in a world that has a growing population, growing purchasing power and a growing consumption of foods heavily reliant on cereals for their production. For example, meat uses a lot more basic agricultural production than does the consumption of grain. Water is a concern and so too is the use of potential arable land. When arable land is diverted to non-agricultural uses, it usually raises world GDP, but it also has the effect of reducing the incomes of those already at the bottom of the earning scale.

We had a very serious outbreak of human suffering and political instability resulting from a really quite brief spike in the price of food. It was not an extended period and it was overtaken by the events of the broad collapse of economic activity due to the financial crisis. Had it gone on any longer, it might have been much worse, and all indications are that the food crisis of 2008 was a dress rehearsal for future crises. There are no such mechanisms in place yet to deal with these issues.

Energy security

Energy prices have seen a steady decline (in constant dollars) over the last 200 years. The latest energy price hikes have not even brought us back to the price levels of some 30 years ago. The tragic reality is that political zeal has led governments to keep energy prices as low as possible, thus frustrating most attempts to increase energy productivity. Energy price elasticity is very much a long-term rather than a short-term affair, yet the investments in infrastructure that are crucial to the creation of an energy efficient society are very long term. Creating a long-term trajectory of energy prices that slowly, steadily and predictably rise in parallel with our energy productivity would give a clear signal to investors and infrastructure planners that energy efficiency and productivity are going to become ever more necessary and profitable (Krugman, 2009).

There is much debate about the potential contribution of agriculture to renewable energies. The problem is that with existing technology, renewable energies may be renewable, but they are mostly not green. Whether second generation biofuels can escape most of the pitfalls of the first generation is open to doubt, although admittedly they do not use the food component of plants.

Biofuel policy is a major aggravating factor even if not really discussed at present because of the decline in oil prices, which reduced the demand and at the same time food prices have gone down. It is pushed to the background because of the current financial crisis, but it will be a problem that will come back as the financial crisis will end and crude oil prices will increase.

Biofuels

Bioenergy covers approximately 10% of total world energy supply. Traditional unprocessed biomass accounts for most of this, but commercial bioenergy is assuming greater importance. Liquid biofuels for transport are generating the most attention and have seen a rapid expansion in production. However, quantitatively their role is only marginal; they cover 1% of total transport fuel consumption and 0.2–0.3% of total energy consumption worldwide. Large-scale production of biofuels implies large land

requirements for feedstock production. Liquid biofuels can therefore be expected to displace fossil fuels for transport to only a very limited extent. Even though liquid biofuels supply only a small share of global energy needs, they still have the potential to have a significant effect on global agriculture and agricultural markets, because of the volume of feedstocks and the relative land areas needed for their production.

The contribution of different biofuels to reducing fossil-fuel consumption varies widely when the fossil energy used as an input in their production is also taken into account. The fossil energy balance of a biofuel depends on factors such as feedstock characteristics, production location, agricultural practices and the source of energy used for the conversion process. Different biofuels also perform very differently in terms of their contribution to reducing greenhouse gas emissions. Second-generation biofuels currently under development use lignocellulosic feedstocks such as wood, tall grasses, and forestry and crop residues. This should increase the quantitative potential for biofuel generation per hectare of land, and could also improve the fossil energy and greenhouse gas balances of biofuels. However, it is not known when such technologies will enter production on a significant commercial scale.

Liquid biofuels such as bioethanol and biodiesel compete directly with petroleum-based petrol and diesel. Because energy markets are large compared with agricultural markets, energy prices will tend to drive the prices of biofuels and their agricultural feedstocks. Biofuel feedstocks also compete with other agricultural crops for productive resources; therefore energy prices will tend to affect prices of all agricultural commodities that rely on the same resource base. For the same reason, producing biofuels from non-food crops will not necessarily eliminate competition between food and fuel. For certain technologies, the competitiveness of biofuels will depend on the relative prices of agricultural feedstocks and fossil fuels. The relationship will differ among crops, countries, locations and technologies used in biofuel production.

With the important exception of ethanol produced from sugar cane in Brazil, which has the lowest production costs among the large-scale biofuel-producing countries, biofuels are not generally competitive with fossil fuels without subsidies. In the case of low crude oil prices, even ethanol production in Brazil is not competitive with petroleum. However, competitiveness can change as feedstock and energy prices and developments in technology change.

Biofuel development in developed countries has been promoted and supported by governments through a wide array of policy instruments; a growing number of developing countries are also beginning to introduce policies to promote biofuels. Common policy instruments include the mandated blending of biofuels with petroleum-based fuels, and subsidies. The exact contribution of expanding biofuel demand to these price increases is difficult to quantify. However, with increasing oil prices, biofuel demand will continue to exercise upward pressure on agricultural prices.

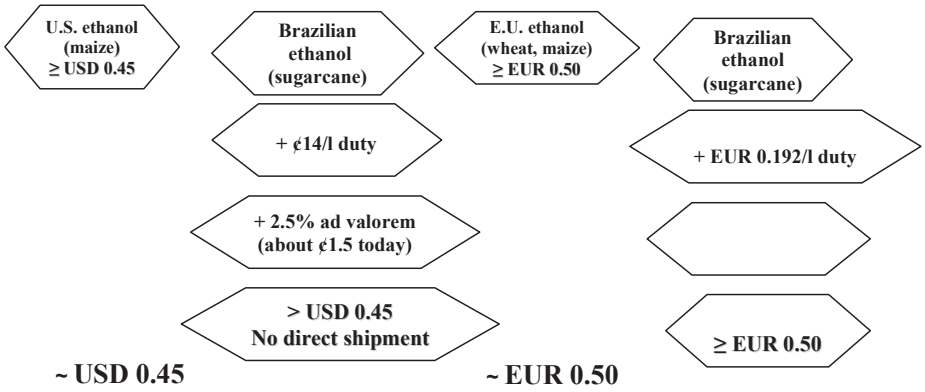
Modern bioenergy represents a new source of demand for farmers' products. At the same time, it generates increasing competition for natural resources, notably land and water, especially in the short run, although yield increases may mitigate such competition in the longer run. Competition for land becomes an issue especially when some of the crops (*e.g.* maize, oil palm and soybean) that are currently cultivated for food and feed are redirected towards the production of biofuels, or when food-oriented agricultural land is converted to biofuel production. Biofuel policies have significant implications for international markets, trade and prices for biofuels and agricultural commodities. Current trends in biofuel production, consumption and trade, as well as the global outlook, are

strongly influenced by existing policies. Policies implemented in the EU and USA, which promote biofuel production and consumption, while protecting domestic producers especially in case of ethanol production, typically exert much influence (Figure 8.2).

Trade policies *vis-à-vis* biofuels discriminate against developing country producers of biofuel feedstocks, and impede the emergence of biofuel processing and exporting sectors in developing countries. Many current biofuel policies distort biofuel and agricultural markets and influence the location and development of the global industry, such that production may not occur in the most economically or environmentally suitable locations. International policy disciplines for biofuels are needed to prevent a repeat of the kind of global policy failure that exists in the agriculture sector.

Currently, around 80% of the global production of liquid biofuels is in the form of ethanol. In 2009 global ethanol production reached 73 billion litres, global biodiesel production amounted to 15 million tonnes. The two largest ethanol producers, the United States and Brazil, account for 90% of total production, with the remainder accounted for mostly by the EU (mainly France and Germany), China and Canada (Figure 8.3).

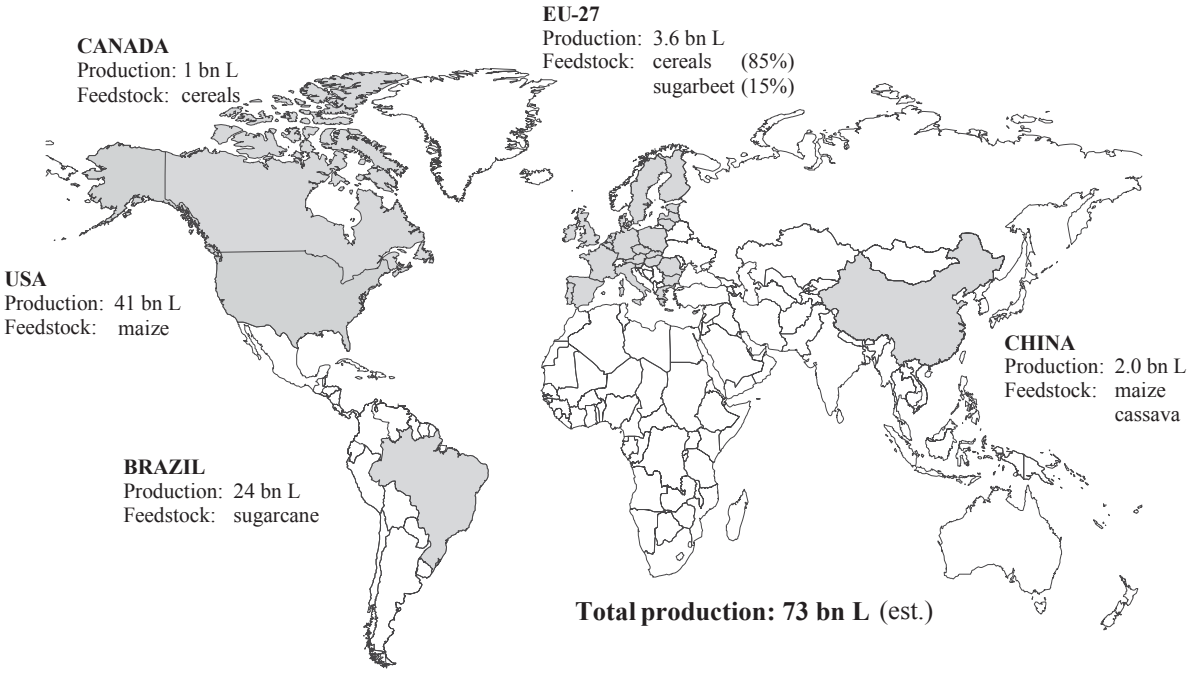
Figure 8.2. Trade distortion in the EU and USA in 2009 (Ethanol)



Notes: Rotterdam cif (T1): USD 0.43/L (EUR 0.33/L) + EUR 0.192/L duty = EUR 0.51/L (ethanol price in the EU is largely determined by the exports from Brazil). Rotterdam fob inc. duty: EUR 0.51/L.

Source: F.O. Licht (2009) and own calculations.

Figure 8.3. Global fuel ethanol production, 2009



Source: F.O. Licht (2010) and own calculations.

In the USA, fuel ethanol production reached 41 billion litres in 2009. In 2008 and 2009 Brazil shipped around 2.8 billion litres (740 million gallons) of ethanol either directly to the USA or through Caribbean Basin Initiative (CBI) countries. The trade programmes known collectively as the CBI is intended to facilitate the economic development and export diversification of the Caribbean Basin economies. The CBI currently provides 19 beneficiary countries with duty-free access to the US market for most goods. These countries are: Antigua and Barbuda, Aruba, Bahamas, Barbados, Belize, British Virgin Islands, Costa Rica, Dominica, Grenada, Guyana, Haiti, Jamaica, Montserrat, Netherlands Antilles, Panama, St. Kitts and Nevis, St. Lucia, St. Vincent and the Grenadines, and Trinidad and Tobago. Whether or not Brazilian alcohol can be mobilised for US trade will crucially depend on the price. Direct exports of anhydrous ethanol are out of the question now that the re-export loophole in the customs regulations has been closed in the latest Farm Bill.

The year 2008 was a defining one for the US ethanol sector. A combination of high maize prices and rock-bottom petroleum values threatened the industry. Higher grain costs put margins under pressure and then the meltdown in the financial markets prompted gasoline prices to tumble. In addition, there was surprisingly little of substance for biofuels in the American Recovery and Reinvestment Act (ARRA). Of critical importance will be the trend in petroleum prices. The collapse of the oil price benefitted American motorists much more than those in countries where tax forms a higher proportion of the retail price than in the USA. Thus, lower values have made all types of alcohol uncompetitive in the USA (Figure 8.2).

Brazil produced 24 billion litres of ethanol in 2009. Before 2009 almost two-thirds of Brazil's ethanol exports went to the United States, some via states in the Caribbean and Central America (CBI countries). These countries were able to re-export up to 2.35 billion litres of dehydrated alcohol to the USA in 2009 free of the high duty imposed on any ethanol imported directly from Brazil. Before oil values collapsed in 2008, alcohol imported directly from Brazil was competitive with petroleum, even after the high duty had been paid. In addition, some oil firms took advantage of a loophole which allowed ethanol to be imported tax free on a "draw-back" scheme if an identical amount of some other fuel was exported, a trade which was halted at the end of September 2008 (F.O. Licht, 2009).

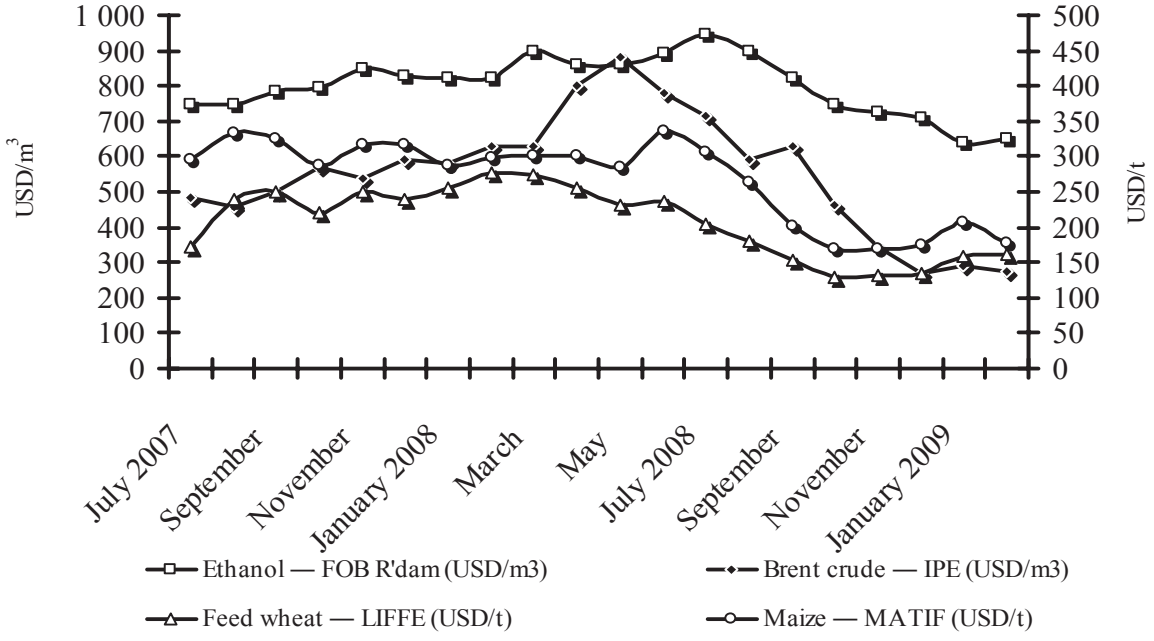
The country's ethanol exports fell to 3.3 billion litres in 2009/10 from 4.8 billion litres the year before. This was mainly due to bad weather conditions causing a reduction in the sugar content of cane, and therefore in the amount of alcohol which could be distilled, which resulted in a sharp decline in the national ethanol output. The consequence was a quite unprecedented rise in values which soon made the Brazilian ethanol uncompetitive on the world market. Furthermore, the development of large-scale trade with Japan remains a pipe dream. On the other hand, the fact that the EU has now also determined that 10% of motor fuels consumed within the Community must be renewable from 2020 onwards should also favour the country. Brazil has a good chance to supply a large chunk of the 18 billion litres market which could well develop as a result of these provisions. Although developments in the USA and the EU mean the long term demand for alcohol looks guaranteed, the sector in Brazil will face extremely difficult times until that happens.

With sugar values low and demand for ethanol being so strong, the proportion of cane distilled into alcohol exceeded 60% in 2008. This trend reversed in 2009, partly because much less extra alcohol was needed and partly because a world deficit of 3-4 million tonnes of sugar has led to increasing international sugar prices. Relatively firm sugar values will make the choice for the sector easy. The consequence of this could be a restriction of the country's exports. It was anticipated that green fuel would become steadily more competitive and popular and consequently the requirement for increased supplies would continue to grow. This scenario still holds true, which explains why many investors have not abandoned their plans but are merely postponing them. The current difficult phase may last some time. However, once the economies of enough countries start to grow fast enough to transform the present surplus of oil into a shortage again, the price of oil will quickly rise above USD 100 per barrel.

In the EU, total fuel ethanol production in 2009 was 3.6 billion litres. Ethanol imports decreased by 300 million litres to almost 1.1 billion, of which around 400 million litres came from Brazil. The EU's continued commitment to 10% mandate for 2020 is welcomed. The package will require the EU to derive 20% of its energy from renewables, mostly from biofuels, by 2020, including 10% of its transportation energy. Starting in 2014, biofuels will have to achieve GHG savings of 35% relative to fossil fuels. This figure is to rise to 50% by 2017. Biofuel plants beginning operation in 2017 and beyond will have to achieve savings of 60%. Biofuels consumption in Eastern Europe is expected to rise due to increasing biofuel mandates. A significant share of this demand will be met by domestic production. To a growing extent, markets in the new Member States (EU-12) will however have to compete with EU-15 and non-Community imports. Competitiveness of ethanol production depends on the relative prices of feedstock and fossil fuel (Figure 8.4). At the moment, exporters compete on price and price alone, at least in the fuel ethanol trade. First and foremost, the EU's sustainability criteria will have to be

addressed by the exporters, mainly by the industry in the USA if it wants to be able to compete with Brazil in this market as well.

Figure 8.4. Prices of ethanol, crude oil, feed wheat and maize in the EU (July 2007-February 2009)



Notes: Barrel = 159 L; 1 m^3 = 6.3 barrel.
Ethanol and crude oil parity prices (February 2009): at EUR 0.50/l ethanol and USD 103/b crude oil price (but crude oil price was USD 44/b).
Source: HGCA (2009).

In Asia, biofuels in general, and ethanol in particular, have been introduced as one method of alleviating the chronic energy shortage which is dogging many of the region's economies. With crude oil prices around USD 50 a barrel, the need to develop domestic sources of energy has lost some of its urgency in 2009. Even though the lower commodity values seen in recent months have reduced the cost of production for ethanol, this fall has not been sufficient to compensate for the sharp decline in crude oil prices.

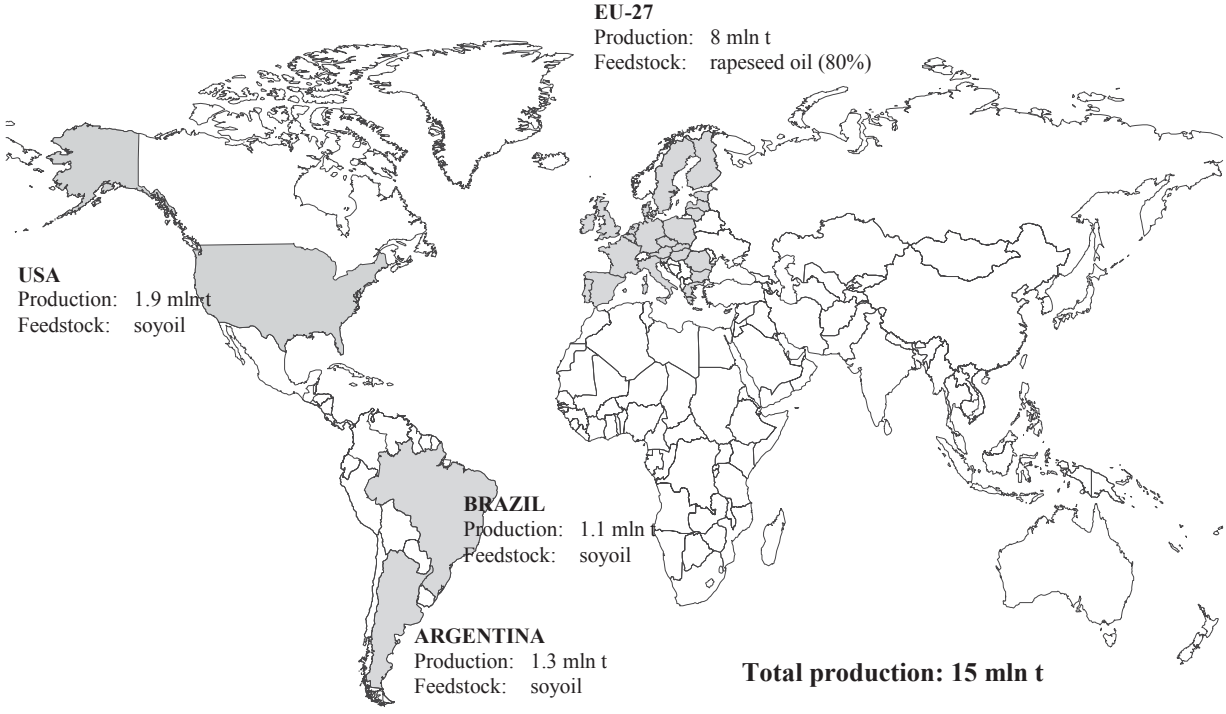
Thailand has been promoting biofuels with a comprehensive package of policy measures since 2003 but in 2008-09 the country's distilleries worked at less than capacity due to limited foreign opportunities and disappointing domestic gasohol demand. However, the strongest growth is likely to occur in Thailand where a number of new tapioca-based units have come online. Traditionally, China has used grains for the manufacture of fuel ethanol. Currently, most plants in the country use cereals with the rest using tapioca starch. The use of this substrate in various forms to produce fuel alcohol is a relatively recent development and it still has to prove its economic viability. While the government's policy to limit the use of cereals for ethanol production effectively puts a lid on new investments, it will be the relatively low price of oil which will act as a disincentive. India's output of sugar and molasses was considerably lower in 2008-09 than in the previous 12 months. The downturn has already boosted values of the sugar co-product and, as a result, those of alcohol as well. The country's output of ethanol may also rebound on the back of the higher sugar output expected in 2009-10.

The Philippines government remains committed to biofuels. The local alternative-fuels sector should grow further despite the low world oil prices. The introduction of E-5 blends in 2009 and an E-10 blend by 2011 will raise bioethanol consumption. There are a number of newcomers like Vietnam and Cambodia that are quickly ramping up production.

Biodiesel production is principally concentrated in the EU (with around 55% of the total), with a significantly smaller contribution coming from the USA. In Brazil, biodiesel production is a more recent phenomenon and production volume remains limited. Other significant biodiesel producers include Argentina and to a lesser extent India, Indonesia and Malaysia. Brazil, the EU and the USA are expected to remain the largest producers of liquid biofuels, but production is also projected to expand in a number of developing countries (Figure 8.5).

After several years of strong growth rates, world biodiesel production remained virtually flat in 2009. The outlook strongly depends on the present low fuel prices. On one hand, low energy prices reduce feedstock manufacturing costs. On the other, they decrease sales values for biofuels and thus production margins. Actual biodiesel consumption figures will rely strongly on the blending demand outlook for conventional fuels as there is currently no real B-100 market. However, the latest data from the International Energy Agency (IEA) show a decline in conventional fuel consumption. Not only will the expected two-year contraction in oil demand be the first since the early 1980s, but 2009's decline was also the largest since 1982 (IEA, 2009).

Figure 8.5. Global biodiesel production, 2009

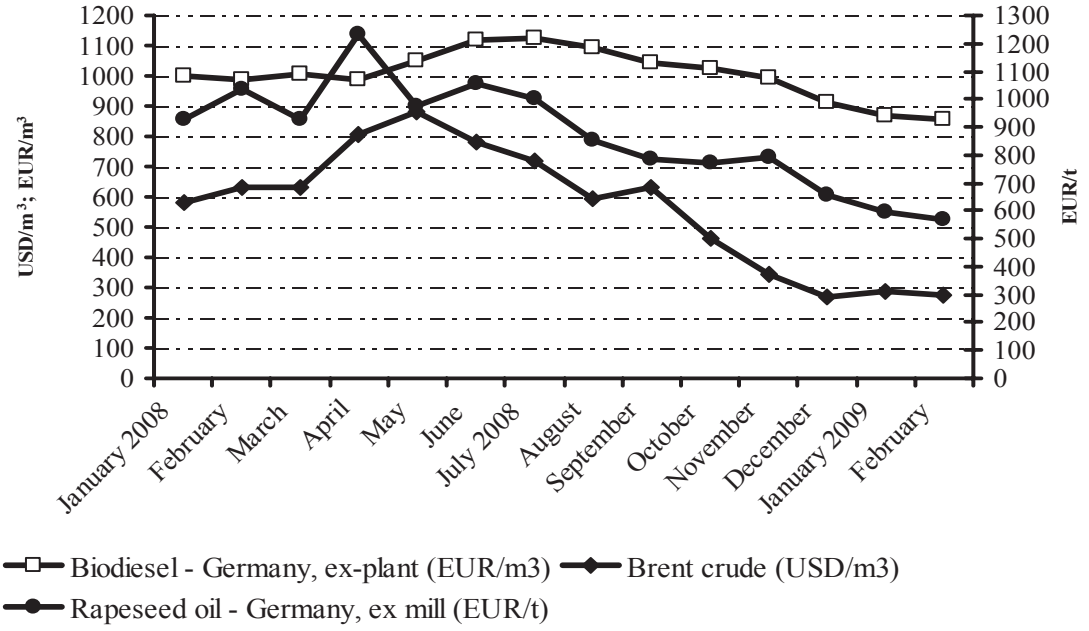


Source: F.O.Licht (2010) and own calculations.

In 2009 biodiesel production reached 8 million tonnes in the EU. The greatest potential for feedstock suppliers inside and outside the EU-27 is offered by the vegoils market since there is a significant import demand from the European Community. The average spread between average biodiesel ex-works prices and total net production costs narrowed but remained negative in 2009. However, the main problem is relatively low fuel prices.

The competitiveness of biodiesel production depends on the relative prices of feedstock and fossil fuel (Figure 8.6). The dispute between the USA and the EU over the biodiesel trade has come to an end. The EU announced an import duty on American biodiesel imports as US blends of the fuel, mainly the so-called SME B-99.9, qualify for a tax credit of USD 1 per gallon, around USD 300 per ton, which more than offsets the cost of freight and the Community's import tariff of 6.5%. The US federal tax credit expired on 31 December 2009 reducing profitability for less efficient producers.

Figure 8.6. Prices of biodiesel, crude oil and rapeseed oil in the EU (January 2008-February 2009)



Notes: Barrel = 159 L; 1 m^3 = 6.3 barrel.
Biodiesel and crude oil parity prices (February 2009): at EUR 0.85L biodiesel and USD 174/b crude oil price (but crude oil price was USD 44/b.

Source: HGCA (2009).

The EU's sustainability requirements could fundamentally change the Community's import demand for biodiesel. According to the EU's Joint Research Committee's figures published in 2008, the use of SME reduces GHG emissions by only 31% while PME without methane capture at the oil mill is even worse at only 19%. Biodiesel exporters from South America and Southeast Asia as well as the Community's biodiesel producers using these feedstocks may face severe problems from 2010. There may be significant growth in the use of waste cooking oil and animal fat in the EU as in both cases GHG reductions stand at 83%. There is a logistical cost to using these feedstocks (collection of

the oils, refining, etc.) and the feedstock supply itself is limited. There are also discussions on the sustainability of SME in the USA where the Environmental Protection Agency (EPA) is currently assessing the national ecological aspects of biofuels.

Hydro treated and co-processing are technical procedures which have the potential to substitute biodiesel. Hydro cracking is a process in which a synthetic fuel is made from biodiesel feedstocks such as animal fat or vegoil without esterification. Co-processing means that conventional fuel is directly mixed with vegoil. Several oil companies such as ConocoPhillips in the USA and Finland's Neste Oil have invested significant amounts in plants which are already operating, although so far only at modest levels. Taking into account the sustainability issue mentioned above, the majority of these hydro-treated vegoils would meet the GHG reduction levels under the Commission's proposal.

All the biofuels produced from wastes, residues, non-food cellulosic material, and ligno-cellulosic material shall be considered to be twice that made by other biofuels. This means that only half the volume of this type of biofuel is needed to achieve the 10% target. However, it does not automatically mean that this biofuel will have a double economic value, nor is it certain whether this double counting will offset the higher production costs of most of the advanced biofuels. It is equally unclear if higher CO_2 savings will be realised; after all, less volume could result in less net emission reductions.

Judging by the quantitative targets at European and national level, and the EU's present biodiesel manufacturing capacity of about 15 million tonnes, it is clear that there is no need for more biodiesel plants. On the contrary, European biodiesel manufacturers need to make the effort to develop export markets and new sales markets (*e.g.* biofuel oil). At the same time, they should, as far as possible, make better use of their advantages in terms of cost and the CO_2 balance in a situation where cut-throat international competition is substantially greater. From this perspective, it does not make sense for further subsidies to be provided from either EU or national budgets for the construction of more biodiesel capacity.

The end of the SME B-99.9 business also meant significantly lower biodiesel output in the USA in 2009 compared to 2.4 million tons in 2008. There is also the biodiesel mandate under the Energy Independence and Security Act, which may help make up for the loss of the biodiesel business, although the sector is suffering from the expiration of the blender's tax credit (USD 1 per gallon of blended biodiesel). However, there is support from the B-19 trade with Europe. In addition hydro treated vegoils may play a growing role in the mid-term because, according to EU legislation, hydro treated palm oil with methane capture has a 65% GHG reduction, which would guarantee its position in the EU.

Brazil's B-3 mandate introduced in 2008 raised output to one million tonnes. Continuously expanding biodiesel mandates boosted annual output to 1.4 million tonnes in 2009. With the B-5 mandate introduced in 2009, 2010 consumption and production are expected to be 1.7 million tonnes. Almost all of the domestic output is destined for domestic use, due to the relatively high cost of production. Due to industry overcapacity, the manufacturers are asking for a B-4 mandate which could be introduced during this calendar year according to recent official announcements.

Argentina's manufacturers see Europe as their main outlet. The EU's special import tariffs on biodiesel, introduced in 2009, have made direct shipment from Argentina competitive in this key import market and have definitely closed the door for US B-99.

There is still much overcapacity in the sector locally as local plants can produce almost 3 million tonnes. Production in 2009 was around 1.3 million tonnes.

Southeast Asian producers were seen to benefit from the end of SME B-99.9 as there is a significant biodiesel import demand from the EU. Marketing the product itself is difficult due to technical problems (*i.e.* the issue of cold filter plugging point, as well as doubts over the sustainability of biodiesel production from palm and soyoil), which are continually being raised in the destination markets, particularly in the EU. Indonesia and Malaysia may continue to ship to the EU, and to a lesser extent to the USA, in the summer months. However, the volumes exported will remain markedly below these countries' potential.

Challenges

There are three traditional biofuels options: bioethanol, biodiesel and biogas. Each differs in terms of feedstock source, net energy yield per hectare and investment cost. The net energy yield per hectare with biogas can be much higher than with bioethanol production, provided the entire crop is fermented in the biogas plant. However, bioethanol would come closer to the net energy yield of biogas when cellulose is fermented to alcohol. Additionally, the investment costs are much higher for biogas than for bioethanol.

These differences explain why bioethanol is predominantly produced in countries with an abundance of agricultural areas, such as the USA or Brazil. The analysis of ethanol production from maize in the USA is totally different from that from sugarcane in Brazil due to the availability of land, energy conversion rates and technologies used. In more densely populated regions such as the EU, farmland is more expensive. Therefore, the net energy yield per unit area is more important and, thus, so is biogas production. Additionally, the population density results in more waste from food use and livestock production. The more expensive the farmland – and the more waste and manure available – the more attractive option biogas may become.

The main challenge of the biofuels industry in the coming years is how to cope with relatively low fuel prices. The longer-term outlook for fuel prices however remains bullish. The question for the biodiesel sector will be – how many companies will survive the hard times? An adjustment in production capacity seems inevitable and manufacturers which are part of conglomerates and/or are integrated in the value chain usually have better chances of survival.

The economics of first generation biofuels are location specific – as are environmental benefits. Both the USA and the EU have many of the same players supporting and resisting biofuels growth. The EU appears to be further ahead in raising issues of sustainability, including mitigating the threat to biodiversity, the effect on climate change, and concerns related to food supply. However, these issues are gaining attention on both sides of the Atlantic. The growth of biofuels and the impending evolution to second-generation biofuels present considerable challenges in terms of policy development, trade and certification of sustainability. Heretofore, these issues have been dealt with on a "local" basis; but the time has come to take a global approach as well.

Is there any market relationship between the agriculture of foodstuffs and that of energy? Is there available land? Biofuels are not the primary, nor a major, driver affecting

worldwide food prices. However, the role of biofuels in food prices has been limited so far. At present, feedstock for biofuel occupies just 1% of global cropland. Rising population, changing diets and demand for biofuels will increase demand for cropland. The balance of evidence indicates there will be sufficient appropriate land available to meet this demand to 2020, but this must be confirmed before global supplies of biofuel increase significantly. Current policies are not entirely effective in assuring that additional production moves exclusively to suitable areas – and attempts to do so will face challenges in terms of implementation and enforcement. Governments should amend but not abandon biofuel policy in an effort to recognise these issues and ensure their policies deliver net GHG benefits.

In 2009, an increase in the use of grains for fuel ethanol occurred, mainly due to a higher output in the USA and Europe. This was the equivalent of 7% of 2009 grain consumption (*cf.* 6% the previous season). Net use of grains for fuel ethanol is actually one third lower (4.7%), as ethanol yields dried distiller grains (DDGS) as by-product. The bulk of the worldwide use of grains in alcohol production comprises maize in the USA and China. However, an increase in the offtake of wheat for fuel ethanol can also be observed in Canada and the EU. The share of biodiesel in total vegoils use was 11% (*cf.* 11% the previous season) as non-fuel vegoils consumption has increased at a faster pace (F. O. Licht, 2010). The EU is set to remain the largest biodiesel producer, and thus the main consumer of vegoils for fuels, but growth rates are also declining with lower fuel prices.

What about the impact on use of agricultural land? In Brazil, sugarcane is grown on 2.5% of the arable land and 1.5% of arable land is dedicated to ethanol production. In the USA, according to the Renewable Fuel Standard (RFS), 136 billion litres of biofuels will be needed by 2022 requiring feedstock production on up to 15% of total arable land (own calculation). In the EU, by 2020 the 10% of biofuel impact on land use means that 15% of EU-27 total arable land will be used for biofuel feedstock production (EC, 2009).

The development and evolution of trade rules regarding biofuels is becoming a pivotal issue in both the EU and the USA. Europe is questioning biofuel production on agricultural lands. While the USA has more land, it does appear that substantial farmland could be made available in new EU Member States. Otherwise, biofuels will need to be supplied by countries outside the EU. The existence of a global market of food and biofuel requires the development of expertise in building agribusiness systems that are increasingly transnational and sustainable. This global biofuel market will involve more production, compulsory legislation and the standardisation and certification of the ethanol itself. Market structure has been influenced by policy, so strengthening the market is essential. Stakeholders focus on their local markets first (the concept of "home grown" is attractive) and international investment in biofuels has been limited. Oil prices are largely demand driven, but global recession has led to significant price falls. Investments in alternative energy sources are risky in this environment without policy measures that ensure against major drops in oil prices. Policy is a key to promote sustainable biofuel trade. At present, uncertain classification, a wide range of government measures (tax incentives, tariffs, subsidies), and a web of varying technical and environmental standards do not facilitate trade.

It should be possible to establish a genuinely sustainable biofuels industry, provided that robust, comprehensive and mandatory sustainability standards are developed and implemented. The risks of indirect effects can be significantly reduced by ensuring that the production of feedstock for second-generation biofuels takes place mainly on idle and

marginal land – and by encouraging technologies that take best and appropriate advantage of wastes and residues. Sustainable production is being increasingly regarded as a prerequisite for market access. Sustainability certification has three main dimensions: environmental, economic and social. A schematic for certification must overcome the difficulty inherent in measuring and verifying what, in many cases, are aspirations or principles. Certification requires an institutional environment with requirements that can be effectively and consistently implemented, and an organisational environment that supports reliable monitoring and evaluation.

The main initiative for certification of biofuels has come from national governments, private companies, non-governmental organisations and international organisations. Most are in the early stages, while others may come into force in the near term. There is considerable variance in terms of the principles they include and the procedures and organisational processes involved. And most are based on existing systems for the agriculture, forestry or energy sectors. This certification system must cover all biomass (regardless of the end use) and all relevant bioenergy – and it must take a global approach as biomass and bioenergy sources become internationally traded commodities. Systems that focus simply on national or EU-wide implementation, for example, will not help solve major sustainability issues. Additionally, the system must take a holistic approach or risk forfeiting all relevance. For example, if the relatively small quantities of palm oil used for biodiesel production are produced in a sustainable manner, but the large volumes consumed in the food sector are not, all the effort expended would be invalidated.

As certification criteria are considered, each country should prioritise the areas of law, production and products, communications, distribution and logistics, and human resources. Higher targets for biofuels in the marketplace should be implemented carefully to ensure these fuels are demonstrably sustainable. Any criterion related to competition, or demanding more than just a reporting obligation, could potentially lead to an infringement of the World Trade Organization (WTO) rules.

Environmental security

Biodiversity losses have accelerated, most notably in the tropics. The depletion of fisheries and fish stocks has continued, and in some cases has accelerated. China's growing appetite for mineral and energy resources in Africa and elsewhere is cause for concern, and India, Brazil, South Africa, Angola and others are all aiming to fuel their high growth rates with accelerating resource extraction, and there is no end in sight to this trend.

In terms of climate change and the overall ecological situation, the picture is even grimmer. By adopting the right policy mix, we can decouple wealth creation from energy and material consumption just as we decoupled wealth creation from the total number of hours of human labour. That was the great achievement of the industrial revolution, and labour productivity has risen at least twentyfold in the course of mankind's last 150 years of industrialisation. Resource productivity should become the core of our next industrial revolution. Technologically speaking, this should not be more difficult than the rise in labour productivity.

We now start to recognise that the (over)exploitation of our entire ecosystem and the depletion of natural resources (the reserve/production ratio of oil reserves is rapidly declining) must carry a price which must be paid today to compensate future generations for the loss (or costs of substitution) they will be faced with tomorrow. Moreover, world

population growth by 30% during the next 40 years, causing new scarcities (*e.g.* water) and pollution (*e.g.* CO_2 emission rights), is reinforcing this issue. Corporations in energy-intensive sectors need to start taking future CO_2 prices into account in their investment decisions and public disclosure policies now. Because the scarcity of emission rights has been recognised, an active market has been created in the EU and CO_2 emission rights now have a price; more regional cap and trade markets for CO_2 have been (in the USA), or are in the process of being created.

The environment is now back at centre stage, after a quarter century of denial among the political and business elite in the USA. The weight of evidence from the IPCC, and the devastating levels of pollution in the industrial centres of the high growth countries, like China, have at last shifted opinion behind tough new controls. The EU has taken the political lead in addressing global warming, setting up the European Trading System (ETS) for CO_2 emissions. President Obama has given clear commitments to mitigating global warming, and China too has become very serious about tackling pollution, climate change and energy efficiency. Renewable energy sources now constitute a dynamic growth sector, and the Convention on Biological Diversity (CBD) is enjoying increasing visibility in the signatory states which means nearly all countries around the world except the USA.

Never waste a good crisis. Joseph Stiglitz and Nicholas Stern have made a joint appeal to use the financial crisis as an opportunity to lay the foundations for a new wave of growth based on the technologies for a low carbon economy (Financial Times, 2009). The investments would drive growth over the next two or three decades, ensuring it becomes sustainable. They added that "providing a strong, stable carbon price is the single policy action that is likely to have the biggest effect in improving economic efficiency and tackling the climate crisis." Lord Stern calculated that governments should spend at least 20% of their stimulus on green measures to achieve the emission targets (Stern, 2006).

The environmental resource scarcity issues also still look entirely real. Depending on the extent of climate changes, many agricultural patterns may become disrupted, and the poorest countries are the ones most vulnerable in the face of this. In the long term, environmental security is the mirror image of food security, because there is no food without substantial clean water resources, productive soils, and appropriate climate. In turn, failure to tackle environmental degradation jeopardises the future of agriculture and the countryside. Climate change puts all businesses and society at cumulative, long-term risk. The failure of agriculture alone would lead to widespread hunger in developing countries and mass migration of people (half a billion according to the UN), mostly to developed countries.

The search for more environmentally friendly agricultural inputs and practices must continue. Scientists are working to improve the efficiency of photosynthesis, carbon capture, nitrogen fixation and many other cellular processes that boost biomass yields. It may also become possible to plant crops in soils lost to salinisation, and develop genetically modified plants that can grow in marginal or otherwise unusable farmland.

Mankind is directly influenced by the loss of biodiversity. With the extinction of species we lose possibly crucial opportunities and solutions to problems of our society. Biodiversity provides us directly with essentials like clean water and air, fertile soil, and protects us from floods and avalanches. These aspects can all be economically valued. It is a difficult and complex task, but through this valuation it becomes clear how important they are for human well being and economic development (Table 8.3).

Many people are unaware of the speed at which we are using up our natural resources, and that we are producing waste far faster than it can be recycled. It is important to clarify the items of public goods and services with arguments whether or not market failures are linked to the provision of services. Market failure is a crucially important justification for taking measures to protect our landscapes. Corrections in market failures could also be achieved through investments and the provision of payments to reward land managers who provide public goods and services (EC, 2008).

Table 8.3. Scenario of the future: 2050

Actual	2000	2010	2050	Difference	Difference	Difference
Area	million km^2	million km^2	million km^2	2000 to 2010	2010 to 2050	2000 to 2050
Natural areas	65.5	62.8	58.0	-4%	-8%	-11%
Bare natural	3.3	3.1	3.0	-6%	-4%	-9%
Forest managed	4.2	4.4	7.0	5%	62%	70%
Extensive agriculture	5.0	4.5	3.0	-9%	-33%	-39%
Intensive agriculture	11.0	12.9	15.8	17%	23%	44%
Woody biofuels	0.1	0.1	0.5	35%	437%	626%
Cultivated grazing	19.1	20.3	20.8	6%	2%	9%
Artificial surfaces	0.2	0.2	0.2	0%	0%	0%
World Total	108.4	108.4	108.4	0%	0%	0%

Source: Braat *et al.* (2008), Cost of Policy Inaction, OECD, COPI.

It is important to demonstrate the economic value of ecosystem goods and services. We not only need to know costs, but also to be assured of the benefits. There is increasing consensus about the importance of incorporating these "ecosystem services" into resource management decisions, but quantifying the levels and values of these services has proven difficult.

Our research has revealed a disappointingly small set of attempts to measure and value these services (Amstrong-Brown *et al*. 2009). Chronologically the first is the quantification of global ecosystem services by Constanza *et al. (*1997). Estimates were extracted from the literature of values based on willingness to pay for a hectare's worth of each of the services. These were all expressed in 1994 USD per hectare and there was some attempt to adjust these values across regions by purchasing power. The results were that a central estimate of the total value of annual global flows of ecosystem services in the mid 1990s was USD 33 trillion (*i.e.* 10^{12}) and the range was thought to be USD 16-54 trillion. To put this figure into some kind of context, their central estimate was 1.8 times bigger than global Gross Domestic Product (GDP) at that time. We should take the figures only as the roughest of approximations – indeed the authors warn of the huge uncertainties involved in making calculations of this kind.

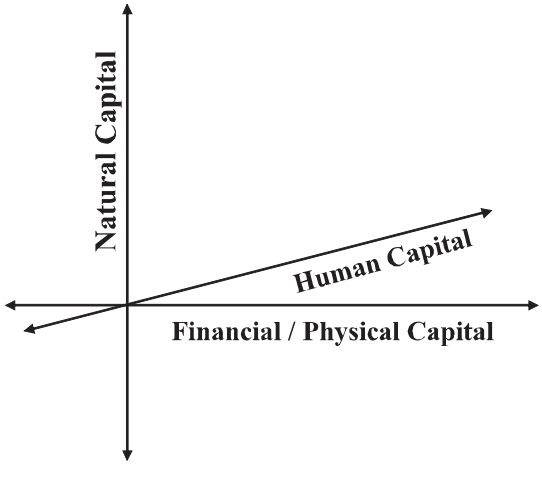
The "Stern Review" parallels "The Economics of Ecosystems and Biodiversity" (TEEB) study into the economics of climate change (Stern, 2006). Climate change could have very serious impacts on growth and development. The costs of stabilising the climate are significant but manageable; delay would be dangerous and much more costly. The review estimates that if we do not act, the overall costs and risks of climate change will be equivalent to losing at least 5% of global GDP each year, now and forever. In contrast, the costs of action – reducing greenhouse gas emissions to avoid the worst

impacts of climate change – can be limited to around 1% of global GDP each year. Key to understanding the conclusions is that as forests decline, nature stops providing services which it used to provide essentially for free. So the human economy either has to provide them instead, perhaps through building reservoirs, building facilities to sequester carbon dioxide, or farming foods that were once naturally available.

The World Wildlife Fund's "Living Planet" Report demonstrates that mankind is living way beyond the capacity of the environment to supply us with services and to absorb our waste (WWF, 2008). They express this using the concepts of ecological footprints and biocapacity, each expressed per hectare per person.[2] Humanity's footprint first exceeded global biocapacity in 1980 and the overshoot has been increasing ever since. In 2005 they calculated the global footprint on average across the world was 2.7 global hectares (gha) per person[3] compared to a biocapacity they calculated as 2.1 gha per person: a difference of 30%. That is, each person on earth is on average consuming 30% more resources and waste absorption capacity than the world can provide. We are therefore destroying the earth's capacity and compromising future generations.

The study on TEEB is fundamentally about the struggle to find the value of nature (Figure 8.7). There are about 100 000 terrestrial protected areas on Earth, covering 11% of the land mass of our planet. These protected areas provide ecosystem services and biodiversity benefits to people valued at USD 4.4 trillion to USD 5.2 trillion (*i.e.* million millions) per annum. As a comparison, that is more than the revenues of the global car manufacturing sector, steel sector and IT services sector combined! Calculations show that the global economy is losing more money from the disappearance of forests than through the recent banking crisis, as forest decline could be costing about 7% of global GDP. It puts the annual cost of forest loss at between USD 2 trillion and USD 5 trillion. The figure comes from adding the value of the various services that forests perform, such as providing clean water and absorbing carbon dioxide. But the cost falls disproportionately on the poor because a greater part of their livelihood depends directly on the forest, especially in tropical regions. The greatest cost to western nations would initially come through losing a natural absorber of the most important greenhouse gas (EC, 2008).

Figure 8.7. The economics of ecosystems and biodiversity (TEEB): navigation challenge ahead



Can we navigate a complex, three-dimensional, economic space...

... with a simple economic compass ?

Source: European Commission (2008).

The study shows that diversity is crucial for survival and the importance of biodiversity for economic development. It might be possible to substitute some of the ecosystem services by human-made technologies, but the study results clearly show that it is often cheaper to invest in the conservation of biodiversity than to invest in new technologies to substitute the services nature provides for us. Therefore, it is essential for the safeguarding of our natural resources to jointly create a co-ordination of economic interests. We need to give the ecosystem services of biodiversity a market value to create incentives for developing countries to conserve their biodiversity.

Market-based instruments are helpful for giving the peoples of the world a chance to secure the natural resources and secure their livelihood simultaneously. In this context the inclusion of the private sector into the process of conservation and sustainable use of biodiversity has high priority. The goals of conservation and sustainability will only be achieved if the main drivers of ecosystem and biodiversity loss are actually addressed through appropriate intervention and response based on credible valuations. Businesses have to accept biodiversity as the indispensable resource which it is and have to treat this resource with respect and care.

The Global Canopy Programme's report concludes: "If we lose forests, we lose the fight against climate change". International demand has driven the intensive agriculture, logging and ranching which have lead to deforestation. Standing forest was not included in the original Kyoto protocols and stands outside the carbon markets. The inclusion of standing forests in internationally regulated carbon markets could provide cash incentives to halt this disastrous process. Marketing these ecosystem services could provide the added value forests need and help dampen the effects of industrial emissions. Those countries wise enough to have kept their forests could find themselves the owners of a new billion-dollar industry (Parker *et al.*, 2008).

Currently, there are two paradigms for generating ecosystem service assessments that are meant to influence policy decisions. Under the first paradigm, researchers use broad-scale assessments of multiple services to extrapolate a few estimates of values, based on habitat types, to entire regions or the entire planet (Costanza *et al.*, 1997). This "benefits transfer" approach incorrectly assumes that every hectare of a given habitat type is of equal value – regardless of its quality, rarity, spatial configuration, size, proximity to population centres, or the prevailing social practices and values. Furthermore, this approach does not allow for analyses of service provision and changes in value under new conditions. By contrast, under the second paradigm for generating policy-relevant ecosystem service assessments, researchers carefully model the production of a single service in a small area with an "ecological production function" – how provision of that service depends on local ecological variables (Kaiser and Roumasset 2002; Ricketts *et al.*, 2004). These methods lack both the scope (number of services) and scale (geographic and temporal) to be relevant for most policy questions (Nelson *et al.*, 2009).

Spatially explicit values of services across landscapes that might inform land-use and management decisions are still lacking. Quantifying ecosystem services in a spatially explicit manner, and analysing tradeoffs between them, can help to make natural resource decisions more effective, efficient, and defensible (Nelson *et al.*, 2009). Both the costs and the benefits of biodiversity-enhancing land-use measures are subject to spatial variation, and the criterion of cost-effectiveness calls for spatially heterogeneous compensation payments (Drechsler and Waetzold, 2005). Cost-effectiveness may also be achieved by paying compensation for results rather than measures. We have to ensure that

all possibilities for creating markets to provide environmental services are fully exploited to minimise the public costs (and the extent of government bureaucracy etc).

Creating markets for environmental services could encourage the adoption of farming practices that provide cleaner air and water, and other conservation benefits. Products expected to generate the greatest net returns are the ones generally selected for production. Since environmental services generally do not have markets, they have little or no value when the farmer makes land-use or production decisions. As a result, environmental services are under-provided by farmers. The biggest reason that markets for environmental services do not develop naturally is that the services themselves have characteristics that defy ownership. Once they are produced, people can "consume" them without paying a price. Most consumers are unwilling to pay for a good that they can obtain for free, so markets cannot develop. Can anything be done other than relying on government programmes to provide publicly funded investments in environmental services?

Governments play a central role in creating markets for environmental services, as has been done for markets in water quality trading, carbon trading and wetland damage mitigation. These markets would not exist without government programmes that require regulated business firms (such as industrial plants and land developers) to meet strict environmental standards. In essence, legally binding caps on emissions (water and carbon), or mandatory replacement of lost biodiversity (wetland damage mitigation) create the demand needed to support a market for environmental services. So-called cap and trade programmes create a tradable good related to an environmental service (Ribaudo *et al.*, 2008).

Mandatory reduction pledges can be experienced in all developed nations apart from the USA. The same is true for project-level reductions in developing countries. Mandatory cap and trade programmes have been introduced in north eastern USA and the EU. The USA and Australian governments announced that they will also institute a mandatory cap and trade programme to create financial incentives to limit energy use or reduce emissions.

In the case of water quality, it is necessary to establish caps on total pollutant discharges from regulated firms in some watersheds, and issue discharge allowances to each firm specifying how much pollution the firm can legally discharge. In markets for greenhouse gases, carbon credits are exchanged. Contracts also include renewable energy credits and voluntary carbon credits.

No-net-loss requirements for new housing and commercial development require that damaged/lost wetland services be replaced, creating demand for mitigation credits, which are produced by creating new wetlands. In all of these cases, the managing or regulatory entity defines the tradable good and enforces the transactions.

Simply creating demand for an environmental service does not guarantee that a market for services from agricultural sources will actually develop. A number of impediments affect agricultural producers' ability to participate in markets for environmental services. Purchasers may be unwilling to enter into a contract with a farmer who cannot guarantee delivery of the agreed-upon quantity of pollution abatement, wetlands services, or other environmental service. Some markets prevent uncertain services from being sold. For example, the Chicago Climate Exchange does not certify credits from soil types for which scientific evidence is lacking on the soil's ability

to sequester carbon. Transaction costs can also undermine the development of markets for environmental services (Ribaudo *et al.*, 2008).

If markets are to become important tools for generating resources for conservation on farms, government or other organisations may have to help emerging markets overcome uncertainty and transaction costs. Government can reduce uncertainty by setting standards for environmental services and can play a major role in reducing uncertainty by funding research on the level of environmental services from different conservation practices. For example, the government can develop an online Nitrogen Trading Tool to help farmers determine how many potential nitrogen credits they can generate on their farms for sale in a water quality trading programme.

While markets have many desirable properties, they are limited in what they can accomplish, even with government assistance. Public good characteristics that defy ownership discourage markets for environmental services from developing – and prevent the full value of environmental services from being reflected in prices. The prices of credits in water, carbon, and wetland markets also may not reflect their full social value, only their value to the regulated community. A national cap and trade programme could establish a national market for carbon credits. Others, such as water quality trading or wetland damage/loss mitigation, may be limited to a few specific geographic areas.

A significant role will be given for EU policy and budget in the appropriate land and environmental management. The EU needs regulation defining its policy on markets for environmental services. This policy would co-operate with Member State and local governments to establish a role for agriculture in environmental markets. We have to find ways to make EU policies and programmes support producers wanting to participate in such markets. Conducting research and developing tools for quantifying environmental impacts of farming practices is of great importance as well. Requirements are needed to establish technical guidelines for measuring environmental services from conservation and other land management activities, with priority given to participation in carbon markets. Guidelines are also to be established for a registry to record and maintain information on measured environmental service benefits, and a process for verifying that a farmer has implemented the conservation or land management activities reported in the registry.

Enthusiasm can be observed for green public procurement, linked to certification/ labelling, and supported by due information on embedded water/carbon/biodiversity or simply guidance to help public procurers buy less biodiversity harmful goods/ commodities. It is a useful stepping stone towards biodiversity reflective procurement in public sector establishments in due course (schools, hospitals).

"Ecosystems" markets will change the present, economics-only value-paradigm, with winners and losers. As an example, countries and companies with significant carbon-sink potential will benefit. On the other hand, applying the "polluter pays" principle, CO_2 emitters must pay a price for continuing to be able to do so. The concept of limiting (capping), auctioning and trading emission/access/user rights must be further developed beyond CO_2, in scope (*e.g.* water) and scale (worldwide). On the basis of valuing our ecosystems and regulating the access thereto, a market will be created for payment for ecosystem-access entitlements and for ecosystem services. We really need to upgrade our performance metrics. The same is true with respect to human/social capital: also here the metrics, the value of education, culture, social cohesion, etc. should be established and more prominently included in investment/development decisions (Figure 8.7).

Notes

1. An estimated 40 000 ha of land are needed for basic living space for every one million people added.
2. The Ecological Footprint "measures the amount of biologically productive land and water area required to produce the resources an individual, population or activity consumes and to absorb the waste it generates, given prevailing technology and resource management" (WWF, 2008).
3. A global hectare is a hectare with a global average ability to produce resources and absorb wastes.

Bibliography

Amstrong-Brown, S., *et al.* (2009): *RISE Task Force on Public Goods from Private Land*, Brussels, p. 66.

Braat, L. and Brink, ten P. (eds.) (2008), "Contribution of Different Pressures to the Global Biodiversity Loss Between 2000 and 2050 in the OECD Baseline", The Economics of Ecosystems and Biodiversity (TEEB): an interim report, Brussels.

Braun, J. von, *et al* (2008), "High Food Prices. The What, Who, and How of Proposed Policy Actions", *Policy Brief* 1A, International Food Policy Research Institute (IFPRI), Washington, D.C.

Braun, von J. and R. Meinzen-Dick (2009), "Land Grabbing" by Foreign Investors in Developing Countries: Risks and Opportunities", *Policy Brief* 13, International Food Policy Research Institute (IFPRI), Washington D.C.

Costanza, R., *et al.* (1997), "The Value of the World's Ecosystem Services and Natural Capital", *Nature,* 387: 253-60.

Drechsler, M. and F. Waetzold (2005), "Spatially Uniform Versus Spatially Heterogeneous Compensation Payments for Biodiversity-Enhancing Land-Use Measures", *Environmental and Resource Economics,* 31: 73-93.

Earth Institute of Columbia University (2005), *The Growing Urbanization of the World*, Columbia University, New York.

EC (2008), "The Economics of Ecosystems and Biodiversity (TEEB)", an Interim Report Resources, Brussels. *http://ec.europa.eu/environment/nature/biodiversity/economics/index_en.htm*

EC (2009), *Prospects for Agricultural Markets and Income in the European Union 2008-2015",* Directorate-General for Agriculture and Rural Development, Brussels.

FAO (2003), *World Agriculture: Towards 2015-2030,* Food and Agriculture Organization of the United Nations, Rome.

FAO (2008), *The State of Food Insecurity in the World, High Food Prices and Food Security – Threats and Opportunities,* Food and Agriculture Organization of the United Nations, Rome.

Financial Times (2009), "Obama's Chance to Lead the Green Recovery", *Financial Times*, 3 March 2009.

F.O. Licht (2010), *World Ethanol and Biofuel Report* (Jan.-June. 2010), Agra Informa Ltd, United Kingdom.

Fraiture, Ch. de and D. Molden (2009), "Balancing Global Water Supply and Demand", Presentation: Challenges for Agricultural Research, OECD, 6-8 April 2009 Prague, Czech Republic.

HGCA (Home Grown Cereals Authority) (2009), The Agriculture and Horticulture Development Board (AHDB), Subdivision GGCA, London, United Kingdom, Link to website: *http://www.hgca.com/content.output.*

IEA (International Energy Agency) (2008), *World Energy Outlook 2008*, International Energy Agency, Paris, France.

IWMI (2007), "*Water for Food, Water for Life: A Comprehensive Assessment of Water Management in Agriculture"*, Earthscan and Colombo: International Water Management Institute, London, United Kingdom.

Kaiser, B. and J. Roumasset (2002), "Valuing Indirect Ecosystem Services: the Case of Tropical Watersheds", *Environment and Development Economics*, 7: 701-14.

Krugman, P. (2009), "Is a New Architecture Required for Financing Food and Environmental Security?", Paul Krugman, Professor of Economics and International Affairs, Princeton University, Summary of the speech made during the launching event of the 2nd Forum for the Future of Agriculture, 17th of March in Brussels, *http://www.elo.org* (accessed April 15, 2009).

Nelson, E., *et al.* (2009), "Modelling Multiple Ecosystem Services, Biodiversity Conservation, Commodity Production, and Tradeoffs at Landscape Scales, *Front Ecol Environ*; 7(1): 4–11.

OECD (2007), "*Biofuels: Is the Cure Worse than the Disease?"*, Organisation for Economic Co-operation and Development, Paris, France.

Parker, Ch., *et al.* (2008), "The Little Redd Book (Reducing Emissions from Deforestation and (Forest) Degradation: Redd)", Global Canopy Programme, Oxford: John Krebs Field Station.

Reid, W. *et al.* (2005), *Millennium Ecosystem Assessment: Ecosystems and Human Well-Being – Biodiversity Synthesis*, World Resources Institute, Washington D.C.

RFA (The Renewable Fuels Agency) (2008), *The Gallagher Review of the Indirect Effects of Biofuels Production*, The Renewable Fuels Agency, United Kingdom.

Ribaudo, M. *et al.* (2008), *The Use of Market to Increase Private Investment in Environmental Stewardship*, USDA-ERS, Washington D. C.

Stern, N. (2006), *Stern Review: The Economics of Climate Change*, Cambridge University Press, Cambridge, United Kingdom.

UNEP/GRID-Arendal and UNEP- WCMC (2009), *The Environmental Food Crisis,* edited by Joel Benoit, United Nations Environment Programme (UNEP), Link to website *http://www.grida.no/publications/rr/food-crisis/.*

United Nations (2003), *Millennium Ecosystem Assessment: Ecosystems and Human Wellbeing,* Island Press, Washington D.C.

USDA (United States Department of Agriculture) (2008), *USDA Agricultural Projections to 2017,* Interagency Agricultural Projections Committee, United States Department of Agriculture, Washington D.C.

WWF (World Wildlife Fund) (2008), *Living Planet Report*, World Wildlife Fund, Gland, Switzerland.

Chapter 9

Genetic Technology, Sustainable Animal Agriculture and Global Climate Change

John P. Phillips, Professor Emeritus,

Department of Molecular and Cellular Biology,
University of Guelph, Ontario, Canada

World food demand is expected to more than double in the next 50 years. During this time, our planet will likely undergo dramatic climate change that will impose new challenges on our capacity to maintain even current levels of food production let alone meet the anticipated demand. All of us at this conference were born and raised during the last century when the globe experienced a doubling of the human population. Little did we know then how our lives would depend on the remarkable increase in global food production that characterises that century, an increase underwritten by astonishing advances in genetics and agricultural science. Nor did we realise that the 20th century expansion of the global larder came at such great environmental cost, a cost born largely by the conversion of natural ecosystems to agriculture with the resulting destruction of the essential services those ecosystems provide. Genetics has always been the currency for assuring population success in changing environments. Although technology alone will be insufficient, the development and application of new advanced genetic technologies will be absolutely necessary to feed the world our children and grandchildren will know as their own. The Enviropig™ *represents a model of environmental-genetic innovation with the potential to dramatically enhance the sustainability of animal agriculture in an increasingly hungry world intoxicated by its own waste.*

The global environmental challenge

> "During the next 50 years…, demand for food by a wealthier and 50% larger global population will be a major driver of global environmental change. Should past dependences of the global environmental impacts of agriculture on human population and consumption continue, 10^9 hectares of natural ecosystems would be converted to agriculture by 2050. This would be accompanied by 2.4-to-2.7 fold increases in nitrogen- and phosphorus-driven eutrophication of terrestrial, freshwater, and near-shore marine ecosystems…. This eutrophication and habitat destruction would cause unprecedented ecosystem simplification, loss of ecosystem services, and species extinctions. Significant scientific advances and regulatory, technological, and policy changes are needed to control the environmental impacts of agricultural expansion." (D. Tilman *et al.*, 2001)

Although the Green Revolution has seen a doubling of global grain production in the last 35 years, it has done so at high environmental cost. In their landmark paper, David Tilman and colleagues (2001) present a convincing but sobering forecast of current and future agricultural impacts on global ecosystems. Agriculture impacts ecosystems through (i) the generation of greenhouse gases, (ii) the consumption and release of limiting resources like N, P and water that affect ecosystem function and (iii) the conversion of natural ecosystems to agriculture. Tilman *et al.* (2001) predict that these sources of global transformation could rival those arising from climate change in environmental and societal impacts. Clearly, the status quo in agriculture cannot continue; an environmentally sustainable revolution (Conway, 1997) is needed.

Global pork production

Pork is one of the principal global sources of dietary animal protein (43% Pork, 27% Poultry, 26% Beef/veal, 4% Other). By 2004, world pork consumption had reached approximately 15.9 kg/person/year, having risen from 9.2 kg/person/year in 1970, and is predicted to reach 17.9 kg/person/year in 2015. The top five consumer countries (China, European Union, United States, Brazil and Canada) consume 76.1% of global pork production while the top 20 countries consume 93.7%. If the predicted consumption of 17.9 kg per person per year in 2015 is reached, pork production will need to grow to 130 Mmt (Roppa, 2005). To support the 2004 level of consumption a global swine herd totalling 1.278 billion will be required, with China contributing over half of this total at 622 million, the EU 246 million, USA 103 million, Brazil 38 million and Canada 23 million, to list the top five.

Pigs and phosphorus pollution

Phosphorus pollution is one of the greatest threats to freshwater and marine environments. Animal waste is a leading source of phosphorus pollution from agriculture (Jongbloed and Lenis, 1998), and its effect exceeds that of inorganic fertilisers or other anthropogenic fluxes (Smil, 2000). In the USA alone, over 100 mt of animal manure is produced annually with the liberation of 1 mt of phosphorus into the environment each year (Walsh *et al.*, 1993). Freshwater eutrophication degrades the quality of drinking water creating an offensive taste and odour (Smil, 2000). Increased nutrient inputs into near-coastal waters cause serious environmental degradation that is a major threat to

coastal environments upon which large populations in developing countries depend for survival (Jickells, 1998; Harvell *et al*., 1999; Jackson *et al*., 2001).

As so starkly demonstrated by Tilman (2001), "…the demand for food by a wealthier and 50% larger global population over the next 50 years will be a major driver of global environmental change." Moreover, the effects of food shortages are compounded by decreasing availability of unpolluted potable water. Given past experience, limitations on the availability of potable water in the future will be compounded and exacerbated by more intensive agricultural activities (Tilman *et al*., 2001). A large part of this pollution is expected to rise from increased production of monogastric food animals, pigs and poultry, primarily in developing countries (Delgado, 2003), but contributions will come from other food animals as well. Pig production in developing countries has increased at a linear rate of 10% per year since the early 1970s while pig production in developed countries has remained comparatively constant over the same time period.

Because the burden of increased food demand is certain to be borne largely by monogastric food animals, a major effort should be made to increase the capacity of these animals to utilise dietary nutrients more efficiently. As with other human-caused burdens, the best way to reduce the phosphorus impact of animal agriculture is to minimise the inputs at source. The production of food animals will continue to be a key contributor to the agricultural economy in developing countries, and depending upon geographic location the challenges will include one or all of the following: (i) production of sufficient animal feeds, (ii) prevention and treatment of animal diseases, and (iii) development of systems to reduce pollution from animal waste. Meeting these objectives will require innovations at many different levels and at many different points in diverse animal production systems.

Enhancing phosphorus utilisation and reducing P output in pork production

Cereal grains such as corn and barley, and plant-based protein supplements fed to pigs and poultry contain upwards to 80% of their P in the form of *myo*-inositol hexakis dihydrogen phosphate (phytate) complexed with minerals (Jongbloed and Kemme, 1990). Pigs do not digest P in this form, instead it is concentrated in the feces by a factor of three- to four-fold (unpublished data). As a consequence of the poor digestibility of P in cereal grains, supplemental phosphate is included in the ration to meet the dietary requirement for optimal growth. The resulting high P manure makes an excellent fertiliser when properly applied to P-depleted soils. However, when the P concentration exceeds the retention capacity of the soil, P leaches rapidly into normally phosphate-limited freshwater and marine systems causing eutrophication (nutrient enrichment with subsequent algal growth) with the death of fish and aquatic animals, and impacting on water quality (Diaz, 2001; Jongbloed and Lenis, 1998). Animal waste is a leading source of phosphorus pollution from agriculture (Jongbloed and Lenis, 1998) and its effect exceeds that of inorganic fertilisers or other anthropogenic fluxes (Smil, 2000).

Consequently, reducing the fecal and urinary output of nutrients from pigs is a clear and urgent requirement. To achieve this, several different approaches can be taken, including (i) formulation of rations to avoid exceeding the dietary requirements of the animal, for example, reduction of the concentration of supplemental phosphate in rations (Shen *et al*., 2002), or replacement of a portion of the crude protein by essential amino acids (Lenis *et al*., 1999); (ii) improvement in feed digestibility by addition of supplemental enzymes including phytase (Simons *et al*., 1990) or β-glucanase and

xylanase (Bedford and Schulze, 1998); (iii) feeding of more digestible cereal grains, for example, low phytate cereal grains (Sands *et al*., 2001) and (iv) establishing genes in the host that enhance the metabolic potential of food animals (Ward, 2000). The expression of genes coding for novel enzymes in food animals constitutes a rational strategy for enhancing digestive capabilities. Development of the Enviropig™ represents the leading edge of a revolution that will ultimately change the pork industry, and directly tackles the elusive goal of producing animals with markedly reduced environmental impact.

The Enviropig™: a genetic technology for meeting the global environmental challenge

The Enviropig™ is a trademark for pigs expressing the PSP/APPA salivary phytase transgene. The generation of pigs expressing this transgene has been described in detail (Golovan *et al*., 2001a and 2001b) and is the subject of recent reviews (Forsberg *et al*., 2005; Forsberg *et al*., 2003). From 33 initial independent founder lines carrying the transgene, several lines were selected for further development and testing. Selected data will be used here to illustrate the efficacy of the transene in these lines. For example, hemizygous weanling and growing-finishing pigs from the WA line tested for true digestibility of dietary P in soybean meal as the sole source of P using an ileal cannulation methodology (Fan *et al*., 2001) were found to digest 88% and 99%, respectively, of the dietary P, as compared with non-transgenic pigs that digested 49% and 52% of dietary P, respectively (Golovan *et al*., 2001b). Fecal matter from the weanling and growing-finishing hemizygotes contained 75% and 56%, respectively, less P than that of non-transgenic pigs fed the same diet. Because the transgenic phytase pigs digest practically all of the dietary P, the residual P entering the terminal ileum of these pigs presumably consists primarily of differentiated enterocytes released from the mucosa during the process of continual epithelial regeneration (Ramachandran *et al*., 2000).

Boars and gilts hemizygous for the phytase transgene fed a conventional cereal grain diet lacking supplemental P during the finishing phase had fecal P concentrations that were 67% and 64% less than the corresponding non-transgenic pigs in the same trial (Golovan *et al*., 2001b). The initial observations on the G_o pigs have been reinforced by more comprehensive data obtained from feeding trials with other lines of phytase transgenic pigs. Although the amount of P excreted in the urine was not determined in the initial studies, more recent data on weanling, growing and finishing pigs shows that Enviropigs™ fed on diets without supplemental P excrete substantially less phosphorus in the urine than conventional non-transgenic pigs fed on diets containing supplemental P (unpublished data). It has been reported that urinary P accounts for 6%, 9% and 27% of P excreted by weanling pigs, growing pigs and sows, respectively (Poulsen, 2000). Overall, our combined urine and fecal P data from several lines of the Enviropig™ clearly demonstrates that pigs expressing the salivary phytase transgene digest and utilise virtually all of the phytate P in their diet throughout their growth to market weight. Moreover, recent studies demonstrate that when fed diets that do not contain traditional P supplements, Enviropigs™ perform equal to or better than their conventional counterparts fed on diets containing supplemental P as measured against commercial production indices such as rate of gain, reproduction, susceptibility to disease, and industry-standard carcass characteristics. Overall, the data predict that in settings of commercial production, total P output (urinary + fecal) from Enviropig™ herds will be at least 50% lower than that of conventional herds. By any measure, this represents a quantum phenotype of astonishing environmental potential in meeting the goal of environmental sustainability of animal agriculture.

The Enviropig™ provides a simple and reliable means for reducing the environmental impact of pork production. Although P is the third most expensive nutrient fed to pigs, the cost of phosphate is not a major constraint and overfeeding of this compound has been a common practice. However, in many jurisdictions, the land base for spreading of manure is a serious limitation. To assess the benefit of Enviropig™ genetics in terms of land area for spreading manure, we used the NMAN 2001 manure management computer simulation program developed by the Ontario Ministry of Agriculture and Food (*www.omafra.gov.on.ca/scripts/english/engineering/nman/default.asp*). Simulating a 350 sow farrowing-to-finishing pig operation, the spreading of manure from non-transgenic pigs on low-erodable soil theoretically requires 151 hectares to avoid application of excess P. Replacing conventional pigs with Enviropigs™ would reduce the land area required for manure spreading by 33% at which point manure N – not P – would become limiting. It is generally recognised that for each 1% decrease in crude protein in the diet there is an 8% to 10% reduction in manure N (Le Bellego *et al*., 2001; Lenis and Jongbloed, 1999). Using the NMAN program to simulate the relationship between decreasing manure N and reduction in land required for spreading of manure, it can be shown that if the N content of the manure was reduced by up to 40%, the area of low-erodable soil required for spreading could be reduced by 60% (*i.e.* to 100 hectares), before P would be applied in excess.

Introducing the genetics for salivary phytase into swine herds around the world using artificial insemination will be relatively straight forward and has the potential to markedly reduce P-loading into the environment on a global scale. This represents the kind of quantum technology that will be required for animal agriculture to attain a sustainable global equilibrium. As a technology it is simple, effective and stable and requires little management. The Enviropig™ is on the leading edge of genetic advancements that will reduce the environmental footprint of animal agriculture through enhanced metabolic capacity. These pigs, and other transgenic animals under development elsewhere, must undergo safety and quality testing and approval in the country of origin and in countries to which the product is exported before being released into the marketplace. Such testing of the Enviropig™ is currently in progress.

Bibliography

Bedford, M. R. and H. Schulze (1998), "Exogenous Enzymes for Pigs and Poultry", *Nutrition Research Reviews* 11: 91-114.

Conway, G. (1997), *The Doubly Green Revolution*, Penguin Books, London.

Delgado, C.L. (2003), "Rising Consumption of Meat and Milk in Developing Countries Has Created a New Food Revolution", *Journal of Nutrition* 13 (11 Suppl. 2):3907S-3910S.

Diaz, R. J. (2001), "Overview of Hypoxia Around the World", *Journal of Environmental Quality* 30:275-281.

Fan, M. Z., *et al.* (2001), "Novel Methodology Allows Simultaneous Measurement of True Phosphorus Digestibility and the Gastrointestinal Endogenous Phosphorus Outputs in Studies with Pigs", *Journal of Nutrition* 131:2388-2396.

Forsberg, C.W., *et al.* (2003), "The Enviropig™ Physiology, Performance, and Contribution to Nutrient Management Advances in a Regulated Environment: the Leading Edge of Change in The Pork Industry", *Journal of Animal Science* 81 (E. Suppl. 2):E68–E77.

Forsberg, C.W., *et al.* (2005), "Genetic Opportunities to Enhance Sustainability of Pork Production in Developing Countries: A Model for Food Animals", In: *Application of Gene-Based Technologies for Improving Animal Production and Health in Developing Countries*, H.P.S. Makkar and G.J. Viljoen (eds.), Springer, New York.

Golovan, S.P., *et al.* (2001a), "Transgenic Mice Expressing Bacterial Phytase as a Model for Phosphorus Pollution Control", *Nature Biotechnology*. 19:429-433.

Golovan, S.P., *et al*. (2001b), "Pigs Expressing Salivary Phytase Produce Low Phosphorus Manure Through Complete Digestion of Dietary Phytate", *Nature Biotechnology* 19:741-745.

Harvell, C.D., *et al*. (1999), "Emerging Marine Diseases-Climate Links and Anthropogenic Factors", *Science* 285:1505-1510.

Jackson, J.B. *et al.* (2001), "Historical Overfishing and the Recent Collapse of Coastal Ecosystems", *Science* 293:629-637.

Jickells, T.D. (1998), Nutrient Biogeochemistry of the Coastal Zone, *Science* 281:217-221.

Jongbloed, A.W. and P.A. Kemme (1990), "Apparent Digestible Phosphorus in the Feeding of Pigs in Relation to Availability, Equipment and Environment. 1. Digestible Phosphorus in Feedstuffs from Plant and Animal Origin", *Netherlands Journal of Agricultural Science* 38:567-575.

Jongbloed, A.W. and N.P. Lenis (1998), "Environmental Concerns About Animal Manure", *Journal of Animal Science* 76:2641-2648.

Le Bellego, L., *et al.* (2001), "Energy Utilization of Low-Protein Diets in Growing Pigs", *Journal of Animal Science* 79:1259-1271.

Lenis, N.P., *et al.* (1999), "Effect of the Ratio Between Essential and Non Essential Amino Acids in the Diet on Utilization of Nitrogen and Amino Acids by Growing Pigs", *Journal of Animal Science* 77:1777-87.

National Research Council (1998), *Nutrient Requirements of Swine*, National Academy of Sciences, Washington.

Poulsen, H.D. (2000), "Phosphorus Utilization and Excretion in Pig Production", *Journal of Environmental Quality* 29:24–27.

Ramachandran, A., M. Madesh and K.A. Balasubramanian (2000), "Apoptosis in the Intestinal Epithelium: its Relevance in Normal and Pathophysiological Conditions", *Journal of Gastroenterology and Hepatology* 15:109-120.

Roppa, L. (2005), "Competition from South American Pork Production", *Advances in Pork Production* 16:29-42.

Sands, J.S., *et al*. (2001), "Phosphorus Bioavailability, Growth Performance, and Nutrient Balance in Pigs Fed High Available Phosphorus Corn and Phytase", *Journal of Animal Science* 79:2134-2142.

Shen, Y., *et al.* (2002), "Use of the Regression Analysis Technique to Determine the True Phosphorus Digestibility and the Endogenous Phosphorus Output Associated with Corn in Growing Pigs", *Journal of Nutrition* 132:1199-1206.

Simons, P.C.M., *et al.* (1990), "Improvement of Phosphorus Availability by Microbial Phytase in Broilers and Pigs", *British Journal of Nutrition* 64:525-540.

Smil, V. (2000), "Phosphorus and the Environment: Natural Flows and Human Interferences", *Annual Review of Energy and the Environment* 25:53-88.

Tilman, D., *et al.* (2001), "Forecasting Agriculturally Driven Global Environmental Change", *Science* 292:281-284.

Walsh, G.A., R.F. Power and D.R. Headon (1993), "Enzymes in the Animal Feed Industry", *TIBTECH* 11:424-430.

Ward, K.A. (2000), "Transgene-Mediated Modifications to Animal Biochemistry", *Trends in Biotechnology* 18:99-102.

Chapter 10

Challenges and Opportunities for Further Improvements in Wheat Yield

Gustavo A. Slafer

ICREA (*Catalonian Institution for Research and Advanced Studies*)
and Department of Crop and Forest Sciences, University of Lleida, Spain

Wheat is one of the most critical food crops. Globally wheat yield has been growing slower than wheat demand. Further improvements in yield are required. Due to environmental concerns, much of these improvements must come from genetic gains. As wheat yield potential is expressed across a wide range of environments, breeding cultivars of higher-yield potential than that of most modern cultivars is critical. The challenge is that the main physiological avenues for improving yield in the future must be different than that on which past breeding (including the "green revolution") was based. Major improvements in yield potential were achieved by increased harvest index based on plant height reduction, but any further reductions in plant height would bring about yield penalties rather than gains. In this paper I will discuss alternative opportunities for future improvements beyond modifications in height or partitioning of dry matter.

Introduction

Wheat is likely our most critical crop. It was central to the beginning of agriculture (*e.g.* Harlan, 1981; Araus *et al.*, 2001), which in turn produced one of the most revolutionary changes in history shaping the future development of our societies (Araus *et al.*, 2003); and it continues to be our most largely grown crop (wheat is grown over roughly one sixth of the total arable land in the world) as well as our main source of protein (Slafer and Satorre, 1999). During the 20th century, wheat production has almost constantly increased, first from major increases in growing area (up to approximately the 1950s), followed by a dramatic increase in yields from then to the 1990s (*e.g.* Calderini and Slafer, 1998), associated with genetic and agronomic improvements in yield (Slafer and Andrade, 1991; Calderini *et al.*, 1999; Evenson and Gollin, 2003; Reynolds and Borlaug, 2006).

However, since the 1990s global wheat yield has been growing slower than wheat demand. Even worse, the predictions are that global demand for wheat (Rosegrant and Cline, 2003) will increase at a faster rate than the genetic gains that have been achieved lately (Calderini *et al.*, 1999; Denison *et al.*, 2003; Fischer, 2007). In this context, there seems to be little doubt that further improvements in yield are required. Due to environmental concerns, much of these improvements must come from genetic gains (Araus *et al.*, 2007; Reynolds *et al.*, 2009). As genetic gains must be increased with a crop that already possess a high yield potential, which implies the process will be more difficult than in the past (Slafer *et al.*, 1994), and breeding under high-yielding conditions seems far less complex than under stressful environments (R. Richards, 1996a; Araus *et al.*, 2002), the chances are that attempting to increase wheat yield potential would be the most promising alternative to face the future demand. But breeding to further raise yield potential would only be useful if it brings about improvements in yield under environmental constraints (Slafer *et al.*, 1999; Araus *et al.*, 2002).

Can we breed for yield potential with benefits in realistic growing conditions?

As discussed recently (Slafer and Araus, 2007) there is a debate in the literature on whether it might be more beneficial to breed for yield potential or for tolerance to stressful conditions, with examples supporting both views available in the literature. As discussed in that paper, it seems fair to assume that, with the likely exception of environments characterised by very severe stresses, with yields lower than 1-2 Mg ha^{-1} (in which higher yield potential does not translate into higher actual yields; *e.g.* Ceccarelli and Grando, 1996), selecting for higher yield potential would result in concomitant improvements in adaptation to stress (Richards, 2000; Araus *et al.*, 2002; Slafer *et al.*, 2005), including environments affected by water deficit (Trethowan *et al.*, 2002), high temperatures (Reynolds *et al.*, 1998), and salinity (Richards, 1995; Isla *et al.*, 2003).

Empirical evidence supporting that increased yield potential would concomitantly increase yield in a wide range of conditions is that modern cultivars largely selected under high-yielding conditions are widely adopted by farmers whose crops are grown under more stressful conditions. This might well be the basis for the frequently found parallelism between potential and farmers' average yields over the years (Evans, 1993; Abeledo *et al.*, 2003a; Slafer and Calderini, 2005). Documenting experimentally the association between yield potential and yield under stressful conditions, Calderini and

Slafer (1999) showed that modern wheats over-yielded their predecessors throughout a wide range of environmental conditions (see also Ortiz Monasterio *et al.*, 1997; Abeledo *et al.*, 2003b; Tambussi *et al.*, 2004).

As wheat yield potential is expressed across a wide range of environments, breeding cultivars of higher-yield potential than that of most modern cultivars is critical. Although genetic gains under potential conditions are more likely than under stress, it is nothing but simple: to achieve the rates of gains required in the future, I believe that further improvements need the integration of new tools and strategies to complement traditional breeding approaches.

Major advances achieved in the field of molecular biology are no doubt of enormous importance for breeding for relatively simple traits. The success of GMO cultivars in countries with no major restrictions to their cultivation speaks for itself. However, when it comes to complex traits, heavily dependent on the interactions within the genetic background and with the environment, the powerfulness of biotechnological tools is strongly restricted. Empirical evidence of the difficulties is that whilst the literature is full of papers reporting quantitative trait *loci* (QTLs) for yield in wheat, there are no examples of breeding programmes introgressing those QTLs and ending up with a consistent yield gain (Slafer, 2003); in fact examples of ending up with yield penalties can be found, as reviewed by Slafer *et al.* (2005).

Molecular biology would only become a strong contributor to the actual breeding for complex traits such as potential yield when they acquire capabilities to manipulate predictably complex traits (Goodman, 2004). One way in which this predictability may increase is by using crop physiological knowledge, to identify relatively simple traits putatively associated with yield potential. We need an improved crop-physiological knowledge of which relatively simple traits may be putatively associated with yield under a wide range of conditions (Slafer, 2003).

What physiological traits may be useful in future improvements of wheat yield potential?

The challenge is that the main physiological avenues for improving yield in the future must be different from those on which past breeding (including the "green revolution") was based. Major improvements in yield potential were achieved by increased harvest index based on plant height reduction (Calderini *et al.*, 1999 and several references quoted therein), but any further reductions in plant height would bring about yield penalties rather than gains (Richards, 1992; Miralles and Slafer, 1995; Flintham *et al.,* 1997).

Determination of yield potential

To identify physiological traits that may be useful in future improvements of wheat yield potential, we must first understand the determination of yield potential. Although there are different approaches to understand yield in terms of relatively simpler traits, since the pioneer work by Fischer (1985), it has been popularly recognised that although yield components are formed throughout the whole growing season (Slafer and Rawson, 1994), wheat yield is predominantly determined during a relatively short period from about four weeks before to one week after anthesis, mostly the period of stem elongation (Fischer and Stockman, 1980; Thorne and Wood, 1987; Savin and Slafer, 1991; Slafer

et al., 1994; Miralles *et al.*, 1998; Wang *et al.*, 2003; Demotes-Mainard and Jeuffroy, 2004; González *et al.,* 2005a; Fischer, 2008), when the number of fertile florets, and then grains, of the crop is largely determined (*e.g.* Kirby, 1988; Siddique *et al.*, 1989; Slafer and Andrade, 1993; Miralles and Slafer, 2007).

This is so because the number of grains per unit land area of the crop is a clear determinant of yield, as wheat grains hardly compete strongly for assimilates during grain filling (Borrás *et al.*, 2004; Bingham *et al.*, 2007) and any negative relationship between grains per m^2 and average grain weight seems to be independent of a strong competition for assimilates (Acreche and Slafer, 2006). This means that, in most conditions, the capacity of the crop canopy to provide assimilates to the growing grains is more or less adequate to allow grain filling (Savin and Slafer, 1991; Richards, 1996b; Reynolds *et al.*, 2004), and consequently average grain weight is far less variable than grain number (Slafer *et al.*, 2006; Peltonen-Sainio *et al*., 2007) as due to evolutionary causes, the reproductive fitness of the crop is expressed in terms of the number of offspring it produces (Sadras, 2007).

It can be concluded that to further raise yield potential we must somehow increase the number of grains per m^2, which is strongly related to the growth of the spikes during the last half of stem elongation (Slafer *et al.*, 2005). This is so critical that actual gains achieved in the past in virtually any environmental condition in which the breeding programme was developed, including the green revolution, were almost entirely related to increases in the partitioning of dry matter to the spikes during stem elongation (Siddique *et al.*, 1989; Slafer and Andrade, 1993). To further raise the dry weight of the spikes at anthesis, as a way to improve the number of grains per unit land area of the crop, the opportunities from additional gains in spike-stem partitioning seem limited (Slafer *et al.*, 1999). Alternatives must be focused on improving growth during this critical pre-anthesis period in which wheat yield, oppositely to what occurs during grain filling, is strongly limited by the strength of the source (Slafer and Savin, 2006). Evidence of such limitation may be found in experiments in which yield is promoted by means of N fertilisation in which the driving force for increasing yield has been the improved growth during the stem elongation phase and the concomitant increase in spike dry weight at anthesis and number of grains per m^2 (*e.g.* Fischer, 1993; Prystupa *et al.*, 2004). As recently revised in depth (Araus *et al.*, 2008; Reynolds *et al.*, 2009), there are two alternative ways to genetically improve growth during the critical period of stem elongation: increasing crop growth rate, or lengthening the duration of that phase. For a full treatment of these alternatives please see the quoted references. I will only recapitulate briefly here some the main concepts behind these two alternatives.

Opportunities to improve crop growth rate

Crop growth is the product of radiation interception and radiation use efficiency (Sinclair and Muchow, 1999). As well managed crops fully intercept the incoming radiation during the critical period, the opportunity is restricted to particular conditions (such as those of Nordic growing areas) in which radiation interception is not maximised in well managed modern cultivars. In these conditions advantages of improving early vigour (*e.g.* Richards, 1996*a*) may be capitalised in improvements in radiation interception during the stem elongation phase. Early vigour has been dissected and found related to a number of seedling characteristics (Liang and Richards, 1994; López-Castañeda and Richards, 1994; López-Castañeda *et al.*, 1995). Fortunately for those regions in which this may be an important source of improvements in growth, substantial

variation in traits associated with early vigour has been documented (*e.g.* Rebetzke *et al.*, 1996).

In all other cases the alternative to improve crop growth rate during stem elongation would be restricted to improvements in radiation use efficiency. This depends on improving either the arrangement of the canopy structures so that the light is more evenly distributed and then used more efficiently or the photosynthetic capacity of the leaves and spikes. Although the former is unquestionably true, most modern, high-yielding cultivars already possess an erect canopy, which makes the possibilities for further raising radiation use efficiency difficult from altering the canopy structure in the near future. This leaves the actual possibility to improve radiation use efficiency into finding ways of improving the photosynthetic capacity of the leaves and spikes.

Rubisco, the enzyme involved in the photosynthetic capacity of wheat (and other C3 crops), is naturally the first alternative to attempt achieving genetic gains in radiation use efficiency (Reynolds *et al.*, 2009). One alternative would be through engineering Rubisco so that it becomes more active as a carboxylase and less active as an oxygenase (the latter responsible of the "waste" of energy involved in photorespiration, that reduces the photosynthetic activity). There is a large degree of variation for relative specificity for CO_2 among sources of Rubisco (*e.g.* Delgado *et al*., 1995; Galmés *et al*., 2005), that could be exploited (Parry *et al*., 2007). Another alternative is attempting to introduce pump mechanisms in order to increase noticeably the concentration of CO_2 in the carboxilation site, thus empirically reducing photorespiration by competition (*e.g.* Leegood, 2002).

Opportunities to lengthen the stem elongation phase

The other hypothetical alternative to improve growth during the critical period of stem elongation would be lengthening the stem elongation phase (Slafer *et al.*, 2001; Slafer *et al.*, 2005; Miralles and Slafer, 2007). The rationale is that if making this phase longer does not affect the daily radiation use efficiency, the accumulated growth during stem elongation would increase proportionally to the extension of the phase. As photoperiodic responses of the length of different phases seem to differ depending on the genotype (Slafer and Rawson, 1996) and different combinations of timing to onset of stem elongation for similar time to anthesis may be found in detailed screenings of cereals (Whitechurch *et al.*, 2007), it seems possible to explore this alternative (Slafer *et al.*, 2009).

Evidence that increases in grain number would be feasible if we were able to genetically manipulate sensitivity to photoperiod during stem elongation can be found in experiments in which the duration of stem elongation has been artificially extended for particular genotypes. For instance by exposing the crop to different photoperiods only during the stem elongation phase, we were able to raise the number of grains that the plants produced (Miralles *et al.*, 2000; González *et al.*, 2003, 2005b; Serrago *et al.*, 2008; Borràs *et al.*, 2009).

The existence of healthy genetic variation is a requirement for considering a trait in breeding. But it would be extremely useful to identify proper genetic bases for this trait if the breeding process is to maximise its efficiency. Although we analysed experimentally the opportunity of increasing grain number through sensitivity to photoperiod, another alternative might be the selection for differences in earliness *per se* of the stem elongation phase. The fact that the stem elongation phase is sensitive to photoperiod and that there is genetic variation for that sensitivity has been evidenced several times (Slafer and

Rawson, 1994; 1997, Miralles and Richards, 2000; González *et al.*, 2002); whilst differences in earliness per se for this particular phase have not been explored widely, chances are that they exist (Slafer, 1996).

To the best of my knowledge, so far there have been studies aimed to identify genetic bases of photoperiod sensitivity during stem elongation. Attempts so far consisted of comparative of performance of recombinant inbred lines or isogenic lines for major Ppd alleles. As reviewed by González *et al.* (2005c) these approaches have mostly failed in identifying reliable genetic bases for the specific sensitivity to photoperiod in the stem elongation phase. Alternative approaches, including the analysis of genes that are up- or down-regulated when the wheat plants respond to the exposure to different photoperiods exclusively during the stem elongation phase (*e.g.* Ghiglione *et al.*, 2008) and the behaviour of mapping populations (Borràs *et al.*, 2009) are undergoing.

Bibliography

Abeledo, L.G., D.F. Calderini, and G.A. Slafer (2003a), "Genetic Improvement of Barley Yield Potential and its Physiological Determinants in Argentina (1944-1998)", *Euphytica*, 130:325-334.

Abeledo, L.G., D.F. Calderini and G.A. Slafer (2003b), "Genetic Improvement of Yield Responsiveness to Nitrogen Fertilization and its Physiological Determinants in Barley", *Euphytica*, 133:291-298.

Acreche, M.M. and G.A. Slafer (2006), "Grain Weight Response to Increases in Number of Grains in Wheat in a Mediterranean Area", *Field Crops Research*, 98:52-59.

Araus, J.L., *et al.* (2001), "Estimated Wheat Yields During the Emergence of Agriculture Based on the Carbon Isotope Discrimination of Grains: Evidence from a 10th Millennium BP Site on the Euphrates", *Journal of Archaeological Science*, 28:341-350.

Araus, J.L., *et al.* (2002), "Plant Breeding and Water Relations in C_3 Cereals: What Should we Breed for?", *Annals of Botany*, 89:925-940.

Araus, J.L., *et al.* (2003), "Productivity in Prehistoric Agriculture: Physiological Models for the Quantification of Cereal Yields as an Alternative to Traditional Approaches", J*ournal of Archaeological Science*, 30:681-693.

Araus, J.L., *et al.* (2008), "Breeding for Yield Potential and Stress Adaptation in Cereals", *Critical Reviews in Plant Science*, 27:377-412.

Bingham, I.J., *et al.* (2007), "Is Barley Yield in the UK Sink Limited? I. Post-Anthesis Radiation Interception, Radiation Use Efficiency and Source-Sink Balance", *Field Crops Research*, 101:198-211.

Borràs, G., *et al.* (2009), "Genetic Variability in Duration of Pre-Heading Phases and Relationships with Leaf Appearance and Tillering Dynamics in a Barley Population", *Field Crops Research*, 113:95-104.

Borrás, L., G.A. Slafer and M.E. Otegui (2004), "Seed Dry Weight Response to Source-Sink Manipulations, In "Wheat, Maize and Soybean. A Quantitative Reappraisal", *Field Crops Research*, 86:131-146.

Calderini, D.F. and G.A. Slafer (1998), "Changes in Yield and Yield Stability in Wheat During the 20th Century", *Field Crops Research*, 57:335-347.

Calderini, D.F. and G.A. Slafer (1999), "Has Yield Stability Changed with Genetic Improvement of Wheat Yield?", *Euphytica*, 107:51-59.

Calderini, D.F., M.P. Reynolds and G.A. Slafer (1999), "Genetic Gains in Wheat Yield and Main Physiological Changes Associated with Them During the 20th Century", In:

Wheat: Ecology and Physiology of Yield Determination, E.H. Satorre and G.A. Slafer (Eds), Food Product Press, New York, pp. 351-377.

Ceccarelli, S. and S. Grando (1996), "Drought as a Challenge for the Plant Breeder", *Plant Growth Regulation*, 20:149-155.

Delgado, E., *et al.* (1995), "Species Variation in Rubisco Specificity Factor", *Journal of Experimental Botany*, 46:1775-1777.

Demotes-Mainard, S. and M.H. Jeuffroy (2004), "Effects of Nitrogen and Radiation on Dry Matter and Nitrogen Accumulation in the Spike of Winter Wheat", *Field Crops Research*, 87:221-233.

Denison, R.F., E.T. Kiers and S.A. West (2003), "Darwinian Agriculture: When Can Humans Find Solutions Beyond the Reach of Natural Selection? *The Quarterly Review of Biology*, 78:145-168.

Evans, L.T. (1993), *Crop Evolution, Adaptation and Yield*, Cambridge University Press, Cambridge, 512 pp.

Evenson, R.E. and D. Gollin (2003), "Assessing the Impact of the Green Revolution, 1960 to 2000", *Science*, 300:758-762.

Fischer, R.A. (1985), "Number of Kernels in Wheat Crops and the Influence of Solar Radiation and temperature", *Journal of Agricultural Science,* 105:447-461.

Fischer, R.A. (1993), "Irrigated Spring Wheat and Timing and Amount of Nitrogen Fertiliser. II. Physiology of Grain Yield Response", *Field Crops Research*, 33:57-80.

Fischer, R.A. (2008), "The Importance of Grain or Kernel Number in Wheat: a Reply to Sinclair and Jamieson", *Field Crops Research*, 105:15-21.

Fischer, R.A. and Y.M. Stockman (1980), "Kernel Number per Spike in Wheat (*Triticum aestivum L.*): Responses to Preanthesis Shading", *Australian Journal of Plant Physiology*, 7:169-180.

Flintham, J.E., *et al.* (1997), "Optimizing Wheat Grain Yield: Effects of Rht (Gibberellin-Insensitive) Dwarfing Genes", *Journal of Agricultural Science*, 128:11-25.

Galmés, J., *et al.* (2005), "Rubisco Specificity Factor Tends to be Larger in Plant Species from Drier Habitats and in Species with Persistent Leaves", *Plant, Cell and Environment* 28, 571-579.

Ghiglione, H.O., *et al.* (2008), "Autophagy Regulated by Day Length Determines the Number of Fertile Florets in Wheat", *The Plant Journal*, 55:1010–1024.

González, F.G., G.A. Slafer and D.F. Miralles (2002), "Vernalization and Photoperiod Responses in Wheat Reproductive Phases", *Field Crops Research*, 74:183-195.

González, F.G., G.A. Slafer and D.J. Miralles (2003), "Grain and Floret Number in Response to Photoperiod During Stem Elongation in Fully and Slightly Vernalized Wheats", *Field Crops Research*, 81:17-27.

González, F.G., G.A. Slafer and D.J. Miralles (2005a), "Floret Development and Survival in Wheat Plants Exposed to Contrasting Photoperiod and Radiation Environments During Stem Elongation", *Functional Plant Biology*, 32:189-197.

González, F.G., G.A Slafer and D.J. Miralles (2005b), "Photoperiod During Stem Elongation in Wheat: Is Its Impact in Fertile Floret and Grain Number Determination Similar to That of Radiation?", *Functional Plant Biology*, 32:181-188.

González, F.G., G.A. Slafer and D.J. Miralles (2005), "Pre-Anthesis Development and Number of Fertile Florets in Wheat as Affected by Photoperiod Sensitivity Genes *Ppd-D1* and *Ppd-B1"*, *Euphytica*, 146:253–269.

Goodman, M.M. (2004), "Plant Breeding Requirements for Applied Molecular Biology", *Crop Science*, 44:1913-1914.

Harlan, J.R. (1981), "The Early History of Wheat", In: *Wheat Science Today and Tomorrow*, L.T. Evans and W.J. Peacock (Eds.), Cambridge University Press, Cambridge, pp. 1-19.

Isla, R., Aragüés, R. and A. Royo (2003), "Spatial Variability of Salt-Affected Soils in the Middle Ebro Valley (Spain) and Implications in Plant Breeding for Increased Productivity", *Euphytica*, 134:325-334.

Kirby, E.J.M. (1988), "Analysis of Leaf, Stem and Ear Growth in Wheat from Terminal Spikelet Stage to Anthesis", *Field Crops Research*, 18:127-140.

Leegood, R.C. (2002), "C_4 Photosynthesis: Principles of CO_2 Concentration and Prospects for its Introduction into C_3 Plants", *Journal of Experimental Botany*, 53:581-590.

Liang, Y.L. and R.A. Richards (1994), Coleoptile Tiller Development is Associated with Fast Early Vigour in Wheat, *Euphytica*, 80:119-124.

López-Castañeda, C. and R.A. Richards (1994), "Variation in Temperate Cereals in Rainfed Environments. I. Grain Yield, Biomass and Agronomic Characteristics", *Field Crops Research*, 37:51-62.

López-Castañeda, C., R.A. Richards and G D. Farquhar (1995), "Variation in Early Vigour Between Barley and Wheat", *Crop Science*, 35:472-479.

Miralles, D.J. and R.A. Richards (2000), "Response of Leaf and Tiller Emergence and Primordium Initiation in Wheat and Barley to Interchanged Photoperiod", *Annals of Botany*, 85:655-663.

Miralles, D.J. and G.A. Slafer (1995), "Yield, Biomass and Yield Components in Dwarf, Semi-Dwarf and Tall Isogenic Lines of Spring Wheat under Recommended and Late Sowing Dates", *Plant Breeding*, 114:392-396.

Miralles, D.J. and G.A. Slafer (2007), "Sink Limitations to Yield in Wheat: How Could it be Reduced?", *Journal of Agricultural Science*, 145:139-149.

Miralles, D.J., R.A. Richards and G.A. Slafer (2000), "Duration of the Stem Elongation Period Influences the Number of Fertile Florets in Wheat and Barley", *Australian Journal of Plant Physiology*, 27:931-940.

Miralles, D.J., *et al.* (1998), "Floret Development in Near Isogenic Wheat Lines Differing in Plant Height", *Field Crops Research*, 59: 21-30.

Parry, M.A.J., *et al.* (2007), "Prospects for Increasing Photosynthesis by Overcoming the Limitations of Rubisco", *Journal of Agricultural Science*, 145:31-43.

Peltonen-Sainio, P., *et al*. (2007), "Grain Number Dominates Grain Weight in Temperate Cereal Yield Determination: Evidence Based on 30 Years of Multi-Location Trials", *Field Crops Research*, 100:179-188.

Prystupa, P., R. Savin and G.A. Slafer (2004), "Grain Number and Its Relationship with Dry matter, N and P in the Spikes at Heading in Response to NxP Fertilization in Barley", *Field Crops Research*, 90:245–254.

Rebetzke, G.J., A.G. Condon and R.A. Richards (1996), "Rapid Screening of Leaf Conductance in Segregating Wheat Populations", In *Proceedings of the Eighth Assembly of the Wheat Breeding Society of Australia*, RA Richards *et al.* (Eds), Canberra: Wheat Breeding Society of Australia.

Reynolds, M., *et al.* (2004), "Evidence for Excess Photosynthetic Capacity and Sink-Limitation to Yield and Biomass in Elite Spring Wheat", In *New directions for a diverse planet*, Proceedings of the 4th International Crop Science Congress (Fischer, R.A., Editor-in-Chief). The Regional Institute Ltd, Gosford.

Reynolds, M. *et al*. (2009), "Raising Yield Potential in Wheat", *Journal of Experimental Botany*, 60:1899-1918.

Reynolds, M.P. and N.E. Borlaugh (2006), "Impacts of Breeding on International Collaborative Wheat Improvement", *Journal of Agricultural Science*, 144:95-110.

Reynolds, M.P. *et al.* (1998), "Evaluating Physiological Traits to Complement Empirical Selection for Wheat in Warm Environments", *Euphytica*, 100:85-94.

Richards, R.A. (1992), "The Effect of Dwarfing Genes in Spring Wheat in Dry Environments. I. Agronomic Characteristics", *Australian Journal of Agricultural Research*, 43:517-527.

Richards, R.A. (1995), "Improving Crop Production on Salt-Affected Soils: by Breeding or Management", *Experimental Agriculture*, 31:395-408.

Richards, R.A. (1996a), "Defining Selection Criteria to Improve Yield Under Drought", *Plant Growth Regulation,* 20:57-166.

Richards, R.A. (1996b), "Increasing Yield Potential in Wheat - Source and Sink Limitations", in *Increasing Yield Potential in Wheat: Breaking the Barriers*, M.P Reynolds, S. Rajaram and A. McNab (Eds.), Mexico DF: CIMMYT, pp. 134-149.

Richards, R.A. (2000), "Selectable Traits to Increase Crop Photosynthesis and Yield of Grain Crops", *Journal of Experimental Botany*, 51:447-458.

Rosegrant, M.W. and S.A. Cline (2003), "Global Food Security: Challenges and Policies", *Science*, 302:1917-1919.

Sadras, V.O. (2007), "Evolutionary Aspects of the Trade-Off between Seed Size and Number in Crops", *Field Crops Research*, 100:125-138.

Savin, R. and G.A. Slafer (1991), "Shading Effects on the Yield of an Argentinian Wheat Cultivar", *Journal of Agricultural Science*, 116:1-7.

Serrago, R.A., D.J. Miralles and G.A. Slafer (2008), "Floret Fertility in Wheat as Affected by Photoperiod During Stem Elongation and Removal of Spikelets at Booting", *European Journal of Agronomy*, 28:301-308.

Siddique, K.H.M., *et al*. (1989), "Growth, Development and Light Interception of Old and Modern Wheat Cultivars in a Mediterranean Environment", *Australian Journal of Agricultural Research*, 40:473-487.

Sinclair, T.R. and R.C. Muchow (1999), "Radiation Use Efficiency", *Advances in Agronomy*, 65:215-265.

Slafer, G.A. (1996), "Differences in Phasic Development Rate Amongst Wheat Cultivars Independent of Responses to Photoperiod and Vernalization. A Viewpoint of the Intrinsic Earliness Hypothesis", *Journal of Agricultural Science*, 126:403-419.

Slafer, G.A. (2003), "Genetic Basis of Yield as Viewed from a Crop Physiologist's Perspective", *Annals of Applied Biology*, 142:117-128.

Slafer, G.A. and F.H. Andrade (1991), "Changes in Physiological Attributes of the Dry Matter Economy of Bread Wheat (*Triticum Aestivum*) through Genetic Improvement of Grain Yield Potential at Different Regions of the World. A Review.", *Euphytica*, 58:37-49.

Slafer, G.A. and F.H. Andrade (1993), "Physiological Attributes Related to the Generation of Grain Yield in Bread Wheat Cultivars Released at Different Eras", *Field Crops Research*, 31:351-367.

Slafer, G.A. and J.L. Araus (2007), "Physiological Traits for Improving Wheat Yield Under a Wide Range of Conditions", In: *Scale and Complexity in Plant Systems Research*, Gene-Plant-Crop Relations, J.H.J. Spiertz, P.C. Struik and H.H. van Laar (Eds.), Springer, Dordrecht, the Netherlands, pp. 147-156.

Slafer, G.A. and D.F. Calderini (2005), "Importance of Breeding for Further Improving Durum Wheat Yield", In: *Durum Wheat Breeding: Current Approaches and Future Strategies,* C. Royo *et al.* (Eds.), The Haworth Press, Inc., New York, pp. 87-95.

Slafer, G.A. and H.M. Rawson (1994), "Sensitivity of Wheat Phasic Development to Major Environmental Factors: a Re-Examination of Some Assumptions Made by Physiologists and Modellers", *Australian Journal of Plant Physiology*, 21:393-426.

Slafer, G.A. and H.M. Rawson (1996), "Responses to Photoperiod Change with Phenophase and Temperature During Wheat Development", *Field Crops Research*, 46:1-13.

Slafer, G.A. and H.M. Rawson (1997), Phyllochron in Wheat as Affected by Photoperiod Under Two Temperature Regimes, *Australian Journal of Plant Physiology*, 24:151-158.

Slafer, G.A. and E.H. Satorre (1999), "An Introduction to the Physiological-Ecological Analysis of Wheat Yield", In: *Wheat: Ecology and Physiology of Yield Determination*,E.H. Satorre and G.A. Slafer (Eds), Food Product Press, New York, pp. 3-12.

Slafer, G.A. and R. Savin (2006), "Physiology of Crop Yield", In: *Encyclopedia of Plant and Crop Science*, R. Goodman (Ed.), Taylor and Francis, New York.

Slafer, G.A., E.H. Satorre and F.H. Andrade (1994), "Increases in Grain Yield in Bread Wheat from Breeding and Associated Physiological Changes", In: *Genetic Improvement of Field Crops*, G.A. Slafer (Ed.), Marcel Dekker, Inc., New York, pp. 1-68.

Slafer, G.A., J.L. Araus and R.A. Richards (1999), "Physiological Traits to Increase the Yield Potential of Wheat, In: *Wheat: Ecology and Physiology of Yield Determination*, E.H. Satorre and G.A. Slafer (Eds.), Food Product Press, New York, pp. 379-415.

Slafer, G.A., *et al.* (1994), "Preanthesis Shading Effects on the Number of Grains of Three Bread Wheat Cultivars of Different Potential Number of Grains", *Field Crops Research*, 36:31-39.

Slafer, G.A., *et al.* (2001), "Photoperiod Sensitivity During Stem Elongation as an Avenue to Raise Potential Yield in Wheat", *Euphytica*, 119:191-197.

Slafer, G.A., *et al.* (2005), "Promising Eco-Physiological Traits for Genetic Improvement of Cereal Yields in Mediterranean Environments", *Annals of Applied Biology*, 146:61-70.

Slafer, G.A., *et al.* (2006), "Grain Number Determination in Major Grain Crops", In: *Handbook of Seed Science and Technology*, A.S. Basra (Ed.), The Haworth Press, Inc. New York, pp. 95-123.

Slafer, G.A., *et al.* (2009), "Crop Development: Genetic Control, Environmental Modulation and Relevance for Genetic Improvement of Crop Yield", In: *Crop Physiology: Applications for Genetic Improvement and Agronomy,* V.O Sadras and D.F. Calderini (Eds.), Elsevier, The Netherlands, pp. 277-308.

Tambussi, E.A., *et al.* (2004), "Growth and Photosynthesis During Early Plant Cycle of Two Barley Genotypes Which Differ in Yield Potential and Adaptation to Mediterranean Conditions", *Field Crops Research*, 91:149-160.

Thorne, G.N. and D.W. Wood (1987), "Effects of Radiation and Temperature on Tiller Survival, Grain Number and Grain Yield in Winter Wheat", *Annals of Botany*, 59:413-426.

Trethowan, R.M., M. van Ginkel and S. Rajaram (2002), "Progress in Breeding for Yield and Adaptation in Global Drought Affected Environments", *Crop Science*, 42:1441-1446.

Wang, Z., *et al.* (2003), Allocation of Photosynthates and Grain Growth of Two Wheat Cultivars with Different Potential Grain Growth in Response to Pre- and Post-Anthesis Shading, *Journal of Agronomy and Crop Science*, 189:280-285.

Whitechurch, E.M., G.A. Slafer and D.J. Miralles (2007), Variability in the Duration of Stem Elongation in Wheat Genotypes and Sensitivity to Photoperiod and Vernalization, *Journal of Agronomy and Crop Science*, 193:131-137.

Chapter 11

Replacement of Fish Meal in Aquaculture Diets with Plant Ingredients as a Means of Improving Seafood Quality

Konrad Dabrowski

School of Environment and Natural Resources,
Ohio State University, Columbus, Ohio, USA

The enhanced metabolic efficiency of aquatic animals such as fish and crustaceans over terrestrial homotherms includes the fact that they do not expend energy for body temperature regulation and excretion of toxic ammonia (without the need of synthesising its non-toxic derivatives). Therefore, utilisation of dietary nutrients for body deposition/growth can be higher in fish than in domestic mammals or birds. There is evidence that seafood quality can be enhanced by using specifically modified diets for cultured fish while simultaneously avoiding environmental pollutants in controlled farming. The question remains if fish can utilise feed stuffs of plant, bacterial, or yeast origin with low nutrient concentrations. There is increasing pressure to substitute fish meal protein with plant protein in aquafeeds for both carnivorous and omnivorous fish. In 2006 over 50% of the world fish meal supply was used for feeding cultured aquatic organisms. The price of fish meal has been fluctuating between USD 1 100 and 1 400 per MT since 2006. Plant protein concentrates and distillers' dried grains with solubles (DDGS, after ethanol extraction) are competitively priced relative to fish meal. If the concentration of proteins and essential amino acids (lysine, methionine) in plant proteins can be enhanced it may prove to be a valuable alternative to fish meal. As a result of a three month long study, we can provide evidence that entirely replacing fish meal (but not fish oil) with extracted cottonseed meal does not negatively impact the growth performance of carnivorous rainbow trout. Similarly, replacing 75–85% of the animal protein with plant proteins in the diets of other species of marine and freshwater fish, yield no observable detrimental effect on food intake and growth performance. Protein concentrates from oilseeds, such as soy or rapeseed/canola, contain minimal amounts of anti-nutrients that are not likely to restrict their use in aquafeeds. Therefore, their use has great potential in aquaculture.

Fish metabolic advantages over terrestrial animals

Aquatic organisms are poikilothermic, meaning that the energy requirement for maintenance is lower than in terrestrial homeotherms and affects food utilisation. Based on direct calorimetry Smith *et al.* (1978) established that maintenance energy expenditure differs between warm blooded animals (350-550 kJ per kg body weight per day) and fish (10-50 kJper kg per day) by one order of magnitude. Aquatic organisms are ammonotelic in comparison to terrestrial animals that synthesise urea (ureotelic, mammals) or uric acid (uricotelic, birds), so there is no metabolic need to detoxify ammonia (which results in energy loss). Net energy obtained by ammonotelic fish, ureotelic mammals, and uricotelic birds based on metabolic loss and waste product synthesis, concentration and excretion was estimated to provide 4.24, 3.37, and 2.92 kcal per g dietary protein. Consequently, the energy cost of animal protein production amounted to 2.3, 6.4, 15.9 and 40 g protein per Mcal of digestible energy for beef, pork, poultry and salmonid fish, respectively.

Human health advantages resulting from seafood consumption

In developing countries fish are frequently the protein of highest value in the diet. In developed countries fish oils are recognised for reducing serum triglyceride levels and systolic blood pressure, reducing plasma cholesterol and platelet adhesiveness. In the end, fish consumption correlates with a decrease in coronary heart diseases. There are multiple comprehensive projects addressing the role of fish in human diets.

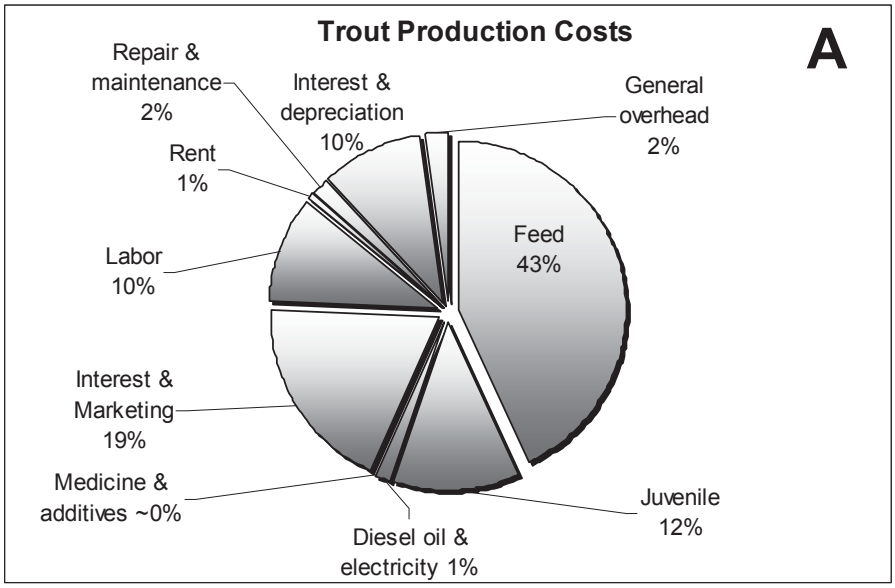
Effects of fish oil (or placebo as olive oil) supplementation during pregnancy on fatty acid composition of breast milk have been documented (Dunstan *et al.*, 2004). As the follow up to these findings, allergic women received four capsules daily of highly concentrated docosahexaenoic acid (DHA) which is equivalent to one fatty-fish meal per day as determined by the eicosapentaenoic acid (EPA) (with no more than one fish meal per week permitted). Dunston *et al.* (2008) found out that cognitive assessments of their children at the age of 2.5 years after maternal polyunsaturated fatty acids (PUFA) supplementation during pregnancy revealed that fish oil supplement is safe and may have beneficial effects on the child. Mental development, receptive language and child behaviour were also examined and showed improvements.

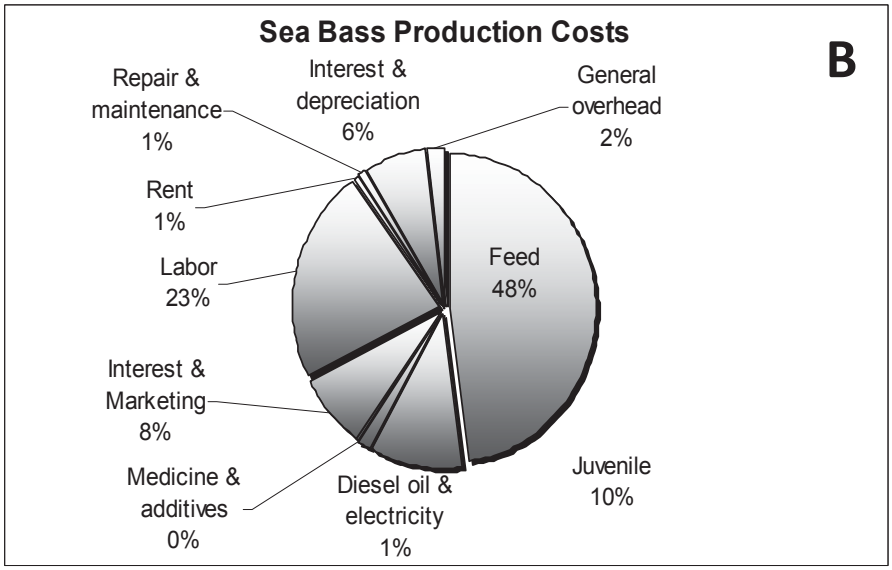
In another study, men between the ages of 40 and 49 years old from Kusatsu, Shiga, Japan, as well as Allegheny County, Pennsylvania, USA, and offspring of ethnic Japanese born in Honolulu, Hawaii (926 men) were examined for serum fatty acids. Transverse images of the aortic root at the apex of the heart were obtained by tomography. Coronary artery calcification (CAC) and intima media of the carotid artery were identified. Japanese men were found to be significantly less obese than the two other groups. Japanese men were found to have two-fold higher levels of n3 fatty acids than both US populations and it inversely correlated with intima-media thickness (Sekikawa *et al.*, 2008). Therefore, the authors concluded that high levels of marine oils-derived n3 fatty acids have anti-atherogenic effects that are independent of traditional cardiovascular risk factors in the Japanese population and it is unlikely to be the result of genetic factors.

The third example comes from Finland's (Kuopio) ischaemic heart disease risk factor studies that involved middle age men (52 years old). These men (1 871 subjects) were followed for ten years (194 coronary events; 160 coronary infarction). Serum fatty acids and hair mercury (Hg) levels were measured. Hg levels from 0 to 15.7 ug per g were observed (Rissanen *et al.*, 2000). Men with high DHA and docosapentaenoic (DPA) in

their blood and lower than 2 ug per g Hg had a 67% lower risk of acute heart events. The authors concluded that due to possible peroxidation of unsaturated fatty acids by mercuric compounds, the decreasing risk of DHA and DPA on acute coronary disease can be attenuated.

Figure 11.1. Cost analysis of trout and sea bass production in a Mediterranean country





Source: Bozoglu and Ceyhan (2009).

Cost of feeds in aquaculture

Aquaculture facilities such as culture ponds can be built in areas unsuitable for other agriculture activities: poor land, river flood plain, swamp land, natural prairies lakes, water enclosures and cages. Fish can be produced in rice paddies or rotated with agricultural crops. Despite several major farming systems used in aquaculture, *i.e.* ponds, tanks, or cages, the associated financial calculations point out unequivocally that the cost of feed is the major expenditure in the process of producing fish (Bozoglu and Ceyhan, 2009; D'Abramo *et al.*, 2008). In the case of freshwater rainbow trout and seawater sea bass at the medium level of intensification (20-30 kg per m^3) feed costs constituted 45–47% of the total production costs (Figure 11.1). The costs of production of trout and sea bass in Turkey was perhaps one of the lowest in Europe, USD 2.58 and USD 4.77 per kg respectively.

In a highly intensive system of channel catfish production in the USA (10-17 tons per ha) the cost of feed amounted to 27–35% of total production costs (Figure 11.2). Although in those studies the low-cost and high-cost diet formulations were not precisely defined, catfish diets do not in general contain more than 4–8% of fish meal. In fact, the low cost diet (USD 310) contained cottonseed meal as the protein component (replacing expensive menhaden fish meal in the high-cost diet with costs about USD 378/ton). Despite the fact that feeding coefficients in pond cultured catfish did not differ significantly, there were substantial differences in the mean fish size. This analysis points out that in highly intensive systems diet-dependent cost is the major single factor in the cost-profit ratio.

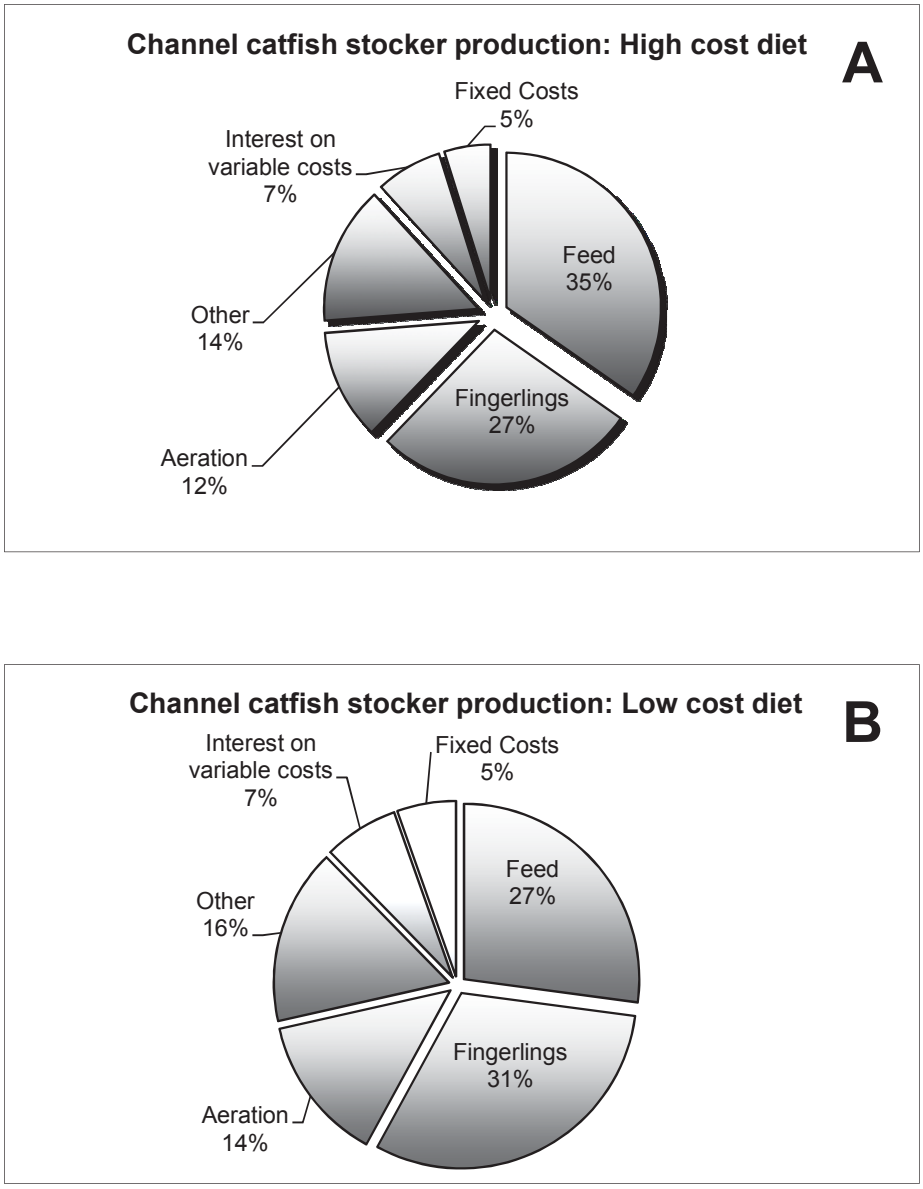
Cost of individual dietary components

Both researchers and practitioners, and feed manufacturers in particular must concentrate on the cost and profitability analysis that would include cost of individual components in diet formulation. In general, high protein levels (30–55%) and in salmonid diets high lipid levels (30–45%) dictate the major part in percentage cost breakdowns. Higgs (Department of Fisheries and Oceans, Vancouver, Canada) estimated that the cost share in Atlantic salmon diet (39% protein, 33% lipid) is as follows: protein, 52.1%, lipids 32%, vitamins and minerals 2.3%, binder 2.9%, canthaxanthin 10.7%. Therefore, the most practical cost saving option in aquatic diets is the use of a cheaper protein carrier.

Fish meal replacement

Plant protein concentrates and distiller's dried grains with solubles (DDGS, after ethanol extraction) are competitively priced relative to fish meal. There is an array of studies in which plant ingredients and plant protein concentrates were used in fish diets. However, one of the major problems in the studies of fish meal replacement with non-animal products has been the duration of the experiment, or simply that conclusions were made based on digestibility, *i.e.* nutrient absorption following a single meal (or a short series of feeding a diet with an inert marker). These results severely limit predictions related to the utility of plant ingredients for long term use in aquatic diets.

Figure 11.2. Cost analysis of channel catfish production in the USA



Note: Illustration was drawn based on data presented for pond cultured channel catfish in Mississippi, U.S.A.

Source: D'Abramo *et al.* (2008).

Plant protein substitution in fish meal was recently reviewed by Gatlin *et al.* (2008) and most of the information included in that paper is pertinent to the discussion of the current status of research in this field, that authors also highlighted further research avenues. Therefore, we deal here just with one example of a comprehensive approach to fish meal replacement in the diet of rainbow trout.

Cottonseed meal is among the largest high protein (30–40%) oil-seed meal produced in the world after soybean and rapeseed meal. The processing technology is being

continuously improved and the concentration of the major phytochemical limiting cottonseed use in animal diets, namely gossypol, was substantially decreased in the last decade. It is the cheapest plant protein concentrate and it appears that "carnivorous" coldwater salmonids have higher capacities to utilise this ingredient than warm water carps, catfishes and tilapia (cyprinids, ictalurids, cichlids). Two aspects are critical, the use of attractants with plant proteins and the masking of the texture of plant ingredients which may possibly negatively affect feed palatability. For instance, de Oliveira *et al.* (2004) were able to double the weight gain of carnivorous largemouth bass when diets were supplemented with small proportions of lipid-containing attractants.

Figure 11.3. Facilities used in inland aquaculture

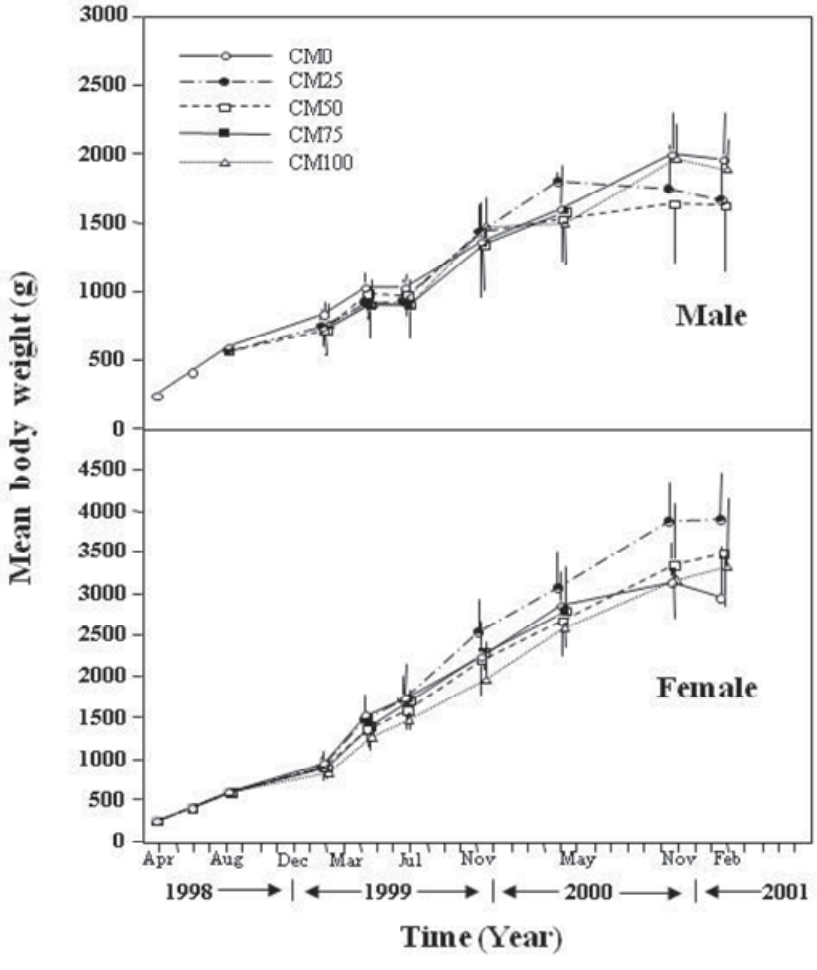
Note: Indoor (A) and outdoor (B) production tanks for culture of rainbow trout (C); controlled reproduction of this species involves stripping gametes and artificial fertilization (D).

Source: Pictures taken by Jacques Rinchard and Konrad Dabrowski.

A study by Lee *et al.* (2007) stands out because of its long term research approach. Namely, cottonseed meal utilisation was examined for nearly three years and the rainbow trout grow out experiment constituted several different life stages, and addressed possible genetic and epigenetic effects (Figure 11.3). General physiological parameters were examined along with effects on fish reproduction, gamete quality, performance of the progeny, and quality of fish flesh. Three aspects are important to mention, supplementation with indispensable amino acids (lysine and methionine), addition of animal tissue attractants (krill meal), and a proportional increase in fish oil with a decrease of fish meal, to compensate for energy content and mask possible "detracting"

chemicals in plant ingredients. Overall, we were able to conclude that if fish gender is separated (Figure 11.4) there is no significantly different growth of trout fed fish meal-free and control (40% fish meal) diets.

Figure 11.4. Mean body weight of rainbow trout fed five practical diet formulations for 35 months



Note: The level of fish meal protein substitution by cottonseed meal protein is listed in diet description (Upper, left corner). There was no significant difference between fish meal-free diet (100% cottonseed meal protein) and control diet based on fish meal protein (CM0) within the same gender groups.

Source: Lee *et al.* (2005).

Fish oil replacement

There is a consensus that replacement of fish oil in aquatic diets may become more urgent then that of fish meal.

Plant ingredients with novel functions: gossypol, saponins, quercetin, hydroxytyrosol, steroid-inhibitors

Several phytochemicals are known for their toxic, pharmacological, endocrine, immunostimulating, animal and human diseases preventing capacities. Gossypol, as an example, is a well known antifertility agent in animals and men. Less known is its cancer cell growth inhibiting capacity that was revealed in mice (Ko *et al.*, 2007). It should be stressed that gossypol concentrations in trout muscle after three years of feeding with a diet containing 58.8% cottonseed amounted to 0.68 mg per kg (ppm). That is almost a 500 fold lower concentration than the limit set by the US Food and Drug Administration (FDA) for human consumption. We suggest that it can be safely consumed and perhaps constitutes another preventive measure against human diseases.

Research needs to facilitate wider/larger use of plant ingredients in aquafeeds

- Studies involving interactions of proteins in the food, protein synthesis, protein deposition, metabolites must continue. Testing new hypotheses challenging "ideal protein" concept with, for instance, imbalance indispensable amino acid concept should be encouraged.
- Studies of "food chain" involved in effects of fish diet on quality of fish muscle (meat storage) and tests on mice/rat models (health promoting effects) are almost not available in the literature.
- Studies of plant specific substances, such as appetite and growth promoters, sex reversal, immune resistance enhancers, antioxidants should be followed with the use of semi-purified diets to avoid side-effects of practical ingredients (Dabrowski *et al.* 2010). Isolation, testing, synthesis and use of phytochemicals are urgently needed.
- Studies addressing the mechanisms of action of nutrients in all ontogenic stages of fish development. Genomic, metabolomic and proteomic techniques need to be used.
- Preparation of predictive models and conduct of studies that would optimise (economise) aquafeed formulations based on current commodity prices would greatly improve profitability of aquaculture.

Bibliography

Bozoglu, M. and V. Ceyhan (2009), "Cost and Profitability Analysis for Trout and Sea Bass Production in Black Sea", *J. Animal and Vet. Advances* 8: 217-222, Turkey.

D'Abramo, L.R., T.R Hanson and J.A. Steeby (2008), "Production and Associated Economics of Channel Catfish Fed Different Practical Diets in the Fingerling-Stocker Phase of Culture", *North Am. J. Aquaculture* 70: 154-161.

Dabrowski, K., Y. Zhang, K. Kwasek, P.Hliwa and T. Ostaszewska (2010), "Effects of Protein-, Peptide-, and Free Amino Acid-Based Diets in Fish Nutrition", *Aquaculture Res.* 41: 668-683.

De Oliveira, A.M.B.M. and J.E.P. Cyrino (2004), "Attractants in Plant Protein-Based Diets for Carnivorous Largemouth Bass, *Micropterus salmoides*", *Sci.Agric*. 61: 326-331.

Dunstan, J.A., K. Simmer, G. Dixon and S.L. Prescott (2004), "The Effect of Supplementation with Fish Oil During Pregnancy on Breast Milk Immunoglobulin A, Soluble Cd14, Cytokine Levels and Fatty Acid Composition", *Clin. Exp. Allergy* 34: 1237-1242.

Dunstan, J.A., K. Simmer, G. Dixon and S.L. Prescott (2008), "Cognitive Assessment of Children at Age 2 ½ years After Maternal Fish Oil Supplementation in Pregnancy: a Randomized Controlled Trial", *Arch. Dis. Child Fetal neonatal Educ.* 93: F45-F50.

Gatlin III, D.M., *et al.* (2007), "Expanding the Utilization of Sustainable Plant Products in Aquafeeds: a Review", *Aquaculture Res.* 38:551-579.

Ko, C-H., *et al.* (2007), "Effect of Gossypol Treatment on Inhibition of Human Colorectal Carcinoma Cells Transplanted to Nude Mice", *Internat. J. Cancer* 121: 1670-1679.

Lee, K-J., *et al.* (2005), "Long-Term Effects of Dietary Cottonseed Meal on Growth and Reproductive Performance of Rainbow Trout: Three-Year Study", *Animal Feed Sci.Technol.*

Rissanen, T., *et al.* (2000), "Fish Oil-Derived Fatty Acids, Docosahexaenoic Acid, and Docosapentaenoic Acid, and the Risk of Acute Coronary Events: the Kuopio Ischaemic Heart Disease Risk Factor Study", *Circulation* 102: 2677-2679.

Sekikawa, A., *et al.* (2008), "Marine-Derived n-3 Fatty Acids and Atherosclerosis in Japanese, Japanese-American, and White Man", *J. American College of cardiol.* 52: 417-424.

Smith, R.R., G.L. Rumsey and M.L. Scott (1978), "Net Energy Maintenance Requirements of Salmonids as Measured by Direct Calorimetry: Effect of Body Size and Environmental Temperature", *J. Nutrition* 108: 1017-1024.

Part IV

Food Safety Today and Tomorrow: the Challenges in Changing Food and Farming Practices

Summary of discussions

Dr. Allan King

Department of Biomedical Sciences, University of Guelph, Ontario, Canada

There are significant challenges for providing sufficient food to sustain the growing population which are further compounded by the link between quality and quantity of food and health status. Malnutrition is no longer the main nutritional side effect. Food and feed borne diseases are an increasing threat to human and animal health. In addition, association between diet and chronic diseases such as cardio vascular disease, diabetes and certain cancers has brought the quality of foods to the forefront of health research as well as consumer awareness. Research in these areas being conducted against the backdrop of diminishing biodiversity, climate change and changing agricultural practices are facing unprecedented challenges. This session, which consisted of lectures by five international scientists and a panel discussion, was devoted to addressing specific topics related to future food production and delineating associated research challenges and needs in general.

Dr. László Hornok, Szent István University, Hungary, provided an update and insights into future initiatives in research on mycotoxins, feed borne pathogens that have an adverse effect upon human and animal health. In the same vein, Dr. Jaap Wagenaar, Utrecht University, presented an insightful overview of causes and effects and possibilities for controlling food and feed borne zoonotic diseases. Dr. Stefaan De Smet, Ghent University, discussed the possibilities altering and enriching the health promoting edible animal products through altering the diets of production animals. Dr. Mark Baron Van Montagu, a pioneer in plant transgenesis, provided an insightful view of the future possibilities for plants and plant derived product. In the final lecture of the session, Dr. José Esquinas Alcázar, former General Secretary of Genetic Resources Conference, FAO, discussed the importance of maintaining biodiversity and utilising these genetic resources for breeding to meet agricultural challenges of the future.

During the round table and audience discussion, a number of important issues and knowledge gaps were identified. The issues and knowledge gaps pose challenges for the

quality and safety of our food supply and need to be prioritised for further research. Areas that were identified as key to being able to provide safe pathogen free foods include:

a) increasing the understanding of plant, animal and microbial genome;

b) host pathogen interactions; and

c) development of molecular markers to identify pathogens and toxicogenic organisms.

The effective application of new molecular monitoring technology at all levels of the food chain is warranted and bioinformatics and modelling was seen as potentially playing an increasing and effective role in food quality and safety and controlling food borne disease. At the national and international levels, greater information sharing, particularly concerning public health issues pertaining to food borne disease, was seen as an important initiative to address the issues of supplying safe and healthy foods. Research directed towards more efficient utilisation of nutrients and development of abiotic/biotic stress tolerant plants were considered important for increasing production efficiency. A greater awareness and access to information of genetic resources are necessary to identify species that can tolerate the changing climate and environment. Although we have the tools and knowledge to develop new genotypes or improve food quality by traditional breeding or through transgenesis, the applications and priorities need to be identified and determined on both national and international levels. To this end, the involvement of breeders, farmers and consumers is essential. Particularly in the case of novel food technologies where international harmonisation of the regulatory framework was viewed as key to not duplicate limited resources.

Chapter 12

Major Trends in Mycotoxin Research

Dr. László Hornok

Szent István University, Mycology Group of the Hungarian Academy of Sciences, Institute of Plant Protection, Gödöllö, Hungary

Mycotoxins, produced by fungi that colonise foods and feeds may be carcinogenic, cytotoxic, oestrogenic, immunosuppressant, nephrotoxic, neurotoxic or teratogenic compounds and pose, therefore, serious public and animal health hazards. Food and feed safety, as a major concern all over the world, is the driving force of mycotoxin research and development activity. The present study provides an overview of the major mycotoxins and mycotoxicoses including chemistry, toxicity, and detection of mycotoxins. Special attention is devoted to biodiversity, genetic variation, life cycle strategies, pathogenicity and identification of toxigenic fungi. Risk assessment and climatic models developed to predict mycotoxin contamination of crop products are considered as potential solutions of reducing the threat of mycotoxicoses. The role of storage conditions and food processing technologies in the reduction of mycotoxin concentrations are also discussed.

Introduction

Mycotoxins are secondary fungal metabolites with chemical structures suitable to cause a variety of toxic effects in humans and animals. Some of these compounds may be carcinogenic, cytotoxic, oestrogenic, immunosuppressive, mutagenic, nephrotoxic and teratogenic. If ingested, they may cause severe disorders, including alimentary toxic aleukia (ATA), diarrhoea, oesophageal cancer, feed refusal, irregular oestrous cycle, nervous system disturbances, pulmonary oedema, and vomiting.

The risk of mycotoxin contamination arises in the field, where susceptible plants are infected with potentially toxigenic fungi. During ripening, plant tissues enter into a senescent state, their basal resistance declines and weak parasites or even saprophytes may initiate colonisation. Under favourable environmental conditions invasion by toxigenic fungi becomes more serious. Colonisation by fungi proceeds during storage especially if plant products, foods and feeds are stored under warm and moist conditions or the products are inadequately dried.

History of mycotoxins and mycotoxicoses

Cases of mycotoxicoses have been recorded in historical times. One of the Ten Plagues of Egypt, death of the first borns, as we know from the Old Testament, was probably caused by consumption of mould infected grains (Marr and Malloy, 1996). St. Anthony's Fire syndrome, as described in the Middle Ages was, in fact, ergotism. Horses of the Mongol hordes invading Europe during the 13th century suffered serious stachybotrytoxicoses contributing to the military defeat of the invaders. Ergotism was also involved in the Salem Witchcraft Trials. During the Second World War a lethal outbreak of Alimentary Toxic Aleukia occurred in the Soviet Union caused by ingestion of grains infected with *Fusarium sporotrichioides*, a T-2 toxin producing fungus (Joffe, 1986).

Major mycotoxins

More than 400 mycotoxins are currently known, but only a subset of these compounds poses direct toxic hazards. Considering their frequency of occurrence and the severity of the toxicoses they may cause, aflatoxins, deoxynivalenol, fumonisins, ochratoxin A, T-2 toxin, and zearalenone are classified as major mycotoxins (Richard, 2007). Nowadays, massive human mycotoxicoses are restricted to developing countries; one of the sad examples occurred in 2004 in Kenya, where a serious aflatoxicosis claimed more than 120 victims (Muture and Ogana, 2005). In OECD countries the major concerns are chronic mycotoxicoses that occur when people ingest small concentrations of these compounds for a long period.

Aflatoxins constitute a group of chemically related compounds, including aflatoxin B_1, B_2, G_1 and G_2. They are produced by certain isolates of *Aspergillus flavus, Aspergillus nomius* and *Aspergillus parasiticus*. The major crops exposed to aflatoxin contamination are corn, cottonseed, peanuts and tree nuts. These compounds are carcinogenic, immunosuppressive, mutagenic, and teratogenic and cause liver damage in humans and animals. Aflatoxin M_1 a hydroxylated metabolite may accumulate in milk and meat of animals fed by contaminated food. Both the US FDA and the EC issued action levels for

aflatoxins in food and feed; the EC levels are more restrictive. Aflatoxin producing fungi occur mainly in warm arid, semi-arid, sub-tropical and tropical regions and, therefore crops grown in these regions have greater likelihood of contamination with aflatoxins. The global climatic warming favours the spread of aflatoxin producing fungi and vast human populations are expected to be exposed to aflatoxicosis, especially in Africa (Cotty and Jaime-Garcia, 2007).

Deoxynivalenol (DON), a type B trichothecene is accumulated mainly in corn and small grain cereals infected with *Fusarium graminearum* and, to a lesser account with *F. culmorum*. *Fusarium* head blight (FHB) is an irregularly occurring but serious disease of wheat and other small grain cereals throughout the temperate zone. *F. graminearum* survives on plant residues left on the field from the previous year's crop and provide an efficient ascospore inoculum the following spring, when wheat is in heading stage. The fungal inoculum infects florets leading to the development of FHB (Francl *et al.*, 1999). Of the domestic animals, swine is mostly affected by DON toxicosis: animals may refuse the intake of contaminated feeds, or if they eat such feeds, they may vomit them. Both feed refusal and vomiting result in decreased weight gain (Marasas *et al.*, 1984). The FDA and the EC have issued advisory levels for DON contamination; the EC regulations are again more stringent.

Fumonisins (FB_1, FB_2 and FB_3 are the major forms, FB_1 is the most toxic) are long-chain amino polyalcohols produced primarily by *F. proliferatum* and *F. verticillioides*, fungi that prefer warm, semi-arid conditions. These compounds inhibit sphingolipid metabolism and cause leucoencephalomalacia in horses, pulmonary oedema in swine, tumours of kidney and liver in rodents and oesophageal cancer in humans (Marasas, 1996). The major source of fumonisin ingestion is sweet corn, but rice, wheat and sorghum may also be seriously infected by fumonisin producing fungi. Strict FDA and EC regulations are issued for these mycotoxins.

T-2 toxin belongs to type A trichothecenes, its major producer is *F. sporotrichioides*, a psychrotrophic fungus prevailing in Northern Europe and Northern America. Like other trichothecenes, T-2 toxin inhibits protein synthesis and is regarded as a virulence factor of phytopathogenic fungi. The major sources of T-2 toxicoses are sorghum and small grain cereals (Marasas *et al.*, 1984).

Ochratoxin A (OTA) is primarily produced by *Aspergillus niger, Aspergillus ochraceus* and *Penicillium verrucosum*. Under field conditions, these fungi occur on grapevine and fruits; they are, however more important as storage pathogens due to their xerophilic nature. OTA is nephrotoxic and has been identified as the causative agent of Balkan Endemic Nephropathy (Pfohl-Leszkowicz *et al.* 2002). The major sources of OTA accumulation are raisins, barley (and hence malting products), coffee, grapevine (and hence vine). The EC has strict regulations for OTA.

Zearalenone (ZEA), mainly produced by *F. graminearum* and related fungi (like *F. culmorum, F. equiseti, F. semitectum*) is a phenolic resorcyclic acid lactone with estrogenic effects on swine and other mammals, including humans (Hidy *et al.*, 1977). Of the major crops, corn is most frequently exposed to ZEA contamination. Ingestion of ZEA is associated with hyperestrogenic syndromes, precocious development of mammae, weak piglets and small litter size (Prelusky *et al.*, 1994).

Other important mycotoxins

Other mycotoxins with low or moderate toxicity are also subjects of research interest, as they may cause local incidents or act synergistically if associated with other secondary metabolites of microbial origins.

Beuvericin and enniatins are cyclic hexadepsipeptides with ionophore and antibiotic activities and are produced by *Beuveria bassiana* and selected species of *Fusarium* (Moretti *et al.*, 1997). Ergot alkaloids, such as clavine alkaloids, lysergic acids, lysergic acid amides, and peptide alkaloids are produced by sclerotium forming *Claviceps* species, pathogens of cereals and a variety of grass species. Other ergot producing organisms are fungal endophytes belonging to *Neotyphodium* or *Epichloe.* Symptoms of ergotism range from nervous signs (nausea, star gazing, staggering) to gangrenous symptoms, including the loss of extremities (Demeke *et al.*, 1979). Ergot toxicoses have caused severe economic losses in sheep, cattle and horse industries in the USA and New Zealand. Butenolide, a 4-acetamido-4-hydroxy-2-butenoic acid lactone is produced by *Fusarium* species causing oedema, lameness and gangrenous loss of appendages. Equisetin, a N-methyl-2,4-pyrrolidone derivative is also produced by *Fusarium* species; there is a pharmaceutical interest towards this compound due to its anti-HIV (human immunodeficiency virus) activity (Hazuda *et al.*, 1999). Fusarins are 2-pyrrolidones, produced by *F. graminearum* and *F. verticillioides*. Fusarin C, the most notable member of this group proved to be mutagenic in the Ames test (Wiebe and Bjeldanes, 1991). Moniliformin produced by several species of *Fusarium* (Chelkowski *et al.*, 1990) is acutely toxic to ducklings and rats. The major sources of patulin, a potentially genotoxic compound are apples colonised by a variety of *Penicillium* and *Aspergillus* species, most notably by *P. expansum* (Anderson *et al.*, 2004). Citrinin, also produced by *Aspergillus* and *Penicillium* species, causes nephropathy in livestock, but its acute toxicity greatly varies. This mycotoxin increases mitochondrial membrane permeability transition (da Lozzo *et al.*, 1998), inhibits respiration and probably contributes to programmed cell death.

Research and development priorities

Biodiversity of toxigenic fungi

In most cases, mycotoxin contamination starts in the field, where complexes of pathogenic or weak parasite fungi attack and colonise plant tissues. Strains of the same species may show qualitative differences in their secondary metabolite profiles and there are great within species differences in the amounts of a specific toxin, produced by one or other strain of a fungus. For example, strains of *F. graminearum* differ in their trichothecene production profiles: DON chemotype strains produce deoxynivalenol, nivalenol (NIV) chemotype strains produce nivalenol, whereas DON-NIV chemotype strains produce both deoxynivalenol and nivalenol (Sugiura *et al.*, 1990). Genetically isolated lineages of *F. sporotrichioides*, a fungus with no known sexual stage also show strikingly different secondary metabolite profiles (Nagy and Hornok, 1995). Continuous monitoring of field populations of toxigenic fungi is an important research priority. Such surveys help to assess mycotoxin risks in a given region and forecast changes of populations of toxigenic fungi. Restriction fragment length polymorphisms (RFLPs), amplified fragment length polymorphisms (AFLPs) and single nucleotide polymorphisms (SNPs) of selected genes or gene fragments are widely used to assess within species

diversity. Divergence in molecular markers may be coupled with significant differences in toxin production: two subgroups (sibling species) of *Fusarium subglutinans*, a maize ear rot pathogen identified by RFLPs in the histone H3 and β-tubulin sequences have recently been found to differ in beauvericin production (Moretti *et al.*, 2008).

Biology of mycotoxin producing fungi

Environmental conditions have a direct influence on toxigenic fungi, but affect plant-pathogen interactions as well. An adequate knowledge on the environmental requirements of toxigenic fungi helps to improve control measures used against these organisms.

Environmental factors, like temperature, nitrogen depletion, pH conditions have been demonstrated to trigger secondary metabolite production of fungi (Sagaram *et al.*, 2006). Identification of the stress-factors and the signalling pathways that induce mycotoxin production would certainly (Choi *et al.*, 2008; Kohut *et al.*, 2009) improve measures aimed to reduce mycotoxin accumulation both in the field and during storage.

Toxigenic fungi follow different reproduction strategies for their survival and spread. Some of them use regular sexual reproduction, while others prefer clonal propagation. In sexually reproducing heterothallic species, meiosis generates recombinants with new genetic traits and hence novel pathotypes or mycotoxin chemotypes may arise at high frequency (Cumagun *et al.*, 2002). On the contrary, in homothallic species the sexual events occur in the same thallus, and therefore the frequency of genetic recombination is limited. The advantage of this type of reproduction can be the large number of ascospores produced without the need for a compatible mating partner; the ascospores serve then as primer inocula in FHB of cereals (Francl *et al.*, 1999). Species with no known sexual stage follow an R-strategic way of living and reproduce clonally preventing the dilution of their genetic pool. Depending on a specific reproduction strategy, the frequency of mating and hence meiotic recombination can be high in female fertile heterothallic fungi, rare in homothallic fungi and "zero" in clonally reproducing fungi. The frequency of sexual reproduction is an important parameter for deciding control measures. A high level of race specific resistance can be built into plant cultivars against clonally reproducing organisms, whereas horizontal resistance can be more efficient against pathogens comprising genetically diverse populations as a result of frequent mating and meiotic recombination.

Identification of toxigenic fungi

Molecular biology of toxigenic fungi would certainly be a prominent research priority both in the present and the next decade. Complete genome sequences of several mycotoxin producing fungi, including *Aspergillus flavus, A. nidulans, A. oryzae, A. niger*, *F. graminearum, F. verticillioides,* and *Penicillium chrysogenum*, as well as a number of expressed sequence tags (EST) databases are by now available (Broad Institute/MIT Center for Genome Research). Functional analyses of the exponentially growing sequence data resulted in the identification of mycotoxin biosynthesis genes, as well as genes with a regulatory role on mycotoxin biosynthesis. In *Fusarium* and *Aspergillus*, gene clusters for aflatoxins, butenolide, enniatins, equisetin, fumonisins, fusarins, ochratoxins, trichothecenes, and zearalenone (Desjardins and Proctor, 2007; Yu *et al.*, 2008) have been identified. The results of these studies are potentially exploited for mycotoxin control and plant breeding efforts aimed to select cultivars, resistant against

toxigenic plant pathogens. On the other hand, the prompt exploitation of nucleic acid sequence data results in the development of nucleic acid sequence based diagnostic tools.

Identification of mycotoxin producing fungi by using traditional cultural and microscopic practices needs high expertise and costs time. To overcome these problems rapidly, nucleic acid based methods have been developed in the last 15 years. Polymerase chain reaction (PCR) proved to be the most successful approach to replace the time-consuming microbiological identification methods.

Of the aflatoxin producing fungi *Aspergillus flavus, A. parasiticus* and *A. versicolor* can be identified selectively by using specific primers based on the *nor-1* gene and the ITS1-5.8 S region of the ribosomal ribonucleic acid (rRNA) gene (Geisen, 1996). More recently, a quantitative real-time PCR (q-rt-PCR) assay was developed to detect aflatoxin producing in contaminated food samples (Bu *et al.*, 2005).

Owing to the ample sequence information on the trichothecene gene cluster, a number of PCR diagnostic techniques have been developed to detect trichothecene producing *Fusarium, Myrothecium,* and *Trichoderma* fungi (Tan and Niessen, 2003; Demeke *et al.*, 2005). Most workers used primers, based on sequences of the *tri5* (trichodiene synthase) gene, but other members of the trichothecene gene cluster, like *tri6*, *tri7*, and *tri13* could also be utilised in designing primers. RAPD and ITS based primers were also successfully used for specific identification of toxigenic *Fusarium* species (Nicholson *et al.*, 1998; Kulik *et al.*, 2004).

Fumonisin producing members of the *Gibberella fujikuroi* complex, including *F. proliferatum, F. subglutinans* and *F. verticillioides* have been identified by PCR using primers based on either the *fum* gene sequences (Gonzales-Jaen *et al.*, 2004) or the ITS1 region of the rRNA genes (Grimm and Geisen, 1998). The *idh* gene, coding for isoepoxidon dehydrogenase, a key enzyme of patulin biosynthesis was used to design specific PCR primers to detect patulin producing *Penicillium expnasum* and *P. griseofulvum* strains (Paterson *et al.*, 2000).

The simple, user-friendly PCR-based methods are suitable for the rapid detection of selected toxigenic fungi in a range of products, but they can only give qualitative information, limited to one or a few species. DNA microarray techniques solve this problem. Schmidt-Heydt *et al.* (2008) developed a microarray procedure based on cDNAs of ochratoxin genes and found good correlation between the intensity/range of hybridization signals and the fungal biomass present in the samples. Furthermore, correlation also existed between the signals and the amount of ochratoxin A detected in the same sample. The number of mycotoxin producing species detected in a single assay can also be increased by the DNA microarray method as demonstrated by Kristensen *et al.* (2006), who could detect 16 different toxigenic Fusarium species in a single multiplex assay.

Detection and identification of mycotoxins

Sensitive, exact chromatographic methods are available allowing the detection and quantification of any known mycotoxin. These methods are widely used in food safety but most of them are suitable for detecting a single class of mycotoxins with similar physicochemical parameters. To speed up mycotoxin analysis and detect potentially synergistic, co-occurring toxins and/or their conjugates multi-mycotoxin methods have been developed. One of them, a sophisticated liquid chromatography-mass spectrometry

approach allowed the simultaneous detection and quantification of as much as 90 mycotoxins (Berthiller *et al.*, 2007),

For the rapid, user friendly detection of mycotoxins various immunochemical methods have been developed. Most of these methods are based on enzyme-linked immunoassay (ELISA) and use monoclonal antibodies. Other qualitative detection tools, suitable for *in situ* (at the field, in storehouses, etc.) detection, are immunostrips and lateral flow devices. A list of commercial immuno-kits with detailed descriptions is provided by the European Mycotoxin Awareness Network (*www.mycotoxins.org)*.

Pre-harvest control of toxigenic fungi

Efficient control measures including agrotechnical practices, fungicide treatments, biocontrol methods, breeding for host-plant resistance, integrated management systems and genetic engineering have been developed and widely used to combat mycotoxin producing fungi (Cleveland *et al.*, 2003; Tóth *et al.*, 2008). However, these measures should be cost responsive and therefore there is an increasing demand for predictive models to assist growers in their pest management or grain marketing decisions. To date, the most successful forecast model is DONcast developed by Hooker *et al.* (2002) to predict DON accumulation in wheat. This and other similar models use agronomic and meteorological variables (including varietal resistance, cropping history, soil and plant nutrition parameters, temperature, rainfall, relative humidity and the duration of leaf wetness) when calculating the risk of mycotoxin contamination.

Post-harvest control strategies, food processing

The best way of mycotoxin control is to produce healthy crops, a requirement difficult to meet in every growing season and any region. Spoilage moulds, especially xerotolerant species of *Aspergillus, Fusarium* and *Penicillium* continue to grow and colonise stored plant products contributing to mycotoxin accumulation in these products. Post-harvest control strategies have been developed to avoid or reduce this kind of risk (Magan and Aldred, 2007). These strategies include maintaining elevated CO_2 levels (~75%) in partially dried grain lots or the use of essential oils and anti-oxidants. However, these technologies are not widely utilised and further experiences are needed to see their future. The most efficient mycotoxin prevention post-harvest management today is to maintain good storage conditions paralleled with appropriate monitoring systems suitable to detect any onset of spoilage.

Mycotoxins are difficult to destroy during food processing operations. Sorting and trimming of crop products lower mycotoxin concentrations by removal of fractions that became contaminated with fungi. Milling processes only redistribute mycotoxins and concentrate these compounds in selected mill fractions, such as bran. In general, brewing results only in low levels of reduction. Of thermal processing technologies roasting, extrusion and alkaline cooking are the most efficient ways of reducing mycotoxin contamination of food products, although very high temperature is needed to attain substantial reduction of toxin levels (Bullerman and Bianchini, 2007).

Conclusions

A certain degree of mycotoxin contamination is unavoidable under the current crop production and storage technologies. Although our knowledge on these compounds and

the producing organisms is far from complete, enough is known to face the problems they may cause. There is a need for the continuous monitoring of populations of toxigenic fungi to follow their changes driven by genetic and environmental factors. New and/or more complex diagnostic methods are also needed to provide a rapid and reliable identification of these organisms, as well as the secondary metabolites they produce. Although a great choice of control methods, both pre-harvest and post-harvest are available, improved, more efficient technologies based on mycotoxin prediction models are expected to be introduced and commercialised in the near future. Education, extension and consultation activities should be improved to distribute information on these compounds that are among the most dangerous undesirable substances in foods and feeds.

ACKNOWLEDGEMENTS

I am grateful to the organising committee of the OECD CRP conference on "Challenges for Agricultural Research" (6-8 April, 2009 in Prague, Czech Republic) for inviting me to present this work. This study was in part supported by the Hungarian National Scientific Research Fund (OTKA) (K 76067) and the Office for Subsidised Research Units of the Hungarian Academy of Sciences.

Bibliography

Andersen, B., J. Smedsgaard and J.C. Frisvad (2004), "*Penicillium Expansum*: Consistent Production of Patulin, Chaetoglobosins, and Other Secondary Metabolites in Culture and their Natural Occurrence in Fruit Products", *Journal of Agricultural and Food Chemistry,* 52, 2421-2428.

Berthiller, F. *et al.* (2007), "Chromatographic Methods for the Simultaneous Determination of Mycotoxins and their Conjugates in Cereals", *International Journal of Food Microbiology* 119**,** 33-37.

Bu, R., *et al.* (2005), "Monochrome Lightcycler PCR Assay for Detection and Quantification of Five Common Species of *Candida* and *Aspergillus", Journal of Medical Microbiology* 54**,** 243-248.

Bullerman, L.B. and A. Bianchini (2007), "Stability of Mycotoxins During Food Processing", *International Journal of Food Microbiology* 119**,** 109-115.

Cleveland, T.E., *et al.* (2003), "United States Department of Agriculture – Agricultural Research Service Research on Pre-harvest Prevention of Mycotoxins and Mycotoxigenic Fungi in US Crops", *Pest Management Science* 59**,** 629-642.

Chelkowski, J., *et al.* (1990), "Moniliformin Production by *Fusarium* Species", *Mycotoxin Research* 6**,** 41-45.

Choi Y-E., *et al.* (2008), "GAC1, a Gene Encoding a Putative GTPase-Activating Protein, Regulates Bikaverin Biosynthesis in *Fusarium verticillioides", Mycologia* 100, 701-709.

Cotty, P.J. and R. Jaime-Garcia (2007), "Influences on Climate on Aflatoxin Producing Fungi and Aflatoxin Contamination", *International Journal of Food Microbiology* 119, 109-115.

Cumagun, C.J.R., R.L. Bowden and T. Miedaner (2002), "Segregation of Agressiveness in a Crossing Population of *Fusarium graminearum*, *Journal of Applied Genetics* 43A, 39-44.

da Lozzo, E.J., M.B. Oliveira and E.G. Carnieri (1998), "Citrinin-Induced Mitochondrial Permeability Transition", *Journal of Biochemical and Molecular Toxicology* 12, 291-197.

Demeke, T., Y. Kidane and E. Wyhib (1979), "Ergotism: a Report of an Epidemic, 1977-78", *Ethiopian Medical Journal* 17, 107-114.

Demeke, T., *et al.* (2005), "Species Specific PCR-based Assays for the Detection of *Fusarium* Species and a Comparison with the Whole Seed Agar Plate method and Trichothecen Analysis", *International Journal of Food Microbiology* 103, 271-284.

Desjardins, A.E., and R.H. Proctor (2007), "Molecular Biology of *Fusarium* Mycotoxins", *International Journal of Food Microbiology* 119, 47-50.

Francl, L., *et al.* (1999), "Daily Inoculums Levels of *Gibberella Zeae* on Whet Spikes", *Plant Disease* 83, 662-666.

Geisen, R. (1996), "Multiplex Polymerase Chain Reaction for the Detection of Potential Aflatoxin and Sterigmatocystin Producing Fungi", *Systematic and Applied Microbiology* 19, 388-392.

Gonzales-Jaen, M.T., *et al.* (2004), "Genetic Markers for the Analysis of Variability and for Production of Specific Diagnostic Sequences in Fumonisin-Producing Strains of *Fusarium Verticillioides", European Journal of Plant Pathology* 110, 525-532.

Grimm, C. and R. Geisen (1998), "A PCR-ELISA for the Detection of Potential Fumonisin Producing *Fusarium* Species", *Letters in Applied Microbiology* 26, 456-462.

Hazuda, D., *et al.* (1999), "Isolation and Characterization of Novel Human Immunodeficiency Virus Integrase Inhibitors from Fungal Metabolites", *Antiviral Chemistry and Chemotherapy* 10, 63-70.

Hidy, P.H., *et al.* (1977), "Zearalenone and Some Derivatives: Production and Biological Activities", *Advances in Applied Microbiology* 22, 59-82.

Hooker, D.C., A.W. Schaafsma and L. Tamburic-Ilincic (2002), "Using Weather Variables Pre- and Postheading to Predict Deoxynivalenol in Winter Wheat", *Plant Disease* 86, 611-619.

Joffe, A.Z. (1986), *Fusarium Species: Their Biology and Toxicology*, John Wiley and Sons, New York City.

Kohut, G., *et al.* (2009), "N-Starvation Stress Induced *FUM* Gene Expression and Fumonisin Production is Mediated via the HOG-type MAPK Pathway in *Fusarium proliferatum", International Journal of Food Microbiology* 130, 65-69.

Kristensen, R., K.G. Berdal and A. Holst-Jensen (2006), "Simultaneous Detection and Identification of Trichothecene- and Moniliformin-Producing *Fusarium* Species Based on Multiplex SNP Analysis", *Journal of Applied Microbiology* 102, 1071-1081.

Kulik, T., *et al.* (2004), "Development of PCR Assay based on ITS2 rDNA Polymorphism for the Detection and Differentiation of *Fusarium sporotrichioides", FEMS Microbiology Letters* 239, 181-186.

Magan, N. and D. Aldred (2007), "Post-harvest Control Strategies: Minimizing Mycotoxins in the Food Chain", *International Journal of Food Microbiology* 119, 131-139.

Marasas, W.F.O. (1996), "Fumonisins: History, World-wide Occurrence and Impact", In: L.S. Jackson *et al.* (Eds.), *Fumonisins in Food*, Plenum Press, New York, pp. 1-17.

Marasas, W.F.O., P.E. Nelson and T.A. Toussoun (1984), *Toxigenic Fusarium Species: Identity and Mycotoxicology*, The Pennsylvania State University Press, University Park, Pennsylvania

Marr, J.S., and C.D. Malloy (1996), "An Epidemiologic Analysis of the Ten Plagues of Egypt", *Caduceus* 12, 7-24.

Moretti, A., *et al.* (1997), "Diversity in Beuvericin and Fusaproliferin Production by Different Populations of *Gibberella Fujikuroi* (*Fusarium* section *Liseola*)", *Sydowia* 48, 44-56.

Moretti, A., *et al*. (2008), "Cryptic Subspecies and Beauvericin Production by *Fusarium subglutinans* from Europe", *International Journal of Food Microbiology* 127, 312-315.

Muture, B.N., and G. Ogana (2005), "Aflatoxin Levels in Maize and Maize Products During the 2004 Food Poisoning Outbreak in Eastern Province of Kenya", *East African Medical Journal* 82, 275-279.

Nagy, R., É. Táborhegyi, A. Wittner, and L. Hornok (1995), "Mini-Chromosomes in *Fusarium Sporotrichioides* are Mosaics of Dispersed Repeats and Unique Sequences", *Microbiology* 141, 713-719.

Nicholson, P., *et al.* (1998), "Detection and Quantification of *Fusarium Culmorum* and *Fusarium Graminearum* in Cereals Using PCR Assays", *Physiological and Molecular Plant Pathology* 53, 17-37.

Paterson, R.R.M., *et al.* (2000), "A Gene Probe For the Patulin Metabolic Pathway with Potential for Use in Patulin and Novel Disease Control", *Biocontrol Science and Technology* 10, 509-512.

Pel, H.J., *et al.* (2007), "Genome Sequencing and Analysis of the Versatile Cell Factory *Aspergillus niger* CBS 513.88", *Nature Biotechnology* 25, 221–231.

Pfohl-Leszkowicz, A., *et al.* (2002), "Balkan Epidemic Nephropathy and Associated Urinary Tract Tumours: A Review on Aetiological Causes and The Potential Role of Mycotoxins", *Food Additives and Contaminants* 19, 282-302.

Prelusky, D.B. (1994), "Residues of food products of animal origin", In: J.D. Miller and H.L. Trenholm (Eds.), *Mycotoxins in Grain Compounds other than Aflatoxin*, Eagan Press, St. Paul, pp. 404-419.

Richard, J.L. (2007), "Some Major Mycotoxins and their Mycotoxicoses – An Overview," *International Journal of Food Microbiology* 119, 3-10.

Sagaram, U.S., M.V. Kolomiets and W.B. Shim (2006), "Regulation of Fumonisin Biosynthesis in *Fusarium verticillioides*-Maize System", *Plant Pathology Journal* 22, 203-210.

Schmidt-Heydt, M., *et al.* (2008), "Comprehensive Molecular System to Study the Presence, Growth and Ochratoxin – A Biosynthesis of *Penicillium Verrucosum* In

Wheat", *Food Additives and Contaminants Part A – Chemistry Analysis Control Exposure and Risk Assessment* 25, 989-996.

Sugiura, Y., *et al.* (1990), "Occurrence of *Gibberella zeae* Strains that Produce Both Nivalenol and Deoxynivalenol", *Applied and Environmental Microbiology* 56, 3047–3051.

Tan, M.K. and L. Niessen (2003), "Analysis of rDNA ITS sequences to determine genetic relationships among, and provide a basis for simplified diagnosis of *Fusarium* species causing crown rot and head blight of cereals", *Mycological Research* 107, 811-821.

Tóth, B., *et al.* (2008), "Common Resistance of Wheat to Members of the *Fusarium graminearum* Species Complex and *F. culmorum*", *Plant Breeding* 127, 1-8.

Wiebe, L.A., and L.F. Bjeldanes (1991), "Fusarin C, a Mutagen from *Fusarium moniliforme* Grown on Corn", *Journal of Food Sciences* 46, 1424-1426.

Yu, J.J., *et al.* (2008), "*Aspergillus Flavus* Genomics as a Tool for Studying the Mechanism of Aflatoxin Formation", *Food Additives and Contaminants Part A – Chemistry Analysis Control Exposure and Risk Assessment* 25, 1152-1157.

Chapter 13

Food without Zoonotic Agents: Fact or Fiction?

Jaap A. Wagenaar

Department of Infectious Diseases and Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, the Netherlands

Central Veterinary Institute, Lelystad, The Netherlands

Danilo M.A. Lo Fo Wong

Department of Food Safety and Zoonoses, Health Security and the Environment, World Health Organization, Geneva, Switzerland

and

Arie H. Havelaar

Laboratory for Zoonoses and Environmental Microbiology, Centre for Infectious Diseases Control Netherlands, National Institute for Public Health and the Environment, Bilthoven, the Netherlands

Division of Veterinary Public Health, Institute for Risk Assessment Sciences, Utrecht University, Utrecht, the Netherlands

Over the last decades considerable investment has been made to produce safe food. In many industrialised countries food is safer than ever before due to continuous efforts, but this can never be taken for granted. Some existing microbiological food safety problems still remain a challenge; well-known pathogens may be transmitted by hitherto unknown vehicles and new pathogens will continue to emerge. Many factors influence the changing epidemiology of pathogens and their emergence is only partly predictable or explainable. The majority of foodborne pathogens have their reservoir in the animal population. Therefore, one of the keys for future preparedness to detect new trends, to implement control measures and to predict the effect of interventions is intersectoral collaboration between animal health, the food sector and public health.

Introduction

Zoonotic diseases are a group of infectious diseases that are naturally transmitted between vertebrate animals and humans (*www.who.int/topics/zoonoses/en/*). A literature search showed that more than 800 human pathogens are zoonotic (Taylor *et al.*, 2001; Woolhouse and Gowtage-Sequeria, 2005). The majority of these infections originate from wildlife. Transmission to humans may occur through a variety of transmission routes including food, the environment, and direct animal contact. Secondary spread may occur through human-to-human transmission. Foodborne zoonotic diseases are a public health concern worldwide (Anonymous, 1984).

Certain zoonotic pathogens have been well known for a long time and are still a persisting problem in many areas of the world. Examples of these pathogens are non-typhoidal *Salmonella* (*e.g. S. Enteritidis, S. Typhimurium*), *Brucella* spp., and *Bacillus anthracis*. Examples of pathogens that were detected relatively recently (the last third of the 20th century) are *Campylobacter* spp. (causing mainly gastro-intestinal problems but also neurological and rheumatological disorders in humans), *E. coli* O157 (causing diarrhoea in humans and HUS – Hemolytic Uremic Syndrome – mainly in children), and Transmissible Spongiform Encephalopathy (the BSE prion in cattle as cause of the variant Creutzfeldt–Jakob disease in humans).

Zoonotic pathogens that have been detected recently are referred to as emerging zoonoses. According to the definition given by World Health Organization (WHO) these are "zoonoses that are newly recognised or newly evolved, or that have occurred previously but show an increase in incidence or expansion in geographic, host, or vector range" (Anonymous, 2004). Over the last 20 years, 73% (114/156) of all emerging human infections are zoonotic (Taylor *et al.*, 2001). The emerging zoonoses are a major concern as they pose a significant burden on global economies and public health. A recent example of an emerging zoonosis originating from wildlife and spreading rapidly through the human population in various parts of the world is SARS (Drosten *et al.*, 2003). In addition to the threat of the emerging infectious diseases, pathogenic organisms resistant to antimicrobials continue to emerge, caused by both human and non-human antimicrobial usage, leading to increased morbidity and mortality through treatment failure.

The global burden of foodborne diseases is largely unknown. Virtually no data on morbidity and mortality of foodborne diseases exist in large areas of the world. The WHO has recently launched a new initiative to estimate the burden of foodborne diseases on a global scale (Stein *et al.,* 2007).

Control of infectious diseases

Several foodborne infectious diseases have been successfully controlled over the last century, in particular in industrialised countries. Data from the USA shows that five pathogens that were major causes of foodborne disease before 1900 (*Brucella* spp., *Clostridium botulinum*, *Salmonella* Typhi, *Trichinella* spp. and toxigenic *Vibrio cholerae*) account for only 0.01% of the disease cases and less than 1% of the deaths in 1997 (Tauxe, 2002). This reduction over time can be explained by the implementation of general and specific control measures. In general, the improvement of sanitation (municipal water supply, sewage systems) has contributed enormously to the control of

infectious diseases. Pasteurisation of milk and other food products has reduced tuberculosis and brucellosis in humans. Control measures along the food chain (pre- and post-harvest) have reduced the burden of foodborne diseases. The consequences of a failing control system are illustrated by the biggest *Salmonella* Typhimurium outbreak ever reported that happened in Illinois (USA) in 1985. It was estimated that between 168 791 and 197 581 people were affected (Ryan *et al.*, 1987) due to a *Salmonella* contamination in a single production plant.

Besides the success-stories on aforementioned pathogens, other pathogens like *Campylobacter* spp. are much harder to control (Wagenaar *et al.*, 2006). Also, we have to realise that the implementation of effective control measures for foodborne diseases is usually reported from industrialised countries. Due to economic and logistic constraints implementation of interventions in developing countries is much more difficult.

(Re)emerging infectious diseases

The change in epidemiology and (re)emergence of foodborne pathogens is influenced by many factors (Todd, 1997; Havelaar *et al.*, 2010). A selection is listed below.

International trade and travel: there is a growing international trade of food. This may facilitate the spread of infectious agents and antimicrobial resistance around the globe. Outbreaks with a common contamination may occur in several countries at the same time. Increasing travel of people increases the risk of acquiring "foreign" pathogens (Sirichote *et al.*, 2010). People may come in contact with organisms to which they have not been exposed earlier and are immunologically naive. For *Campylobacter* these aspects of immunity have been reviewed (Havelaar *et al.*, 2009).

Changing consumer lifestyles, habits and demands: compared with the situation in the second half of the 20th century, consumers chose increasingly fresh, minimally processed or ready-to-eat foods. These food items pose a greater risk for foodborne diseases (*e.g. Listeria* and *Yersinia* in ready-to-eat foods kept in the refrigerator, sporeforming micro-organisms that survive minimal processing).

Susceptibility of hosts: the number of people with an impaired immune system is increasing due to the further developed life saving health care of premature children and the increase of the population of elderly (Ohlsen and Hacker, 2005). This will lead to an increased susceptible fraction of the population.

Changing animal production systems: starting in the 1950s animal production systems changed into more large-scale indoor kept animals. From a biosecurity point of view (prevention of contact with wild animals, prevention of pathogen introduction) this was a positive development. However, increased attention to animal welfare and focus on sustainable production systems have led to more extensive farming and organic production. These systems have more outdoor production and potential contact with wildlife with consequently the re-introduction of *e.g. Trichinella spiralis* and *Toxoplasma gondii* (Kijlstra *et al.*, 2009). In poultry almost all flocks with outdoor access are colonised with *Campylobacter* spp., whereas for poultry kept in more biosecure housing systems the prevalence of *Campylobacter* colonised flocks is lower (Näther *et al.*, 2009)

Improved diagnostics: some pathogens were previously not detected due to the lack of detection methods. One example is *Campylobacter*, a pathogen that was most probably "always" present but only detected in human stools after the development of sensitive and selective detection media in the 1970s (Butzler, 2004). Even with the same occurrence of

pathogens, the introduction of improved diagnostic assays can suggest an increased prevalence of disease.

Changing microbes: not only is the world around the microbes changing but also the microbes themselves. Verotoxin containing *E. coli* (*e.g. E. coli* O157) is an example of a pathogen that evolved from an *E. coli* after acquiring additional virulence traits (verotoxic genes) resulting in a pathogen causing severe disease. Another example is the worldwide alarming increase in antimicrobial resistance in bacterial pathogens. This development is the result of the use of antimicrobials in animals and humans. As this is a major risk for public health, the prudent use of antimicrobials must be advocated.

Climate change: the association of climate change and the changing epidemiology of infectious diseases is extremely complex. Changes in water supply (shortage *versus* floodings) can have a huge impact on the food supply and contamination of food and therewith on the epidemiology of pathogens.

Challenges in the control of foodborne diseases

The reason why, when and where formerly unknown pathogens are introduced into the human population is influenced by a large and complex set of factors. Therefore, the (re)emergence of pathogens seems to be rather unpredictable. However, an analysis of 335 emerging infectious diseases between 1940 and 2004 showed that the emergence is a non-random process. There is an association with socio-economic, environmental and ecological factors (Jones *et al.*, 2008). This analysis provides the basis for the identification of regions where emerging infectious diseases are most likely to originate ("hot-spots"). Newly developed tools (*e.g.* molecular typing, predictive mathematical modelling, and understanding of adaptation of microbial pathogens) may identify risks more precisely and support risk assessment of pathogens (Havelaar *et al.*, 2010).

Although theoretical science-based predictions are of great value, the monitoring of contamination in the food chain, combined with surveillance of human illness and epidemiological investigations of outbreaks and sporadic cases continue to be important. Monitoring and surveillance provide data on (changing) trends, have an early warning function and will potentially detect emerging infections.

International co-operation and communication

International co-operation and communication are essential to develop an effective control strategy for foodborne diseases. International organisations (*i.e.* WHO, FAO, and the World Organisation for Animal Health (OIE)) have developed supranational information systems for the detection and timely reporting of infectious diseases and contaminants. These systems include the International Health Regulations (IHR) (human infectious diseases), the International Food Safety Authorities Network (INFOSAN) (food contamination) and The Global Early Warning and Response System (GLEWS) (major animal diseases, including zoonoses). As there is a major threat from the animal reservoir for (re)emerging zoonoses, the collaboration between the veterinary sector, food sector, and public health are crucial in addressing zoonotic risks (Newell *et al.*, 2010).

An integrated approach to food safety and zoonoses: global foodborne infections network

Due to the nature of zoonotic infections in animals and contamination of foods, visual inspection is not enough to prevent the spread of infection between animals and to ensure safe food and ingredients. Laboratory-based surveillance of animals, food and humans is important, both to detect and prevent foodborne pathogens from entering or spreading through the food chain, as well as to identify foodborne disease outbreaks so that appropriate control measures can be taken.

Many countries still lack the necessary surveillance capacity for outbreak detection and response. In addition, foodborne disease outbreaks go undetected, in part due to lack of communication between the human, veterinary, and food sectors. Due to the globalisation of animal and food trade, national issues can have global implications. It is, therefore, imperative that countries are able to detect and deal with clusters of foodborne pathogens and disease.

In 2000, WHO initiated WHO Global Salm-Surv (GSS), now called Global Foodborne Infections Network (GFN), to enhance countries' capacities to conduct integrated surveillance for foodborne and other enteric infections from the farm to the table. Recognising that zoonotic risks require multi-sectoral co-operation and strong partnerships with strong linkages between human and animal detection and response systems, GFN promotes integrated, laboratory-based surveillance, and fosters intersectoral collaboration and communication among microbiologists and epidemiologists in human health, veterinary, and food-related disciplines.

Conclusion

We conclude that food production systems are continuously challenged by existing and (re)emerging pathogens. Food production should aim for safe products but the reality dictates that zero risk is non-existent. Therefore monitoring and surveillance systems should be in place worldwide to detect and respond to food safety events. Implementation of these systems is required to reduce the burden of foodborne diseases in developing and industrialised countries.

Bibliography

Anonymous (1984), World Health Organization, "The Role of Food Safety in Health and Development: Report of a Joint FAO/WEHO Expert Committee on Food Safety", *WHO Technical Report Series*, no 705. Geneva: The Organization; 1984.

Anonymous (2004), "Report of the WHO/FAO/OIE Joint Consultation on Emerging Zoonotic Diseases", 3-5 May 2004, Geneva, Switzerland.

Butzler, J.P. (2004), "Campylobacter, from Obscurity to Celebrity", *Clinical Microbiology and Infection* 10:868-876.

Drosten, C., *et al.* (2003), "Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome", *The New England Journal of Medicine* 348:1967-1976.

Havelaar, A.H, *et al.* (2009), "Immunity to *Campylobacter*: its Role in Risk Assessment and Epidemiology", Critical Reviews in Microbiology 35:1-22.

Havelaar, A.H., *et al.* (2010), "Future Challenges to Microbial Food Safety", *International Journal of Food Microbiology 2009, Oct 23*, (Epub ahead of print) PubMed PMID: 19913933.

Jones, K.E., *et al.* (2008), "Global Trends in Emerging Infectious Diseases", *Nature* 451:990-993.

Kijlstra, A., B.G. Meerburg and A.P. Bos (2009), "Food Safety in Free-Range and Organic Livestock Systems: Risk Management and Responsibility", *Journal of Food Protection* 72:262926-37.

Näther, G., *et al.* (2009), "Analysis of Risk Factors for Campylobacter Species Infection in Broiler Flocks", *Poultry Science* 88:1299-1305.

Newell, D.G., *et al.* (2010), "Food-borne Diseases - The Challenges of 20 Years Ago Still Persist While New Ones Continue to Emerge", *International Journal of Food Microbiology*, 2010 Jan 22, [Epub ahead of print].

Ohlsen, K. and J. Hacker (2005), "Infections in Elderly", *International Journal of Medical Microbiology* 294:471-472.

Ryan, C.A., *et al.* (1987), "Massive Outbreak of Antimicrobial-Resistant Salmonellosis Traced to Pasteurised Milk", *JAMA* 258:3269-74.

Sirichote, P., *et al.* (2010), "Molecular Characterization of Extended-Spectrum Cephalosporinase-Producing *Salmonella Enterica* Serovar Choleraesuis Isolates from Patients in Thailand and Denmark", *Journal of Clinical Microbiology* 48:883-888.

Stein, C., *et al.* (2007), "The Global Burden of Disease Assessments-WHO Is Responsible?", *PLoS Neglected Tropical Diseases* 1, e161.

Tauxe, R.V. (2002), "Emerging Foodborne Pathogens", *International Journal of Food Microbiology* 78:31-41.

Taylor, L.H., S.M. Latham and M.E. Woolhouse (2001), "Risk Factors for Human Disease Emergence", *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences* 356:983-989.

Todd, E.C.D. (1997), "Epidemiology of Foodborne Diseases: a Worldwide Review", World Health Stat. Q. 50:30-50.

Wagenaar, J.A., D.J. Mevius and A.H. Havelaar (2006), "*Campylobacter* in Primary Animal Production and Control Strategies to Reduce the Burden of Human Campylobacteriosis", *Rev Sci Tech*. 25:581-94.

Woolhouse, M.E. and S. Gowtage-Sequeria (2005), "Host Range and Emerging and Reemerging Pathogens", *Emerging Infectious Diseases* 11:1842-7.

Chapter 14

Altering Foods Derived from Animals for the Future?

Stefaan De Smet

Laboratory for animal production and animal product quality
Ghent University, Belgium

Breeding and feeding of food-producing farm animals has long been mainly oriented to maximising production efficiency. High-yielding dairy cattle and layers produce nowadays cheap milk and eggs respectively, and fast-growing pigs, broilers and beef cattle provide us with lean meat. However, the transition from a producer-driven to a consumer-oriented market forces the animal industry to pay more attention to the sensory and technological properties and the health value of their products. The immense ongoing research on improving the fatty acid composition of animal products mainly through altered feeding strategies is a good example thereof. In monogastric animals, the potential of nutrition for steering the fatty acid composition of raw meats and eggs is now relatively well established, whereas in ruminants the fatty acid metabolism is more complex as a result of the rumen processes. The potential of animal genetics for modifying the fat content and the fatty acid composition of animal products should also be further explored. Animal products are also safe carriers of essential trace elements and other nutrients, and more research for upgrading the value of animal products in this respect is warranted. The effects of altering the composition and properties of raw animal products on the sensory quality and the health value of the end products should be better established. In particular, human intervention studies are required to evaluate the impact on human health of consuming animal products. Overall, a cost-benefit evaluation of the potential contribution of altering raw animal products to improving the health of consumers should be made. It is evident that this requires a fork-to-farm chain approach, taking into account the needs of the animals, the farmers, the food processing industry and the end consumer.

Decrease production and consumption of animal-derived foods or alter their composition?

Foods derived from farm animals (meats, milk and eggs) contribute significantly to the intake of energy and nutrients and to the taste and enjoyment of meals (Hulshof *et al.*, 1999; Givens, 2005; Wood *et al.*, 2008). The livestock sector is also a dynamic part of the agricultural economy supporting the livelihoods of many families and in particular the poorest households in developing countries (Delgado *et al.*, 1999; FAO, 2009). On the other hand, animal production is increasingly criticised for its possible contribution to the burden of chronic diseases, for its negative environmental impact and for compromising animal welfare (Pimentel and Pimentel, 2003; McMichael *et al.*, 2007; Michaelowa and Dransfeld, 2008). However, there are very large differences among societies in the level of consumption of animal-derived foods and in the types and characteristics of the prevailing animal production systems. Consequently the impact of the production and consumption of animal-derived foods on human health and on the environment is diverse (Delgado *et al.*, 1999; Steinfeld *et al.*, 2006; FAO, 2009). For example, the current global average meat consumption is 100 g per person per day, with about a ten-fold variation between high-consuming and low-consuming populations (McMichael *et al.*, 2007; FAO, 2009). It is expected that the demand for animal-derived foods will continue to grow strongly in the coming decades, especially in the developing countries, driven by increasing purchasing power, population growth and urbanisation (FAO, 2009). A much smaller increase is projected for the OECD countries. This growing demand in developing countries implies challenges in terms of efficient use of natural resources, managing animal- and human-health risks, environmental sustainability, poverty reduction and ensuring food security (FAO, 2009). One of the ten universal guidelines for healthy nutrition in a report of the World Cancer Research Fund released end of 2007 was to "limit intake of red meat and avoid processed meat", as a result of the "convincing evidence" for an association with an increased risk of colorectal cancer development (WHO, 2007). An international contraction and convergence strategy with a reduction of the average worldwide consumption level of animal products has been suggested to counteract the risks associated with the growth in meat consumption (McMichael *et al.*, 2007). It is beyond the scope of the present manuscript to discuss these global perspectives, but it must be clear that this is a very important yet also complex issue. For example, the question if the use of feeds for animal production reduces the availability of food for human consumption is not easy to answer and involves both physical and economic dimensions. It is felt that one global policy is neither possible nor desirable.

Another option for animal production to meet changing consumer demands lies in developing strategies to improve the health value and sensory quality of animal-derived foods, taking at the same time other sustainability issues into account. It is clear that meeting these different criteria simultaneously will be a difficult task. Animal product quality comprises sensory, technological, nutritional, microbiological and chemical-toxicological characteristics. Each of these characteristics is determined by several factors, *i.e.* animal genetics, husbandry and feeding factors, harvesting conditions, processing factors, etc. (Hocquette and Gigli, 2005). The management of these factors determines the direct, intrinsic quality of the product and the indirect quality of the production system, *i.e.* the impact of animal-derived food production on the environment, animal welfare and worldwide food security. Furthermore, livestock production systems range from extensive systems that mainly rely on herbivore ruminants exploiting grasslands with few external inputs to intensive so-called landless systems in which feeds are converted to animal-derived foods using considerable amounts of external inputs

(Steinfeld *et al.*, 2006). Again, to alter animal-derived foods one single approach is not feasible. Some examples will therefore be given to illustrate the potential and limitations of this approach.

Gross composition of animal products

Much of the criticism on the impact of the consumption of animal-derived foods on human health stems from the fat content and the fatty acid composition of these food commodities (Givens, 2005). Although meats, milk and eggs and the products derived thereof are primarily sources of protein of high nutritional value, they do also contain variable amounts of fat. On a fresh matter basis, the total fat content of raw milk and eggs is approximately 4% and 9% respectively, whereas the protein content is approximately 3.5% and 12.5% respectively. In meat cuts devoid of external fat, the protein content is relatively constant at approximately 19% on a fresh matter basis, whereas the fat content is more variable. The fat content of fresh meat is generally low, between 1% and 2.5%, but may be higher too, depending on species, muscle, nutrition etc. (Chizzolini *et al.*, 1999). However, the fat content of carcasses is higher with again large variability among and within species and breeds. Fat depots are removed from carcasses during cutting but are to a variable extent used in the processing of meat products. Hence, whereas fresh meat is relatively lean containing only intra- and intermuscular fat, the fat content of meat products may vary strongly and be as high as over 30% (Chizzolini *et al.*, 1999). Processing easily allows to separate protein and fat in raw milk and to use these fractions in variable proportions during food processing, yielding products with a wide protein to fat ratio. The yolk and white of eggs can also be separated easily, with the yolk containing almost all the egg fat and both the egg white and yolk yielding protein for food processing purposes. Processing of raw animal-derived foods thus offers a lot of opportunities to steer the composition of the final food products. However, most of the animal fat from raw animal-derived materials is used somehow in the food industry. The relatively large fat content of carcasses, raw milk and eggs, thus contributes significantly to the overall average energy intake in populations with a large consumption of these products and processed products derived thereof. Of course, the individual consumer has a large choice among the type of products in terms of composition and nutritional quality. A key question therefore is to what extent efforts should be made in the animal industry to alter products compared to technological alternatives in the processing industry.

Because the demand for animal protein has been growing at the expense of animal fat, there has been for a long time and there is still a large interest in the animal industry to change the fat and protein content of animal produce towards increasing the protein to fat ratio, at least in meat- and milk-producing animals. Quantitative animal genetic selection has been successfully applied for this purpose in meat producing animals. Muscle protein accretion and body fat accretion in growing animals are negatively genetically correlated, hence it has been possible to select for animals with a high body protein to fat content (Sellier, 1998). In addition, the efficiency of feed to food conversion is higher in the case of protein deposition versus fat deposition. Lean animals do consume less feed than fat animals. Since feed costs are the major cost item in most animal production systems, the economic incentive to genetically select for lean meat producing animals and to optimise feeding systems in terms of balancing nutrient supplies for fat and lean muscle accretion has been great. The Piétrain breed is an example of an extremely lean breed of pigs. The carcass fat to lean ratio in this breed dropped from 0.49 to 0.19 between 1970 and 2000 (Roehe *et al.*, 2003). In milk it appears much more difficult to steer the fat to protein ratio

because of a positive, unfavourable genetic correlation between the fat and protein concentration of milk. Although nutrition offers some potential in this respect, the fat to protein ratio of milk has not dramatically changed over the last decades.

New genetic selection approaches needed

Classical breeding programmes in farm animals have been very effective in many ways, and although there is still room for progress, it seems that this type of selection starts to face its limits (Rauw *et al.*, 1998). Not only is progress levelling off, side-effects of mass selection for animal productivity are also appearing, such as reduced animal fertility, increased prevalence of metabolic disorders and problems with intrinsic product quality. One example is the very low intramuscular fat content of lean meats, reducing the flavour and juiciness of cooked meats. Muscle cuts from very lean animals also seem to have reduced suitability for processing. The incidence of PSE meat (pale, soft and exudative meat) is higher in very lean pigs and modern broilers resulting in more quality defects upon transformation to high quality cooked products. The use of additives during processing may overcome part of these problems, but this is not always allowed or desired in case of high quality or minimally processed products. Theoretically, it is possible to include specific quality traits in breeding objectives. Intramuscular fat content and eating quality traits such as tenderness have a moderately high to high heritability (Sellier, 1998). However, product quality traits except for milk gross composition are generally not included in breeding objectives for several reasons. One exception is several decades of selection for meat quality in Swiss pig breeding (Schwörer *et al.*, 1994). For meat quality traits, there is still a lack of methods that allow measuring different traits on a large number of animals in a sufficiently fast, cost-effective and accurate way. In addition, there are often opposite conflicts of interest in the meat chain in terms of the economic value for animal performance traits compared to meat quality traits. Finally, meats are much more heterogeneous compared to milk and eggs because they are derived from many different muscles that vary in their composition and biochemical characteristics. This hampers the assessment of the meat quality of carcasses. Conventional animal genetic selection and management strategies will not be able to solve these issues. The implementation of new molecular-genetic technologies may offer perspectives in this respect, and their potential should at least be investigated. While allowing further progress in terms of overall animal productivity to be made, these tools should enable to steer tissue-specific expression of traits, *e.g.* to produce lean carcasses with higher intramuscular fat content and improved eating quality. However, there is still much research needed before this becomes feasible.

Fatty acid composition of animal-derived foods

Apart from the gross composition, the nutrient composition of animal-derived foods is also a matter of intense debate and research. Whereas the amino acid profile of animal products is relatively conserved and difficult to modify, the fatty acid composition of animal products is dependent on both the genetic determination of fat metabolism and the dietary fatty acid composition (De Smet *et al.*, 2004; Raes *et al.*, 2004; Givens, 2005). Animal fats strongly differ in fatty acid composition, but are generally considered too high in saturated and too low in polyunsaturated fatty acids (Givens and Shingfield, 2004; Wood *et al.*, 2003 and 2008). On the other hand, apart from the major supply by fish consumption, meats and eggs are the sole source of long-chain n-3 polyunsaturated fatty

acids, of which the intake is far below the recommended levels in many industrialised countries (Givens and Gibbs, 2008). In addition, products from ruminants do contain a lot of minor fatty acids such as trans fatty acids, conjugated linoleic and α-linolenic fatty acids and odd- and branched-chain fatty acids, resulting mainly from rumen microbial biohydrogenation and metabolism (Jensen, 2002; Vlaeminck *et al.*, 2006). The human health effects of these individual fatty acids are still unclear and will differ for each of these specific fatty acids. Consequently, the effects of the regular intake of foods containing these fatty acids are also not fully established at present.

The contribution of food items to the intake of total and specific fatty acids is the resultant of the food item intake, its fat content and its fatty acid profile (De Henauw *et al.*, 2007; Gibbs *et al.*, 2009). Meats strongly differ in fat content and fatty acid profile, dependent on the animals' potential for fat deposition and fatty acid metabolism, and the dietary fatty acid supply. The source and content of dietary fat, and the duration and time of feeding all affect meat fatty acid composition. Monogastric animals are particularly responsive to changes in the dietary fat supply. There is abundant literature on the effect of α-linolenic acid supply on the n-3 polyunsaturated fatty acids content of meats (Raes *et al.*, 2004; Wood *et al.*, 2008). Within the range of currently applied dietary fat levels, linear relationships are generally found between the supply of α-linolenic acid and the total n-3 polyunsaturated fatty acids content of meats. However, the elongation and desaturation to long-chain n-3 polyunsaturated fatty acids is limited, requiring the direct supply by fish oil or marine algae to obtain a meaningful increase in the content of long-chain n-3 polyunsaturated fatty acids. Adding (long-chain) n-3 polyunsaturated fatty acids to the diets of pigs and poultry at modest inclusion rates significantly increases the contribution of meats from these animals to the human intake of long-chain n-3 polyunsaturated fatty acids at the current levels of meat intake (Raes *et al.*, 2002; Raes *et al.*, 2004; Rymer and Givens, 2005). Because the use of fish oil for farm animal feeding is not sustainable in the long term, there is now increasing interest in the use of marine algae that are the primary producers of long-chain n-3 polyunsaturated fatty acids and that may be cultivated (Boeckaert *et al.*, 2008; Gibbs *et al.*, 2009). These are feasible and worthwhile feeding strategies that have no negative impact on animal performances and welfare, and that may be beneficial to human health.

In ruminants, steering the fatty acid composition of products is more complex compared to monogastrics because of the rumen fatty acid metabolism. Rumen lipolysis and biohydrogenation of polyunsaturated fatty acids results in a more saturated fatty acid profile with also the formation of a lot of intermediates as mentioned above. To increase the polyunsaturated fatty acids content of ruminants' meats and milk, feeding strategies need to be developed to bypass these rumen processes. Feeding "rumen-protected" polyunsaturated fatty acids-rich oils has been successfully applied, but the search for safe and effective methods continues (Scollan *et al.*, 2006). The type of forage fed to ruminants also has an effect on the fatty acid profile. Forages with a higher botanical diversity, *e.g.* by the presence of clover, affects the fatty acid profile favourably compared to intensive ryegrass (Lourenço *et al.*, 2007).

There is also significant genetic variation for fatty acid deposition and metabolism. In milk, there is considerable genetic variation for the major fatty acids (Soyeurt *et al.*, 2007). Similarly, in pigs and beef cattle, moderate to high heritabilities were found for the proportions of intramuscular polyunsaturated fatty acids. This offers opportunities for genetic selection. However, the phenotypic and genetic correlations between the proportions of polyunsaturated fatty acids in meat and carcass lean meat content or intramuscular fat content are negative (De Smet *et al.*, 2004). Mass selection for lean

carcasses thus results in higher proportions of polyunsaturated fatty acids in meats. On the other hand, this is accompanied by lower levels of intramuscular fat, reducing the polyunsaturated fatty acids content in a meat portion and hence also the contribution to human intake. Further lowering the intramuscular fat of pork is also not warranted because of the negative impact of too low levels of intramuscular fat on the taste of meat. As mentioned above more generally, it seems that molecular-genetic approaches will be required to differentially affect the levels of carcass and intramuscular fat, and to steer the fatty acid composition favourably at the same time. As an example, the functional expression of a delta-12 fatty acid desaturase gene from spinach in transgenic pigs was reported by Saeki *et al.* (2004), resulting in levels of linoleic acid that were approximately 10-fold higher in adipocytes differentiated in vitro and approximately 20% higher in backfat in vivo. This was the first time a plant gene was expressed in a complex mammalian system. The generation of cloned pigs that express a humanised *Caenorhabditis elegans* gene, fat-1, encoding an n-3 fatty acid desaturase is also reported (Lai *et al.*, 2004). Alternatively, research is going on to create transgenic oilseeds that are able to synthesize long-chain (C chain $\geq$ 20) polyunsaturated fatty acids. These long-chain derivatives are normally absent in all agronomically important plants. Hence, different approaches may become available in the long term to improve the supply of long-chain n-3 polyunsaturated fatty acids. It remains to be evaluated which approach offers the best potential in terms of improving human health and has the greatest chance of being successfully implemented.

Side-effects of improved fatty acid composition

Altering the fatty acid composition of meats, milk and eggs may have an impact on other quality traits, in particular on the oxidative stability, shelf-life and taste (Havemose *et al.*, 2004; Scollan *et al.*, 2006; Wood *et al.*, 2008). Long-chain polyunsaturated fatty acids are more prone to radical induced peroxidation than less unsaturated fatty acids. Peroxidation of polyunsaturated fatty acids reduces the nutritional value and results in the formation of harmful oxidation products. These oxidation products also contribute to rancid off-flavours. Fish oil in the diet of farm animals above certain levels may lead to a fishy taste and reduced shelf-life of the products. At low levels, these negative side-effects of enrichment with long-chain n-3 polyunsaturated fatty acids may be absent and may be controlled by the use of antioxidants in the diets and by appropriate storage and packaging conditions. The use of α-linolenic acid rich ingredients in the diet of farm animals increases the level of n-3 polyunsaturated fatty acids in the products, with however modest increases in the long-chain n-3 polyunsaturated fatty acids. These products do not or much less suffer from rancid off-flavours (Smet *et al.*, 2009). Processed meat products, particularly fat-rich fermented meat products, are much more sensitive to oxidative deterioration compared to fresh meats. High levels of antioxidants added to the diet of the animals or during processing are able to retard oxidative rancidity (Decker *et al.*, 2000), but do not allow the off-flavours to be overcome in cases where animals were fed high levels of fish oil. High levels of vitamin E in the diet of animals are very effective in retarding lipid and colour oxidation (Decker *et al.*, 2000; Wood *et al.*, 2008). There is currently large interest in the role of antioxidants and other minor compounds that are naturally present in feeds or that may be added during processing on oxidative stability and meat quality in general. However, more work is required in this area to produce meat and meat products with an improved composition without compromising sensory quality.

Altering the content of other minor compounds in animal-derived foods

In addition to altering the fatty acid composition of animal products in line with human dietary recommendations, animal products are also carriers of essential micro-nutrients. Milk is a good source of calcium (Ca), and meats are good sources of Fe, manganese (Mn), Zn and Se (Givens, 2005). All animal products are natural sources of vitamin B12. As for the essential fatty acids, the intake of some essential trace elements is below the recommended intake. The potential to enrich animal products by including higher levels of these trace elements in the diet of animals will differ according to the element and will depend on the source and concentration in the diet, interaction with other feed components and the food item that is considered. The flux of trace elements through the body is generally well regulated. Major sites of homeostatic regulation are absorption for Zn, Fe, copper (Cu) and Hg, and urinary excretion for Se and I (Windisch, 2002). This means that increasing the levels of Se and I in meats, milk and eggs is easier to accomplish than for other elements. The source of the element is also important. The use of an organic source of Se (Se containing yeast protein) compared to inorganic Se results in a substantially higher transfer efficiency of Se from diet to milk, and thus in levels of Se in milk that may alleviate part of the deficiencies (Givens *et al.*, 2004). The meat of pigs was enriched in I by including the brown seaweed *Ascophyllum nodosum* in the feed (Dierick *et al.*, 2009). These brown algae are also a source of bioactive polysaccharides that may function as alternatives to nutritional antibiotics and improve gut health of pigs. This example shows that the search for novel, natural feed ingredients that are beneficial to the health of both humans and animals should be continued.

Conclusions and additional considerations

It is clear that animal-derived foods are an important source of nutrients in the diet. On the other hand, there are also concerns about the fatty acid composition of these products not being in line with human dietary recommendations. However, the fatty acid composition of these foods is not constant and can be enhanced by animal nutrition. Nutrition strategies offer the largest potential, but molecular-genetic approaches should also be considered. The role of animal nutrition in creating foods with increased levels of other beneficial minor compounds also needs further investigation. In general, meats can be considered as a safe but more resistant product to modify compared to milk and eggs. Optimising the eating quality of meats is another permanent concern that needs to be tackled at all levels of the production chain.

To allow successful introduction of meats, milk and eggs in the market with an improved nutrient composition, human intervention studies are needed that examine the effect of intake of these foods on human metabolic parameters. Only a few studies are available in this respect, but there are indications that altered animal-derived foods may indeed have a positive impact on health indicators (Noakes *et al.*, 1996; Weill *et al.*, 2002). More generally, cost-benefit analyses are required to evaluate altering the nutrient profile of various types of animal-derived foods by breeding and feeding strategies versus approaches at the level of the food processing industry or public health services. Enhancing the nutrient profile of animal products by novel feeding strategies is less versatile compared to processing strategies. The outcome is also less standardised and the allocation of the added value in the production chain is sometimes questionable. On the other hand, this approach has also some clear advantages. It is a natural approach that

may be easily accepted by consumers. There is no shift in the eating pattern required. There is generally no risk of overdosing compared to the direct intake of supplements. Finally, it may offer added-value to primary producers.

Bibliography

Boeckaert, C., *et al.* (2008), "Effect of Dietary Starch or Micro Algae Supplementation on Rumen Fermentation and Milk Fatty Acid Composition of Dairy Cows", *Journal of Dairy Science*, Vol. 91, pp. 4714-4727.

Chizzolini, R., *et al.* (1999), "Calorific Value and Cholesterol Content of Normal and Low-Fat Meat and Meat Products", *Trends in Food Science and Technology*, Vol. 10, pp. 119-128.

Decker, E.A., C. Faustman and C.J. Lopze-Bote (eds.) (2000), *Antioxidants in Muscle Foods*, Wiley Interscience, New York.

De Henauw, S., *et al.* (2007), "Response to n-3 Fatty Acid Enrichments of Foods From Animal Origin", *Journal of the Science of Food and Agriculture*, Vol. 87, pp. 200-211.

De Smet, S., K. Raes and D. Demeyer (2004), "Meat Fatty Acid Composition as Affected by Fatness and Genetics Factors: A Review", *Animal Research*, Vol. 53, pp. 1-18.

Delgado, C., *et al.* (1999), "Livestock to 2020, The Next Food Revolution", Food, Agriculture, and the Environment Discussion Paper 28.

Dierick, N., A. Ovyn and S. De Smet (2009), "Effect of Feeding Intact Brown Seaweed Ascophyllum Nodosum on Some Digestive Parameters and on Iodine Content in Edible Tissues in Pigs", *Journal of the Science of Food and Agriculture*, Vol. 89, pp. 548-594.

Food and Agriculture Organization of the United Nations (2009), "The State of Food and Agriculture, Livestock in the balance", Rome.

Gibbs, R.A., C. Rymer and D.I. Givens (2009), "Long-Chain n-3 PUFA: Intakes in the UK and the Potential of a Chicken Prototype to Increase Them", *Proceedings of the Nutrition Society*, Conference on "Over- and Undernutrition: Challenges and Approaches", pp. 1-12.

Givens, D.I. (2005), "The Role and Animal Nutrition in Improving the Nutritive Value of Animal-Derived Foods in Relation to Chronic Disease", *Proceedings of the Nutrition Society*, Vol. 64, pp. 395-402.

Givens, D.I. and K.J. Shingfield (2004), "Foods Derived from Animals: The Impact of Animal Nutrition on their Nutritive Value and Ability to Sustain Long-Term Health", *British Nutrition Foundation Nutrition Bulletin*, Vol. 29, pp. 325-332.

Givens, D.I., E.K. Kliem and R.A. Gibbs (2006), "The Role of Meat as a Source of n-3 Polyunsaturated Fatty Acids in the Human Diet", *Meat Science*, Vol. 74, pp. 209-218.

Givens, D.I., *et al.* (2004), "Enhancing the Selenium Content of Bovine Milk Through Alteration of The Form and Concentration of Selenium in the Diet of the Dairy Cow", *Journal of the Science of Food and Agriculture*, Vol. 84, pp. 811-817.

Havemose, M.S., *et al.* (2004), "Influence of Feeding Different Types of Roughage on the Oxidative Stability of Milk", *International Dairy Journal*, Vol. 14, pp. 563-570.

Hocquette, J.F. and S. Gigli (eds.) (2005), *Indicators of Milk and Beef Quality*, EAAP Publication No. 112, Wageningen Academic Publishers.

Hulshof, K.F.A.M., *et al.* (1999), "Intake of Fatty Acids in Western Europe with Emphasis on Trans Fatty Acids: The TRANSFAIR Study", *European Journal of Clinical Nutrition*, Vol. 53, pp. 143-157.

Jensen R.G. (2002), "Invited Review: The Composition of Bovine Milk Lipids: January 1995 to December 2000", *Journal of Dairy Science*, Vol. 85, pp. 295-350.

Lai, L., *et al.* (2006), "Generation of Cloned Transgenic Pigs Rich in Omega-3 Fatty Acids", *Nature Biotechnology*, Vol. 24, No. 4, pp. 435-436.

Lourenço, M., *et al.* (2008), "Influence of Different Dietary Forages on The Fatty Acid Composition of Rumen Digesta as Well as Ruminant Milk and Meat", *Animal Feed Science and Technology*, Vol. 145, pp. 418-437.

McMichael, A.J., *et al.* (2007), "Food, Livestock Production, Energy, Climate Change, and Health", *Lancet*, Vol. 370, pp. 1253-1263.

Michaelowa, A. and B. Dransfeld (2008), "Greenhouse Gas Benefits of Fighting Obesity", *Ecological Economics*, Vol. 66, pp. 298-308.

Noakes, M., P.J. Nestel and P.M. Clifton (1996), "Modifying the Fatty Acid Profile of Dairy Products Through Feedlot Technology Lowers Plasma Cholesterol of Humans Consuming the Products", *American Society for Clinical Nutrition*, Vol. 63, pp. 42-46.

Pimentel, D. and M. Pimentel (2003), "Sustainability of Meat-Based and Plant-Based Diets and the Environment", *American Society for Clinical Nutrition*, Vol. 78 (suppl), pp. 660S-663S.

Raes, K., *et al.* (2002), "The Deposition of Conjugated Linoleic Acids in Eggs of Laying Hens Fed Diets Varying in Fat Level and Fatty Acid Profile", *The Journal of Nutrition*, Vol. 132, pp. 182-189.

Raes, K., S. De Smet and D. Demeyer (2004), "Effect of Dietary Fatty Acids on Incorporation of Long Chain Polyunsaturated Fatty Acids and Conjugated Linoleic Acid in Lamb, Beef and Pork Meat: A Review", *Animal Feed Science and Technology*, Vol. 113, pp. 199-221.

Rauw, W.M., *et al.* (1998), "Undesirable Side Effects of Selection for High Production Efficiency in Farm Animals: A Review", *Livestock Production Science*, Vol. 56, pp. 15-33.

Roehe, R., G.S. Plastow and P.W. Knap (2003), "Quantitative and Molecular Genetic Determination of Protein and Fat Deposition", *Homo*, Vol. 54/2, pp. 119-131.

Rymer, C. and D.I. Givens (2005), "n-3 Fatty Acid Enrichment of Edible Tissue of Poultry: A Review", *Lipids*, Vol. 401, No. 2, pp. 121-130.

Saeki, K., *et al.* (2004), "Functional Expression of a Δ12 Fatty Acid Desaturase Gene from Spinach in Transgenic Pigs", *Proceedings of the National Academy of Sciences of the United States of America*, Vol. 101, No.17, 6361-6366.

Schwörer, D., A. Rebsamen and D. Lorenz (1994), "Twenty years of selection for meat quality in Swiss pig breeding", *Pig News and Information*, Vol. 15, No.2, 63N-66N.

Scollan, N., *et al.* (2006), "Innovations in Beef Production Systems that Enhance the Nutritional and Health Value of Beef Lipids and Their Relationship with Meat Quality", *Meat Science*, Vol. 74, pp. 17-33.

Sellier, P. (1998), "Genetics of Meat and Carcass Traits", in M.F. Rothschild and A. Ruvinsky (eds.), *The Genetics of the Pig* (eds.), pp. 463-510.

Smet, K., *et al.* (2009). "Oxidative Stability of UHT Milk as Influenced By Fatty Acid Composition and Packaging", *International Dairy Journal*, Vol. 19, pp. 372-379.

Soyeurt, H., *et al.* (2007), "Estimation of Heritability and Genetic Correlations for the Major Fatty Acids in Bovine Milk", *Journal of Dairy Science*, Vol. 90, pp. 4435-4442.

Steinfeld, H., *et al.* (2006), "Livestock's Long Shadow, Environmental Issues and Options", Food and Agriculture Organization of the United Nations, Rome.

Vlaeminck, B., *et al.* (2006), "Factors Affecting Odd- and Branched-Chain Fatty Acids in Milk: A Review", *Animal Feed Science and Technology*, Vol. 131, pp. 389-417.

Weill, P., *et al.* (2002), "Effects of Introducing Linseed in Livestock Diet on Blood Fatty Acid Composition of Consumers of Animal Products", *Annals of Nutrition and Metabolism*, Vol. 46, pp. 182-191.

Windisch, W. (2002), "Interaction of Chemical Species with Biological Regulation of the Metabolism of Essential Trace Elements", *Analytical and Bioanalytical Chemistry*, Vol. 372, pp. 421-425.

Wood, J.D., *et al.* (2003), "Effects of Fatty Acids on Meat Quality: A Review", *Meat Science* Vol. 66, pp. 21-32.

Wood, J.D., *et al.* (2008), "Fat Deposition, Fatty Acid Composition and Meat Quality: A Review", *Meat Science*, Vol. 78, pp. 343-358.

World Cancer Research Fund/American Institute for Cancer Research (2007), *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective*, Washington D.C., American Institute for Cancer Research.

Chapter 15

Plants for the Future

Dulce E. de Oliveira and Marc Van Montagu

Institute of Plant Biotechnology for Developing Countries (IPBO)
Department of Molecular Genetics, Ghent University, Belgium

The present millennium has started with unprecedented global menaces with serious implications for mankind. The management of the planet's resources, the consequences of climate change, the problems generated by the food crisis require prompt actions. Actions at political and managerial level that take into account the contributions that science and technology can bring. The main challenges are: food and feed security; a much more sustainable agriculture; improved cash crops as raw material for the chemical and manufacturing industry; and, above all, actions for the preservation of the last surviving wildlife areas. The challenge is to produce better and more. The millennium goals are far from met. The number of undernourished people is reaching 1 billion. We need to produce more, to fulfil the demand of diversified agricultural products, and to guarantee a decent income to the farmers in the developing and emerging countries. To produce better, to satisfy sanitary and environmental requirements, biotechnologists have developed prototype plants that take up fertilisers more efficiently, need less irrigation and are more resistant to biotic and abiotic stresses. It is our mission to ensure that this knowledge is used in a wide range of breeding programmes, to generate the crops of the future.

Despite the enormous increase of our knowledge on plant genomes, their dynamics and evolution as well as on gene expression and its link to agronomic traits, we have seen that the best of plant sciences cannot help if society is not confident in the technology. Every effort should be made in creating awareness on how plant biotechnology can play a major role in meeting the main environmental and nutritional challenges we are facing. Society's support of the technology is needed for rationalising and harmonising the regulatory and biosafety policies which presently stop all introductions of transgenic plants by SMEs. It is the duty of the scientists in the public sector to explain to society and to policy makers the important benefits of these novel achievements in plant sciences to the economy, the environment and the global well-being of our societies.

Ten thousand years of genetically modified plants

Agriculture can be considered as a changing relation of the human being with the environment. It started more than ten thousand years ago when nomad gatherers started to put some roots back into the soil for the next time they would visit the site. The process of plant domestication gradually progressed in different parts of the world from selective gathering to the conscious exploitation of the genetic malleability of a dozen plants. Domestication slowly brought about large changes in morphological, physiological and biochemical characters on those plants to make them more suited to human needs. During the last century, this ancient technique was sped up with the rediscovery of Mendel's laws of inheritance in 1900. Knowledge based plant improvement started with hybridisation to combine the desired characters from different accessions and the exploitation of hybrid vigour. New laboratory techniques were then developed to oversee the breeding and selection process. The use of radiation and chemical mutagens to induce mutations and chromosome translocation, and the selection of embryos by tissue culture to the development of polyploids and amphiploids further hastened the pace of change.

As a human endeavour, agriculture is a resounding success. Food is more abundant and healthier than it has ever been in the past. Thanks to the Green Revolution food production has kept pace with population growth. The success of Norman Borlaug and the International Maize and Wheat Center (CIMMYT) team in producing dwarf wheat and, later, rice high yield varieties, together with innovative cultivation methods, brought huge increases in grain yield without which current human population levels would already be unsustainable. Unfortunately it was not without costs. The need to increase yields launched an intensive agriculture system characterised by high inputs of capital, labour, intensive irrigation and heavy use of pesticides and chemical fertilisers relative to land area. The bottom line is that agriculture is a major cause of environmental degradation.

Agriculture now faces several important challenges. It has to tackle: (i) food security issues of a still-growing human population, estimated at 8 billion by 2025. Already more than 1 billion people are chronically undernourished and one in six people do not get enough food to be healthy (FAO, 2009); (ii) the need to reduce the environmental footprint not only of agriculture but also of industry; and (iii) the increasing demand for renewable fuels and many additional non-food agricultural applications.

Biotechnology as a coherent answer to these challenges

Scientific breakthroughs continue to be the major source of innovation in agriculture. The tools to manipulate DNA together with the discovery of the Ti plasmid of *Agrobacterium tumefaciens* and the demonstration that crown gall induction was a phenomenon of natural genetic engineering opened the era of plant molecular genetics and laid the foundations for today's plant sciences (for review see Gelvin, 2003). These important milestones made *Agrobacterium*-mediated gene transfer possible and enabled the construction of the first transgenic plants which expressed important agricultural input traits and which are still hugely popular with farmers the world over 13 years on. From the first commercial launch in 1996, the global GM crop area has increased more than 50-fold in the first decade of adoption, and in 2009 14 million farmers planted 134 Mha (330 million acres) of biotech crops in 25 countries, up from 13.3 million farmers and 125 Mha (7%) in 2008. Notably, 13 of the 14 million farmers, or 90%, were small and resource-poor farmers from developing countries (James, 2009).

Already, significant developments related to improving quality of life or furthering economic productivity have been made. The crops produced by biotechnology and smart breeding currently on the market are helping agriculture to achieve higher yields in a more sustainable way. At the same time, novel applications that provide environmental benefits are becoming more visible as technologies mature and are more widely adopted (see Table 15.1 and references therein). Remarkable progress in genomics and functional genomics has brought the first insights into the gene pool and transcriptional regulation of model plants and of some important crop species. The rapid and long-term adaptation of plants to biotic and abiotic stress conditions is now open to molecular analysis and manipulation. Through these approaches, the next wave of crops presently under evaluation will have resistance to biotic and abiotic stresses and will be able to grow productively on marginal land. The productivity gains will be important for food security and land conservation, particularly in a shifting climate. As temperatures rise the land suitable for agriculture diminishes. Overall healthier and more resilient plant varieties adapt better to climate change.

Besides increasing yields the nutritional value of crops can also be enhanced by increasing the nutritional quality of food. There have been a number of breakthroughs in transgenic approaches to increase the nutritional quality of food crops. These include (i) the enhancement of vitamin levels in staple crops; (ii) GM plants that produce healthful omega-3 fatty acids; and (iii) GM rice with heightened iron levels. Recent developments are now aiming at combinatorial gene transfer systems to tackle multiple metabolic pathways at the same time. The idea is to use this tool to metabolically engineer all essential nutritional compounds in a given crop.

Green biotechnology is transforming bio-economy. Not only because it is revolutionising the oldest bio-economic sector of human civilisation – agriculture for food – but also because it is opening new possibilities for the sustainable use of plants as feedstock for industry and energy. The remarkable innovative breakthroughs being made in the fundamental plant sciences are fuelling new opportunities in an agriculture-based bio-industry. Significant sums have already been invested in the technologically proficient countries, but much needs to be done to promote an enabling environment for the development of a plant-based industry in the least developed countries.

Faced with a global energy crisis and concerns over climate change, the genetic improvement of forest trees is an area that will grow in importance through renewed interest in plants as a source of biofuels. This is reflected in the race for sequencing the genome of energy crops. Whilst some of the world's energy needs may be met through the adoption of nuclear technologies, much of the demand will be met through the exploitation of plant-based resources. Modification of lignin biosynthesis, increased biomass production and yield, resistance to abiotic stress, and metabolic engineering to improve oil content and composition for biodiesel as well as sugar and starch for ethanol, are examples of biotechnology solutions for bioenergy.

Metabolic engineering will also become an important approach for increasing non-fuel bioproducts. Plants are being used more and more as a source of raw material for a non-polluting industry that is not dependent upon the refining of petroleum, such as biodegradable plastic or intermediates for the chemical industries and advanced bioproducts might be the greatest long-term benefit of the current biofuels research race. There is significant scope for growth of this sector since 60% of the chemical industry is carbon based. It is highly likely that a large number of presently underutilised plant

commodities will emerge in the coming years as sources of raw material for the carbon-based chemical industry.

Plants also are being manipulated to be used as vehicles for the development and manufacture of high value pharmaceuticals. The production of pharmaceutical proteins in plants has several potential advantages over current systems such as mammalian and bacterial cell cultures, including the lower costs and scalability of agricultural production, and the absence of human pathogens. Another interesting aspect is that in some cases crops, *e.g.* fruit, leaf vegetables, or grains, can also serve as delivery systems of these high-value proteins to human and animal populations. Research and development in the area of plant-made pharmaceuticals include a number of vaccines already progressing to clinical trials, antibodies and nutraceuticals.

Policy framework priorities

Investments in university basic research and the creation of many start ups and small and medium sized enterprises (SMEs) were central to the growth of the USA and EU biotechnology industry around clusters of scientific excellence. This experience has taught us that the inclusion in the new knowledge-based bio-economy requires a complex interplay between a number of critical factors:

- An education system designed to produce a large pool of qualified and skilled workforce in science, technology and other innovative, creative and enterprising professions. A dynamic interaction between molecular geneticists, biochemists, ecologists and plant breeders;
- An R&D system able to generate knowledge at the frontiers as well as new technologies demanded by the production and services sectors;
- A strong intellectual property regime that provides effective protection and appropriation of intellectual property rights;
- A technology transfer system that ensures efficient transfer of knowledge and technology from the R&D system to the industry and business sectors;
- A critical mass of innovative firms and entrepreneurs to exploit knowledge to produce goods and services for the local and global market;
- A financial system that promotes investment in high risk ventures;
- An international network of scientists for sharing of resources and best practice that facilitates knowledge flow and capture;
- A market structure that enables the conversion of knowledge into products.

It is important to highlight that the present success of green biotechnology has been developed by wealthy countries to address the needs of their own farmers. It is now essential that developing countries develop their own products rather than depend on technological "spill-over" from the North. As Table 15.1 shows, plant biotechnological research, funded primarily by public research institutions, has produced numerous breakthroughs that can help to alleviate many of the entrenched problems of impoverished nations, including hunger, malnutrition, diseases and environmental degradation. Notwithstanding the scientific success, the rate of development of new biotech crops to tackle the problems of subsistence farmers is frustratingly slow, despite

the fact that it has been repeatedly stated that there is a common moral imperative to ensure that pro-poor, pro-environment and pro-economy technologies find their way to those who need them the most.

Table 15.1. Plant Biotechnology present and future – Scientific achievements and innovations in plant biotechnology[a]

Application	Biotechnology	Products/Proof-of-concept innovations (References)
Sustainable intensification	Tolerance to broad-spectrum herbicide	(Royal Society of London 2009 and references therein)
	Biotic stress tolerance (pest, pathogens)	(Christou 2006 and references therein, Dow AgroSciences 2009, Baum 2007, Mao 2007, Degenhardt 2009, Wang 2007, Shimizu 2008, Wang 2007)
	Higher-yield plants	(BASF n.d., Zha 2009, Sakamoto 2005)
	Abiotic tress tolerance (drought, salinity, flooding)	(Lee 2007, Nelson 2007, Hattori 2009, Hu 2008, James 2008)
	Increased nutrient-use efficiency	(Arcadia biosciences n.d.)
	Improved processing and storage	(Bijman n.d., Stone 1994)
Increasing nutritional density	Essential aminoacids	(Wu 2007, Frizzi 2008)
	Vitamins	(Ye 2000, Zhu 2008, Fujisawa 2009, Díaz de la Garza 2007, Naqvi 2009)
	Minerals	(Wirth 2009, Morris 2008, Park 2009)
	Very Long Chain polyunsaturated fatty acids	(Burgal 2008, Hoffmann 2008, Kajikawa 2008)
Value-added products	Plant-made pharmaceuticals (vaccines, antibodies, nutraceuticals)	(Spok 2008 and references therein, Yang 2007, Ma 2005, Ramessar 2008, Rademacher 2008, Sexton A 2009, Ventria Bioscience n.d., SemBoSys n.d.)
	Biofuels (Down-regulation lignin, cell wall biogenesis and degradation, increase lipid and sugar production)	(Coleman 2008, Vanholme 2008, Ransom 2007, Dai 2004, Chapman 2001, Vigeolas 2007, Mu 2005, Wu 2007)
	Renewable polymers (protein fibres, bioplastics)	(Yang 2005, Bohmert 2005)
Environmental sanitation	Phytoremediation (mercury, herbicides, explosives)	(Ruiz 2009 and references therein, Kawahigashi 2009 and references therein, Van Akena 2009 and references therein)
Biosafety	Biocontainment	(Mlynarova 2006, Li 2007, Luo 2007)

[a]This table cannot be considered a comprehensive list.

Source: Authors based on the literature herein.

However, the next step – the development of new products from the results of this research – is beyond the scope of public research institutions. Historically, it has been the private sector that has been responsible for the application of knowledge advances, and herein lies the shortcoming. Commercial interests drive investments of the private sector in R&D both in developed and developing countries. Neglect of pro-poor traits and orphan crops will remain as such if the returns on investments are not attractive. It is

therefore absolutely essential that measures are immediately taken to realise this fundamental humanitarian task. Without strong political support, sadly, much of this promise stagnates.

Specifically, we urgently need to:

i) Increase funding for public sector programmes that aim to address the major constraints of poor farmers trying to provide a sustainable, sufficient and safe supply of foods. As outlined above, these include higher productivity, enhanced nutrition, improved disease and insect resistance, drought tolerance, increased fertiliser use efficiency, etc.

ii) Establish, promote and fund international co-operation networks to allow an efficient knowledge transfer to scientists of developing countries for the establishment of relevant crop improvement programs.

iii) Support existing breeding programmes and quality seed production systems, particularly in those developing countries where a strong seed industry is non-existent.

iv) Develop the mechanisms to empower scientists of developing countries to allow them to participate in – and contribute to – the emerging global knowledge-based bio-economy.

v) Promote efficient, science-based regulatory frameworks for GM crop introduction, to avoid the costly overregulation that is currently limiting the introduction of pro-poor GM crops.

Public perception and regulatory framework

The tools of molecular biology applied to evolution have made us aware that: (i) the living world is one large gene-pool of functional genes and pseudogenes; (ii) this gene pool is permanently evolving – indeed this is the basis of evolution; (iii) nature itself is one big genetic laboratory and; (iv) it is very misleading to talk about human genes, pig genes, rat genes, etc.

There is nothing special or unique about GMO traits and behaviour that are not seen in plants obtained by conventional breeding and mutagenesis technologies. Traditional agriculture imposes threats to the environment arising out of monoculture, including susceptibility to pathogens and biodiversity loss, as well as ethical problems such as farmers' exploitation by hybrid seeds producers. Yet this agricultural system is not subject to the additional level of regulation which is demanded of the GMOs.

National and international regulations have been created since the introduction of GM crops to allow policymakers to make informed decisions based on an evaluation of potential benefits and potential risks. However, the requirements for field trials or placing on the market are expensive and largely unnecessary. The decisions are often delayed or denied without balanced, science-based assessment. It is this cumbersome and costly regulatory infrastructure in particular that is the major obstacle to the development and widespread adoption of new biotech crops. All our progress will be worthless if society is unwilling or unable to embrace the benefits of agricultural biotechnology.

Indeed the cost of regulatory filings to bring new biotech products to the market is so astronomical that only multinational firms are able to afford it, and even so, for very few

crops where there is a clear financial reward. The bottom line is that plant genetic engineering is a methodology that we cannot afford to use. No SME or third world country can develop and market a plant biotech product. There is no SME or developing country that is able to develop and market a plant biotech product. Moreover, regulatory frameworks that are widely diverse between countries limit international trade as developing countries will not be able to keep pace with the regulatory requirements of the developed world and eventually will not maintain their supply contract.

The benefits of GM crops have been largely ignored in the assessment of green biotechnology. The risk factor receives disproportionate weight despite scientific evidence. Sadly, any rational discussion on the subject of GMO regulation has been seriously hampered by the adamant opposition of the critics of the technology. Unfortunately, critics of plant biotechnology have mounted an active campaign of misinformation and obfuscation around GM crops, claiming that their introduction will lead to a loss of biodiversity and that they have not been sufficiently tested. In fact this is not the case. Despite intensive testing, absolutely no adverse effects of GM crops on consumer health or the environment have been substantiated; on the contrary, a number of potentially beneficial health and environmental effects have been noted. While the detractors continue to claim that GM crops are the monopoly of the multinationals and will only serve to enslave the third world, the truth is that it is the developing countries that stand to gain most from this technology, particularly in times of a shifting climate. The adoption of GM crops will help these lands to stabilise agricultural production and to provide food and economic security for their populations.

The result of the present "anti-GM" environment is that GM crops are one of the most over-regulated technology sectors in existence. It is therefore of critical importance to move beyond the populist, ill-informed biases against agricultural biotechnology, and instead to develop transparent regulatory frameworks based on robust scientific evidence. This will help to lower the financial barriers of regulatory filings that are restricting the introduction of new biotech products into the market. For as long as decision-making bodies continue to ignore the science behind the rationale, threats to food security and health problems will remain in these regions.

However, it is also the responsibility of scientists to create the necessary channels to share facts and information with all the different stakeholders, and to provide a platform to openly discuss the concerns, benefits and opportunities associated with this new technology. The following actions are recommended: (i) improve science education and awareness of the importance of science in decision making; (ii) but move from "educating the public" to engaging with the public; (iii) discuss new products with consumer organisations and; (iv) explain the social and environmental costs of not using GM plants.

Above all, we need to impress upon society at large that current agricultural techniques, be it classical or organic, are non-sustainable and highly detrimental to both the environment and to biodiversity. GM crop-based agriculture remains our greatest opportunity for the development of a modern, environmentally friendly agriculture that is still able to meet the food needs of our ever-growing population. In fact through biotechnology innovations it will be possible to intensify agriculture while maintaining the sustainable practices highly praised by organic agriculture. We all want the same more equitable, liveable and environmentally stable society. We can only reach this ideal through co-operation and mutual understanding.

Bibliography

Arcadia biosciences, *http://arcadiabio.com/nitrogen.php* (accessed February 22, 2010).

BASF, Higher-yield plant – BASF – The chemical company - corporate website. *http:/www.basf.com/group/corporate/en/products-and-industries/agriculture/higher-yielding-crop* (accessed February 22, 2010).

Baum, J.A., *et al.* (2007), "Control Coleoptran Insect Pests Through RNA Interference", *Nature Biotechnology* 25: 1322-1326.

Bijman, W. J., "The Development and Introduction of Genetically Modified Potatoes in the Netherlands", Access Excellence*, http:/www.accessexcellence.org/RC/AB/potatos-in-netherlands.php* (accessed February 23, 2010).

Bohmert, K., *et al.* (2005), "Transgenic Arabidopsis Plants Can Accumulate Polyhydroxybutyrate to up to 4% of Their Fresh Weight", *Planta* 211: 841-845.

Burgal, J., *et al.* (2008), "Metabolic Engineering of Hydorxy Fatty Acid Production in Plants: RcDGAT2 Drives Dramatic Increases in Ricinoleate Levels in Seed Oils", *Plant Biotechnol J* 6: 819-831.

Chapman, K.D., *et al.* (2001), "Transgenic Cotton Plants with Increased Seed Oleic Acid Content", *J Am Oil Chem Soc* 78: 941-947.

Christou, P., *et al.* (2006), "Recent Developments and Future Prospects in Insect Pests Control in Transgenic Crops", *Trends in Plant Science* 11: 302-308.

Coleman, H. D., *et al.* (2008), "RNAi-mediated Suppression of p-coumaroyl-CoA 3-hydroxylase in Hybrid Poplar Impacts Lignin Deposition and Soluble Secondary Metabolism", *Proc Natl Acad Sci* 105: 4501-4506.

Dai, Z. (2004), "Optimization Of Acidothermus Cellulolyticus Endoglucanase (E1) Production in Transgenic Tobacco Plants by Transcriptinal, Pos-Transcription and Pos-Translacional Modification", *Trangenic Res* 14: 627-643.

Degenhardt, J., *et al.* (2009), "Restoring a Corn Root Signal that Attracts Insect-Killing Nematodes to Control a Major Pest", *Proc Natl Acad Sci USA* 106: 13213-13218.

Díaz de la Garza, R., *et al.* (2007), "Folate Biofortification in Tomatoes by Engineering the Pteridine Branch of Folate Synthesis", *Proc Natl Acad Sci USA* 104: 4218-4222.

Dow AgroSciences (2009), Dowagro,*http://www.dowagro.com/newsroom/corporatenews/2009/200990731a.htm*.

FAO (2009), "The State of Food Insecurity in the World: Economic Crisis - Impacts and Lessons Learned"*, ftp://ftp.fao.org/docrep/fao/012/i0876r/i0876e00.pdf.*

Frizzi, A., *et al.* (2008), "Modifying Lysine Biosynthesis and Catabolism in Corn with a Single Bifunctional Expression/Silencing Transgene Cassette", *Plant Biotechnology J* 6: 13-21.

Fujisawa, M., *et al.* (2009), "Pathway Engineering of *Brassica Napus* Seeds Using Mulitple Key Enzyme Genes Involved in Ketocarotenoid Formation", *J Exp Bot* 60: 1319-1332.

Gelvin, Stanton B. (2003), "Agrobacterium-Mediated Plant Transformation: the Biology behind the 'Gene-Jockeying' Tool", *Microbiology and Molecular Biology Reviews* 67: 16-37.

Hattori, Y., *et al.* (2009), "The Ethylene Response Factors SNORKEL1 and SNORKEL2 Allow Rice to Adapt to Deep Water", *Nature* 460: 1026-1030.

Hoffmann, M., *et al.* (2008), "Metabolic Engineering of Omega3-VLCPUFA production by an Exclusively Acyl-Coa-dependent Pathway", *J Biol Chem* 283: 22352-22362.

Hu, H., *et al.* (2008), "Characterization of Transcription Factor Gene SNAC2 Conferring Cold and Salt Tolerance in Rice", *Plant Mol Biol* 67: 169-181.

James, V. A., I. Neibaur and F. Altpeter (2008), "Stress inducible expression of the DREB1A transcription factor from xeric, *Hordeum spontaneum* L in turf and forage grass (*Paspalum notatum* Flugge) enhances abiotic stress tolerance", *Transgenic research* 17: 93-104.

James, C. (2008), *Global Status of Commercialized Biotech/GM Crops,* ISAAA Briefs 39-2008, ISAAA: Ithaca, New York.

Kajikawa, M., *et al*. (2008), "Production of arachidonic and eicosapentaenoic acids in plants using bryophyte fatty acid delta6-desaturase, delta6-elongase and delta5-desaturase genes", *Biosci Biotechnol Biochem* 72: 435-444.

Kawahigashi, H. (2009), "Transgenic Plants for Phytoremediation of Herbicides", *Curr Opin Biotechnol* 20, no. 2: 225-230.

Lee, S.H., *et al.* (2007), "Simultaneous Overexpression of Both CuZn Superoxide Dismutase and Scrobate Peroxidase into a Wide Range of Abiotic Stress", *J Plant Physiol* 164 (2007): 1626-1638.

Li, S. F., S. Iacuone and R. W. Parish (2007), "Suppression and Restoration of Male Fertility Using a Transcription Factor", *Plant Biotechnol J* 5: 297-312.

Luo, K., *et al.* (2007), "GM-gene-deletor: fused loxP-FRT recognition sequences dramatically improve the efficiency of FLP or CRE recombinase on transgene excision from pollen and seed of tobaco plants", *Plant Biotechnol J* 5 (2007): 263-274.

Ma, J. K. C., *et al.* (2005), "Molecular Farming for New Drugs and Vaccines. Current Perspectives on the Production of Pharmaceuticals in Transgenic Plants", *EMBO Rep* 6: 593-599.

Mao, Y. B., *et al.* (2007), "Silencing a Cotton Bollwrom P450 Monooxygenase Gene By Plant-Mediated Rnai Impairs Larval Tolerance to Gossypol", *Nature Biotechnology* 25 (2007): 1307-1313.

Mlynarova, L., A. J. Conner and J.-P. Nap (2006), "Directed Microspore-Specific Recombination of Transgenic Alleles to Prevent Pollen-Mediated Transmission of Transgene", *Plant Biotechnol J* 4: 445-452.

Morris, J., *et al.* (2008), "Nutritional Impact of Elevated Calcium Transport Activity in Carrots", *Proc Natl Acad Sci USA* 105: 1431-1435.

Mu, G., *et al.* (2005), "Stepwise Engineering to Produce High Yield of Very-Long Chain Polyunsaturated Fatty Acids in Plants", *Nature Biotechnol* 23: 1013-1017.

Naqvi, S., *et al.* (2009), "Transgenic Multivitamin Corn: Biofortification of Corn Endosperm with Three Vitamins Representing Three Distinct Metabolic Pathways", *Proc Natl Acad Sci USA* 106: 7762-7767.

Nelson, D. E, *et al.* (2007), "Plant Nuclear Factor Y (NF-Y) B Subunitis Confer Drought Tolerance and Lead to Improved Cron Yields on Water-Limited Acres", *Proc Natl Acad Sci USA* 104: 16450-16455.

Park, S., *et al.* (2009), "Sensory Analysis of Calcium-Biofortified Lettuce", *Plant Biotechnol J* 7: 106-117.

Rademacher, T., *et al.* (2008), "Recombinant Antibody 2G12 Produced in Corn Endosperm Efficiently Neutralises HIV-1 and Contains Predominantly Single-GlcNac N-glycans", *Plant Biotechnol J* 6: 189-201.

Ramessar, K., *et al*. (2008), "Cost-Effective Production of a Vaginal Microbicide to Prevent HIV Transmission", *Proc Natl Acad Scie USA* 105: 3727-3732.

Ransom, C., *et al.* (2007), "Heterologous Acidothermus Cellulolyticus 1,4-beta-endoglucanase E1 Produced Within the Corn Biomass Converts Corn Stover into Glucose", *Appl Biochem Biotechnol* 137: 207-219.

Royal Society of London (2009), *Reaping the Benefits: Science and Sustianable Intensification for Global Agriculture,* Royal Society, London.

Ruiz, O. and H. Daniel (2009), "Genetic Engineering to Enhance Mercury Phytoremediation", *Curr Opin in Biotechnol* 20, no. 2: 213-219.

Sakamoto, T., *et al.* (2005), "Erect Leaves Caused by Brassionsteroid Deficiency Increase Biomass Production and Grain Yield in Rice", *Nature Biotechnol* 24: 105-109.

SemBioSys, SemBioSys - In Development *http://www.sembiosys.com/Products/Development.aspx* (accessed 22 February 2010).

Sexton, A. *et al.* (2009), "Transgenic Plant Production of Cyanovirin-N, an HIV Microbicide", *FASEB J* (doi: 10.1096/fj.09-131995).

Shimizu, T., *et al.* (2008), "Silencing by RNAi of the Gene for Pns12, A Viroplasm Matrix Protein If Rice Dwarf Virus, Results in Strong Resistance of Transgenic Rice Plants to the Virus", *Plant Biotechnology* 7: 24-32.

Spok, A., *et al.* (2008), "Evolution of a Regulatoy Framework For Pharmaceuticals Derived from Genetically Modified Plants", *Trends in Biotechnol* 26, no. 9: 506-517.

Stone, B. (1994), "The Flav Savr Arrives", *Access excellence, http:/www.accessexcellence.org/RC/AB/BA/flav_savr_arrives.php* (accessed 23 February 2010).

Van Akena, B. (2009), "Transgenic Plants for the Enhanced Phytoremediation of Toxic Explosives", *Curr Opin in Biotechnol* 20, no. 2: 231-236.

Vanholme, R., *et al.* (2008), "Lignin engineering", *Curr Opin Plant Biol* 11: 278-286.

Ventria Bioscience, *http://www. ventria.com/products/* (accessed February 22, 2010).

Vigeolas, H., *et al.* (2007), "Increasing seed oil content in oil-seed rape (*Brassica napus* L.) by over-expression of a yeast glycerol-3-phosphate dehydorgenase under the control of a seed-specific promoter", *Plant Biotechnol J* 5: 431-441.

Wang, C. and R. J. Leger (2007), "A Scorpion Neurotoxin Increases the Potency of Fungal Insecticide", *Nature Biotechnology*, 1455-1456.

Wirth, J., *et al.* (2009), "Rice Endosperm Iron Biofortification by Targeted and Synergistic Action of Nicotinamide Synthase and Ferritin", *Plant Biotechnol J* 7: 1-14.

Wu, G. and R. G. Birch (2007), "Doubled Sugar Content in Sugarcane Plants Modified to Produce a Sucrose Isomer", *Plant Biotechnol J* 5: 109-117.

Wu, X. R. *et al.* (2007), "Altered Expression of Plant Lysyl tRNA Synthetase Promotes tRNA Misacylation and Translational Recoding of Lysine", *Plant J* 50: 627-636.

Yang, J., *et al.* (2005), "High Yield Recombinant Silk-Like Protein Production in Transgenic Plants Through Protein Targeting", *Transgenic Res* 14 (2005): 841-845.

Yang, L., *et al.* (2007), "Development of Transgenic Rice Seed Accumulating a Major Japanese Cedar Pollen Allergen (Cry j 1) Structurally Disrupted for Oral Immunoterapy", *Plant Biotechnol J* 5: 815-826.

Ye, X.D., *et al*. (2000), "Engineering the Provitamin A (Beta-Carotene) Biosynthetic Pathway into (Carotenoid-Free) Rice Endosperm", *Science* 287: 303-305.

Zha, X., *et al.* (2009), "Over-Expression of the Rice LRK1 Genes Improves Quantitative Yield Components", *Plant Biotechnol J* 7: 611-620.

Zhu, C., *et al.* (2008), "Combinatorial Genetic Transformation Generates a Library of Metabolic Phenotypes for the Carotenoid Pathway in Corn", *Proc Natl Acad Sci USA* 105: 1832-1837.

Chapter 16

Genetic Resources as the Building Blocks for Breeding: Current Status and Challenges

Dr. José T. Esquinas-Alcázar

Politechnical University of Madrid, Spain; Director of the "Catedra" of Studies on Hunger and Poverty, University of Cordoba, Spain; former Secretary, FAO Intergovernmental Commission on GRFA and Chair FAO's Sub-Committee on Ethics in Food and Agriculture

During the 20th century among plant and animal land species, the sources of genetic diversity have disappeared at an alarming rate for most domesticated species. Furthermore, no country is self-sufficient in this area. Geographical and intergenerational dependency on genetic resources for food and agriculture is very high and access to them continues to be a prerequisite for effective agricultural research and breeding. The OECD member countries are among the most dependent on genetic resources from abroad. International co-operation is therefore a must. The negotiation in FAO, and wide ratification of the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA) early this century, have been a significant achievement and a hope for the conservation, sustainable use, and continuous availability of these resources. However, a considerable effort is still needed, including making the ITGRFA fully operative in all countries and at all levels. In addition, many crops of the past which are neglected today, as well as many wild species, are expected to play a critical role in food, medicine and energy production in the near future.

Rapid changes in environmental conditions as well as in farmers' needs and consumers' demands pose new and important challenges for the conservation and sustainable utilisation of a wide range of species and genetic resources as a major base for food security and sustainable agricultural development.

Introduction

Selection is only possible in the presence of diversity. Genetic diversity or genetic resources for food and agriculture provide the building blocks for farmers, breeders and biotechnologists to develop new plant varieties (see Box 16.1) and animal breeds necessary to cope with unpredictable human needs and changing environmental conditions, including those due to climate change. Genetic resources are considered the storehouse which provides humanity with food, clothes and medicines. They are essential for sustainable agriculture and food security.

Box 16.1. Some illustrative examples of the importance of conserving and using plant genetic resources
(based on Esquinas-Alcázar, 2005a)

The value of both farmers' traditional varieties and wild relatives of cultivated plants in crop improvement and agricultural development cannot be overemphasised. The examples that follow are illustrative.

i) Farmers' traditional varieties have provided many individual traits that have been introduced into existing, improved breeding lines.

One local variety of wheat found in Turkey, collected by J. R. Harlan in 1948, was ignored for many years because of its many negative agricultural characteristics. But in the 1980s, it was discovered that the variety carries genes resistant to fungi such as *Puccinia Striiformis*, 35 strains of *Tilletia caries* and *T. foetida*, and 10 varieties of the fungus *T. controversa*, and is also tolerant to certain species of *Urcocystis*, *Fusarium* and 1 yphula. It was therefore used as a source of resistance to a whole array of diseases (Kronstad, 1986).

Zerazera sorghums from Ethiopia have provided resistance to downy mildew in many inbred lines widely used in the United States and Mexico. Farmers' varieties of Italian ryegrass (*Lolium multiflorum*), collected in Uruguay in the 1950s, were the source of resistance to crown rust. Local Iranian alfalfa landrace collected in Iran in 1940 has been widely used to introduce resistance to stem nematodes (FAO, 1998).

The primitive Japanese dwarf wheat variety, Norin 10, introduced into America in 1946, played a key role in the genetic improvement of wheat during the so-called "Green Revolution". It was used as a donor of the genes responsible for dwarfism, which allow increased nitrogen uptake and thus increased production (Kihara, 1983).

ii) Wild relatives of our present crop plants, although agronomically undesirable, may also have acquired many desirable characteristics as a result of their long exposure to nature's pressures, and can therefore make enormous useful contributions to crop improvement.

An outstanding example is the genus *Lycopersicon*, many wild species of which can be crossed with cultivated tomato (*L. esculentum*) and have been successfully used as donors of fungus-resistant genes (*L. hirsutum*, *L. peruvianum*), nematode-resistant genes (*L. peruvianum*), insect-resistant genes (*L. hirsutum*), genes for quality improvement (*L. chirnielewskii*), and genes for adaptation to adverse environments (*L. cheesmanii*). Similar examples could be cited for most crops (Esquinas-Alcázar, 1981).

Resistance in cultivated rice, *Oryza sativa*, to grassy stunt virus has been introduced from the wild rice, *Oryza nivara*, (Khush and Beachell, 1972) and resistance to brown planthopper for *Oryza officinalis*.

Box 16.1. Some illustrative examples of the importance of conserving and using plant genetic resources (*continued*)

Wild forms of *Beta* collected in the 1920s were utilised in the 1980s in California as a source of resistance to *Rhizomania*, a devastating sugar beet root disease; meanwhile, it was found that the collections also show *Erwinia* root rot resistance, sugar beet root maggot tolerance, and moderate leaf spot resistance (Doney and Whitney, 1990).

These examples show that genetic material that once appeared to be of no particular value has proved to be crucial in crop improvement. The concept of "usefulness" is a relative one, which may vary according to needs and to the information available.

In spite of its vital importance for human survival, agricultural biodiversity is being lost at an alarmingly increased rate. Hundreds of thousands of farmers' heterogeneous plant varieties and landraces that existed, for generations, in farmers' fields until the beginning of the twentieth century, have been substituted by a small number of modern and highly uniform commercial varieties. In the USA alone, more than 90% of fruit trees and vegetables that were grown in farmers' fields at the beginning of the twentieth century can no longer be found and only a few of them are maintained in gene banks. In Spain, in 1970, the author of this article collected and documented over 350 local varieties of melons; today no more than 5% of them can still be found in the field. The picture is much the same throughout the world (see Box 16.2). Similar alarming figures can be given for the genetic erosion of domestic animal breeds. Actually out of 7 616 breeds that have been reported to FAO, 9% are extinct and another 20% are classified as at risk. Almost one breed per month was lost during the last six years (FAO, 2007a). The loss of agricultural biological diversity has drastically reduced the capability of present and future generations to face unpredictable environmental changes and human needs.

Box 16.2. Increase of agricultural productivity and lost genetic diversity

Global average yearly yields (kg/ha) evolution of six major crops

	1961	1961-70	1971-80	1981-90	1991-00	2000-07
Wheat	1.089	2.208	1.855	2.561	2.720	2.792
Barley	1.328	2.202	1.998	2.412	2.442	2.406
Rice	1.869	3.138	2.748	3.528	3.885	4.152
Maize	1.869	3.417	3.154	3.680	4.242	4.971
Soybean	1.129	1.748	1.600	1.896	2.171	2.278
Potato	12.216	14.738	12.817	15.129	16.339	16.647

Source: FAO statistics on agricultural production.

This table shows the dramatic increase in crop yields over the last few decades; this is partially due to the use of a number of new high yield commercial uniform varieties (Fehr, 1984) that have substituted innumerable heterogeneous farmers' varieties. Although we do not have adequate information to show a correlation, it appears clear from the data below that an undesired negative aspect of this development has been a dramatic increase in genetic erosion; that is the loss of genetic diversity contained in the farmers' varieties that were replaced (Frankel and Soule, 1981; Harlan, 1975). The loss of local genetic diversity has been documented in certain cases. According to the State of the World PGRFA (FAO, 1998) which is based on national and regional reports:

One cultivar accounted for 94% of the spring barley planted. In 1982, the rice variety "IR36" was grown on 11 million hectares in Asia. Over 67% of the wheat fields in

Box 16.2. Increase of agricultural productivity and lost genetic diversity (*continued*)

Bangladesh were planted with the same cultivar ("Sonalika") in 1983. Reports from the USA in 1972 and 1991 indicate that for each of eight major crops fewer than nine varieties made up between 50% and 75% of the total. By the 1990s in Ireland, 90% of the total wheat area is sown to just six varieties.

Out of the 7 098 apple varieties that were documented in the USA at the beginning of the twentieth century, approximately 96% have been lost. Similarly 95% of cabbage varieties; 91% of field maize varieties; 94% of pea varieties; and 81% of tomato varieties cannot be found anymore. In Mexico, only 20% of the maize varieties reported in 1930 are now known. In the Republic of Korea, only 26% of the landraces of 14 crops cultivated in home gardens in 1985 were still present in 1993. In China, in 1949, nearly 10 000 wheat varieties were used in production; by the 1970s, only about 1 000 remained in use.

Furthermore no country is self-sufficient in terms of genetic resources. Geographical and intergenerational dependency on genetic resources for food and agriculture is very high and access to them continuous to be a prerequisite for effective agricultural research and breeding. The OECD member countries are amongst the most dependent ones on genetic resources from abroad. International co-operation is therefore a must (see Box 16.3). It follows that matters related to the conservation and sustainable use of genetic resources and the management of related biotechnologies may appear to be technical, but they have in fact strong socio-economic, political, cultural, legal, institutional and ethical implications and problems in these fields can put at risk the future of humanity.

Box 16.3. Estimated range of dependency (%) from genetic resources from elsewhere

(a) By regions

Region	Minimum (%)	Maximum (%)
Africa	67.24	78.45
Asia and the Pacific Region	40.84	53.30
Europe	76.78	87.86
Latin America	76.70	91.39
Near East	48.43	56.83
North America	80.68	99.74
GLOBAL	**65.46**	**77.28**

(b) For each OECD member country

OECD Member Countries	Minimum (%)	Maximum (%)
Australia	88.40	100
Austria	80.94	97.54
Belgium/Luxembourg	82.26	97.73
Canada	84.00	99.48
Czech Republic	87.87	97.40

Box 16.3. Estimated range of dependency (%) from genetic resources from elsewhere (*continued*)

(b) For each OECD member country (continued)

Denmark	81.18	91.96
Finland	88.96	98.99
France	75.55	90.67
Germany	83.36	98.46
Greece	54.24	68.94
Hungary	86.85	98.04
Iceland	83.82	99.21
Ireland	84.59	99.45
Italy	70.82	81.21
Japan	43.15	61.29
Korea	30.47	54.41
Mexico	45.12	59.48
Netherlands	87.94	98.49
New Zealand	87.40	100
Norway	90.67	98.94
Poland	90.06	99.32
Portugal	78.86	90.88
Slovak Republic	85.10	96.60
Spain	71.41	84.84
Sweden	88.79	98.70
Switzerland	81.79	98.43
Turkey	32.21	43.16
United Kingdom	89.23	99.10
United States	77.36	100
AVERAGE	**83.36**	**98.04**

Source: Based on the study by X. Flores Palacios (1998).

Ftp://ftp.fao.org/docrep/fao/meeting/015/j0747e.pdf.

The table shows, for each region, the mean of countries' degree of dependency on crop genetic resources which have their primary centre of diversity elsewhere. The indicator used is the food energy supply in the national diet provided by individual crops. On the basis of the primary area of diversity of each crop, it has been calculated the estimated dependency that has maximum and minimum indices, showing there is a high rate of dependency in practically all cases.

The negotiation in FAO, and wide ratification of the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA) (*http://www.planttreaty.org*) at the beginning of the century are a significant achievement and a hope for the conservation, sustainable use, and continuous availability of these resources (see Box 16.4). However much effort is still needed, including effort to fully implement the Treaty in all countries concerned.

Box 16.4. The international treaty on plant genetic resources for food and agriculture (ITPGRFA)

The Treaty provides a bridge between agriculture, commerce and the preservation of the environment, and is the result of 23 years of debate, including 7 years of formal negotiations among UN Member Nations in FAO. This process also involved participation by representatives from non-governmental institutions and the private sector.

The Treaty became operational with the first meeting of its Governing Body in Madrid in June 2006. Its objectives are the conservation and sustainable use of plant genetic resources for food and agriculture and the fair and equitable sharing of benefits that arise from their use. The core of the treaty is its innovative Multilateral System of Access and Benefit-sharing, which ensures continuous availability of important genetic resources for research and plant breeding, while providing for the equitable sharing of benefits, including monetary benefits that are derived from commercialisation. Another innovative feature is its provisions for farmers' rights. The ITPGRFA relies on several supporting components that were previously developed by the Commission on Genetic Resources for Food and Agriculture (CGRFA), in particular the Global Plan of Action, the Global Information System, international networks, and terms and conditions for the conservation of and access to *ex situ* collections that are maintained by the International Agricultural Research Centers (IARCs).

An essential element for its funding strategy is the Global Crop Diversity Trust (*http://www.croptrust.org/main/*). This was established under international law as an independent organisation in October 2004. It was constructed largely as an endowment fund, with a target of USD 260 million. As per June 2009, USD 152 million have been pledged out of which USD 124 million have already been paid, with contributions coming from both public and private sources. The Trust is being used to ensure financial sustainability for the conservation of the world's most important crop diversity *ex situ* collections, as a "genetic pantry" for mankind.

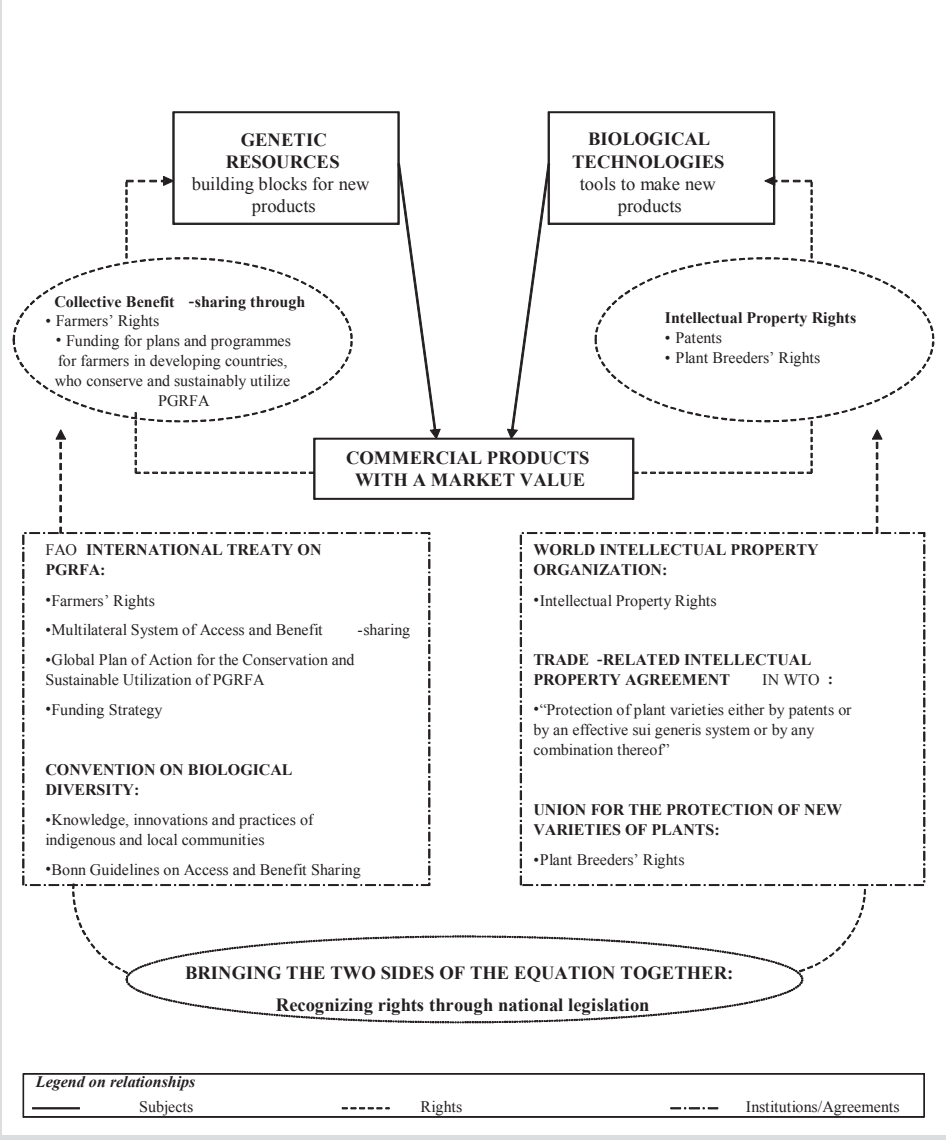
The Treaty has already been ratified by 121 countries. In the period August 2007 to July 2008 alone, more than 440 000 accessions were sent from the Multilateral System for Access and Benefit Sharing to possible users, through the Standard Material Transfer Agreement agreed by Contracting Countries, representing then more than 8 500 accessions per week.

The Third Session of the Governing Body of the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA) took place from 1-5 June 2009, in Tunis, Tunisia. Delegates agreed to: a set of outcomes for implementation of the funding strategy, including a financial target of USD 116 million for the period July 2009 to December 2014; a resolution on the implementation of the Treaty's Multilateral System including the setting up of an intersessional advisory committee on implementation issues; a resolution on farmers' rights; and procedures for the Third Party Beneficiary. They also adopted the work programme and budget for the next biennium, established intersessional processes to finalise compliance procedures by the Fourth Session, and reviewed the Standard Material Transfer Agreement. The Fourth Session of the Governing Body is scheduled to be held in March 2011, in Bali (Indonesia), (*ftp://ftp.fao.org/ag/agp/planttreaty/gb3/gb3repe.pdf*).

Society benefits from the Treaty in different ways: consumers benefit because of a greater variety of foods and agricultural products, as well as increased food security; the scientific community benefits through access to the plant genetic resources that are crucial for research and plant breeding; IARCs benefit because their collections have been put on a safe and long-term legal footing by the Treaty; and both the public and private sectors benefit because they are assured facilitated access to a wide range of genetic diversity for agricultural development.

The Treaty is not the only international agreement dealing with Genetic Resources for Food and Agriculture (GRFA); others such as the CBD (*http://www.biodiv.org/handbook/*), International Union for the Protection of New Varieties of Plants (UPOV) and WTO Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS/WTO) are also directly or indirectly related to access to GRFA and their related knowledge, technologies and information. Complementarities and synergies must be ensured in the interpretation and implementation of their provisions both at national and international levels (see Box 16.5).

Box 16.5. Balancing the value of GRFA and of biological technologies that use them



Box 16.5. Balancing the value of GRFA and of biological technologies that use them (*continued*)

Genetic resources provide the building blocks that allow classical plant breeders and biotechnologists to develop new commercial varieties and other biological products. Although nobody can deny their importance, neither genetic resources, nor the biological technologies that apply to them, have an appropriate market value by themselves, while a clear market value often exists for the commercial products obtained through them.

Since the 1960s, a number of international bodies and agreements (TRIPS/WTO, the World Intellectual Property Organization (WIPO) and UPOV), have included provisions setting minimum standards for, or conferring on the developers of biological technologies individual rights (IPRs such as Plant-Breeders Rights and patents) that allow the right-holders to appropriate part of the profits from any commercial products that may result from the use of those technologies.

Since the 1990s, other international agreements (the CBD and the International Treaty) have conferred equivalent but collective rights (farmer's rights and benefit-sharing) on the providers of the genetic resources. This allows for a symmetrical and balanced system of incentives to promote, on one hand, the developments and application of new biotechnologies and to ensure, on the other hand, the continued conservation, development and availability of genetic resources to which these technologies apply. It is now up to national governments to implement these provisions, including the development, as appropriate, of national legislation that takes fully into account the two "pillars" of the system represented in the diagram, thereby allowing for harmony and synergy in the implementation of the various binding international agreements.

Source: Esquinas-Alcázar, 2005a.

This document provides information on the current status and challenges ahead.

Current status

Status of plant genetic resources

The last decade has witnessed a number of changes on the situation of *ex situ*, "on-farm" and *in situ* conservation and management. Much of the data provided below is based on information available on World Information and Early Warning (WIEWS) 2009 (*http://apps3.fao.org/WIEWS*) and will be reflected in the Second Report on the State of the World on Plant Genetic Resources (SW/PGRFA) currently under preparation.

***Ex situ* collections** have increased by 20% since 1996 to reach 7.4 million accessions, of which about 25% are believed to be unique and distinct. While the number of accessions of minor crops and crop wild relatives has increased, these categories are still generally under-represented. The number of species stored in national collections has increased, on average by 57% since 1995.

Over the last decade, promoting and supporting the **on-farm management** of genetic resources, whether in farmers' fields, home gardens, orchards or other cultivated areas of high diversity, has become firmly established as a key component of crop conservation strategies. The maintenance of genetic diversity within local production systems also helps to conserve local knowledge. According to FAO, recent national reports indicate

that informal seed systems remain a key element in the maintenance of crop diversity "on-farm" and in some countries account for up to 90% of seed movement.

While *ex situ* conservation and on-farm management methods are most appropriate for conserving domesticated crop germplasm, for crop wild relatives and species harvested from the wild, *in situ* conservation, supported by *ex situ* methods, is generally the strategy of choice.

With respect to ***in situ* conservation**, the number of protected areas in the world has grown from approximately 56 000 in 1996 to about 70 000 in 2007, and the total area covered has expanded in the same period from 13 to 17.5 Mkm^2. However a significant number of wild PGRFA species occur outside conventional protected areas and consequently do not receive any form of legal protection (Maxted and Kell, 2009; Heywood and Dulloo, 2005). Cultivated fields, field margins, grasslands, orchards and roadsides may all harbour important crop wild relatives. Plant diversity in such areas faces a variety of threats including the widening of roads, removal of hedgerows or orchards, overgrazing, expansion in the use of herbicides or even just different regimes for the physical control of weeds (FAO, 2007a).

The threat of climate change to crop wild relatives has been highlighted by a recent study (Jarvis A. *et al*., 2008) that focused on three important crop genera: *Arachis*, *Solanum*, and *Vigna.* The study predicts that 16–22% of species in these genera will go extinct before 2055 and calls for immediate action to preserve crop wild relatives *in situ.* The CGRFA has recently commissioned a report on the "Establishment of a global network for the *in situ* conservation of crop wild relatives: status and needs" (Maxted and Kell, 2009). This report identifies conservation priorities and suggested reserve locations for 14 selected crops.

Status of technologies

Powerful new technologies have increased the value and potential of PGRFA, especially for wild species, as potential donors of useful agricultural traits. Molecular genetics, genomics, proteomics, cryopreservation and ecogeographical remote-sensing techniques (using satellites and aircraft) have greatly expanded the technological bases for the location, conservation, management and use of genetic resources. This includes, for example, techniques for estimating the spatial and temporal distribution of genetic diversity, relationships between and within populations (*http://www.fao.org/biotech/C13doc.htm)*, gaining insights into crop domestication and evolution (Lenstra *et al.*, 2005; Diamond, 2002), monitoring gene flows between domesticated and wild populations (Moraesa, 2007) and increasing the efficiency and effectiveness of gene bank operations (*e.g.* deciding what material to include within a collection, identifying duplicates, increasing the efficiency of regeneration and establishing core collections (de Vicente, 2004; Tivang *et al*., 1994).

Advances in information technology and communication techniques have also markedly increased our capacity to use, analyse and communicate related data and information.

Underutilised crops and promising species

In addition, many crops of the past which are neglected today as well as many wild species are expected to play a critical role in food, medicine and energy production in the

near future. Actually, the FAO's first report on the State of the World on Plant Genetic Resources estimates that some 7 000 species have been used by mankind to satisfy human basic needs, while today no more than 30 cultivated species provide 90% of human caloric food supplied by plants (FAO, 1998). Furthermore 12 plant species and five animal species alone provide more than 70% of all human caloric food and a mere four plant species (potatoes, rice, maize and wheat) and three animal species (cattle, swine and chickens) provide more than half.

Rapid changes in environmental conditions as well as in farmers' needs and consumers' demands put new and important challenges for the conservation and sustainable utilisation of a wide range of species and genetic resources as a major base for food security and sustainable agricultural development.

Challenges ahead

Challenges ahead have technical, scientific, socio-economical, legal and institutional dimensions.

Technical and scientific challenges

Technical research challenges for GRFA have largely to do with the ways in which we need to adjust our thinking on conservation and utilisation methods to cope with climate change, environmental sustainability and food security.

Maintenance and management of genetic diversity

- *In situ* and "on-farm" conservation and management strategies need to provide increased adaptability and resilience and be planned to allow for continuing evolution of populations in the face of change.
- *Ex situ* conservation also needs to be further developed and rationalised to provide the resources that will be needed where change is so great that some kind of transformation of the production system is required. This means in particular increased work on *ex situ* conservation of crop wild relatives which is under-researched. Stored samples also need to be properly characterised, evaluated and documented.

The following includes a number of priorities identified by countries and FAO in the preparatory process of the Second Report on the SW/PGRFA to be published shortly:

- to carry out systematic surveys and to publish inventories to identify existing GRFA both in the field and in germplasm banks;
- to develop methods for reliably estimating plant genetic diversity and to adopt standardised definitions of genetic vulnerability and genetic erosion (Brown, 2008; FAO, 2002);
- to give greater attention to the *in situ* management of wild relatives, neglected crops and promising species, as well as diversity in threatened ecosystems;
- to develop a more rational global system of *ex situ* collections;

- to develop and implement national strategies and to strengthen national capacities to manage and use genetic resources, including a greater use of scientific methods and technologies;
- to broaden the genetic basis in crop improvement;
- to develop appropriate policies, legislation and procedures for collecting crop wild relatives, maybe by revising the 1993 FAO International Code of Conduct for Plant Germplasm Collecting (FAO, 2003);
- to carry out ethnobotanical and socio-economic studies, including the study of indigenous and local knowledge, to better understand the role of farming communities in the management of PGRFA.

Utilisation challenges for food security and environmental sustainability and to face climate change

The likely changes in agriculture production methods, in environment, and in demand are all likely to require increased use of genetic resources. The utilisation of a wide range of GRFA is crucial for food security and environmental sustainability and to face climate change.

- Food security

The main challenge to increase food security is not food production, but access to food. In addition, it is not simply a matter of delivering more calories to more people. It should be noted that most hungry people in the world (70%) are living in rural areas. Solutions are needed to improve stability of production at the local level, to provide increased options for small-scale farmers and rural communities and to improve the quality as well as the quantity of food available. Nutritional security, where dietary diversity plays an important role, is a vital component of food security. To achieve this there is a need to increase emphasis on the many neglected and underutilised crops, as well as on the diversity within crops. These are areas which have time and again been neglected by researchers and plant breeders although there is often much diversity and only a relatively small investment is needed to make good progress.

- Environmental sustainability

Reducing the negative impact that agriculture may have on the environment (*e.g.* water, energy, pesticides, and herbicides) needs to become an absolute priority. This requires increased use of diversity in production systems through the deployment of a wider range of varieties and crops to ensure better ecosystem service provision. A good example would be the use of diversity-rich strategies to reduce damage by pests and diseases. Research is needed on how to make diversity-rich strategies more effective in terms of reaching better agriculture productivity and management.

- Climate change

All the predicted scenarios of the Intergovernmental Panel on Climate Change (IPCC) (*www.ipcc.ch*) will have major consequences for the geographic distribution of crops, individual varieties and crop wild relatives. Some recent studies have used current and projected climate data to predict the impact of climate change on areas suitable for a number of staple and cash crops (Jarvis A. *et al*., 2008; Fisher *et al*., 2002).

Undoubtedly a major research challenge is the development of varieties adapted to changing climate conditions. Although there is substantial variation in many crops to cope with a wide range of conditions we need to note:

- The magnitude of change will require significant adaptation.
- New genetic diversity, within and between species is likely to be needed. This will increase the potential of underutilised crops and other promising species.
- Novel and unstable production environments would require different breeding approaches.
- There is an increasing need for adaptability and resilience, properties that have not been embedded in traditional breeding.

All of these require research not only on the diversity itself but on how it can be most effectively deployed to maintain productivity. There will also be research needed on how genetic resources can be used to support mitigation strategies.

It needs to be emphasised that in all these areas it is not a simple question of finding specific traits from a pool of diverse materials. The research needs to be concerned with functional diversity and with diversity deployment in agricultural systems from farm fields to landscape, watershed and regional scales. The way in which diversity functions in different kinds of production systems including organic agriculture, conservation agriculture, etc., is also a relevant entry point.

Social and economic challenges

Social challenges

To ensure that the benefits derived from plant genetic resources reach all those who need them, public-sector research is needed in areas in which the private sector does not invest. Most commercial crop varieties are not adapted to the needs of poorer farmers, especially in many developing countries, who have limited or no access to irrigation, fertilisers and pesticides. A new environmentally friendly, socially acceptable and ethically sound agricultural model is needed to meet their needs. This could be achieved by publicly supported programmes to breed crops that are able to withstand adverse conditions, including drought, high salinity and poor soil fertility and structure, and that provide resistance to local pests and diseases. Such programmes are likely to build on farmers' existing varieties and local crops, which often contain these traits. This is especially important at times when international prices of major crops have dramatically increased (*e.g.* World food crisis in 2008) and continue to be volatile and unpredictable.

Research emphasis needs to be put at local level, often on local and underutilised crops, to breeding and improving performance of a wide range of crops and varieties well adapted to local conditions and needs rather than just seeking uniform "universal genotypes". This can only be achieved by a systematic and participatory process of co-operation between breeders, farmers and consumers.

Economic challenges

The cost of conserving plant genetic diversity is high, but the cost of not taking action is much higher. Economic resources for the conservation and sustainable use of

agricultural genetic resources are well below adequate levels. This problem is especially serious in the case of the *in situ* conservation of traditional farmers' varieties and, increasingly, of wild relatives of cultivated plants, which are largely found in developing countries. The scarcity of economic resources in these countries is not only an obstacle to the protection of wild species, but also a major cause of genetic erosion, as people search for fuel-wood or convert virgin areas into farmland.

The establishment of the Global Crop Diversity Trust, as an important element of the funding strategy of the ITPGRFA, is a step in the right direction. However, this fund is specifically for *ex situ* conservation. In addition the Third Session of the Governing Body of the Treaty in 2009 has agreed a target of USD 116 million for the next five years for the Funding Strategy of the Treaty, and projects have already been developed in a bottom up, country driven process, but the funds are not yet available and might be difficult to obtain. In this context it should be remembered that only 4% of Official Development Aid (ODA) goes to agriculture, while more than 70% of hungry people live in rural areas. The conservation and use of GRFA should not be seen as part of development assistance only, but also as a matter of national development and national security.

From a macroeconomic perspective, PGRFA have been treated as an unlimited source of continuing benefits. They are in fact a limited resource to be used by all generations to come. The full value of such resources for the future continues not to be reflected in market prices. A sustainable economic solution to the problem is the internalisation of the conservation cost of the resource into the production cost of the product. For example, when buying an apple, we could pay not only the cost of production, but also the costs of maintaining genetic resources that will allow future generations to continue eating apples. The ITPGRFA provisions concerning benefit-sharing, including the sharing of monetary benefits that are derived from commercialisation, represent a first step in that direction.

Taking all the above into account we can conclude that there is an urgent need for research in economics that would provide a better description and quantification of the true value of genetic resources. While we have some conceptual framework in terms of use value, future value, option value, we lack an adequate quantification mechanism to drive investment decisions and research planning.

Legal and institutional challenges

Plant genetic resources for food and agriculture: the international treaty

The entry into force of the International Treaty on Plant Genetic Resources for Food and Agriculture marks a milestone, as it provides a universally accepted legal framework for Plant Genetic Resources. However, mechanisms to promote compliance need to be developed, as the Funding Strategy of the treaty needs to become fully operative.

After a country's ratification, the provisions of the ITPGRFA need to be implemented at the national level, which will require the development of national measures. In some cases legislation will also be needed to prevent genetic erosion, promote the conservation, characterisation and documentation of local genetic resources, implement farmers' rights, facilitate access to genetic resources for research and plant breeding, and promote un equitable sharing of benefit.

The Multilateral System of Access and Benefit-sharing of the Treaty started to operate in January 2007 to facilitate the exchange of 64 crops and wild relatives that are

essential for food security and the first projects under the Funding Strategy have been approved in 2009. Once the benefits are being fully realised, future negotiations would be able to reach consensus in other controversial and challenging issues, such as broadening its scope by increasing the number of crops that are exchanged through the Multilateral System.

Ensuring continuous access and availability of PGRFA for research and breeding

Access to genetic resources and related biotechnologies is threatened by the increasing number of national laws that restrict access to and use of genetic resources, as well as by the proliferation of Intellectual Property Rights (IPRs) and the expansion of their scope (Correa, 2003 and 1994). In this context the adoption of the Treaty represents an important step to facilitate access to PGRFA for research and breeding. However the Treaty cannot be seen in isolation from other relevant national and international legislation on biodiversity and related technologies. Complementarities and synergies in the implementation of existing legal instruments related to GRFA in the agricultural (ITPGRFA), environmental (CBD) and trade (WTO/TRIPs) sectors need to be ensured, possibly through the development of national *sui generis* provisions in line with the requirements of these three international agreements (Box 16.5) (Esquinas Alcázar, 2005). In addition, the interest of the agricultural sector needs to be well represented in these three instances. The effectiveness of the Treaty in halting or reversing the current tendency towards restriction will depend on how its provisions are interpreted and implemented by individual countries and the international community.

Farm animals, forest, fisheries and microbial genetic resources for food and agriculture

Guaranteeing a diversified, sustainable and nutritionally diverse production of food will require the conservation and sustainable use of all genetic resources for food and agriculture, including farm animals, forest, fish and micro-organisms. The Multi-Year Programme of Work (MYPOW) and its road map as negotiated and agreed by the representatives of the agricultural sector of all Member Countries in FAO through its intergovernmental CGRFA (FAO, 2007a) needs to be timely implemented. It includes the periodic publishing of reports on the States of the World of Biodiversity for Food and Agriculture to identify needs, gaps, emergencies and priorities in each sector (farm animals, forest, fisheries and microbial genetic resources). Key milestones for presentation of global assessments, as agreed by all countries, include:

- State of the World's Forest Genetic Resources (2013);
- State of the World's Aquatic Genetic Resources (2013);
- In-depth review of microorganisms (2015);
- State of the World's Biodiversity for Food and Agriculture (2017), which includes updates on status and trends for plant and animal genetic resources.

For Animal Genetic Resources for Food and Agriculture: the State of the World and the first-ever Global Plan of Action for Animal Genetic Resources were recently adopted by more than 100 countries, including the majority of OECD countries, at the Interlaken's Technical Conference on Animal Genetic Resources. The FAO Commission has been

charged with overseeing and assessing the implementation of the Global Plan of Action and developing the funding strategy for its implementation.

The MYPOW includes also consideration of important cross-sectorial matters such as access and benefit-sharing; biotechnologies; targets and indicators on genetic diversity; genetic diversity and the Millennium Development Goals.

International co-operation

A number of regional and international organisations including the European Co-operative Programme on GRFA, Bioversity International and other Centres of the Consultative Group on International Agricultural Research (CGIAR), as well as FAO and its Commission on Genetic Resources for Food and Agriculture are well placed to contribute to the implementation of some of the priority areas identified above.

Also a number of international agreements provide excellent frameworks for international co-operation, including:

- For agrobiodiversity in general: FAO Commission's Multi-year Programme of Work for Genetic Resources for Food and Agriculture, which covers all sectors of agricultural biodiversity and the CBD Agrobiodiversity Programme.
- For Plant Genetic Resources for Food and Agriculture: the International Treaty, the FAO's Commission periodic publication on the State of the World, the rolling Global Plan of Action, and the Global Crop Diversity Trust.
- For Animal Genetic Resources for Food and Agriculture: the FAO's Commission State of the World, Global Plan of Action and Global Strategy on Farm Animals Genetic Resources.

Training and public awareness

Training in this area, as well as raising public awareness on the importance of genetic diversity and the dangers of its loss are other important goals: no system of legal provisions is likely to succeed without public understanding and consensus.

It should not be forgotten that genetic erosion is just one consequence of mankind's exploitation of the planet's natural resources. The fundamental problem is a lack of respect for nature, and any lasting solution will have to involve establishing a new relationship with our planet and an understanding of its limitations and fragility. If mankind is to have a future, it is imperative that children learn this at school, and that adults make it part of their everyday life.

Conclusions

Never have we had such powerful tools to control our future, and yet never has it so been at risk. For agricultural development to be sustainable, and for some harmful processes to be reversible, it is necessary to preserve the natural resources on which development is based. The achievement of a world without hunger or poverty is the responsibility of all of us, which must not be avoided or left to chance.

ACKNOWLEDGEMENTS

I am very grateful to Juan Carlos Gutierrez Ruiz for his important assistance in the preparation and finalisation of this paper and to Francisco López Martin and Angela Hilmi for their editorial comments and corrections. I also want to thank Toby Hodgkin and Nicole Demers from Bioversity, Francisco López Martin from the Secretariat of the Treaty, and Alvaro Toledo, Elcio P. Guimaraes, and Irene Hoffmann from FAO for their contributions and important information provided.

Bibliography

Bezancon, G., *et al*. (2009), Changes in the Diversity and Geographic Distribution of Cultivated Millet (*Pennisetum glaucum* (L.) R. Br.) and Sorghum (*Sorghum bicolor* (L.) Moench) Varieties in Niger Between 1976 and 2003, *Gen Res Crop Evol* 56: 223-236.

Bragdon, S. *et al*. (2009), The Agrobiodiversity Policy Development Process: Exploring Means of Policy Development to Support the On Farm Management of Crop Genetic Diversity, *International Journal of Biodiversity Science and Management*.

Brown, A.H.D. (2008), "Indicators of Genetic Diversity, Genetic Erosion and Genetic Vulnerability for Plant Genetic Resources - A report to the Food and Agriculture Organization", 26 January 2009.

Convention on Biological Diversity, (2003), Convention on Biological Diversity Handbook 3rd ed., *http://www.biodiv.org/handbook/*.

Correa, C. (1994), "Sovereign and Property Rights over Plant Genetic Resources. Commission on Genetic Resources for Food and Agriculture. Background Study Paper No. 2", *ftp://ftp.fao.org/docrep/fao/meeting/015/aj596e.pdf*.

Correa, C. (2003), "The Access Regime and the Implementation of the FAO International Treaty on Plant Genetic Resources in the Andean Group Countries", *J. World Intellect. Prop. Rights* 6, 795-806.

Diamond, J. (2002), "Evolution, Consequences and Future of Plant and Animal Domestication", *Nature*, 418, 700-707.

Doney, D.L. and E.D. Whitney (1990), "Genetic Enhancement in Beta for Disease Resistance Using Wild Relatives - A Strong Case for the Value of Genetic Conservation", *Economy Botany,* 44(4), 445451.

Dulloo, M.E. *et al.* (2008), "Genetic Reserve Location and Design", In: J. Iriondo, N. Maxted and M. E. Dulloo (eds), *Conserving Plant Genetic Diversity in Protected Areas*, CABI Publishing, Wallingford Chapter 2, pp. 23-64.

ECPGR (2008), "A Strategic Framework for the Implementation of a European Genebank Integrated System (AEGIS)", Discussion paper, European Cooperative Programme for Plant Genetic Resources (ECPGR), Bioversity International, Rome, Italy.

Engels, J.M.M., *et al*. (2008), "Robust Seed Systems: Integrating a Genetic Resource Conservation and Sustainable Livelihood Perspective in Strategies Supporting Informal Seed Supply", In: M. H. Thijssen, Z. Bishaw, A. Beshir and W.S. de Boef (eds.), *Farmers, Seeds and Varieties: Supporting Informal Seed Supply in Ethiopia*, Wageningen, Wageningen International.

Esquinas-Alcázar, J. T. (1981), "Genetic Resources of Tomatoes and Wild Relatives", IBPGR, Rome.

Esquinas-Alcázar, J.T. (2005a), "Protecting Crop Genetic Diversity for Food Security: Political, Ethical and Technical Challenges*", Nature Reviews Genetics* Vol. 6, December, 946-953.

Esquinas-Alcázar, J.T. (2005b), "International Treaty on Plant Genetic Resources for Food and Agriculture and Other International Agreements on Plant Genetic Resources and Related Biotechnologies", Chapter 20 of *Agricultural Biodiversity and Biotechnology in Economic Development* by J. Cooper, L.M. Lipper and D. Zilberman, Natural Resource Management and Policy, Ariel Dinar and David Zilberman, Series Editors, Springer, 431-455.

FAO (1996)," Global Plan of Action for the Conservation and Sustainable Utilization of Plant Genetic Resources for Food and Agriculture", International Technical Conference on Plant Genetic Resources, Leipzig, Germany, *www.fao.org/WAICENT/FaoInfo/Agricult/AGP/AGPS/Pgrfa/Pdf/GPAENG.PDF*.

FAO (1998), "The State of the World's Plant Genetic Resources for Food and Agriculture", *www.fao.org/WAICENT/FAOINFO/AGRICULT/AGP/AGPS/Pgrfa/pdf/swrfull.pdf*.

FAO (2001a), "International Treaty for Plant Genetic Resources for Food and Agriculture", FAO Conference, *Rome, http://www.planttreaty.org*.

FAO (2001b), "Nutritional Division. Nutritional Value of Some of the Crops under Discussion in the Development of a Multilateral System", CGRFA Background Study Paper No. 11, *ftp://ftp.fao.org/docrep/fao/meeting/015/j0748e.pdf*.

FAO (2002), "Review and Development of Indicators for Genetic Diversity, Genetic Erosion and Genetic Vulnerability (GDEV): Summary Report of a Joint FAO/IPGRI Workshop", Rome, 11-14 September, 2002.

FAO (2003), "International Code of Conduct for Plant Germplasm Collecting and Transfer", FAO Conference, Rome h*ttp://www.fao.org/docrep/x5586E/x5586e0k.htm#xiv.%20appendix%20e%20%20%2*

0international%20code%20of%20conduct%20for%20plant%20germplasm%20collecting%20a.

FAO (2007a), Report of the Commission on Genetic Resources for Food and Agriculture, 11th Regular Session, 11-15 June, 2007, Rome, Italy, CGRFA-11/07/Report, *http://www.fao.org/nr/cgrfa/cgrfa-meetings/cgrfa-comm/eleventh-reg/en/*.

FAO (2007b), *The State of the World's Animal Genetic Resources for Food and Agriculture*, edited by B. Rischkowsky and D. Pilling, Rome.

Fehr, W.R. (1984), "Genetic Contributions to Yield Gains of Five Major Crop Plants", Madison, WI: *Crop Sci. Soc. Am./Am. Soc. Agron.,* 101 pp.

Fischer, G., *et al*. (2002), "Impacts of Climate on Agro-Ecology", Chapter 3 in *Climate Change and Agricultural Vulnerability*, Report by the International Institute for Applied Systems Analysis. Contribution to the World Summit on Sustainable Development, Johannesburg, 2002.

Flores Palacios, X. (1998), "Contribution to the Estimation of Countries' Interdependence in the Area of Plant Genetic Resources", CGRFA Background Study Paper No. 7 Rev.1, *ftp://ftp.fao.org/docrep/fao/meeting/015/j0747e.pdf*.

Fowler, C. and T. Hodgkin (2004), "Plant Genetic Resources for Food and Agriculture: Assessing Global Availability", *Annu. Rev. Environ. Resour*. 29, 143-179.

Fowler, C. and R. Lower (2004), "The Politics of Plant Breeding", *Plant Breeding Rev.* 25, 21-56.

Frankel, O.H. and M. Soule (1981), "Conservation and Evolution", *Cambridge Univ. Press*, Cambridge, United Kingdom, 327 pp.

Global Crop Diversity Trust, (2009), *http://www.croptrust.org/main/*.

Harlan, J.R. (1975), "Our Vanishing Genetic Resources", *Science*, 188: 618-21.

Heywood V.H. and M.E. Dulloo (2005), "*In situ* Conservation of Wild Plant Species - a Critical Global Review of Good Practices", *Technical Bulletin* No 11, International Plant Genetic Resources Institute.

Hodgkin, T., *et al*. (2003), "The Use of *ex situ* Conserved Plant Genetic Resources", *Plant Genet. Resour.* 1, 19–29.

Intergovernmental Panel on Climate Change (IPCC), (2009), *http://www.ipcc.ch*.

Jarvis, A., *et al.* (2008), "The Effect of Climate Change on Crop Wild Relatives", *Agriculture, Ecosystems and Environment*, 126 (1) 13-23.

Jarvis, D.I. *et al*. (2008), "A Global Perspective of the Richness and Evenness of Traditional Crop Variety Diversity Maintained by Farming Communities", *Proceedings of the National Academy of Sciences, USA,* 108; 5326-5331.

Khush, G.S. and H.M. Beachell (1972), "Breeding for Disease Resistance at IRRI", in *Rice Breeding*, p. 309-322, IRRI, Los Baños, The Philippines.

Kihara, H. (1983), "Origin and History of 'Daruma', a Parental Variety of Norin 10", in *Proceedings of the Sixth International Wheat Genetics Symposium*, 6:13-19.

Kronstad, W.E. (1986), "Germplasm: The Key to Past and Future Wheat Improvement", In Smith *et al., Genetic Improvement of Yield in Wheat*, p. 41-54, Special publication 13, *Crop Science Society of America*, Madison, Wisconsin.

Laliberté, B. and C. Fowler (2007), "The Global Crop Diversity Trust: Developing Strategies towards Efficient and Effective *Ex Situ* PGR Conservation", *Proc. XXVII IHC-S1 Plant Gen. Resources*, Ed.-in-Chief: K.E. Hummer Acta Hort. 760, ISHS.

Lenstra, *et al*. (2005), "Evolutionary and Demographic History of Sheep and Goats Suggested by Nuclear, mtDNA and y-chromosome Markers", Presented at meeting on The Role of Biotechnology, Villa Gualino, Turin, Italy – 5-7 March 2005.

Maxted, N. and L. Guarino (2006), "Genetic Erosion and Genetic Pollution of Crop Wild Relatives", In B.V. Ford-Lloyd, S.R. Dias and E. Bettencourt, (eds), *Genetic Erosion and Pollution Assessment Methodologies*, pp.35- 45, Biodiversity International, Rome, Italy.

Maxted, N. and S.P. Kell (2009), "Establishment of a Global Network for the In Situ Conservation of Crop Wild Relatives: Status and Needs", FAO Commission on Genetic Resources for Food and Agriculture, Rome, Italy, 266 pp, *http://www.fao.org/nr/cgrfa/cgrfa-back/en/?no_cache=1*.

Meilleur, B.A. and T. Hodgkin (2004), "*In situ* Conservation of Crop Wild Relatives: Status and Trends", *Biodiversity and Conservation*, 13:663-684.

Moraesa, A.P. (2007), "Chromosomal Markers Distinguish Hybrids and Non-Hybrid Accessions of Mandarin", *Cytogenet Genome Res* 119:275-281, Spooner, D.M. *et al.*, Molecular Markers for Genebank Management, International Plant Genetic Resources Institute, Rome, 126 pp.

National Research Council (1972), "Genetic Vulnerability of Major Crops", National Academy of Sciences, Washington DC.

Tivang, J.G., *et al.* (1994), "Estimation of Sampling Variance of Molecular Marker Data Using the Bootstrap Procedure", *Theor Appl Genet* 89:259-264.

Vicente, M.C. de (2004), "The Evolving Role of Genebanks in the Fast-Developing Field of Molecular Genetics", Issues in *Genetic Resources* No. XI, IPGRI, Rome, Italy.

WIEWS (2009), World Information an Early Warning Systems, *http://apps3.fao.org/WIEWS*.

Part V

Regulatory Challenges

Summary of discussions

Dr. Ervin Balazs, Agricultural Research Institute, Department of Applied Genomics, Hungarian Academy of Sciences

Changes in the international policy arena have contributed to the reshaping of the environment for agricultural biotechnology research. The adoption of the Cartagena Protocol on Biosafety has brought about immense challenges in terms of establishment, implementation and compliance with regulation.

Agriculture in the twenty-first century is facing unprecedented challenges. The world is already facing a serious food crisis resulting from soaring food prices and climate change. The price rises have plunged an additional 75 million people below the hunger threshold, bringing the estimated number of undernourished people worldwide to above 900 million in 2007. The world's population is estimated to increase up to 10 billion in 2050. There are not many solutions to this challenge, while the measures needed go far beyond the issue of producing more food and agricultural products. The key issue of developing policy for the developing world must include boosting the productivity of small farms through the application of good agricultural practices and improved technologies. Biotechnology can play an important role in combating against food scarcity and can help in maintaining food security. During the last three decades the agricultural sector has experienced attempts to increase crop production and improve life stocks. These efforts raised concerns in the different stakeholders of societies. The spectacular results of genetic engineering and animal cloning due to their high value and unprecedented results initiated their regulation both on national and international levels. Starting with the famous Berg letter of the early seventies, followed by the releases of National Institutes of Health (NIH) guidelines and the OECD Blue book on Recombinant DNA safety consideration in 1986, through to today, this is still a controversial issue in the international political arena. Nevertheless, modern biotechnology could contribute to the fight against hunger and improving human health, besides its positive role in environmental issues. The session devoted to the regulatory challenges of the conference covered two major aspects of this issue, namely, the ethical and regulatory question of animal cloning by comparing the North American and the EU perspectives, and the second, how large international organisations are dealing with these questions.

Larisa Rudenko summarised the recent achievements in and the reputation of animal cloning in the USA. She concluded that food from cattle, swine, and goat clones that meet federal and state requirements is as safe as *food from conventional animals that meet the same requirements. Regarding clone progeny, the food from clone offspring poses no additional risk compared with food from other animals. She also gave an excellent summary of how genetically engineered animals are considered under the regulatory framework of the USA.*

Louis-Marie Houdebine described the latest research results and experiences with animal cloning and transgenesis. He detailed the efficiency of cloning by listing data on clone numbers in the EU and in the USA and the lack of data on life span of those clones. He also mentioned the limited knowledge on the genome of the nuclear donors, that cloning does not increase the mutational number in foetal clones and that the telomere length in cattle, pig and goat clones are normal. In his overview, he summarised the European Food Safety Authority (EFSA) conclusion as being very similar to the US official conclusions on food from clones and from their progeny. He also mentioned in detail the typical European attitude towards cloning that more research is needed.

Peter Kearns in his overview of the OECD activity on biosafety regulatory issues started with the first activity of the Organisation by the publication of the Blue Book followed by the description of the OECD's Working Group on Harmonisation of Regulatory Oversight in Biotechnology, which started its activity in 1995. He gave details on the current and very important activity of this working group by editing and issuing consensus documents on safety assessment of transgenic microbes, plants and animals. These documents can be downloaded from the OECD official web site. He also underlined the importance of the collaborative efforts with different international organisations involved in their activities in this field such as FAO, the International Centre for Genetic Engineering and Biotechnology (ICGEB), UNESCO, CBD and the EFSA.

Detlef Bartsch in his talk described the EFSA GMO panel tasks and mandate. The EFSA examines dossiers submitted by companies for scientific evaluation on environmental and health issues for potential introduction of GMOs, with special emphasis on risk assessment and risk management. Both lectures presented excellent overviews on the regulatory challenges for regulators and for all stakeholders.

Chapter 17

Animal Biotechnology in the United States: the Regulation of Animal Clones and Genetically Engineered Animals

Larisa Rudenko, PhD DABT

Senior Advisor for Biotechnology, Center for Veterinary Medicine
US Food and Drug Administration, United States

The implementation of genetic engineering in animals is a rapidly developing field. In January 2009, the US FDA issued the final version of its Guidance on the Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs. This document clarifies the FDA's statutory and regulatory authority, and provides recommendations to producers of GE animals to help them meet their obligations and responsibilities under the Federal Food, Drug, and Cosmetic Act. The FFDCA defines "articles (other than food) intended to affect the structure or any function of the body of man or other animals" as drugs. Because an rDNA construct in a GE animal is intended to affect the animal's structure or function, it meets the definition of a new animal drug, whether the animal is intended for food, or used to produce another substance. The FDA has developed a risk-based approach to the regulation of these rDNA constructs in GE animals. This approach is cumulative and hierarchical beginning with hazard characterisation of the rDNA construct, phenotypic characterisation of the resulting GE animal, and makes safety determinations on a weight of evidence basis. Producers of GE animals must demonstrate that the rDNA construct is safe for the GE animal, if intended for food or feed, safe to humans or animals consuming edible products from GE animals, or if not, demonstrate that such animal will not enter the food supply. They must also demonstrate that the GE animal is safe for the environment. The FDA must agree that the producers have developed a plan to demonstrate the durability of the genotype and phenotype of the GE animal over the commercial lifetime of the animal. Finally, producers of these animals must demonstrate that the claims being made on behalf of the GE animal can be validated. Because each rDNA construct in each animal poses a different set of risks, all evaluations are made on a case-by-case basis, following close interactions between the agency and the producer of the GE animal. This approach is entirely consistent with that in the Codex Alimentarius Guidelines for the Food Safety Evaluation of Food from rDNA Animals.

Introduction

Animal biotechnology can be thought of as a continuum of the human interventions that began with selective breeding aimed at increasing the prevalence of naturally occurring desirable traits (phenotypes) in individual animals or populations (*e.g.* herds, flocks, schools). Assisted reproductive technologies (ARTs) are a form of animal biotechnology that allow the distribution of genetics beyond natural matings, and include selective breeding, artificial insemination (AI), multiple ovulation embryo transfer, in vitro fertilisation, and embryo splitting. These are in common use in modern agriculture around the world; they have been responsible both for the introduction of geographically disparate genetics and traits into current production herds and the rescue and propagation of rare genotypes.

Two recently developed forms of animal biotechnology that have captured the attention of the USA regulatory community are animal cloning and the genetic engineering of animals. We have determined that cloning, in the absence of the introduction of new genes, falls on the continuum of ARTs. Genetic engineering, on the other hand, introduces new genes that may encode novel traits, and thus does not fall on that continuum. These two technologies are regulated in markedly different ways in the United States.

Regulation of animal clones

Cloning, or somatic cell nuclear transfer (SCNT), is a process by which animals are reproduced asexually (embryo splitting and blastomere nuclear transfer are other ways of reproducing animals asexually). In cloning, a differentiated somatic cell from an existing animal is introduced to an oöcyte that has had its nucleus, and thus its genome, removed. Following some additional manipulations that fused cell is induced to start replicating. If all goes well, the dividing cell is implanted into a female animal (dam), continues to develop normally, and is delivered.

Somatic cell nuclear transfer was pioneered in 1962, when Gurdon first employed a two-step "nuclear transfer" process in frogs (oöcyte enucleation and differentiated cell nuclear transfer). Although the process was successful in that reconstituted cells appeared to reprogramme (dedifferentiate) the transferred nuclei and to produce zygotes that developed into tadpoles, the tadpoles failed to metamorphose into frogs. Subsequent attempts to apply this technique to other species were unsuccessful until 1986, when Prather and colleagues, using nuclear transfer, produced a cow from early embryonic cells (Prather *et al.*, 1987). This blastomere nuclear transfer effectively set the stage for the birth of Dolly the sheep a decade later, on 5 July 1996 (Wilmut *et al.*, 1997). Dolly was the first organism ever to be produced using an adult cell as a nuclear donor (somatic cell nuclear transfer). Since that time, many other species have been cloned, from mice to camels, although in some cases (*e.g.* companion animals) only limited numbers of animals have been generated.

Uses of cloning in agriculture

Clones are intended to be used as elite breeding animals (Clones Are for Breeding, Not Eating). Modern livestock breeding, particularly of cattle, can be described best by the "breeding pyramid", in which elite animals are used as the genetic donors to a production system. These animals are bred to produce "multiplier herds", whose genetic

value has been diluted by one round of sexual reproduction, followed by another round of breeding to generate the "production herd", which are the animals used for food, especially beef. Swine breeding generally uses semen from elite breeders to generate production stock. In general, elite breeders are produced by some sort of ART; when expensive technologies, such as embryo transfer following in vitro fertilisation or embryo splitting, are used, they tend to be used to produce elite breeders. When the resulting multiplier animals (for cattle breeding) are used as sources of genetics, AI tends to be used. Natural mating (NM) can be (and is) used throughout the breeding cycles, as well. Cloning (or SCNT) is now being used to produce elite breeders.

Therefore, although much of the Risk Assessment was concerned with the food consumption risks for animal clones, in reality, only a small number of clones will likely be eaten for meat, or have their milk used for human consumption (See subsequent section "Current Status of Cloning in the USA"). It is highly unlikely that bull clones will end up in the food supply as meat until their intended use as breeders has been accomplished. Boar clones will likely never end up in the food supply in the USA as the testosterone produced when the animals become sexually mature imparts a "taint" that is generally unacceptable to American palates. Because clones are intended as breeding stock, it is extremely unlikely that sexually immature clones would be used for food.

When it became apparent that livestock produced via SCNT or the sexually reproduced offspring of animals produced by SCNT could become sources of food, producers of these animals approached the agency to ask if they would require any further regulation. FDA's Center for Veterinary Medicine (CVM) issued a statement indicating that the agency intended to assess potential risks presented by cloning food-producing animals, and requesting that producers and breeders of clones refrain from introducing meat or milk from animal clones or their progeny into the human or animal food supply pending completion of the risk assessment process (Update on Livestock Cloning: *http://www.fda.gov/AnimalVeterinary/NewsEventsCVMUpdates/ucm127240.htm*).

Among the Risk Assessment's goals were the determination of whether SCNT posed any unique risks to animals involved in cloning compared with other ARTs and whether foods derived from animal clones or their progeny pose consumption risks greater than those posed by foods derived from their conventional counterparts. The focus of the Risk Assessment was on those domestic livestock that have been cloned, *i.e.*, cattle, swine, sheep, and goats. All of the data evaluated in the Risk Assessment are available, either in peer-reviewed publications or in the Risk Assessment itself. In addition, the methodology used to evaluate the data, underlying assumptions used by the risk assessors, residual uncertainties, including sources of potential bias, and the basis for CVM's conclusions are explicitly stated in the Risk Assessment.

When this process began, there were no existing risk assessment paradigms with which to evaluate the safety of food from clones or their progeny. Two complementary approaches were developed: the *Critical Biological Systems Approach* (CBSA) and *Compositional Analysis Approach*, to identify and characterise potential animal health and food consumption hazards. The agency then used a weight of evidence approach to draw conclusions regarding risks to animal health and risks from consumption of food products from clones and their progeny. This approach was presented to the Center's Veterinary Medicine Advisory Committee (VMAC), which concurred with the overall methodology. In addition, an external peer review committee evaluated the draft Risk Assessment prior to its release; this committee also concluded that the approach employed by the agency was appropriate. The Risk Assessment and other related

documents are posted on the agency's website at *http://www.fda.gov/AnimalVeterinary/SafetyHealth/AnimalCloning/default.htm*.

Conclusions of the risk assessment

The Risk Assessment assumed that animal clones, their progeny, and all food products derived from either clones or progeny must meet the same federal, state, and local laws and regulations as food from conventionally bred animals.

Source of hazards

Because the Risk Assessment excluded genetically engineered clones, all of the genes present in clones come from their traditionally bred domestic livestock counterparts. During their long history of safe use as food, domestic livestock have not been found to produce toxic substances. Therefore, hazards to and from clones themselves would result from epigenetic dysregulation of existing genes – their inappropriate expression, including over- or under-expression, or expression at the wrong time. A direct corollary of this underlying biological assumption is that the adverse outcomes associated with clones are all problems of development, and that such errors occur as part of conventional sexual reproduction. The underlying biological assumption, therefore, is that there will be no unique risks associated with cloning, and that all of the adverse outcomes one might reasonably expect have already been observed. The Risk Assessment reviewed all of the available data and determined that, within the limitations of the data, this was indeed the case.

Animal health

The risk assessment concluded that the cloning process poses no unique risks to the animals involved, either the surrogate dam or the clone itself. All of the adverse outcomes that had been noted in these animals were qualitatively the same as those encountered in other assisted reproductive technologies or even natural mating. In some studies, particularly earlier reports, or in reports from laboratories with limited experience, rates of adverse outcomes were higher than those observed for current experiences with other ARTs. A careful look at the historical data indicated that the rates of adverse outcomes noted when ARTs first were employed also were considerably higher than they are now.

Cattle and sheep clones exhibited a syndrome first identified in *in vitro* production (IVP) of embryos called Large Offspring Syndrome (LOS), which appears to result from inappropriate placentation during early embryonic and fetal development. LOS can vary from causing very severe health risks to the surrogate dam and the fetus, resulting in death, to relatively mild outcomes that require little to no supportive care. Symptoms associated with LOS include overly large, edematous (fluid-filled) fetuses, cardiovascular abnormalities, difficulty breathing or maintaining body temperature, and contracted tendons. Surrogate dams can suffer from hydrops, or too much fluid accumulating in the uterus, which can result in death if untreated.

Although LOS poses the highest degree of animal health risk associated with cloning of cattle and sheep, it is important to point out that not all clone pregnancies are affected by LOS. In fact, most calf and lamb clones are born healthy, grow and reproduce normally, and are no more susceptible to health problems than their non-clone counterparts. In swine and goats, cloning-associated abnormalities are far less common

than in cattle and sheep; LOS is not observed in these species, and the vast majority of swine and goat clones are born healthy without subsequent health problems.

Any health problems noted in the perinatal period are generally resolved by the time that clones reach the juvenile period; there is no evidence that clones develop any new health problems after the juvenile period of life. A key study investigated the degree to which the physiological status of cattle clones resembles that of breed, age, and gender-matched comparators by examining the standard panel of 17 clinical chemistry measurements (a panel similar to basic blood work done for humans). This study revealed that at ages 1-6 months, 96% of the parameters were within the same range, and at 6-24 months of age, 99% of the parameters were within range. A similar study demonstrated that by 27 weeks of age, offspring of swine clones were within 98% and 99%, respectively, of the ranges of hematological and clinical chemistry measurements of conventionally bred comparators (*www.fda.gov/AnimalVeterinary/SafetyHealth/ Animal Cloning/ucm055489.htm*).

Some have expressed concerns that clones do not live as long as conventionally bred animals, or that they exhibit premature aging. In fact, recent Japanese studies, which evaluated the health and production status and lifespans of all of the clones and all the sexually reproduced offspring of clones that have ever been produced in Japan, found that these animals do not appear to have any new health issues arising that cannot be traced back to the developmental problems; do not appear to require additional veterinary care; do not show any increased susceptibility to illness; and do not have shorter lifespans than conventionally bred animals (Watanabe and Nagai, 2008; Watanabe and Nagai, 2009)

To help minimise risks to both surrogate dams and clones themselves, FDA worked with the International Embryo Transfer Society (IETS) to develop a set of animal care standards. Written by an international group with expertise cloning diverse species, this set of standards is posted on the IETS web site (*www.iets.org*).

In summary, no unique adverse outcomes are associated with cloning, and evaluation of extensive health records, developmental data, and blood work show that clones that survive the perinatal period are perfectly healthy, and walk, wean, grow, mature, and have behaviours similar to conventionally bred animals. The sexually reproduced offspring of clones were found to be the same as any sexually reproduced animals.

Food consumption conclusions

Clones: As a baseline, clones and food products derived from them would be subject to all of the same federal, state, and local regulations as conventional livestock. By analysing physiological, anatomical, health, and when available, behavioural data, the agency determined that anomalies present in cattle, swine or goat clones are the same as those associated with any other ART. In fact, these animals meet all of the developmental milestones appropriate for their species, and become otherwise indistinguishable from sexually-reproduced comparators. Evaluation of all of the available information on the composition of milk and meat from bovine clones did not reveal any significant differences between milk from clones and milk from sexually-reproduced cows. The agency therefore concluded that edible products derived from cattle, swine, and goat clones pose no more risk than food derived from sexually reproduced animals, *i.e.* they are as safe as the foods we eat every day. Insufficient information was available to make a decision on food consumption risks from clones of species other than cattle, swine, and goats.

Progeny: For clone progeny (*i.e.* sexually-reproduced offspring of clones), the agency agreed with the National Academies of Science (2002) that there is no anticipated additional risk of epigenetic dysregulation compared to animals of conventional breeding lineages. In fact, known aberrant phenotypes caused by epigenetic dysregulation in mouse clones have not been shown to be heritable (Tamashiro *et al.*, 2003). Further, analysis of an extensive set of data on the health and meat composition of the sexually reproduced offspring of swine clones indicated that those animals were indistinguishable from other sexually reproduced animals raised under identical conditions (Walker *et al.*, 2002). The agency therefore concluded that food from the progeny of clone traditionally consumed as food poses no more risk than food from any other sexually-reproduced animal traditionally consumed as food. Food from the progeny of clones is the same as food we eat every day.

Current status of cloning in the USA

On 15 January 2008, the final version of the Risk Assessment and associated documents (A Risk Management document [*www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AnimalCloning/UCM124756.pdf*] and Guidance for Industry #179 [*www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052469.pdf*]) were released by the FDA, jointly with the Undersecretary of Marketing and Research Services of the United States Department of Agriculture. The primary announcement was that the US government (USG) had no further science-based concerns regarding cloning or the food from clones[1] or their sexually reproduced offspring. The USG further determined that cloning falls on the continuum of ARTs, and food from cattle, swine, or goat clones or the sexually reproduced offspring of the clone of any species of animal traditionally consumed as food requires no further regulation beyond that applied to food from animals produced by any reproductive method. The announcement emphasised that the sexually reproduced offspring of clones were not "clones", but rather, were the same as any other sexually reproduced animals.

In order to ensure a smooth and orderly transition to the domestic market, however, and so as not to cause disruptions in trade due to asymmetrical decision-making, USDA asked industry if it would continue to refrain from introducing food from clones themselves (but not their offspring) into the food supply until such time that other governments can develop their own regulatory programmes.

Industry has since developed a supply chain management programme for meat that consists of three components: education, identification and traceability, and financial incentives (*www.clonesafety.org/cloning/scm/*). Briefly, all clones are entered into a registry and provided with identification. At slaughter, clones are directed to food streams that will accept clones. Once the clone owner demonstrates that the carcass has been disposed of in an acceptable manner, a refund exceeding the commercial value of the carcass is issued. USDA is in the process of validating this system.

During the intervening time, meat and milk from the sexually reproduced offspring of clones have been entering the food supply. Because no moratorium had been requested for the genetics from clones, once the draft Risk Assessment and its essentially positive findings on food safety had been released, sales of semen from bull clones proceeded internationally. The USA does not monitor the number of clones or their sexually reproduced offspring. Due to the free flow of genetics across the world, it would be extremely difficult, if not impossible, to determine definitively the extent to which the offspring of clones are found in commerce (or the food supply).

Regulation of genetically engineered animals

Introduction

GE animals have been produced since the early 1980s when Brinster *et al.* (1982) and Palmiter *et al.* (1982) reported on the development of GE mice. Not long thereafter, Hammer *et al.* (1985) demonstrated that rabbits and pigs could also be genetically engineered. Now, more than two decades later, many different species, including those traditionally consumed as food, have been engineered with various rDNA constructs.

GE animals currently being developed can be divided into several broad classes based on the intended purpose of the genetic modification: (i) to enhance food quality or agronomic traits (*e.g.* pigs with less environmentally deleterious wastes, faster growing fish); (ii) to improve animal health (*e.g.* disease resistance); (iii) to produce products intended for human therapeutic use (*e.g.* pharmaceutical products or tissues for transplantation; these GE animals are sometimes referred to as "biopharm" animals); (iv) to enrich or enhance the animals' interactions with humans (*e.g.* hypo-allergenic pets); (v) to develop animal models for human diseases (*e.g.* pigs as models for cardiovascular or inflammatory diseases); and (vi) to produce industrial or consumer products (*e.g.* fibres for multiple uses).

In January 2009, following a formal notice and comment period, FDA issued Guidance for Industry 187: Regulation of Genetically Engineered Animals Containing Heritable Recombinant DNA Constructs (*www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM113903.pdf)*. For the purpose of the guidance, FDA defined "genetically engineered (GE) animals" as those animals modified by rDNA techniques, including all progeny that contain the modification. The term GE animal can refer both to an animal with a heritable rDNA construct and to an animal with a non-heritable rDNA construct (*e.g.* a construct intended as therapy for a disease in that animal).

FDA regulates GE animals under the new animal drug provisions of the Federal Food Drug and Cosmetic Act (FFDCA or the Act), 21 USC 321 *et seq.*, and the National Environmental Policy Act (NEPA). Section 201(g) of FFDCA defines drugs as "articles (other than food) intended to affect the structure or any function of the body of man or other animals." The rDNA construct in the resulting GE animal is thus a regulated article that meets the drug definition; the GE animal itself is not a drug. As a short-hand, the agency sometime refers to regulating the GE animal. All GE animals are captured under these provisions, regardless of their intended use.

Enforcement discretion

In general, premarket approval requirements apply to GE animals before they are commercialised, and potential significant environmental impacts, if any, must be examined before approval as required by NEPA. Under certain conditions, based on risk, the agency may not require an approval for some GE animals. In general, these include GE animals of non-food-species that are regulated by other government agencies or entities, such as GE insects being developed for plant pest control or animal health protection, and GE animals of non-food-species that are raised and used in contained and controlled conditions such as GE laboratory animals (*e.g.* mice, rats, some model fish)

used in research institutions. The agency does not expect to exercise enforcement discretion for any animals not traditionally consumed as food.

In addition, on a case-by-case basis, the agency may consider exercising enforcement discretion for GE animals of very low risk, non-food-species GE animals, such as the *Zebra danio* aquarium fish genetically engineered to fluoresce in the dark (GloFish) (*www.fda.gov/bbs/topics/NEWS/2003/NEW00994.html*). In such cases, producers of those animals should come to CVM to discuss their particular construct and resulting GE animals.

The investigational phase and the investigational new animal drug (INAD) file

In general, approvals are required prior to the commercial introduction of GE animals. During the investigational phase (often referred to as "research and development"), sponsors (the parties legally responsible for meeting the obligations and responsibilities under FFDCA and NEPA), may wish to consult with the agency and submit components of a new animal drug application (NADA) for approval. In order to do so, sponsors should ask CVM to open an investigational new animal drug (INAD) file. This administrative file allows the sponsor to have confidential communications with the agency, to discuss or submit data being developed in support of an NADA, and to receive an exemption from the approval requirement in order to cover shipments in interstate commerce and for clinical investigations [21 CFR 511.1(b)]. This exemption allows for certain activities to occur during the development of a GE animal, imposes certain requirements on the sponsor, and allows the agency to make certain regulatory decisions 21 CFR 511.1(b)(1)-(5). These include providing instructions for shipping and labelling investigational animals and their products, disposition of investigational animals, and possible investigational food use authorisations for some classes of investigational animals. It also allows for an initial look at NEPA driven environmental issues.

Risk-based approach to assessing genetically engineered (GE) animals

CVM has developed a new hierarchical risk-based approach to assess GE animals and their edible products. It does not rely on a single "critical" study, but rather on the cumulative weight of the evidence provided by all of the steps in the review. It is risk-based because it examines both the *potential hazards* (that is, components that may cause an adverse outcome) identified at each step along the hierarchical pathway and *likelihood of harm* among the receptor populations (that is, those individuals or populations exposed to the GE animal(s) or their products.

Consistent with other FDA reviews of the products of biotechnology, this approach is, in general, "event-based." An event can be defined as the result of an insertion(s) of a recombinant DNA construct that occurs as the result of a specific introduction of the DNA to a target cell or organism. Animals derived from different events, even if they are based on the previously approved construct(s), would require separate evaluations.

Step 1: Product definition

The hierarchical process is based on a product definition, which in turn drives subsequent data generation and review. Product definitions ultimately characterise the GE animal intended to enter commerce, and should include the following: the ploidy and zygosity of the GE animal; a description of the animal, including the common name, genus and species; the name and number of copies of the rDNA construct; the location of

the insert; the name of the GE animal line; and the claim being made for the animal. CVM recommends that sponsors identify the GE animal's genomic DNA sequences flanking the integration site(s) of the inserted rDNA to protect their intellectual property. The construct may also be given a proprietary name for similar protection.

Step 2: Molecular characterisation of the construct

CVM recommends that sponsors provide fundamental information for identifying and characterising the rDNA construct intended to be introduced into the GE animal intended for marketing. In general, information should be provided to describe the purpose of the modification; source(s) of the introduced DNA; details of how the rDNA construct was assembled; the intended function(s) of the introduced DNA; the sequence of the introduced DNA; and its purity prior to introduction into the initial animal or cell to be used as a nuclear donor to produce an animal via nuclear transfer.

Step 3: Molecular characterisation of the GE animal

In this step, CVM evaluates the data and information supplied on the event that identifies and characterises the subsequent GE animal, the production of the GE animal(s) intended to enter commerce, and the potential hazards that may be introduced into the animal as part of its production. Key data and information include the method by which the rDNA construct was introduced into the initial GE animal, whether the resulting animal was chimeric, and the nature of the breeding strategy used to produce the lineage progenitor.

The lineage progenitor is defined as the animal from which the animals intended to be commercialised are derived; it contains the final stabilised version of the initial event. To characterise this key animal, sponsors should provide information on the genomic location(s) of the rDNA construct's insertion site(s); number of copies of the rDNA construct at each insertion site; whether the insertion occurs in an active transcriptional region; and whether analysis of flanking sequences can help determine whether harm is likely to result from the interruption of a coding or regulatory region (insertional mutagenesis).

Step 4: Phenotypic characterisation of the GE Animal

In this and the following steps, the agency seeks to determine whether any production of the GE animal poses any public health risks (risks to human health, risks to animal health, or risks to the environment). It does so by evaluating the expression of the introduced trait and its effect(s) on the resulting GE animal. First evaluated are the data that characterise whether the rDNA construct or its expression product(s) cause any direct toxicity – that is, whether there are any adverse effects attributable to the intrinsic toxicity of the construct or its expression product(s). Indirect effects also are evaluated (indirect effects are those that may be caused by the perturbations of physiological systems by the construct or its expression product(s) (*e.g.* the expression product may change the expression level of another protein). In general, CVM recommends that sponsors compile and submit data and information addressing the health of the GE animals, including veterinary and treatment records, growth rates, reproductive function, and behaviour. In addition, CVM recommends that data on the physiological status of the GE animals, including clinical chemistry, hematology, histopathology, and post-mortem results, be submitted for evaluation.

Step 5: Durability: genotypic and phenotypic plan

This step is intended to provide information to ensure that the specific event defining the GE animal being evaluated is durable – that is, that there is a reasonable expectation that the gene construct is stably inherited and that the phenotype is consistent and predictable. CVM's specific intention for this step is for the sponsor to provide a plan to ensure that the GE animals for which data are submitted and evaluated for approval are equivalent to those intended for distribution in commerce over the commercial lifetime of the GE animal (or its products). Particular attention should be paid to the identification of GE animals derived immediately from the lineage progenitor, and the preservation of genetic material that could be used to regenerate the genetic line of the lineage progenitor if necessary. As part of the plan, CVM recommends that sponsors maintain accurate and comprehensive records of their breeding strategy, as well as the actual breeding.

For genotypic stability, CVM recommends that sponsors use the results of studies demonstrating that the inserted transgene is consistently inherited. To demonstrate phenotypic durability, CVM recommends that sponsors submit data on the consistency of the expressed trait (based on the claim being made) over multiple generations. CVM recommends that sponsors gather data on inheritance and expression from at least two generations, preferably more, and recommends that at least two of the sampling points be from non-contiguous generations (*e.g.* F_2 and F_4).

Step 6: Food/feed/environmental safety

a. Food/feed safety

The food and feed safety step of the hierarchical review process addresses the issue of whether food or feed from GE animal poses any risk to humans or animals consuming edible products from GE animals compared with the appropriate non-transgenic comparators.

The risk questions involved can be divided into two overall categories. The first ask whether there is any direct toxicity, including allergenicity, via food or feed consumption associated with the expression product of the construct or components of the construct. The second category of questions addresses potential indirect toxicity associated with both the transgene and its expressed product (*e.g.* will expression of the transgene affect physiological processes in the resulting animal such that unintended food/feed consumption hazards are created, or existing food/feed consumption risks are increased). Potential adverse outcomes via the food/feed exposure pathway can be identified by (i) determining whether there are any biologically relevant changes to the physiology of the animal (assessed partly in *Step 3: Phenotypic characterisation of the GE animal*), and (ii) whether reason for toxicological concern is suggested by any biologically relevant changes in the composition of edible products from the GE animal compared with those from the appropriate non-transgenic comparator.

b. Environmental safety

Because of the requirements set forth in the National Environmental Protection Act (NEPA) and FDA environmental impact regulations in 21 CFR 25, the Agency typically must prepare an environmental assessment (EA) for each NADA approval action. The EA generally focuses on potential impacts related to the use and disposal of the GE animal. In general, the EA should describe and discuss the following: (i) the genotype, phenotype and general biology of the GE animal; (ii) potential sources and pathways of escape (or release) and spread of the GE animal; (iii) the types and extent of physical and biological

confinement, if any that will be implemented; and (iv) the potentially accessible ecosystems and their characteristics. CVM recommends that the sponsor contact CVM before proceeding with preparation of the EA in order to insure that it is appropriately focused. In the event that the EA results in a finding that a significant environmental impact may result, an Environmental Impact Statement may need to be prepared.

Step 7: Claim validation

The previous steps of the hierarchical review approach primarily address identity and safety issues. In the last step of pre-market review, the "effectiveness" portion of the proposed claim for the GE animal is validated. In order to demonstrate effectiveness, sponsors must present substantial evidence – that is, one or more adequate and well controlled investigations [21 U.S.C. 360b(d)(3)] to validate the claim that is being made. Because the product definition contains the eventual claim, CVM recommends that sponsors contact the Center early in the development of the GE animal to reach agreement on (i) what would constitute a suitable claim; (ii) the nature and conduct of studies that would validate that claim.

Transparency and public participation

The FDA is interested in increasing the transparency of its decision-making process. To that end, after CVM has completed its review of the data and information to demonstrate safety and effectiveness, the FDA intends to hold a public Veterinary Medicine Advisory Committee meeting to present its findings and receive input from the committee, as well as comments from the public. Once the FDA has considered both the committee recommendation and the public comments, it can issue a statement regarding approval.

Summary

FDA regulates the products of the two newest forms of animal biotechnology in different ways. Cloning is considered to fall on the continuum of assisted reproductive technologies. Sufficient data were available for the agency to determine that food from cattle, swine, and goat clones is as safe to eat as food from their sexually reproduced counterparts. The sexually reproduced offspring of clones are the same as any other sexually reproduced animals, and food from the sexually reproduced offspring of clones is the same as food from any other sexually reproduced animals. At this time, in order to ensure a smooth transition to the market, the USDA has requested that producers of clones continue to keep food from clones out of the general food supply. Food from the sexually reproduced offspring of clones has been entering the food supply freely.

Genetically engineered animals, on the other hand, are regulated under the new animal drug provisions of the FFDCA, and as such must receive formal approval before they may be introduced into commerce. The agency has issued a Guidance for Industry clarifying its statutory authority to regulate GE animals and a set of recommendations for how data and information may be submitted to the agency for review of applications for approval. The agency stresses that, due to the case by case nature of its evaluations, producers of GE animals approach the agency as early in the development process as possible and work closely with CVM to ensure that the appropriate data are developed in the most efficient and effective manner.

Note

1. For purposes of brevity, "clones" refers to cattle, swine, and goat clones.

Bibliography

Brinster, R. L., *et al.* (1982), "Regulation of Metallothionein--Thymidine Kinase Fusion Plasmids Injected into Mouse Eggs", *Nature* 296, 39-42.

Hammer, R.E., *et al.* (1985), "Production of Transgenic Rabbits, Sheep and Pigs by Microinjection", *Nature*, Vol. 315 No. 6021 pp. 680-683.

Palmiter, R.D., *et al.* (1982), "Dramatic Growth of Mice that Develop from Eggs Microinjected with Metallothionein-Growth Hormone Fusion Genes", *Nature,* Vol. 300 pp. 611-615.

Palmiter, R.D., H.Y. Chen and R.L. Brinster (1982), "Differential Regulation of Metallothionein-Thymidine Kinase Fusion Genes in Transgenic Mice and Their Offspring", *Cell*., Vol. 29 No. 2 pp. 701-710.

Prather, R., *et al.* (1987), "Nuclear Transplantation in the Bovine Embryo: Assessment of Donor Nuclei and Recipient Occyte", *Biol. Reprod.* 37:859.

Tamashiro, K.L., *et al.* (2003), "Cloned Mice Have an Obese Phenotype Not Transmitted to Their Offspring", *Nature Medicine*, Vol. 8 No.3 pp. 262-7.

Walker, S.C., *et al.* (2002), "A Highly Efficient Method for Porcine Cloning by Nuclear Transfer Using *In Vitro*-Matured Oocytes", *Clon. Stem Cells* 4, pp. 105-112.

Walker, S.C. (2007) "Comparison of Meat Composition from Offspring of Cloned and Conventionally Produced Boars", *Theriogenology,* Vol. 67 pp. 178-184.

Watanabe, S. and T. Nagai (2008), "Health Status and Productive Performance of Somatic Cell Cloned Cattle and Their Offspring Produced in Japan", *Journal of Reproduction and Development,* Vol. 54 No.1 pp. 6-17.

Watanabe, S. and T. Nagai (2009), "Death Losses Due to Stillbirth, Neonatal Death and Diseases in Cloned Cattle Derived from Somatic Cell Nuclear Transfer and Their Progeny: a Result of National Survey in Japan", *Animal Science Journal*, Vol. 80 pp. 233-238.

Wilmut, I. (1997), "Viable Offspring Derived from Fetal and Adult Mammalian Cells" *Nature*, 385: 810-813.

Chapter 18

Animal Cloning and Transgenesis

Dr. Louis-Marie Houdebine

Joint Research Unit for Developmental Biology and Reproduction, INRA, France

Two techniques, cloning and transgenesis, offer new possibilities to improve the exploitation of farm animal genomes. Cloning is a way to generate genitors having the same genome as that of their genetic parents. This allows the prolonged use of genitors having a high value genome validated by the properties of their offspring born after sexual reproduction. Transgenesis is a way to introduce known new traits into genitors in only one generation. This implies foreign gene addition to a genome or specific inactivation of endogenous genes. Among the current projects are the generation and the study of animals having resistance to diseases, accelerated growth, improved milk or meat composition, milk containing anti-pathogen proteins or reducing pollution. Cloning and transgenesis are thus opposite but complementary techniques. Cloning is implemented to generate some transgenic animals and it will be implemented to spread the transgenic traits into herds. The EFSA has produced guidelines to define in which conditions food from animal clones and clone offspring generated by sexual reproduction could be used. It is admitted that adult clones appear normal but they are epigenetically modified whereas clone offspring have returned to normality. Convincing but limited data did not point out any significant difference of body composition between clones, clone offspring and comparator animals. The EFSA concluded that i) the food from clones and clone offspring is essentially as safe as that from comparators, ii) more food safety tests are needed to confirm this conclusion, iii) a long-term surveillance of the animals is required to confirm that clone offspring have normal health. The European Group on Ethics in Science and New Technologies concluded that a reduction in animal welfare resulting from cloning is not acceptable. The European Commission took these data into consideration and pointed out that the real benefit of clone use for European consumers remains to be proved. The food from clones or clone offspring is thus not authorised in the EU. Transgenesis to improve animal production has received very little support so far in the EU and the projects are almost nonexistent in this part of the world. The EFSA has been recently mandated to write guidelines to define in which conditions food from transgenic animals could be used safely.

Introduction

Reproduction and selection techniques have played and still play a major role in the improvement of animal production. These two techniques are complementary but not in a symmetrical manner. Improvement of reproduction may aim at enhancing production independently of selection whereas selection is always dependent on reproduction and its efficiency is increased with better control of reproduction. In farm animals, as opposed to plants, the efficiency of selection is strongly dependent on spontaneous mutations which are relatively rare due to long reproduction cycles. The dissemination of the best genomes in farm animals is also limited by their slow natural reproduction and by the fact that cloning, as opposed to plants, is traditionally not a possible reproduction technique. The increasing use of genetic markers enhances the efficiency and the precision of genetic selection in farm animals but the two limiting points remain a reality.

Two techniques, cloning and transgenesis open new avenues to accelerate and direct farm animal reproduction and selection. Cloning allows the prolonged reproduction of elite genitors which generate a large number of high value offspring. Transgenesis is a way to create in only one generation genitors having specific new traits of interest by genetic modifications based on gene transfer into genomes. This may include addition of foreign genes as well as allele replacement and specific gene inactivation.

Although attractive, these two techniques have met limited success in farm animals so far for several reasons. One is the difficulty and the cost of these approaches which are highly dependent on reproduction and thus are slower and less flexible than in plants. These two techniques may also raise biosafety and bioethical problems. The present chapter summarises the state of the art in these two fields including the EU guidelines validated or in course of writing.

Animal cloning

Cloning history

In animals, the differentiation process from embryos to adults is naturally irreversible except for the formation of gametes from somatic cells. The first cloning experiments in animals were carried out successfully half a century ago. Differentiation corresponds to a progressive restriction of gene expression. Indeed, about 10 000 genes are required to support embryo development whereas only 2 000 genes remain active in fully differentiated somatic cells. This means that 23 000 genes are silenced during the differentiation process. It is admitted that the same 1 000 genes, the housekeeping genes, are expressed in each somatic cell and that a combination of 1 000 of the other genes, specific of each cell type, is required to reach the differentiated state.

Gene silencing is achieved by a specific and local DNA methylation and by some specific posttranslational modifications of histones (mainly deacetylation and methylation). These mechanisms are reversible under specific biological situations. Gamete formation is coincident with DNA demethylation and histone acetylation. In mature gametes, genes are silent and this is particularly the case in sperm. In these particular cells, DNA is bound to basic proteins, protamines, preventing DNA replication and transcription. A few hours after fertilisation, protamines are replaced by histones leading to a reactivation of the sperm genome which can replicate the next day and be transcribed after one or a few days. Genes are thus reactivated and DNA is demethylated

at the blastocyst stage. It is progressively and specifically remethylated in the different cell types as differentiation proceeds to select genes to be expressed later in adults (Yang *et al.*, 2007). These very important mechanisms involved in the control of gene expression are known as epigenetic as they are inducible, reversible, and transmittable to daughter cells as well as offspring and not implying any DNA mutation.

It is admitted that proteins present in the cytoplasm of the oocytes are responsible for the reactivation of the sperm genome. It was thus hypothesised 50 years ago that oocyte cytoplasm could reactivate the silent genes in somatic cells leading to the formation of pseudo embryos virtually able to develop and give birth to clones. This hypothesis appeared correct as nuclei from pluripotent cells taken in xenopus morula or blastocysts and transferred into enucleated oocytes gave birth to clones. This experiment was extended successfully to sheep but in all cases using pluripotent cells as nuclear donors. Mammalian clones were obtained for the first from sheep cultured embryonic cells by Campbell *et al.* (1996) and from somatic cells by Wilmut *et al.* (1997). Cloning has now been achieved in more than ten mammals including the major farm animals but not in poultry and fish.

Cloning techniques

In all species but mice, the nuclear donor cells are first injected between the zona pellucida and the plasma membrane of the enucleated oocytes. An electric fusion of oocyte and cell membranes leads to the transfer of the nucleus into the cytoplasm of the oocyte generating a pseudo embryo. The electric treatment also provokes the uptake of calcium which is mandatory for the activation and the development of the embryo (Figure 18.1). Other techniques of activation are alternatively used (Houdebine *et al.*, 2008). The transfer of isolated nuclei is not very efficient suggesting that the nuclear organisation must be preserved to make its reprogramming possible. On the contrary in mice, isolated nuclei are preferably used to generate pseudo embryos capable of developing. These techniques are known as Somatic Cell Nuclear Transfer (SCNT). Clones, which are in fact twins, can be obtained by injecting isolated cells from two cells or four cells embryos which have kept their totipotency, into the uterine horns of recipient females. In these conditions the number of clones is reduced and their genotype is not known until they are born. This precludes their extensive use as a breeding technique.

Cloning efficiency

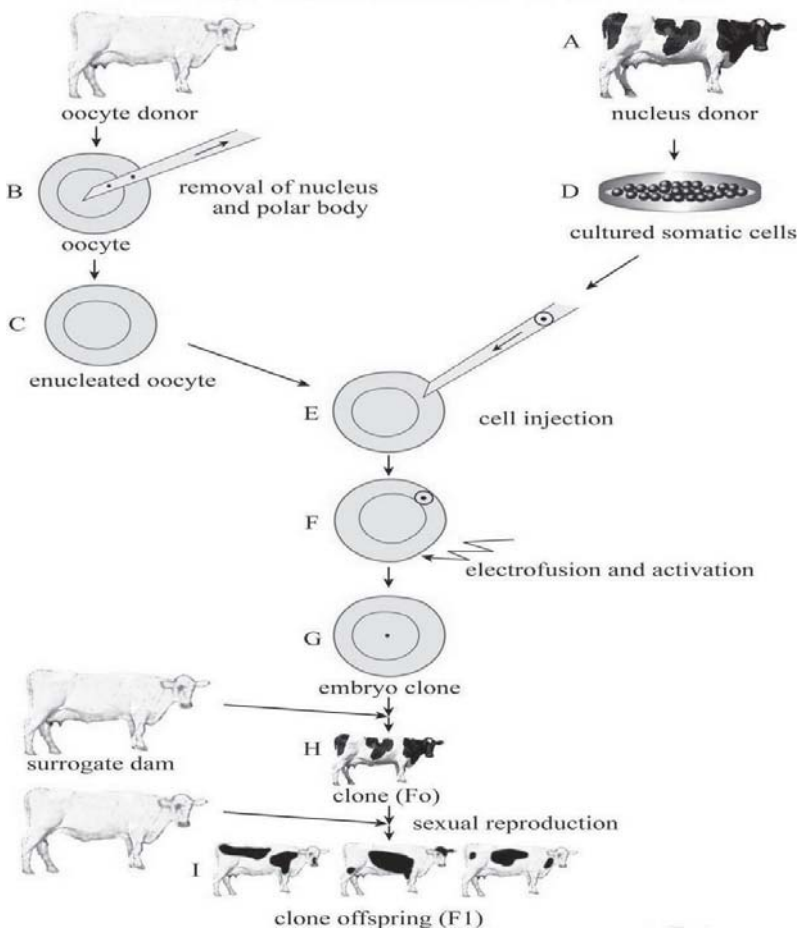
Since the birth of Dolly the sheep in 1996, SCNT has been applied to livestock and to several other species. Cattle, which are reported to be the animals most frequently used for SCNT, were first cloned in 1998 (Cibelli *et al.,* 1998; Yang *et al.,* 2005), goats in 1998 (Keefer *et al.,* 2002), pigs in 2000 (Onishi *et al.,* 2000), rabbits in 2001 (Chesne *et al*., 2002) and horses in 2003 (Galli *et al.*, 2003). For research purposes, clones have also been produced by using cells taken from clones, *i.e.* repetitive-cloning (Cho *et al.*, 2007). The success rate seems to diminish after repeated cloning as though abnormalities accumulate at each round. The overall success rate of the cloning procedure is still low and differs greatly between species ranging approximately from 0.5% to 5%.

The efficiency of cloning cattle in three countries, Brazil, Argentina and the USA, over five years was recently reported (Panarace *et al.*, 2007). From the 3 374 embryo clones transferred into surrogate dams, 317 (9%) live calves were born, 24 hours after birth 278 of these clones (8%) were alive and 225 (7%) were alive at 150 days or more

after birth. The higher overall success rates in cattle are largely due to the extensive knowledge of the female (and male) reproductive physiology in that species because of the importance of reproductive management in breeding schemes and in the economy of milk production.

However, within a given species, success rates can vary extensively reflecting a lack of full understanding of the role of various factors involved in the cloning process, such as somatic cell and oocyte selection, cell cycle stage, culture conditions, etc. This variable efficiency could not be attributed to chromosomal abnormalities in the cell lines resulting in the failure to develop to term (Renard *et al.*, 2007).

Figure 18.1. Main steps of somatic cell nucleus transfer (SCNT)



Note: (A) nucleus cell source; (B) the nucleus and the polar body are removed from oocyte by aspiration giving an enucleated oocyte (C); (D) culture of somatic cells from the nucleus donor; (E) injection of a somatic cell between the zona pellucida and the membrane of the enucleated oocyte; (F) intermediate association of enucleated oocyte and somatic cell followed by introduction of the somatic cell nucleus (and cytoplasm) into the oocyte cytoplasm by electrofusion of the oocyte and cell membranes; (G) embryo clone formed by an oocyte cytoplasm and a somatic cell nucleus containing two copies of chromosomes as normal embryos; (H) embryo transfer into a surrogate dam generating clone (F0) with coat colour similar to that of the nucleus source (A); (I) clone offspring (F1) generated by the sexual reproduction of the clone (F0) with a normal partner, the colour coat of these animals is different from that of the clone and different from each other.

Source: EFSA, 2008.

In the EU there are about 100 cattle clones and fewer pig clones. The estimated number in the USA is about 570 cattle and 10 pig clones. There are also clones produced in Argentina, Australia, China, Japan and New Zealand. The EFSA estimates that the total number of clones alive world wide in 2007 is less than 4 000 cattle and 1 500 pigs. Similarly, the number of clones reported as reared and living for a considerable time is limited. Only a few reports on cattle clones to date refer to animals of 6-7 years of age (Chavatte-Palmer *et al.,* 2004; Panarace *et al.,* 2007) and no data on the full natural life span of livestock clones are available yet.

Health of clones and offspring

The most critical time for the health and development of cattle clones occurs during the perinatal period (Chavatte-Palmer *et al.*, 2004; Wells *et al.*, 2004; Panarace *et al.*, 2007). This can be explained by the fact that most of the observed pathologies are associated with, and secondary to, placental dysfunctions (Constant *et al.*, 2006).

Possible reactivation of bovine endogenous retroviruses was analysed and compared between sexually reproduced cattle and cattle clones (Heyman *et al.*, 2007a). Retroviral sequences were not transcribed and no retroviral ribonucleic acid (RNA) was detected in the blood of clones, donor animals or controls.

LOS has been observed in clones from cattle and sheep that give rise to an increase in perinatal deaths, excess foetal size, abnormal placental development, enlarged internal organs, increased susceptibility to disease, sudden death, reluctance to suckle and difficulty in breathing and standing. LOS is not specific to cloning and it is attributed to epigenetic phenomena triggered during cell manipulation. In a study by Heyman *et al.*, the incidence of LOS at birth was 13.3% for somatic cloning, compared with 8.6% for embryonic cloning and 9.5% for a group of IVF calves (Heyman *et al.*, 2002). There are similar findings in sheep where peri- and post-natal lamb losses were considered to be due to placental abnormalities. One study in cattle reported that a mean of 30% of the calf clones died before reaching 6 months of age with a wide range of pathological causes, including respiratory failure, abnormal kidney development, and liver steatosis (Chavatte-Palmer *et al.*, 2004). However, after one to two months the surviving calf clones became indistinguishable from calves born from artificial insemination. Once past the first few months after birth most calf clones develop normally to adulthood (Chavatte-Palmer *et al.*, 2004; Wells *et al*., 2004; Heyman *et al.*, 2007a). Panarace *et al.* (2007) summarised five years of commercial experience of cloning cattle in three countries. On average, 42% of cattle clones died between delivery and 150 days of life. A large number of physiological parameters including blood profile showed no differences between clones and age-matched controls (Laible *et al.*, 2007; Panarace *et al.*, 2007; Walker *et al.*, 2007; Yamaguchi *et al.*, 2007; Heyman *et al.*, 2007a; Watanabe and Nagai, 2008).

Heifer clones and controls were reared under the same conditions and in one group of experiments the heifer clones reached puberty slightly later than the controls. However, there was no significant variation regarding gestation length, and calf survival (Heyman *et al.*, 2007b). Subsequent 305-day lactation curves taken as a health parameter were also comparable for yield, fat content and mean cell counts. The mean protein content in milk was significantly higher but this could be accounted for by the fact that three of the heifer clones were from the same source mother, which had a lower milk production but higher protein content, and by the small sample size (12 clones and 12 controls). There were no effects on health and subsequent reproductive data showed no significant differences.

Wells *et al.* reported that between weaning and four years of age the annual mortality rate in cattle clones is at least 8% (seven out of 59 died in the age period one to two years; three out of 36 died within the age period of two to three years and one out of 12 died in the age period three to four years) and that the main mortality factor is euthanasia due to musculoskeletal abnormalities (Wells *et al.*, 2004). In a study with 21 heifer clones of four different genotypes, all but one animal survived the study period of four months to three years of age (Heyman *et al.*, 2007a). The animal that did not survive died just after calving during the hot summer of 2003. A comparison in mice, where lifespan and ageing were studied, showed that, on average, mouse clones live for a 10% shorter life than sexually bred mice. However, these data have not been confirmed and mice subjected to reiterative cloning for four and six generations in two independent lines showed no sign of premature ageing as judged by gross behavioural parameters (Wakayama *et al.,* 2000).

Data from several laboratories indicated that the health status of clone offspring and control offspring was the same (Wells *et al.,* 2004; Heyman *et al.,* 2007a; Watanabe and Nagai, 2008; Ortegon *et al.*, 2007).

Genetic and epigenetic properties of clones

The genome of cells used as nuclear donors is not known strictly speaking until a clone is born. Indeed, it is not known up to which point the genome of somatic cells contains mutations. The failure of cloning might therefore be in part due to the fact that some of the genes in nuclear donors are no longer functional. In a recent study, three different cell types from homozygous transgenic mice harbouring the bacteria lac1 gene were retained as nuclear donors to generate clones using SCNT. Although the mutation number of the lac1 gene was higher in adult cumulus cells than in foetal brain cells and still higher in adult skin cells, the mutation number in foetus clones was the same in the clones obtained from the three cell types and also in foetuses generated by normal reproduction (Murphey *et al*., 2009). This experiment demonstrates that neither the natural mutations of the somatic cells nor the cloning process are responsible for any elevated mutation rate in clones. This was attributed to the fact that pluripotent cells as germinal cells have a potent DNA repair mechanism.

Chromosomal disorders after SCNT are routinely observed at a high frequency during the preimplantation stages but mainly in morphologically abnormal embryos (Booth *et al.,* 2003). The chromosomes of 30 healthy offspring from the same bull clone showed no abnormalities (Ortegon *et al.,* 2007). It is thus likely that chromosome instability results from the cloning process and it is blunted during sexual reproduction.

In sexual reproduction, male mitochondria are recognised as foreign and are eliminated in the oocyte cytoplasm in a species-specific manner. After SCNT, embryos can possess mitochondria from the oocyte cytoplasm only (homoplasmy) or from both the donor cell and the recipient cytoplasm (heteroplasmy). The number of mitochondria increases dramatically during oocyte growth and may become as high as 100 000 at the time of fertilisation. It is therefore not surprising that the vast majority of clones analysed so far have shown little evidence of heteroplasmy, but the number of studies is small (Hiendleder *et al.*, 2005).

The low success rates of SCNT and the underlying physiological abnormalities, frequently observed in clones during embryonic and foetal development and also soon after their birth, appear to be caused mainly by epigenetic dysregulation occurring during inappropriate reprogramming of the genome (Yang *et al.*, 2007a). The clone embryos

often show aberrant patterns of global DNA methylation at the zygotic stages. A high degree of variability in the epigenetic changes is also observed among individual embryo clones with regard to methylation levels and mRNA expression patterns of genes (Yang *et al.*, 2007a). In the mouse, the pluripotent cells derived *in vitro* from the inner cell mass of cloned blastocysts have been found to be indistinguishable from those obtained from *in vivo* fertilised embryos, both for their transcriptional activities and their methylation profile restored after SCNT at the blastocyst stage. On the contrary, the DNA of trophectoderm cells, that are the precursors of the placenta, is excessively methylated (Yang *et al.*, 2007a). This may explain why about 400 genes out of 10 000 examined in the placenta of mouse clones showed abnormal expression.

Limited data are available on whether epigenetic dysregulations occurring during the reprogramming of nuclear activities in clones can be transmitted to their sexually reproduced offspring. Several reports on the mouse indicate that, after cloning, epigenetic abnormalities such as those resulting in an obese phenotype are corrected in the germ cells of clones such that the offspring of clone × clone crosses do not exhibit the obese phenotype (Tamashiro *et al.*, 2000). Recent data indicated that 19 female and 11 male offspring generated by the same bull clone, lost all the abnormalities observed at birth and postnatally in the genitor (Ortegon *et al.*, 2007).

Environmental influences may induce a number of epigenetic modifications leading to the silencing or activation of specific genes, especially when pregnant females are maintained in conditions resulting in stress in the dam and foetus. The epigenetic modifications observed in the offspring of those pregnancies may then be transmitted to their progeny. These phenomena, which are considered as mechanisms of adaptation, have been found to be reversible after three generations (Gluckman *et al.*, 2007a; Gluckman *et al.,* 2007b). There is now evidence suggesting that RNA can be a determinant of inherited phenotype. In the mouse *Agouti* phenotype, the white tail tip trait is not transmitted in a Mendelian fashion but by RNAs packaged in sperm and down regulating *Kit* gene expression by an RNA interfering mechanism (Rassoulzadegan *et al.*, 2006).

Telomeres of the first mammalian clone, Dolly the sheep, were found to be shorter than those of the age-matched, naturally bred counterparts. For this reason, clones were first considered to show premature ageing. Subsequently however, the vast majority of studies have reported that telomere length in cattle, pig and goat clones are comparable with or even longer than age-matched naturally bred controls, even when senescent donor cells were used for cloning.

Animal welfare

Due to the effects of SCNT on the placenta and foetal membranes, as well as the large foetuses carried by some of the surrogate dams both during gestation and around parturition, the welfare of the dam is likely to be affected. These effects have been noted primarily in cattle and sheep clone pregnancies. Similar effects have not been reported for swine clone pregnancies.

The various reports suggest that there is an increased risk of mortality and morbidity in perinatal lamb and cattle clones but not in perinatal clone of swine and goat. Clones exhibiting LOS may require additional supportive care at birth. Planned Caesarean sections combined with special postnatal resuscitation measures for the clone neonates may reduce this problem. Calf clones are slower to reach normal levels of various

physiological measures than their conventional counterparts (Chavatte-Palmer and Guillomot, 2007; Batchelder *et al.*, 2007a and 2007b). Stress elicited in the dam carrying cloned foetuses, such as pain or distress during late gestation and calving due to large foetuses, may also affect the foetus. The period immediately after birth is a critical time for all newborns as the cardiovascular, respiratory and other organ systems adapt to life outside the womb. Even though a neonatal animal can certainly show severe signs of abnormal function *e.g.* so-called respiratory distress, it does not necessarily mean it is experiencing or feeling an adverse effect, as adults might experience. In LOS calves and lambs stressors are likely to be detrimental and cause pain, but in apparently normal clones or clones that can be effectively resuscitated after birth the pain and stress experienced during birth or postnatally may be no greater than in their sexually reproduced counterparts, whether they are delivered naturally or by Caesarean section.

A range of behavioural indicators and behaviour challenge tests were performed but no significant differences were observed except that the clones tended to exhibit less play behaviour than the others. Trends were observed indicating that the cattle clones exhibited higher levels of curiosity, more grooming activities and were more aggressive and dominant than controls. An observation of five clones (from three different origins) and five non-clone Holstein heifers has indicated that social relationships (agonistic and non-agonistic behaviours) were not different between the two groups (Coulon *et al.*, 2007). When exposed to an unfamiliar environment, heifer clones showed more exploratory behaviour than control animals. However, the authors concluded that this difference was probably related to the early management of the animals.

No studies on the welfare of the progeny of clones have been reported in livestock species.

Safety of food products from clones

Animals commonly used for food production have never developed pathways specialised for producing toxicants. Therefore, it is highly unlikely in domesticated animals that genes, coding for silent pathways to produce intrinsic toxicants, exist or that their expression is possible even in the case of epigenetic dysregulation. Further, as no new DNA sequences have been introduced into the clones, the occurrence of new substances, such as toxicants or allergens, is not expected.

In the EU, animals belonging to species used for meat production are individually inspected ante- and post-mortem to check whether they meet existing regulatory requirements, without regard for the method employed in their breeding. Moreover, meat and milk are subjected to safety and quality controls, under specific European provisions, before they can be used for human consumption. Therefore, only food products from healthy animal clones and their progeny, which are indistinguishable at veterinary inspection from conventionally-bred animals, would enter the food chain. This means that all animals, including clones for which genome reprogramming has not been successful and which show ill health, would be condemned prior to or at slaughter and would, therefore, be excluded from the human food supply. Milk is also strictly inspected before being marketed.

Several relevant studies have been conducted on the composition of bovine milk and meat from cattle and pigs derived from clones (F0) or their progeny (F1). These analyses included carcass characteristics, water, fat, proteins and carbohydrate content, amounts and distribution of amino acids, fatty acids, vitamins and minerals, and in the case of

milk, volume per lactation (Diles, 1996; Walsh *et al.*, 2003; Takahashi and Ito, 2004; Tome *et al.*, 2004; Norman and Walsh, 2004; Norman *et al.*, 2004; Tian *et al.*, 2005; Shibata *et al.*, 2006; Walker *et al.*, 2007; Heyman *et al.*, 2007a; Yang *et al.*, 2007b).

In an extensive study, more than 150 parameters in 37 cow clones (F0) from three independent cloning experiments and 38 control animals were examined over a three year period and consisted of more than 10 000 individual measurements (Heyman *et al.*, 2007a). In this study some slight changes were observed in all three groups of clones, compared with their controls, *e.g.* in fatty acid composition of milk and muscle of bovine clones (F0) and a slight increase of stearoyl-CoA desaturase in milk and muscle. However, these variations were still within the normal range.

Other data included meat composition data for five pig clones and 15 comparator animals and no biologically relevant differences were observed in fatty acid, amino acid, cholesterol, mineral and vitamin values. In a study of the composition of pig clone offspring, 242 offspring (F1) from one boar clone and 162 control pigs from the same breed were compared (Walker *et al.*, 2007). In this study 58 parameters consisting of more than 24 000 individual measurements were examined. Only three individual values of the offspring were different from the normal range of the controls and two out of the three were within the normal range found in pigs, according to the USDA database.

None of the studies has identified any differences outside the normal variability in the composition of meat (cattle and swine) and milk (cattle) between clones or clone progeny, and their comparators. In addition no novel constituents have been detected in products from clones or their progeny.

A subchronic oral feeding study (14 weeks) was conducted in rats to determine the effects of a diet containing meat and milk derived from embryonic and somatic clones. Rats were not affected by the consumption of meat and milk from bovine clones (Yamaguchi *et al.*, 2007). Similar results were obtained by in a 21-day feeding test with a diet containing milk and meat from cattle clones (F0) (Heyman *et al.*, 2007a). A 12-month oral toxicity study in the rat (including reproduction) with meat and milk from the progeny of cattle clones (F1) is under way in Japan and results are expected in 2009.

Meat derived from cattle clones did not show any genotoxic potential in the mouse micronucleus assay (Takahashi and Ito, 2004).

Rats fed for several weeks with milk and meat from cattle clones and controls developed, as expected, a weak immune reaction. This reaction was qualitatively and quantitatively similar in rats given milk or meat either from clones or controls. The antibodies were in both cases IgG, IgA and IgM but not IgE, indicating that the consumption of the cattle products induced a classical immune response but no allergenic effect (Takahashi and Ito, 2004).

The allergenic potential of several *in vitro* digested samples of meat and milk from cattle clones (F0) and controls was further assessed by intraperitoneal injection into mice following a classical immunisation protocol. No statistically significant difference in the allergenic potential was observed between samples from clones and comparator control cattle (Takahashi and Ito, 2004). Also Heyman *et al.* did not detect differences in the allergenicity of milk and meat obtained from clones, in the rat compared with the same food products derived from non-cloned animals, age and sex-matched, maintained under the same conditions (Heyman *et al.*, 2007a).

These data are limited but they are markedly convergent showing that the food products from clones, clone offspring and control animals have the same level of risk.

Cloning applications

Cloning using SCNT is a new experimental condition which is more and more extensively used to study the mechanisms involved in cell differentiation and dedifferentiation. Moreover, the health status of some foetuses generated by SCNT is similar to that of some human foetuses suffering from development defects. Cloning is becoming a relevant experimental model to study the epigenetic mechanisms controlling development.

Cloning provides a way in which selected characteristics can be propagated more rapidly into production herds. For example, an animal with genetic resistance to a disease could be expanded by cloning to introduce the disease resistance trait via sexual reproduction into herds. SCNT may also prolong the reproductive life of sires or dams that have already produced high value offspring and cannot reproduce anymore due to aging, accident or misadventure. Cloning may also help to diminish the difference that exists for the availability of gametes between male and female genitors. Naturally, females can provide at most a few hundred oocytes whereas male semen can generate thousands of offspring. Cloning thus makes possible a more intensive use of specific female genotypes within a breeding scheme. In all cases so far, the primary use of clones is as elite animals breeding and not for the production of food. Cloning is thus expected to accelerate genetic selection on condition to cross clones with animals having a different and complementary genetic background and to avoid carefully any reduction of biodiversity in herds.

Cloning offers new opportunities to save endangered species or livestock breeds by restoring populations which can include infertile and castrated animals, as it can be used as a tool of preserving genetic material from rare or endangered breeds and species. This is particularly the case for horses used for jumping. These animals are males castrated before their sexual maturity to facilitate training. These animals have started being reproduced by cloning.

Conservation implies the preservation of the DNA in frozen cells from the rare animals of potential high value. Cryopreserved tissue (for example, skin) samples, which are easier to obtain than gametes or embryos, or obtained from infertile animals, can be used to generate reproductively capable animals that could be used to expand endangered populations. It should be noted that saving a breed is generally feasible as oocyte donors and recipient females are available. This is much less likely to occur for the saving of endangered species. This point has been discussed in details for the case of mammoth resurrection (Nicolls, 2008).

The opinion of EU on clone use for food production

The major conclusions of experts from the EFSA (2008) were that i) the food products from clones and clone offspring are essentially as safe as those from comparators, ii) more food safety tests are needed to confirm this conclusion, iii) a long-term surveillance of the animals is required to confirm that the clone offspring have normal health. The first published version of the EFSA opinion was submitted to a public consultation. The final version was published after taking into account the remarks of public opinion. The European Group on Ethics in Science and New Technologies

concluded that the reduction of animal welfare resulting from cloning is not acceptable. The European Commission and the European Parliament took these data into consideration and pointed out that i) the risks for consumers have not been sufficiently evaluated, ii) the suffering of the animals generated by cloning is not acceptable, iii) the real benefit of clone use for European consumers remains to be proved. The food from clones or clone offspring is thus not authorised in the EU.

Animal transgenesis

Transgenesis history

The first transgenic animals, mice, were obtained in 1980. This was achieved by microinjecting gene constructs into embryo pronuclei. Two years later, the birth of giant transgenic mice revealed that a transgene could not only be transmitted to progeny and be expressed but also have a phenotypic effect. In 1985, the microinjection technique was applied successfully to rabbits, sheep and pigs suggesting that transgenesis was possible virtually in all animal species. It soon appeared that microinjection was laborious in all cases and inefficient in some species, indicating that other techniques were required. In 1986, it was shown that gene targeting leading to gene inactivation or allele replacement was possible by using homologous recombination. Other tools to transfer genes such as transposons, lentiviral vectors and cloning have been implemented year after year. These techniques are still being improved but the generation of transgenic animals is no more a strongly limiting technique as it used to be, even if it remains labourious and costly in farm species. Another problem which has not been completely solved is the reliability of transgene expression (Houdebine, 2003, 2007 and 2009a). The present paper summarises the state of the art for animal transgenesis including the guidelines available or in discussion for the applications in food production.

Transgenesis techniques

Two techniques are essential to generate transgenic animals also known as GM animals or r-DNA (recombinant DNA) animals: gene transfer and construction of genes able to express in a reliable manner. Gene transfer is tightly bound to reproduction techniques and different approaches are required for the various animal species.

Direct DNA transfer

In mammals, about 1 000-5 000 copies of the isolated foreign gene contained in 1-2 pl may be injected into one of the pronuclei of one-day embryos. The yield of this method in mice is of 1-2 of transgenics for 100 microinjected and transferred embryos. It is lower in all the other mammalian species and very low in ruminants. It is presently used essentially in mice and rabbits. In non mammalian species, the pronuclei cannot be visualised and DNA must be injected into the cytoplasm of the one-day embryos. This relatively simple technique is efficient in most fish species but highly inefficient in chicken, in Xenopus, in some fish and in insects. For unknown reasons, the integration of the foreign DNA thus does occur in some species.

Foreign genes can be introduced into transposons in vitro. The recombinant transposons may then microinjected into one-day embryos with the transposon integrase or a gene construct able to produce it. The foreign gene thus becomes integrated into the

embryos with a yield of about 1%. All the transgenic insects are being generated by using transposons as vectors. Transposons also proved efficient to generate transgenic fish, chicken and mammals (Ding *et al.*, 2005). Transposons are efficient tools but they can harbour no more than 2-3 kb of foreign DNA.

Lentivirus (a category of retroviruses) genes can be deleted and replaced by the genes of interest. Viral particles are then prepared and used to transfer the foreign genes into oocytes or one-cell embryos. Safe experimental conditions have been defined to use the lentiviral vectors. This method proved highly efficient in several species including mammals (Park, 2007; Whitelaw *et al.*, 2008) and birds (Lillico *et al.*, 2007).

Transgenic animals were obtained by incubating sperm with DNA and by using conventional in vitro fertilisation (Smith and Spadafora, 2005; Shen *et al.*, 2006). The method has been greatly improved by using Intracytoplasmic Sperm Injection (ICSI). This technique which consists of injecting sperm into the cytoplasm of oocytes is currently used for in vitro fertilisation in humans. To transfer genes, sperm from which plasma membrane has been damaged by freezing and thawing were incubated in the presence of the gene of interest and further used for fertilisation by ICSI. This method proved efficient in mice (Moreira *et al.*, 2007; Shinoara *et al.*, 2007) and pigs (Yong *et al.*, 2006). Transposon use and ICSI may be combined to increase the yield of transgenesis (Shinoara *et al.*, 2007; Moisyadi *et al.*, 2009).

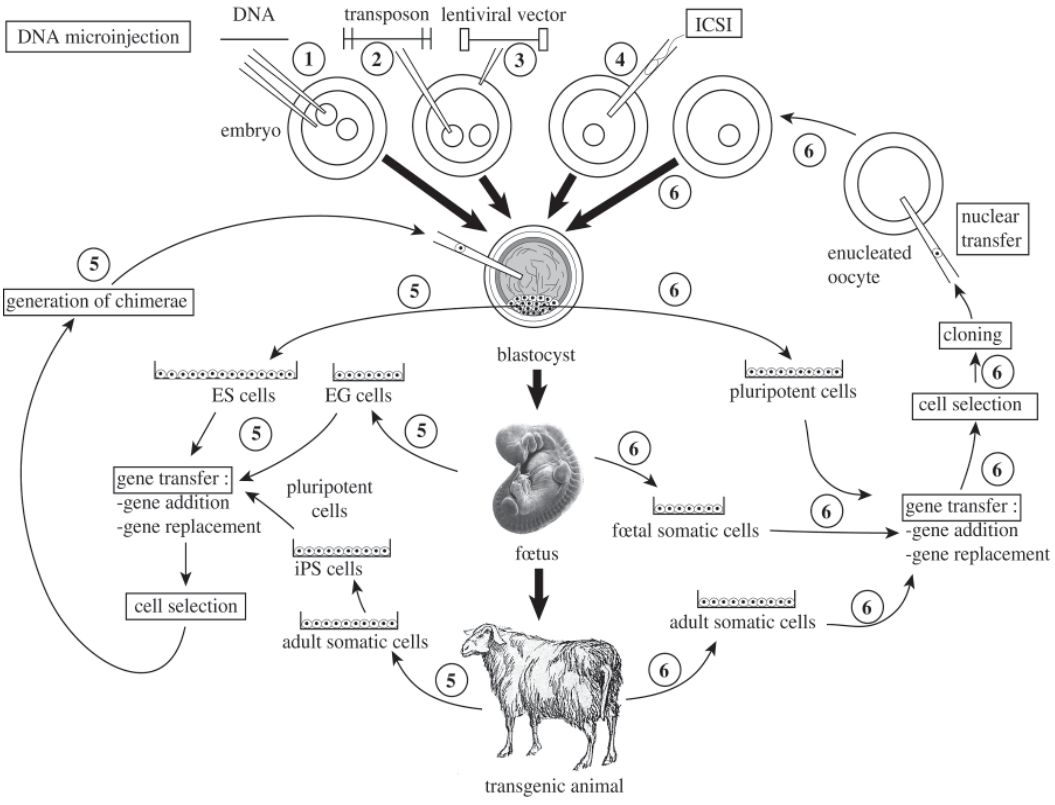
The methods described above to transfer foreign genes rely on the integration of the DNA into the host genome. Another possibility may theoretically be to use episomal vectors capable of autoreplicating in host cells and transferred to daughter cells without being integrated into the genome. Fragments of chromosomes are being used for the transfer of very long DNA fragments. These chromosomal vectors are not of an easy use and they carry a number of genes in addition of the gene of interest. Another possibility consists of using vectors which derive from viruses having the capacity to replicate in animal cells. Herpes viruses are naturally stably maintained as autonomous circular minichromosomes at a low copy number in some animal cells. Foreign genes can be introduced into Herpes viral vectors and be maintained during cell division. Episomal vectors not based on the use of viral elements are available. Such a vector proved efficient to transfer foreign genes into pig embryo using ICSI (Manzini *et al.*, 2006). This vector is maintained without any selection pressure in the cells of the developing embryos but seemingly not later.

DNA transfer via intermediate cells

In some situations, the efficiency of the genetic modification is too low to be achieved by the methods described above. This is particularly the case for gene targeting (see section below on "Targeted gene transfer"). One possibility is to do the genetic modification in pluripotent cells further used to participate in the development of living organisms. Pluripotent cells have the capacity to participate in the development of all the organs. Pluripotent cells known as embryonic stem (ES) cells exist in early embryos (morula and blastocysts). The pluripotent cells can be cultured, genetically modified, selected and transferred into recipient morula or blastocysts. These cells participate in the development of the embryo to give birth to chimeric animals (Figure 18.2). This means that the organs of the animals, including sexual cells, derive from the genetically modified cells or from the recipient embryo. The offspring of these chimeric animals will harbour the genetic modification if they derive from the transplanted cells. This method is

extensively used essentially in mice to inactivate (knockout) genes specifically and for gene replacement (see section below on "Targeted gene transfer").

Figure 18.2. Different methods to generate transgenic animals



Notes: (1) DNA transfer via direct microinjection into pronucleus or cytoplasm of embryo; (2) DNA transfer via a transposon: the foreign gene is introduced in the transposon which is injected into a pronucleus; (3) DNA transfer via a lentiviral vector: the gene of interest introduced in a lentiviral vector is injected between the zona pellucida and membrane of the oocyte or the embryo; (4) DNA transfer via sperm: sperm is incubated with the foreign gene and injected into the oocyte cytoplasm for fertilisation by ICSI (intracytoplamic sperm injection); (5) DNA transfer via pluripotent or multipotent cells: the foreign gene is introduced into pluripotent cell lines (ES, embryonic stem cells: lines established from early embryo or iPS: cells obtained after dedifferentiation of somatic cells) or into multipotent cell lines (EG, gonad cells lines established from primordial germ cells of foetal gonads); the pluripotent cells containing the foreign gene are injected into an early embryo to generate chimeric animals harbouring the foreign gene DNA; the multipotent EG cells containing the foreign gene are injected into recipient foetal gonads; in both cases the transgene is transmitted to progeny; (6) DNA transfer via cloning: the foreign gene is transferred into a somatic cell, the nucleus of which is introduced into the cytoplasm of an enucleated oocyte to generate a transgenic clone. Methods 1, 2, 3 and 4 allow random gene addition whereas methods 5 and 6 allow random gene addition and targeted gene integration via homologous recombination for gene addition or gene replacement including gene knockout and knockin.

Source: Author's own work.

For unknown reasons, ES cell lines have been established and used essentially in two mouse lines. In other lines and species, the ES lose their pluripotency and can no more give birth to chimeric animals transmitting the genetic modification to their offspring. Recent experiments have shown that the transfer of three genes, normally expressed in pluripotent cells, into somatic cells can dedifferentiate these organ cells into pluripotent cells known as induced pluripotent cells (iPS) and almost similar to ES cells (Takahasha

et al., 2007; Wernig *et al.*, 2007; Nakagawa *et al.*, 2008; Pera and Hasegawa, 2008). These experiments open avenues for cell and gene therapy. The approach known as therapeutic cloning becomes no longer necessary and puripotent cells can potentially be obtained in different species by this method. Similarly, iPS might be implemented for transgenesis in species in which ES cells are not available. Recent experiments showed that the culture conditions to maintain the multipotency of chicken embryonic gonad (EG) cells have been found. Foreign genes can be transferred into EG cells which can be reimplanted into recipient gonads and participate to gamete development. This has greatly simplified the generation of transgenic chicken (Van de Lavoir *et al.*, 2006; Han, 2009).

Cloning was initially designed to improve transgenesis efficiency in farm animals but its only real application is presently transgenesis (Robl *et al.*, 2007). The principle of this method is described in Figure 18.2. Genes are transferred into somatic cells which are then used to generate transgenic clones. This method has become the most frequently used for big farm animals.

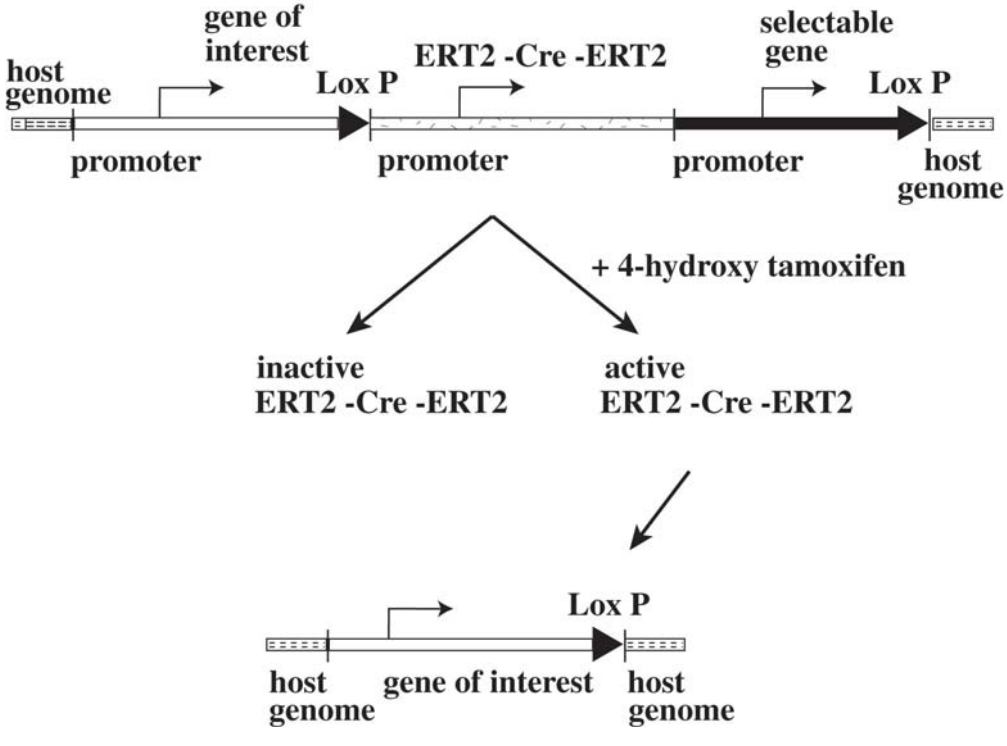
Targeted gene transfer

The techniques described above lead to uncontrolled but not strictly random gene integration. Foreign DNA is preferentially integrated in gene rich genome regions and its location can be precisely identified. A foreign DNA fragment can recombine very precisely with a genomic DNA region containing a similar sequence. This natural mechanism known as homologous recombination makes the precise replacement of a gene by another possible (Figure 18.3). An active gene may thus be replaced by an inactive version leading precisely to an inactivation of the targeted gene (gene knockout). The targeted gene may be as well replaced by an active gene (gene knockin). This technique allows therefore a better controlled transgenesis reducing possible damage of the genomic DNA at the integration site and frequent side effects of the genes located in the vicinity of the transgene on the expression of the transgene (see section below on "Control of transgene expression"). Yet, this approach remains limited by the fact that the homologous recombination required for gene targeting is a rare event. The targeted integrations by homologous recombination of a foreign DNA represents 0.1%-1% of the total integrations. The cells in which targeted integration occurred must be selected and used to generate a transgenic animal. The formation of chimeric embryos using pluripotent cells (see section above on "DNA transfer via intermediate cells") or the cloning technique (see section above on "DNA transfer via intermediate cells") is required to obtain a targeted integration.

The efficiency of homologous recombination can be markedly increased (at least 100 times) by a local break of the two DNA strands in the targeted site of integration. This can be achieved by using special restriction enzymes known as meganucleases. These enzymes have the capacity to cut DNA at sites which are longer than those of the classical restriction enzymes and which are usually not present in animal genomes, avoiding genomic DNA degradation. The DNA sequences recognised by meganucleases must then be added to the genome of animals either at targeted sites by homologous recombination or at random sites. In the latter case, the integration sites must be validated for its capacity to allow a good gene expression before targeting the gene of interest at the meganuclease site. In practice, the recombination vector containing the gene to be transferred bordered by two DNA sequences present in genomic DNA, is introduced in the cell with the meganuclease or the zinc finger nuclease (ZFN). Engineered meganucleases capable of recognising specifically natural genomic DNA sequence make

gene targeting at multiple sites of the genome possible (Porteus and Caroll, 2005). This method which is being developed to improve the efficiency and the precision of gene therapy can be applied to target the integration of foreign genes into experimental animals. Interestingly, when the recombination vector is not added with the meganuclease, the genomic DNA repair takes place but often with alteration of the sequence. This process known as non homologous end joining (NHEJ) corresponds to a knockout (Santiago *et al.*, 2008; Wilson, 2008). This mechanism is efficient and it allowed a knockout using NHEJ in one-cell fish embryos after the injection of an engineered meganuclease (Wood and Shier, 2008). This suggests that gene targeting might be achieved directly in mammal embryos by injecting an engineered meganuclease with or without a homologous recombination vector.

Figure 18.3. Elimination of the marker and selectable genes



Notes: The vector for homologous recombination, not shown here, contained at both ends host DNA sequences targeting the chosen region of the genome. It allowed the targeted integration of the gene of interest. The homologous recombination occurred between the targeted host DNA sequences and the same sequences flanking the vector. The genomic targeted gene was interrupted by a DNA sequence containing the gene of interest which may be an inactive version of the targeted gene leading to a knockout or an active gene for a knockin or an allele replacement, a selectable gene, the gene coding for a form of Cre recombinase (ERT2-Cre-ERT2 active only in the presence of 4-hydroxy tamoxifen) and two LoxP sequences flanking the region containing the Cre gene and the selectable gene. After the targeted integration, 4-hydroxy tamoxifen may be added to the cells used to generate chimerae or clones, to the new embryos or to the embryos of the next generation. This activates the Cre recombinase which recombines the two LoxP sequences leading to the elimination of the selectable gene and of the Cre recombinase gene. The remaining LoxP sequence (32 nucleotides) is not expected to be the source of significant side effects. This approach allows the elimination of the DNA sequences not necessary for the knockout or the knockin and it avoids the toxic effects of overexpressed Cre recombinase.

Source: Author's own work.

Similarly, the bacterial enzyme phiC31, which is an integrase, recognises several sites in various animal genomes and allows the efficient integration of foreign genes at the

targeted sites (Rao, 2008). Several other recombination systems rely on the use of integrases such as Cre and Flp which recognise specific sites of about 30 nucleotides (LoxP and FRT respectively) which must be added to the animal genome (Baer and Bode, 2001). These systems are more often used to delete a DNA region previously bordered by the LoxP or the FRT sequences (see section below on "Control of transgene expression").

Control of transgene expression

The low expression of many transgenes containing only the transcribed regions with a promoter, proximal enhancers, at least one intron and a transcription terminator, revealed that remote regulatory regions must be involved in the control of gene expression. In a limited but significant number of cases, using long genomic DNA regions (up to 200 kb) surrounding the gene of interest increases greatly the proportion of active transgenes and also often the level of their expression (Long and Miano, 2007; Montoliu *et al.*, 2009).

A gene is inactivated usually to eliminate the corresponding protein in the animal. This can be achieved by different techniques and at different levels of the protein synthesis process. The data reported in the section above on "Targeted gene transfer" indicate that gene knockout can be based on homologous recombination or NHEJ. Experimenters may wish to prevent the expression of a gene reversibly, in a given cell type only and at chosen periods of the animal's life. Available methods make possible the gene knockout in a given cell type at a chosen moment.

The discovery of interfering RNA one decade ago has profoundly improved the situation. It was unexpectedly found that long double strand RNAs are randomly cut into 19-21 nucleotide fragments known as small interfering RNA (siRNA). One of the two strands of the siRNA is kept and targeted to an mRNA having a complementary sequence. This induces the degradation of the mRNA. Soon after, the use of promoters directed by RNA polymerase III could synthesise siRNAs. In practise, a synthetic gene containing the targeted 19-21 nucleotide sequence followed a short random sequence and by the targeted sequence in the opposite orientation is linked to a promoter acting with RNA polymerase III (usually U6 or H1 gene promoters). The RNAs synthesised by such vectors form a 19-21 nucleotide double strand RNA known as short hairpin RNA (shRNAs) are processed in cells to generate active siRNAs.

The recent discovery of the role of microRNAs has increased the possibility to use interfering RNAs. MicroRNAs are encoded by short genes expressed under the control of RNA polymerase II promoters. Their primary products are transformed into siRNAs. The mature miRNAs which are fully complementary to the targeted mRNA induce a degradation of this mRNA. The miRNAs which are only partially complementary to the targeted mRNA and which recognise a sequence located in the 3'untranslated region (3'UTR) of the mRNA inhibit translation of this mRNA without inducing its degradation. The possibility known as knockdown to generate transgenic animals expressing siRNAs preventing specifically the expression of a gene by degrading the corresponding mRNA or inhibiting its translation has opened avenues for the control of gene expression in vivo. The application of the siRNA approach is not as easy in animals as in plants for several reasons. Long double strand RNAs induce interferons and some unspecific immune reactions (Sioud, 2006). On the other hand, siRNAs are not autoamplified in higher animals and this reduces their potency. An appropriate expression of siRNA genes in transgenic animals can be obtained when they are introduced into lentiviral vectors (Tiscornia *et al.*, 2003).

All the vectors described above and used to express transgenes contain promoters which are naturally active in the cells of the transgenic animals. This implies that the transgenes are regulated by the natural inducers of the host genes. The induction of a transgene may then be coincidental with the unwanted stimulation of a number of host genes. Artificial promoters containing regulatory elements from both animal genes and bacterial genes have been designed. The resulting promoters are active in animal cells but controlled by substances active in bacteria but not in animals. The most popular system is based on the use the bacterial tetracycline repressor gene. In practice, the transgene becomes reversibly activated only when tetracycline is administered to the animals. A number of similar systems are available and currently used in transgenic animals with good success (Malphettes and Fussenegger, 2006). These tools offer virtually the possibility to express a transgene precisely in a given cell type and at a given moment.

Deletion of genomic DNA region is required in some circumstances. Conventional homologous recombination makes gene deletion known as knockout possible (see section above on "Targeted gene transfer"). Another possibility consists of using the Cre-LoxP or Flp-FRT systems. A LoxP sequence must first be added on both ends of the fragment to delete. The presence of the Cre recombinase will then recombine the two LoxP sites leading to a deletion of the DNA fragment located between the LoxP regions. The Cre recombinase may be synthesised by the corresponding gene under the direction of a cell specific promoter. Another level of control can be obtained by using an engineered Cre recombinase which becomes reversibly active in the presence of an oestrogen analogue, 4-hydroxy tamoxifen. This offers the advantage of having the active Cre recombinase for short periods of time. This prevents the non-specific action of the Cre recombinase which can recognise cryptic sites in the host genome and induce illegitimate recombination damaging the host DNA.

Applications of animal transgenesis

At least 90% of transgenic animals are used to study gene function and mechanisms of action. Many transgenic models are also generated specifically to study human diseases and to validate new medicaments (Houdebine, 2007). The possibility of grafting pig organs to humans requires transgenesis for both studying rejection mechanisms and to generate the pig organ donors in the future (Petersen *et al.*, 2009). Milk from transgenic mammals and the whites of chicken eggs have started being the source of pharmaceutical proteins (Van de Lavoir *et al.*, 2006; Schnieke, 2009; Houdebine, 2009b; see also Multiauthor book, 2009). A number of projects aiming at improving animal production are in progress (Niemann *et al.*, 2009; Laible, 2009). The most advanced project concerns salmon farming. Faster growing salmons have been obtained by overexpressing the salmon growth hormone gene. This project waits until the confinement, either physical or physiological, of these fish becomes a reality before its industrial development (Kaputchinsky, Hayes, Li and Dana, 2007). An important challenge is to generate animals resistant to diseases. One example is catfish which express the gene coding for peptide having anti-bacteria activities and have become resistant to bacterial infections which are a real aquaculture problem (Dunham, 2009). These results are of importance when we consider that wild fish production is becoming limiting. Other projects aim at modifying milk composition to improve its nutritional properties or to use it as a carrier to provide consumers with proteins having anti-pathogen properties (Laible, 2009). Pigs expressing in their milk bovine α-lactalbumine and pig IGF1 have a better capacity to feed their piglets (Wheeler *et al.*, 2001). Pigs having a body composition enriched in omega-3 fatty acids are currently under study to evaluate their potential beneficial effect on human

health (Lai *et al.*, 2006). Another example is pigs expressing phytase in their saliva. This enzyme degrades phytic acid present in feed and not digested by pigs. These animals release much less polluting phosphate into the environment than control pigs (Fosberg *et al.*, 2003).

The guidelines for food from transgenic animals

Several documents aiming at defining in which conditions the products from transgenic animals could be used as food have been published. A first report was established by FAO/WHO in 2003. More recently, the *Codex Alimentarius* published a draft document on this subject (Joint FAO/WHO Food Standards Programme *Codex Alimentarius* Commission, 2008). These data have been summarised by Lema and Burachik (2009). The US FDA has produced a document summarising its guidelines (2009). The EFSA mandated experts to write the European guidelines on the same subject before the end of 2009.

The safety of food from transgenic plants and animals is not expected to be very different. However, domestic animals are maintained in most cases in confined areas and they usually do not transfer their genes to wild relatives. Many plants contain toxins to protect themselves from predators, not domestic animals. Toxicants active in consumers are expected to alter animal health and thus to be detected without proceeding to toxicology tests. Some animals contain toxins like venoms. Moreover, lower vertebrates and invertebrates may contain substances (toxins, anti-nutrients) more deleterious for mammals than in their own species. GM plants and animals may be fortuitously more sensitive to some pathogens than control. This may favour transmission of the pathogens from GM animals but not from GM plants to consumers.

Even the ancient Greeks considered that it is possible to reveal the existence of a risk but not its absence. In plants as in GM animals or normal counterparts, the toxicity cannot be identified with certainty. Indeed, a number of food products considered safe become toxic when they are ingested in large quantity. The safety of GM products can thus be determined by comparing them to control products which must come from animals of the same breed and housed in the same conditions.

The criteria retained to evaluate the safety of products of GM animals are the following:

- The zoological properties of the animals: development, growth, general health, reproduction, aging;
- The gene construct transferred to the animals. Special care must be taken if the coding sequence comes from a living organism known to contain toxicants or allergens. The complete structure of the construct and of the transgene must be shown;
- The method used for gene transfer. Special care must be taken if transposons or lentiviral vectors are used to prevent their uncontrolled dissemination. When intermediate cells are used (ES, EG, iPS, somatic cells for used as nuclear donors) conditions of cell culture must be described;
- The substantial equivalence between the GM animals and the comparators;
- The toxicity of the protein coded by the transgene. This must be demonstrated by giving large amounts of the pure protein to mice for 10 days or more;

- Chronic toxicity tests using meat and milk given to rats for 90 days or more. The implementation of these tests must be decided or not on a case by case basis;
- Allergenicity of the protein coded by the transgene. Allergenicity must be evaluated using the conventional tests: identification of sequences known to be allergens, sensitivity to degradation by pepsin, presence of IgE antibodies against the protein in the blood of consumers or experimental mice.

Two problems were a matter of long discussion in *Codex Alimentarius* meetings on GM animals (FAO/WHO, 2007). One problem is the presence of marker genes in the genome of transgenic animals. Selection genes, essentially for resistance to antibiotics, are needed in vectors (plasmids, BACs) for gene constructions. They are not kept in DNA fragments transferred directly to embryos or gametes as they often interfere negatively with transgene expression. Selection genes are needed to prepare cells used to generate transgenics (ES, EG, iPS, somatic cells). Different marker genes can be used and several systems to delete them are available (Houdebine, 2007b). The most sophisticated tool relies on the use of the Cre-LoxP system. The gene coding for Cre-estrogen receptor fusion protein and the gene coding for the resistance to an antibiotic can be integrated between two LoxP sequences. The administration of 4-hydroxy tamoxifen to the animals or its addition to the culture medium of cells or embryos induces activation of the Cre recombinase and the elimination of the Cre and antibiotic resistance genes from the genome leaving only one LoxP motif (32 nucleotides) (Figure 18.3). The recommendations of the working group were to eliminate the antibiotic resistance gene if the antibiotic is used in human or veterinary medicine. It was also recommended to use the Cre-LoxP system carefully to avoid any alteration of the genome potentially resulting from an exceeding expression of the Cre recombinase.

The other problem was that of non-heritable gene transfer. DNA may be transferred only in the somatic cells, to be integrated, expressed and having a biological effect similar to that obtained in transgenic animals. This may avoid any dissemination of the foreign gene. A non-integrated vector has more chance to escape and be transferred into other cells than integrated DNA. Moreover, a non-integrated vector may provoke unintended recombination more likely than integrated DNA. The working group concluded that the safety depends more upon the fact that the transgene is integrated or not rather than upon its inheritability.

General conclusions

Cloning appears a logical technical approach as the use of elite genitors obtained by conventional genetic selection proved to have a strong impact on animal productions. The future use of this technique is still not clear. The US breeders appreciate that cow clones which are authorised by FDA can be used in herds as other sires. Animal welfare seems not to be a limiting point for implementing cloning in the USA. The consumption of food from clone offspring without any particular traceability and labelling of the products is thus becoming a reality in the USA. The cost of the clones has diminished during the last decade and it is expected to become lower still, making this approach more attractive. In Japan, consumption of cow clones is authorised but essentially for the Kobe beef obtained by nuclear transfer using pluripotent cells as nuclear donors. In the EU, the breeders have not so far expressed a clear will to use clones for genetic selection. This may be due not only to economic problems, but also possibly to the fact that breeders refrain from implementing cloning as they believe consumers will not readily accept food from clones.

The market is uncertain and this is reinforced by the decision of the European Commission not to authorise clone use. The EU situation thus appears blocked.

The biosafety tests for food from clones and clone offspring are limited in number but of high quality and convergence. This led the EFSA to conclude that food from clones is safe. It appears logical and reasonable to confirm these data, to establish a surveillance of clones and clone offspring over several generations to confirm that they do not suffer from any particular disease, to analyse in depth possible remnant epigenetic modifications at the chromatin level in clone offspring and to improve the cloning protocols to reduce the suffering of animals. Clones and their offspring are a particularly costly biological material. The studies mentioned above cannot thus be easily performed. One possibility could be to authorise controlled marketing of the experimental clone offspring. This would bring financial support to their study over several generations, without taking unacceptable risks. One limiting aspect of clone use seems to come from consumers who feel that cloning is an exceedingly sophisticated technique which makes the food products from clones less attractive. It is not clear if consumers realise that it not expected that clones be eaten, but rather their progeny (Suk *et al*., 2007). Another point must also be considered. The committees have analysed essentially the putative biosafety and ethical problems of clone use for consumers and animals respectively. This occulted the comparative evaluation of the benefit of clone use for breeders but also potentially for consumers.

The projects implementing GM animals are not numerous in comparison to those for plants. Several of them appear attractive. This is the case for the fortification of milk by anti bacterial proteins (lysozyme, lactoferrin and lysostaphin), for catfish resistant to bacterial infections, for pigs releasing less polluting phosphate and for pigs secreting a more nourishing milk allowing the survival and the development of a higher proportion of piglets. These projects are facing to variable degrees the opposition or reluctance of some NGOs. The financial support of projects implying GM animals is presently relatively weak all over the world.

The guidelines validated or about to be so appear sufficient to provide consumers with safe food from clones and transgenic animals. Additional tests could be implemented in future. This will be especially the case when the composition and thus the metabolism of the animals is modified in order to improve food properties. Transcriptome, proteome and mainly metabolome might provide experts in future with relevant information reflecting the new biological properties of the animals. A recent study may exemplify this point. Salmon having an accelerated growth after conventional selection appear genetically modified as those having a similar growth after the transfer of the salmon growth hormone gene (Devlin *et al.*, 2009).

Bibliography

Baer, A. and J. Bode (2001), "Coping with Kinetic and Thermodynamic Barriers: RMCE, an Efficient Strategy for the Targeted Integration of Transgenes", *Curr Opin Biotechnol*. 12: 473-480.

Batchelder, C.A., *et al.* (2007a), "Perinatal Physiology in Cloned and Normal Calves: Physical and Clinical Characteristics", *Cloning Stem Cells* 9: 63-82.

Batchelder, C.A., *et al.* (2007b), "Perinatal Physiology in Cloned and Normal Calves: Hematologic and Biochemical Profiles", *Cloning Stem Cells* 9: 83-96.

Booth, P. J., *et al.* (2003), "Numerical Chromosome Errors in Day 7 Somatic Nuclear Transfer Bovine Blastocysts, *Biol Reprod* 68: 922-928.

Bösze, Zs. and L.M. Houdebine (2006), "Application of Rabbits in Biomedical Research: a Review", *World Rabbit Sci.* 14: 1-14.

Campbell, K.H., *et al.* (1996), "Sheep Cloned by Nuclear Transfer from a Cultured Cell Line", *Nature* 380: 64-66.

Chavatte-Palmer, P., *et al.* (2004), Health Status of Cloned Cattle at Different Ages, *Cloning Stem Cells* 6: 94-100.

Chavatte-Palmer, P. and M. Guillomot (2007), "Comparative Implantation and Placentation", *Gynecol Obstet Invest* 64: 166-174.

Chesné, P., *et al.* (2002), Cloned Rabbits Produced by Nuclear Transfer from Adult Somatic Cells, *Nat. Biotechnol.* 20: 366-369.

Cho, S.K., *et al.* (2007), Serial Cloning of Pigs by Somatic Cell Nuclear Transfer: Restoration of Phenotypic Normality during Serial Cloning, *Dev Dyn* 236: 3369-3382.

Cibelli, J.B., *et al.* (1998), "Cloned Transgenic Calves Produced from Nonquiescent Fetal Fibroblasts", *Science* 280: 1256-1258.

Codex Alimentarius (2007), Proposed Draft Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant DNA Animals.

Devlin, R.H., *et al.* (2009), "Domestication and Growth Hormone Transgenesis Cause Similar Changes in Gene Expression in Coho Salmon (*Oncorhynchus Kisutch*)", *Proc Natl Acad Sci USA* 106:3047-3052.

Diles, J.J.B., *et al.* (1996), "Relationships between Body Measurements Obtained on Yearling Brangus Bulls and Measures of Carcass Merit Obtained from their Steer Clone-Mates", *The Professional Animal Scientist* 12: 244-249.

Ding, S., *et al.* (2005), "Efficient Transposition of the PiggyBac (PB) Transposon in Mammalian Cells and Mice", *Cell* 122: 473-483.

Dunham, R. A. (2009), "Transgenic Fish Resistant to Infectious Diseases, their Risk and Prevention of Escape into the Environment and Future Candidate Genes for Disease Transgene Manipulation", *Comp Immunol Microbiol Infect Dis* 32:139-161.

EFSA (European Food Safety Authority) (2008), Draft ''Scientific opinion on food safety, animal health and welfare and environmental impact of animals derived from cloning by somatic cell nucleus transfer (SCNT) and their offspring and products obtained from those animals. *www.efsa.europa.eu/EFSA/DocumentSet/ sc_opinion_ clon_public_consultation.pdf*, accessed 23.06.08.

European Group on Ethics in Science and New Technologies (EGE), (2008), *Ethical Aspects of Cloning for Food Supply*, Opinion N° 23 pp 1-47.

European Parliament resolution of 3 September 2008 on the cloning of animals for food supply.

FAO/WHO (2003), "Expert consultation on the safety assessment of foods from genetically modified animals, including fish".

FAO/WHO (2007), "Expert consultation on safety assessment of foods derived from recombinant-DNA animals (for *Codex Alimentarius*)", (Latest developments in relation to the use of reporter and selectable genes in animal biotechnology), Geneva, Switzerland, 26 February-2 March 2007.

FDA (2009), "Guidance for industry. Regulation of genetically engineered animals containing heritable recombinant DNA construct. Final guidance".

Fosberg, D. and R.R. Hacker (2003), "The Enviropig Physiology, Performance, and Contribution to Nutrient Management, Advances in a Regulated Environment: the Leading Edge of Change in the Pork Industry", *J.Anim.Sci.* 81(E. Suppl. 2):E68-E77.

Galli, C., *et al.* (2003), "Pregnancy: a Cloned Horse Born to its Dam Twin", *Nature* 424: 635.

Gluckman, P.D., M.A. Hanson and A.S. Beedle (2007a), "Early Life Events and Their Consequences for Later Disease: a Life History and Evolutionary Perspective", *Am J Hum Biol* 19: 1-19.

Gluckman, P.D., M.A. Hanson and A.S. Beedle (2007b), "Non-Genomic Transgenerational Inheritance of Disease Risk", *Bioessays* 29: 145-154.

Han, J.Y. (2009), "Germ Cells and Transgenic Chicken", *Comp Immunol Microbiol Infect Dis* 32:61-80.

Heyman, Y., *et al.* (2002), "Frequency and Occurrence of Late-Gestation Losses from Cattle Cloned Embryos", *Biol Reprod* 66: 6-13.

Heyman, Y., *et al.* (2007a), "Assessing the Quality of Products from Cloned Cattle: an Integrative Approach", *Theriogenology* 67: 134-141.

Heyman, Y., *et al.* (2007b), "Quality and Safety of Bovine Clones and their Products", *Animal* 1: 963-972.

Hiendleder, S., V. Zakhartchenko and E. Wolf (2005), "Mitochondria and the Success of Somatic Cell Nuclear Transfer Cloning: from Nuclear-Mitochondrial Interactions to Mitochondrial Complementation and Mitochondrial DNA Recombination", *Reprod Fertil Dev* 17: 69-83.

Houdebine, L.M. (2003), *Animal Transgenesis and Cloning*, Wiley and Sons, 250 pages.

Houdebine, L.M. (2005), "State of the Art in Biotechnology. II. Intended Uses, Scientifically and Commercially, Possible Benefit", *European Bioethical Cours*e (BioTethics), Edited by L. Landeweerd, L. M. Houdebine and R. Ter Meulen, pp 107-134.

Houdebine, L.M. (2007a), "Transgenic Animal Models and Target Validation", *Methods in Molecular Biology* 360: 163-202.

Houdebine, L.M. (2007b), "Latest developments in relation to the use of reporter and selectable genes in animal biotechnology", FAO/WHO Expert Consultation on the Safety Assessment of Foods Derived from Recombinant-DNA Animals, Geneva, Switzerland, (26 February-2 March 2007) .

Houdebine, L.M. (2009a), *Methods to Generate Transgenic Animals in Ethics of Science and Technology Assessment*", Springer-Verlag, Heildelberg Berlin New York, pp. 31-48.

Houdebine, L.M. (2009b), "Production of Pharmaceutical Proteins by Transgenic Animals", *Comparative Immunology, Microbiology and Infectious Diseases* 32: 107-121.

Houdebine, L.M., *et al.* (2008), "Animal Cloning for Food: Epigenetics, Health, Welfare and Food Safety Aspects", *Trends in Food Science and Technology* 19: S80-S95.

Joint FAO/WHO Food Standards Programme *Codex Alimentarius* Commission, 31st Session Geneva Switzerland, (30 June-5 July 2008), Appendix II, pp 35-49.

Kaputchinsky, A.R., *et al.* (2007), *Environmental Risk Assessment of Genetically Modified Organisms, Volume 3, Methodologies for Transgenic Fish*, edited by A. R. Kaputchinsky *et al.*, CAB International Publisher.

Keefer, C.L., *et al.* (2002), "Production of Cloned Goats after Nuclear Transfer Using Adult Somatic Cells", *Biol Reprod* 66: 199-203.

Lai, L. (2006), "Generation of Cloned Transgenic Pigs Rich in Omega-3 Fatty Acids", *Nat. Biotechnol.* 24:435-436.

Laible, G., *et al.* (2007), "Compositional Analysis of Dairy Products Derived from Clones and Cloned Transgenic Cattle", *Theriogenology* 67: 166-77.

Laible, G. (2009), "Enhancing Livestock Through Genetic Engineering – Recent Advances and Future Prospects", *Comp Immunol Microbiol Infect Dis* 32:123-137.

Lema, M.A. and M. Burachik (2009), "Safety Assessment of Food Products from r-DNA Animals" *Comp Immunol Microbiol Infect Dis* 32:163-189.

Lillico, S.G., *et al.* (2007), **"**Oviduct-Specific Expression of Two Therapeutic Proteins in Transgenic Hens", *Proc Natl Acad Sci* 104: 1771-1776.

Long, X. and J.M. Miano (2007), "Remote Control of Gene Expression", *J Biol Chem* 282: 15941-15945.

Malphettes, L. and M. Fussenegger (2006), "Improved Transgene Expression Fine-Tuning in Mammalian Cells Using a Novel Transcription-Translation Network", *J. Biotechnol*. 124: 732-746.

Manzini, S., *et al.* (2006), "Genetically Modified Pigs Produced with a Nonviral Episomal Vector", *Proc Natl Acad Sci USA* 103:17672-17677.

Moisyadi, S., J.M. Kaminski and R. Yanagimachi (2009), "Use of Intracytoplasmic Sperm Injection (ICSI) to Generate Transgenic Animals", *Comp Immunol Microbiol Infect Dis* 32: 47-60.

Montoliu, L., *et al.* (2009), "Design of Vectors for Transgene Expression: the Use of Genomic Comparative Approaches", *Comp Immunol Microbiol Infect Dis* 32:81-90.

Moreira, P.N., *et al.* (2007), "Improving the Generation of Genomic-Type Transgenic Mice by ICSI", *Transgenic Res* 16:163-168.

Multiauthor book (2009), "Pharming. Promises and risks of biopharmaceuticals derived from genetically modified plants and animals". In *Ethics of Science and Technology Assessment*, Edited by E Rehbinder *et al.*, Springer-Verlag, Heildelberg Berlin New York, 35, 332 pages.

Murphey, P., *et al.* (2009), "Epigenetic Regulation of Genetic Integrity is Reprogrammed during Cloning", *Proc Natl Acad Sci* USA 106: 4731-4735.

Nakagawa, M., *et al.* (2008), "Generation of Induced Pluripotent Stem Cells without Myc from Mouse and Human Fibroblasts", *Nat. Biotechnol.* 26: 101-106.

Nicolls, H. (2008), "Let's Make a Mammoth", *Nature* 456: 310-314.

Niemann, H., W. Kues and J.W. Carnwath (2009), *Methods to Generate Transgenic Animals in Ethics of Science and Technology Assessment*, Springer-Verlag, Heildelberg Berlin New York, 34, pp. 1-30.

Norman, H.D., *et al.* (2004), "Performance of Holstein Clones in the United States", *J Dairy Sci* 87: 729-738.

Norman, H.D. and M.K. Walsh (2004), Performance of Dairy Cattle Clones and Evaluation of Their Milk Composition, *Cloning Stem Cells* 6: 157-164.

Onishi, A., *et al.* (2000), "Pig Cloning by Microinjection of Fetal Fibroblast Nuclei", *Science* 289: 1188-1190.

Ono, E., *et al.* (2004), "Transgenic Mice Expressing a Soluble Form of Porcine Nectin-1/herpesvirus Entry Mediator C as a Model for Pseudorabies-Resistant Livestock", *Proc.Natl. Acad. Sci. USA* 10:16150-16155.

Ortegon, H., *et al.* (2007), "Genomic Stability and Physiological Assessments of Live Offspring Sired by a Bull Clone, Starbuck II", *Theriogenology* 67: 116-126.

Panarace, M., *et al.* (2007), "How Healthy are Clones and their Progeny: 5 Years of Field Experience", *Theriogenology* 67: 142-151.

Park, F. (2007), "Lentiviral Vectors: Are they the Future of Animal Transgenesis?", *Physiol Genomics*, 31:159-173.

Pera, M.F. and K. Hasegawa (2008), "Simpler and Safer Cell Reprogramming", *Nat Biotechnol.* 26: 59-60.

Petersen, B., J.W. Carnwath and H. Niemann (2009), "The Perspectives for Porcin-to-Human Xenografts", *Comp Immunol Microbiol Infect Dis* 32:91-105.

Porteus, M.F. and D. Carroll (2005), "Gene Targeting Using Zinc Finger Nucleases", *Nat Biotechnol* 23: 967-973.

Rao, M. (2007), "Scalable Human ES Culture for Therapeutic Use: Propagation, Differentiation, Genetic Modification and Regulatory Issues", *Gene Therapy* 15: 82-88.

Rassoulzadegan, M., *et al.* (2006), "RNA-Mediated Non-Mendelian Inheritance of an Epigenetic Change in the Mouse", *Nature* 441: 469-474.

Renard, J.P., *et al.* (2007), "Nuclear Reprogramming and Pluripotency of Embryonic Cells: Application to the Isolation of Embryonic Stem Cells in Farm Animals", *Theriogenology* 68 Suppl 1: S196-205.

Robl, J.M., *et al.* (2007), "Transgenic Animal Production and Animal Biotechnology", *Theriogenology* 67: 127-133.

Santiago, Y., *et al.* (2008), "Targeted Gene Knockout in Mammalian Cells by Using Engineered Zinc-Finger Nucleases", *Proc Natl Acad Sci USA* 105: 5809-5814.

Schnieke, A. (2009), *Animal Pharming: Past Experience and Future Prospects. Methods to Generate Transgenic Animals in Ethics of Science and Technology Assessment*, Springer-Verlag. Heildelberg Berlin New York, 34, pp 49-69.

Shen, W., *et al.* (2006), "Efficient and Simple Production of Transgenic Mice and Rabbits Using the New DMSO-Sperm Mediated Exogenous DNA Transfer Method", *Mol Reprod Dev* 73:589-594.

Shinohara, E.T., *et al.* (2007), "Active Integration: New Strategies for Transgenesis", *Transgenic Res* 16: 333-339.

Sioud, M. (2006), "Innate Sensing of Self and Non-self RNAs by Toll-like Receptors", *Trends Mol Med* 12: 167-176.

Scientific Opinion on Food Safety, Animal Health and Welfare and Environmental Impact of Animals derived from Cloning (SCNT) and their Offspring and Products Obtained from those Animals, Scientific Opinion of the Scientific Committee (Question No EFSA-Q-2007-092), 2008, The EFSA Journal 767:7-49.

Shibata, M., *et al.* (2006), "Reproductive and Growth Performance in Jin Hua Pigs Cloned from Somatic Cell Nuclei and the Meat Quality of Their Offspring", *J. Reprod Dev* 52: 583-590.

Smith, K. and C. Spadafora (2005), "Sperm Mediated Gene Transfer: Applications and Implications", *BioEssays* 27: 551-562.

Suk, J., *et al.* (2007), "Dolly for Dinner? Assessing Commercial and Regulatory Trends in Cloned Livestock", *Nat Biotechnol*. 25:47-53.

Takahashi, S. and Y. Ito (2004), "Evaluation of Meat Products from Cloned Cattle: Biological and Biochemical Properties", *Cloning Stem Cells* 6: 165-171.

Tamashiro, K.L., *et al.* (2000), "Postnatal Growth and Behavioral Development of Mice Cloned from Adult Cumulus Cells", *Biol Reprod* 63: 328-334.

Tian, X.C., *et al.* (2005), "Meat and Milk Compositions of Bovine Clones", *Proc Natl Acad Sci USA* 102: 6261-6266.

Tiscornia, G., *et al.* (2003), "A General Method for Gene Knockdown in Mice by Using Lentiviral Vectors Expressing Small Interfering RNA", *Proc Natl Acad Sci USA* 100:1844-1848.

Tom, e D., M. Dubarry and G. Fromentin (2004), "Nutritional Value of Milk and Meat Products Derived from Cloning", *Cloning Stem Cells* 6: 172-177.

Van de Lavoir, M.C., *et al.* (2006), "Germline Transmission of Genetically Modified Primordial Germ Cells", *Nature* 441: 766-769.

Wakayama, T., *et al.* (2000), "Cloning of Mice to Six Generations", *Nature* 407: 318-319.

Walker, S., *et al.* (2007), "Comparison of Meat Composition from Offspring of Cloned and Conventionally Produced Boars", *Theriogenology* 67: 178-184.

Walsh, M.K., *et al.* (2003), "Comparison of Milk Produced by Cows Cloned by Nuclear Transfer with Milk from Non-Cloned Cows", *Cloning Stem Cells* 5: 213-219.

Watanabe, S. and T. Nagai (2008), "Health Status and Productive Performance of Somatic Cell Cloned Cattle and their Offspring Produced in Japan", *J. Reprod Develop* 54: 6-17.

Wells, D.N., *et al.* (2004), "The Health of Somatic Cell Cloned Cattle and their Offspring", *Cloning Stem Cells* 6: 101-110.

Wheeler, M.B., G.T. Bleck and S. M. Donovan (2001), "Transgenic Alteration of Sow Milk to Improve Piglet Growth and Health", *Reprod Suppl* 58: 313-324.

Whitelaw, C.B., S.G. Lillico and T. King (2008), "Production of Transgenic Farm Animals by Viral Vector-Mediated Gene Transfer", *Reprod Domest Anim*. 43 Suppl 2:355-358.

Wilmut, I, *et al.* (1997), "Viable Offspring Derived from Fetal and Adult Mammalian Cells", *Nature* 385: 810-813.

Wilson, J.H. (2008), "Knockout Punches with a Fistful of Zinc Fingers", *Proc Natl Acad Sci USA* 105: 5653-5654.

Yamaguchi, M., Y. Ito and S. Takahashi (2007), "Fourteen-Week Feeding Test of Meat and Milk Derived from Cloned Cattle in the Rat", *Theriogenology* 67: 152-165.

Woods, I.G. and A.F. Schier (2008), "Targeted Mutagenesis in Zebrafish", *Nat Biotechnol.* 26: 650-651.

Yang, L., *et al.* (2005), "Expression of Imprinted Genes is Aberrant in Deceased Newborn Cloned Calves and Relatively Normal in Surviving Adult Clones", *Mol Reprod Dev* 71: 431-438.

Yang, X., *et al.* (2007a), "Nuclear Reprogramming of Cloned Embryos and its Implications for Therapeutic Cloning", *Nat Genet* 39: 295-302.

Yang, X., *et al.* (2007b), "Risk Assessment of Meat and Milk from Cloned Animals", *Nat Biotechnol* 25: 77-78.

Yong, H.Y., *et al.* (2006), "Production of a Transgenic Piglet by a Sperm Injection Technique in Which No Chemical or Physical Treatments Were Used for Oocytes or Sperm", *Mol Reprod Dev* 73: 595-599.

Chapter 19

The Biotechnology and Biosafety Activities at the OECD

Peter Kearns, Yukihiko Fukase and Bertrand Dagallier
OECD's Biosafety Team, Paris, France

In order to increase the efficiency of the risk/safety assessment process and to reduce duplication of effort, OECD countries have recognised the value of working together to harmonise approaches and share information used in safety assessment. The need for such co-operation and the value of harmonisation amongst countries has resulted in two closely related programmes at the OECD:

- *The Working Group on Harmonisation of Regulatory Oversight in Biotechnology, established in 1995, addresses aspects of the environmental risk/safety assessment of transgenic organisms;*
- *The Task Force for the Safety of Novel Foods and Feeds, established in 1995, addresses the safety assessment of foods and feeds derived from transgenic organisms.*

The main focus of the work is to ensure that the types of information used in risk assessment, as well as the methods to collect such information, are as similar as possible.

Introduction

For a number of years, the assessment of the safety of products derived from modern biotechnology has been an important challenge for countries as transgenic crops are increasingly cultivated world wide, and as human foods and animal feeds derived from such crops are being marketed. In order to increase the efficiency of the risk/safety assessment process and to reduce duplication of effort, OECD countries recognised, some years ago, the value of working together to harmonise approaches and share information used in safety assessment. The need for such co-operation and the value of harmonisation amongst countries has resulted in two closely related programmes at OECD:

- The *Working Group on Harmonisation of Regulatory Oversight in Biotechnology*, established in 1995, addresses aspects of the environmental risk/safety assessment of transgenic organisms;
- The *Task Force for the Safety of Novel Foods and Feeds*, established in 1999, addresses the safety assessment of foods and feeds derived from transgenic organisms.

The main focus of the work is to ensure that the types of information used in risk assessment, as well as the methods to collect such information, are as similar as possible. The main purpose of the work is threefold:

i) to assist countries evaluate the potential risks of transgenic products to ensure high standards of safety;

ii) to foster communication and mutual understanding of the regulatory processes in different countries;

iii) to reduce the potential for non-tariff barriers to trade.

Environmental risk/safety assessment of transgenic organisms

The work on the environmental risk/safety assessment of transgenic organisms is undertaken through *OECD's Working Group on Harmonisation of Regulatory Oversight in Biotechnology*, a subsidiary body of the Joint Meeting of the Chemicals committee and the Working Party on Chemicals, Pesticides and Biotechnology.

Delegates to the Working Group are nominated by the OECD member countries and the European Commission, typically from ministries or agencies responsible for the environmental risk/safety assessment of transgenic organisms. At the same time, a number of observers participate from non-member economies, to date, Argentina, Brazil, Cameroon, China, Chile, India, Latvia, Philippines, the Russian Federation, Slovenia, South Africa and Thailand. In addition, there is participation from other intergovernmental organisations and programmes such as the United Nations Environment Programme (UNEP), the secretariat of the Convention on Biological Diversity (CBD), the Food and Agriculture Organization of the United Nations (FAO) and the United Nations Industrial Development Organization (UNIDO). Finally, there is also input into the activities from industry via the Business and Industry Advisory Committee to OECD (BIAC).

The main outputs of the work on the environmental risk/safety assessment of transgenic crops are the series of "consensus documents", more than 40 published to date. Many of them address those major crops which have been involved in the development of commercialised transgenic varieties or have the potential for such uses in the near future.

Biology consensus documents

These documents deal with the biology of major crops which have been the subject of genetic engineering. They contain a wealth of information (for use in risk assessment) on the *biology* of specific crops, including: a short natural history of the crop plant, major uses and agricultural practices, taxonomic status; reproductive behaviour; occurrence of wild relatives and possibility of hybridisation with them; centre of origin and diversity of the crop; and potential for weediness. These are considered as key issues for risk/safety assessors.

The crops considered to date include maize, oilseed rape, potato, wheat, rice, soybean, sugar beet, cotton, sunflower, papaya, peppers, rice, bananas and plantains.

Some documents deal with tree species which have also been the subject of genetic engineering, though there are only a few examples of commercialised varieties to date. Nevertheless documents are available on spruces (Norway spruce, White spruce, Sitka spruce); poplars; Douglas fir; pines (Lodgepole pine, Eastern white pine, Western white pine, Jack pine); European white birch; Native North American larches; and Stone fruits.

Future biology documents currently being developed will include cucurbits, cassava, sugarcane, eucalyptus, black spruce and the first document related to an animal species: Atlantic salmon.

Trait consensus documents

The Working Group has also published documents on those traits which are commonly used in transgenic crops. These "trait documents" include topics such as: tolerance to glyphosate herbicide; tolerance to phosphinothricin herbicides; virus resistance through coat protein gene-mediated protection; and insect control through *Bacillus thuringiensis* (*Bt*). As with the biology consensus documents on specific crop plants, the "trait documents" focus on issues which are of great concern to risk/safety assessors.

General biosafety documents

Three additional publications are important in understanding both the process of how these documents are developed and published, as well as the information they contain.

First, the Working Group published an *Introduction to the Biosafety Consensus documents* in 2005. This document describes what is meant by regulatory harmonisation in the context of the work of the Working Group. The document considers the purpose of consensus documents and their intended users who are those involved in regulatory safety assessment. It explains how it is possible to have a common approach to risk/safety assessment at international level. The basis for it lies in the fact that the process of risk/safety assessment, as well as the information used during the process, are very similar among countries. The publication explains why such consensus documents are

considered a useful approach to harmonisation, and notes that the information compiled in them is presented in a form that can readily be used.

Second, the *Guide for Preparation of Consensus Documents* was published in 2008. It describes the important role of lead countries: each document is drafted, in its initial stages, by one or more lead countries that have had experience with the crop in question. It is then circulated to all countries and other stakeholders for their input. This guide also points to potential sources of information for use in consensus documents, as well as guidance on style and layout as well as nomenclature. This document also considers the role of the OECD Secretariat in the preparation of consensus documents, which manages the drafting and revision process and ensures that input is collected from all stakeholders.

Third, a document entitled *Points to Consider for Consensus Documents* was issued in 2006. This publication is important for understanding the types of information included in the consensus documents, because it identifies the type of information that can be provided for a range of items. Crucially, it offers a "Rationale" as to why that information is relevant to environmental risk/safety assessment. The document has six information sections which cover:

- species and taxonomic group
- reproductive biology
- genetics
- hybridisation and introgression
- general interactions with other organisms (ecology)
- human health and biosafety.

To quote just one example from the section on Reproductive Biology, there is an information item:

"Generation time and duration under natural circumstances, and where grown or managed".

The type of information to address this item is noted as follows:

"Important aspects of generation time and duration include the time to first flowering and total life cycle of the plant, and time from planting to plough-down. Include the effects of agronomic, silvicultural, and similar practices when describing generation time and duration of the cultivated plant. Important differences within both the natural and the cultivated regions should be noted."

Then the following rationale explains why this information is relevant to environmental safety:

"Rationale: The generation time and duration are indications of the terms in which environmental effects may occur. Precocious generation times and shorter durations in agriculture affect the likelihood of outcrossing with free-living (wild) relatives, and give a general indication of when outcrossing may first occur."

By reading this document, therefore, one can gain important insights as to why certain information items are considered important to the risk/safety assessment process.

Further Guidance Documents are currently being prepared on other important issues:

- environmental considerations
- low level presence of transgenic grains in conventional seeds and commodities
- molecular characterisation of plants derived from modern biotechnology.

Micro-organisms documents

Finally, the Working Group has undertaken work related to the use of transgenic micro-organisms. Documents have been published on specific groups of micro-organisms which are of interest in biotechnology such as *Acinetobacter, Acidithiobacillus, Pseudomonas* and baculoviruses.

Two other documents relate to the use of bacteria in the environment: *Taxonomy in Risk Assessment*; and *Methods for Detection when Micro-organisms are Introduced into the Environment*. Although there are few examples to date of the use of transgenic micro-organisms in the environment, such uses have been predicted and might occur in the future.

Risk/safety assessment of foods and feeds derived from transgenic organisms

The work on the risk/safety assessment of foods and feeds derived from transgenic organisms is undertaken by OECD's Task Force for the Safety of Novel Foods and Feeds. Its work closely complements that of the Working Group. Both groups address the risk safety assessment of transgenic organisms (primarily crop species) but while the Working Group focuses on environmental safety, the Task Force covers food and feed safety issues.

Participation in the Task Force is primarily delegates nominated by member countries and the European Commission, who are from those ministries and agencies responsible for the risk/safety assessment of novel foods and feeds. There are also delegations from non-member countries as those mentioned above for the Working Group. In addition, other intergovernmental organisations participate such as FAO, WHO and the Secretariat of the *Codex Alimentarius* Commission. Business and Industry also make input into the work.

The risk/safety assessment of foods and feeds derived from transgenic varieties follows a comparative approach. In other words, an essential part of the work of risk/safety assessors is to determine whether or not a new food or feed is "as safe as" a traditional counterpart. In making such a determination, risk/safety assessors use information on key compositional components of a new food to compare it with its traditional counterpart. Such compositional components typically include: key nutrients; anti-nutrients; toxicants; allergens; and secondary metabolites.

To assist in this work, the Task Force publishes a series of "food/feed safety consensus documents" which includes compositional considerations – the typical composition – of specific crops as well as processed foods and feeds derived from them. This information can then be used by risk/safety assessors when considering a new variety. The process by which these documents are developed and published is similar to the way in which the Working Group develops its documents, as described above. However, the most important feature is that these documents are developed through a lead country approach with other delegations and stakeholders having input during the drafting process.

The Task Force has published an *Introduction to OECD's Food and Feed Safety Consensus Documents* which provides a detailed explanation on their content and development.

To date, the Task Force has published 16 food/feed consensus documents which include; soybean; low erucic acid oilseed rape (canola); potato; sugar beet; maize; sunflower; alfalfa and other temperate forage legumes; wheat; rice; cotton; barley; cultivated mushroom (*Agaricus bisporus*); tomato; and cassava.

A general document considering the *safety assessment of animal feedstuffs* is also recognised and used as a basis by many authorities and agencies.

Documents under preparation will cover the following species in the near future: sweet potato, grain sorghum, papaya, and sugarcane.

Conclusions

This paper has explored the activities and publications of OECD's Working Group on Harmonisation of Regulatory Oversight in Biotechnology and the Task Force for the Safety of Novel Foods and Feeds. These groups are working towards the environmental safety and food/feed safety of transgenic crop varieties or the foods and feeds derived from them.

The main outputs of the work are the Series of "consensus documents" of the respective groups. These documents compile information which is intended to be used by those involved in the business of risk/safety assessment. This includes those working for national authorities as well as developers of transgenic crops.

The advantage of the activities of both the Working Group and Task Force is that the "consensus documents" are developed primarily by delegates from national authorities (with input from other stakeholders) who have the responsibility for risk/safety assessment. They give a major insight into those issues and the information that national authorities believe is important for safety.

An increasing trend in both the Working Group and Task Force is to consider crop species which are relevant to tropical regions and therefore to countries that are not necessarily members of the OECD. For example, the Working Group has recently published a consensus document on bananas and plantains while the Task Force has published a document on cassava. This trend towards crops of greater interest in the tropics is likely to continue into the future.

Bibliography

All the documents mentioned in the text can be found in chronological order and downloaded from the OECD Biotrack public web site, *www.oecd.org/biotrack.*

It includes those related to the environmental safety activities of the Working Group that can be found at:

www.oecd.org/document/51/0,3343,en_2649_34387_1889395_1_1_1_1,00.html

and those related to the food and feed safety activities of the Task Force at:

www.oecd.org/document/9/0,3343,en_2649_34391_1812041_1_1_1_1,00.html.

Chapter 20

Biosafety Assessment of the EFSA GMO Panel

Dr. Detlef Bartsch, Federal Office of Consumer Protection and Food Safety, Germany

Federal Office of Consumer Protection and Food Safety, Germany

The European Food Safety Authority (EFSA) is the keystone of European Union (EU) risk assessment regarding food and feed safety. In close collaboration with national authorities like the German Federal Office of Consumer Protection and Food Safety (BVL) and in open consultation with its stakeholders, the EFSA provides independent scientific advice and clear communication on existing and emerging risks. The GMO Panel provides independent scientific advice on the safety of GMOs such as plants, animals and micro-organisms, on the basis of Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms; and of genetically modified food and feed, on the basis of Regulation (EC) No 1829/2003 on genetically modified food and feed.

The Panel carries out risk assessments in order to produce scientific opinions and advice for risk managers. Its risk assessment work is based on reviewing scientific information and data in order to evaluate the safety of a given GMO. This helps to provide a sound foundation for European policies and legislation and supports risk managers in taking effective and timely decisions. The Panel carries out much of its work in the context of authorisation applications, since all GM food and feed products must be evaluated by the EFSA before they can be authorised in the EU. The EFSA integrates the input of Member States in the risk assessment process in a transparent manner. The EFSA frequently sets up Working Groups involving external scientists – also from national Competent Authorities like the German BVL – with relevant expertise to focus on specific matters and help produce scientific opinions. The GMO Panel itself meets regularly in plenary sessions to discuss work in progress and to adopt finalised scientific opinions. The Panel has four main areas of activity: risk assessment of GM food and feed applications; development of guidance documents; scientific advice in response to ad-hoc requests from risk managers; self-tasking activities.

Introduction

The European Food Safety Authority (EFSA) was established and funded by the European Community as an independent agency in 2002 following a series of food scares that caused the European public to voice concerns about food safety and the ability of regulatory authorities to fully protect consumers.

In close collaboration with national authorities and in open consultation with its stakeholders, the EFSA provides objective scientific advice on all matters with a direct or indirect impact on food and feed safety, including animal health and welfare and plant protection. The EFSA is also consulted on nutrition in relation to Community legislation.

EFSA's work falls into two areas: risk assessment and risk communication. In particular, EFSA's risk assessments provide risk managers (EU institutions with political accountability, *i.e.* the European Commission, European Parliament and Council) with a sound scientific basis for defining policy-driven legislative or regulatory measures required to ensure a high level of consumer protection with regards to food and feed safety.

The EFSA communicates to the public in an open and transparent way on all matters within its remit. Collection and analysis of scientific data, identification of emerging risks and scientific support to the Commission, particularly in case of a food crisis, are also part of EFSA's mandate, as laid down in the founding Regulation (EC) No 178/2002 of 28 January 2002 (EC, 2002).

The role of the scientific panel on GMO

Established in May 2003, the Scientific Panels have delivered almost 1 000 scientific opinions on a wide variety of risk issues. These include Bovine Spongiform Encephalopathy (BSE) and Transmissible Spongiform Encephalopathy (TSE), food additives such as aspartame, allergenic food ingredients, GMOs, contaminants in the food chain, pesticides, and animal health issues including Avian Influenza.

EFSA's Scientific Panels are composed of independent experts. They are responsible for EFSA's risk assessment work including delivering scientific opinions. Each Panel is responsible for a different area of the food chain, with their work co-ordinated by the Scientific Committee. Panel members are appointed by the EFSA Management Board for three years renewable. Appointments are made on the basis of proven scientific excellence following an open call for applications and a rigorous selection procedure. The Panel regularly sets up Working Groups involving external scientists with relevant expertise to deal with specific matters and to help produce scientific opinions. All experts working for the EFSA sign a Declaration of Interests to safeguard EFSA's commitment to independence.

The EFSA GMO Panel provides independent scientific advice on the safety of:

- GMOs such as plants, animals and micro-organisms, on the basis of Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms (EC, 2001);
- GM food and feed, on the basis of Regulation (EC) No 1829/2003 on GM food and feed (EC, 2003)

The Panel carries out risk assessments in order to produce scientific opinions and advice for risk managers. Its risk assessment work is based on reviewing scientific information and data in order to evaluate the safety of a given GMO. This helps to provide a sound foundation for European policies and legislation and supports risk managers in taking effective and timely decisions. The Panel carries out much of its work in the context of authorisation applications, since all GM food and feed products must be evaluated by the EFSA before they can be authorised in the EU.

The GMO Panel works independently, openly and transparently to deliver timely scientific advice of the highest standards to support the policies and decisions of risk managers. The GMO Panel brings together highly qualified risk assessment experts from a number of European nationalities with expertise in a range of relevant fields.[1] Since its establishment in 2003, the GMO Panel has issued more than 90 scientific documents.[2]

The GMO Panel carries out its work either in response to requests for scientific advice from risk managers or on its own initiative. It frequently sets up Working Groups involving external scientists with relevant expertise to focus on specific matters and help produce scientific opinions. The Panel itself meets regularly in plenary sessions to discuss work in progress and to adopt finalised scientific opinions. Each opinion results from a collective decision-making process with every Panel member having an equal say.

Risk assessment of GMO

Genetic modification, genetic engineering or recombinant-DNA technology, first applied in the 1970s, is one of the newest methods to introduce novel traits to micro-organisms, plants and animals. Unlike other methods, the application of this technology is strictly regulated. Before any GMO or derived product can be placed on the EU market, it has to pass an approval system in which the safety for humans, animals and the environment is thoroughly assessed.

In line with the provisions of Regulation (EC) 1829/2003 (EC, 2003) on GM food and feed, which came into force on 18 April 2004, the Commission has asked the EFSA to publish detailed guidance to assist the applicant in the preparation and presentation of the application for the authorisation of GM food and/or feed.

The EFSA guidance document (latest published version EFSA 2006a) provides detailed guidance for the assessment of GM plants and food and/or feed containing, consisting of, or produced from these plants. This guidance complements, but does not replace, other requirements, as set out in specific legislation (*e.g.* seed or other plant propagating materials), that a product has to fulfil in order to be approved for the European market. In addition, a guidance document for the risk assessment of GM Microorganisms (GMMs) and derived food and feed was published in 2006 (EFSA, 2006b). The EFSA guidance documents are continuously updated according to latest scientific and policy developments.

The risk assessment strategy for GM plants seeks to deploy appropriate methods and approaches to compare the GMO plant and derived products with their conventional counterpart and other traditionally bred varieties. These non-GM plants can thus serve as a baseline for the environmental and food/feed safety assessment of GMOs. The comparative approach is followed in order to identify intended and unintended differences which are subsequently assessed with respect to their potential impact on environment, food/feed safety and nutritional quality. The underlying assumptions of the

comparative assessment approaches for GM plants is that the biology of traditionally cultivated crops the conventional counterparts from which the GM plants have been derived, is well known and that they have a history of safe use for the average consumer or animal and the environment. To this end the concept of familiarity and substantial equivalence was developed by the OECD (OECD, 1993a; OECD, 1993b) and further elaborated by WHO/FAO (WHO/FAO, 2000 and 2001) for the assessment of the environmental and food/feed safety of GMOs, respectively.

The GMO risk assessment is split into three parts: Molecular characterisation, Food and Feed safety assessment, and Environmental Risk assessment (ERA). The objective of the Risk Assessment is on a case-by-case basis to identify and evaluate potential adverse effects of the GMO, either direct or indirect, immediate or delayed (including cumulative long-term effects[3]), on human health and the environment which the placing on the market of GMOs may have.

The EFSA GMO Panel currently works on:

- an update of the guidance document for the risk assessment of genetically modified micro-organisms and their derived products intended for food and feed use;
- a general mandate on aspects of the ERA and the ERA guidance (outcome expected for 2010);
- a guidance document for the risk assessment of GM Plants and derived food and feed;
- a guidance for the assessment of genetically modified plants used for non-food or non-feed purposes (EFSA, 2008b).

The risk assessment process consists of four steps *i.e.* hazard identification, hazard characterisation, exposure assessment, and culminates in the final integrative risk characterisation.

Risk characterisation is defined as: "The quantitative or semi-quantitative estimate including attendant uncertainties, of the probability of occurrence and severity of adverse effect(s)/event(s) in a given population under defined conditions based on hazard identification, hazard characterisation and exposure assessment" (SSC, 2000). This chapter describes how the risk characterisation step should be carried out and gives examples of issues to be addressed.

Where the total scientific information is insufficient, inconclusive, or uncertain, or where there are indications that the possible effects on human/animal health and the environment may be potentially dangerous and inconsistent with the chosen level of protection, the precautionary approach may be invoked (EC, 2000b). Application of the precautionary approach is distinct from the normal conservative scientific approach in the assessment of data based on safety or extrapolation factors. Application of the precautionary approach is the responsibility of the risk manager and not of the risk assessor.

Risk analysis starts with defining the proper questions which should be addressed during the risk assessment, *i.e.* identification of potential risks of cultivation of GM plants and/or human/animal consumption of derived food/feed. Problem formulation should involve risk managers, risk assessors and stakeholders *e.g.* producers, growers, environmental and consumer groups. For instance, cultivation areas, exposure routes and

intake, target populations (humans/animals/environment) and health end-points should be identified for the GM plant and its derived foods/feed and existing knowledge on the use of the non-modified parent plant and derived foods/feed should be collected.

The final risk characterisation of GM plants and derived foods/feed is focused on data from hazard identification and hazard characterisation, using laboratory and target animal studies, environmental studies (laboratory scale, greenhouse) and field trials, and on exposure/intake data. A comprehensive risk characterisation should be carried out, *i.e.* considering all the available evidence from several approaches including molecular analysis, agronomical and compositional analysis, toxicity and allergenicity testing, and environmental impact analysis. The risk characterisation may give indications for the requirement of specific activities for post-market monitoring of GM food/feed and for environmental monitoring of GM plants.

The risk characterisation should provide evidence whether the hazard identification and subsequent characterisation is complete. It is essentially an iterative process. Integration and evaluation of data from hazard characterisation and exposure assessment may indicate that appropriate risk estimation can be made, or that further data should be generated in order to complete the risk characterisation. For instance if an increased intake of a GM derived food/feed by humans or animals may be expected further data on toxicity at extended dose ranges may have to be generated. The absence of data essential for the risk assessment and the quality of existing data should be discussed. It should be clear from the discussion how this body of information has been taken into account when the final risk estimation is determined.

The six steps in risk assessment applied by the EFSA GMO Panel in line with EU legislation are:

i) the identification of characteristics which may cause adverse effects;

ii) the evaluation of the potential consequences of each adverse effect, if it occurs;

iii) the evaluation of the likelihood of the occurrence of each identified potential adverse effect;

iv) the estimation of the risk posed by each identified characteristic of the GMO(s);

v) the application of management strategies for risks from the deliberate release or marketing of GMO(s);

vi) the determination of the overall risk of the GMO(s).

A crucial step in the risk assessment (prior to the six steps described in the Directive 2001/18/EC) is to identify the assessment endpoints of the ERA. Defining the assessment endpoints is necessary to focus the risk assessment on aspects of the environment that need protection (*e.g.* protection of endangered species). Risk assessment endpoints derive from management objectives set by public policy.

Legal background for the risk assessment of GMOs, GM food and GM feed at European Community level

The EU Regulations, Directives and Decisions published in the Official Journal of the European Communities establish the procedures to be followed in seeking approval for GMOs as well as the requirements for the applications and are, therefore, always the primary source of advice.

General food law (Regulation (EC) 178/2002)

Regulation (EC) 178/2002 (EC, 2002c) lays down the general principles of food law and procedures in food safety including the tasks of the EFSA. It defines food law broadly, including animal feed and other agricultural inputs at the level of primary production.

In the general food law 'food' means any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans. 'Food' includes any substance intentionally incorporated into the food during its manufacture, preparation or treatment. "Feed" means any substance or product, including additives, whether processed, partially processed or unprocessed, intended to be used for oral feeding to animals. The general food law defines "hazard", "risk", "risk analysis", "risk assessment", "risk management" and "risk communication".[4]

Articles 14 and 15 of the general food law set the food and feed safety requirements, respectively, in order to determine whether any food or feed is injurious to health.

According to Regulation (EC) 1829/2003, GM food and feed should only be authorised for placing on the market after a scientific assessment of any risks which they might present for human and animal health and, as the case may be, for the environment. GM food and feed mean GMOs for food/feed use; food/feed containing or consisting of GMOs; food/feed produced from GMOs; and food containing ingredients produced from GMOs. Food products containing, consisting of, or produced from GMOs were previously regulated by Regulation (EC) 258/97 on novel foods and novel food ingredients, which has been amended by Regulation (EC) 1829/2003.

For feed containing or consisting of GMOs, no specific Community legislation has been in place prior to the entering into force of this Regulation, the safety of GM feed being assessed under Directive 90/220/EEC (repealed by Directive 2001/18/EC). Articles 8 and 20 of Regulation (EC) 1829/2003 establish transitional measures for existing products. Food and feed which have been lawfully placed on the EU market before 18 April 2004 continue to be allowed on the market, used and processed provided that they were notified to the Commission before 18 October 2004.

The Regulation requires that GM food/feed must not (i) have adverse effects on human health, animal health or the environment; (ii) mislead the consumer/user; (iii) differ from the food/feed which it is intended to replace to such an extent that its normal consumption would be nutritionally disadvantageous for the consumer/animals. In addition, GM feed must not harm or mislead the consumer by impairing the distinctive features of the animal products. Products will be authorised only when the applicant has adequately demonstrated that they satisfy these requirements. All these points have to be considered within the scientific risk assessment and applicants have to provide reliable and comprehensive data.

The application shall be submitted to the national competent authority of a Member State, who makes it available to the EFSA which then makes the application available to the other Member States and the Commission, and makes the summary of the application available to the public. The scientific assessment of the application will be undertaken under the responsibility of the EFSA. The EFSA may ask the appropriate food/feed assessment body of a Member State to carry out a safety assessment of the food/feed in accordance with Article 36 of Regulation (EC) 178/2002. The EFSA may also ask a competent authority designated in accordance with Article 4 of Directive 2001/18/EC to carry out an environmental risk assessment. However, if the application concerns GMOs

to be used as seeds or other plant-propagating material, the Authority shall ask a national competent authority to carry out the environmental risk assessment. The EFSA will conclude on the final assessment.

From the receipt of a valid application, the EFSA shall endeavour to comply with a time limit of six months to provide its opinion. The clock will be stopped whenever the EFSA seeks supplementary information from the applicant.

Taking into account the opinion of the EFSA, the Commission shall submit to the Standing Committee on the Food Chain and Animal Health a draft decision within three months of receipt of the opinion. A final decision shall be adopted in accordance with the Committee procedure. The authorisation is valid throughout the Community for ten years. The authorised product will have to comply with the provisions of Regulation (EC) 1830/2003 concerning the traceability and labelling of GMOs and the traceability of food and feed products produced from GMOs (EC, 2003b). The authorised product shall be entered in a Community Register of GM food and feed, which will be made available to the public. Where appropriate, and based on the conclusions of the risk assessment, post-market monitoring requirements for the use of the GM foods for human consumption or GM feeds for animal consumption may be imposed.

Deliberate release of GMOs (Directive 2001/18/EC)

The principles regulating the deliberate release into the environment of GMOs are laid down in Council Directive 2001/18/EC (EC, 2001), which repeals Directive 90/220/EEC (EC, 1990). This Directive puts in place a step-by-step approval process made on a case-by-case assessment of the risk to human health and the environment before any GMOs can be released into the environment, or placed on the market as, or in, products. The step-by-step principle means that the containment of GMOs is reduced and the scale of release increased gradually, but only if assessment of the earlier steps indicates that the next step can be taken.

Part B of the Directive deals with the deliberate release of GMOs for any other purpose than for placing on the market. For these releases, a notification must be submitted to the competent authority of the Member State within whose territory the release is to take place. The applicant may proceed with the release only when they have received a written consent of the competent authority. A format for presenting the results of the release is established by Commission Decision 2003/701/EC (EC, 2003e).

Part C of the Directive deals with the placing on the market, *i.e.* making available to third parties, of GMOs as, or in, products. The applicant must submit an application to the competent authority of the Member State where the GMO is to be placed on the market for the first time. The application must include a risk assessment. Annex IIIB of the Directive details the required information on which to base the risk assessment for higher plants.

The principles for the environmental risk assessment, including aspects of human and animal health, are laid down in Annex II of the Directive. Several supporting documents have been prepared to assist the applicant. Commission Decision 2002/623/EC (EC, 2002a) establishes guidance notes on the objective, elements, general principles and methodology of the environmental risk assessment referred to in Annex II to Directive 2001/18/EC.

Council Decision 2002/811/EC (EC, 2002b) establishes guidance notes supplementing Annex VII to the Directive, describing the objectives and general principles to be followed to design the monitoring plan. Council Decision 2002/812/EC (EC, 2002c) establishes the summary information format. The EU Scientific Steering Committee published on March 2003 the "Guidance document for the risk assessment of genetically modified plants and derived food and feed" prepared by the Joint Working Group on Novel Foods and GMOs (EC, 2003). The present guidance document is an updated replacement of that guidance.

If the national competent authority gives a favourable opinion on the GMO, this Member State must inform the Commission and other Member States.

If no objections are raised either by the Commission or by any other Member State, or if outstanding issues are resolved within the 105 days period, the assessor Member State grants an authorisation and the product may then be marketed throughout the Community. If, however, any objections are raised and maintained, a decision has to be taken at Community level. If an objection relates to risks of the GMO to human health or to the environment, the Commission must then consult the EFSA. The Directive introduces a time limit for the authorisation, which cannot be given for more than ten years. Authorisations can be renewed on the basis of an assessment of the results of the monitoring and of any new information regarding the risks to human health and/or the environment. The Directive also introduces the obligation to propose a monitoring plan in order to trace and identify any direct or indirect, immediate, delayed or unforeseen effects on human health or the environment of GMOs as, or in, products after they have been placed on the market.[5]

Interplay between Regulation (EC) 1829/2003 and Directive 2001/18/EC

It is necessary for the environmental risk assessment to comply with the requirements referred to in Directive 2001/18/EC. In case of food and/or feed containing or consisting of GMOs, the applicant has the choice of either supplying an authorisation for the deliberate release into the environment already obtained under part C of Directive 2001/18/EC, without prejudice to the conditions set by that authorisation, or of applying for the environmental risk assessment to be carried out at the same time as the safety assessment under Regulation (EC) 1829/2003.

Interplay between Directive 2001/18/EC and Regulation (EC) 2009/1107

The regulation and risk assessment of plant protection products used directly in the cultivation of crop plants, including GM plants, falls within the scope of Regulation (EC) 2009/1107/EEC.

The wider environmental impact of changes in the management of the GM plants including, where applicable, changes in agricultural practices, is considered under Directive 2001/18/EC. The environmental consequences of each Herbicide Tolerant (HT) crop will depend on the cultivation of the crop, the non-selective herbicide used, the dose being applied, the time and frequency of applications of the specific non-selective and other herbicides, special management features of the HT crop and of other crops in rotation with the HT crop (EFSA, 2008a). These factors will vary from region to region, from Member State to Member State, and from season to season, depending on the nature of the particular environment, weed pressure, soil type and climatic conditions. Similarly, environmental impacts of the conventional herbicides applied to non-GM comparator

crops vary because of these same factors, so that it is very difficult to establish detailed baselines in these dynamic situations for comparison of Genetically Modified Herbicide Tolerant (GMHT) systems with other systems.

An assessment of the environmental impacts of the herbicide applied to a GMHT crop will thus need to consider these variables associated both with the GM crop and with the many herbicide programmes used now and likely to be adopted in the future on the comparative conventional crop, in order to come to conclusions about whether the GMHT system is likely to result in a decrease in biodiversity. The EFSA GMO Panel considers that no meaningful conclusions on the environmental consequences of the use of herbicide can be made that include consideration of every issue involved, over the full range of possible parameters that may be varied in the management of the GMHT crops in Europe.

The registration and use of herbicides in the EU, including their use on GMHT crops, is an issue for Regulation (EC) 2009/1107 as operated by individual Member States within three different zones of the EU. Potential adverse environmental effects of the cultivation of HT crops are likely to be entirely associated with the use of the complimentary herbicide regimes. However, studies have shown that careful management of herbicides and mitigation measures can be used to minimise these potential environmental effects (Pidgeon *et al.*, 2007).

GM seeds and other plant-propagating material

GM varieties shall only be accepted for inclusion in a national catalogue according to Directive 2002/53/EC (EC, 2002d) and 2002/55/EC (EC, 2002e) after having been accepted for marketing in accordance with Directive 2001/18/EC (90/220/EEC), which ensures that all appropriate measures have been taken to avoid adverse effects on human health or the environment of the release into the environment of the GM variety.

If the application concerns GM plants to be used as seeds or other plant-propagating material falling within the scope of Regulation (EC) 1829/2003, and the applicant has chosen to apply for the environmental risk assessment under the above mentioned Regulation, the EFSA shall, in order to prepare its opinion, ask a national competent authority designated in accordance with Directive 2001/18/EC to carry out an environmental risk assessment.

New ERA Guidance document EFSA

The EFSA is currently revising its ERA guidelines. The current draft document is the result of two years' work by scientists from all over Europe and demonstrates EFSA's commitment to staying at the forefront of recent developments in the field of GM plant environmental risk assessment. In the current draft, the scientific experts have strengthened requirements for GM applications submitted to the EFSA for evaluation with respect to data generation, collection and analysis. EFSA's GMO Panel has in addition further developed specific guidance on the evaluation of possible effects of GM plants on non-target organisms (EFSA, 2010).

Outlook

EFSA's role is to assess and communicate on all risks associated with the food chain. Since EFSA's advice serves to inform the policies and decisions of risk managers, a large part of EFSA's work is undertaken in response to specific requests for scientific advice. Requests for scientific assessments are received from the European Commission, the European Parliament and EU Member States. The EFSA also undertakes scientific work on its own initiative, so-called self-tasking.

Accordingly, EFSA's advice frequently supports the risk management and policy-making processes. These may involve the process of adopting or revising European legislation on food or feed safety, deciding whether to approve regulated substances such as pesticides and food additives, or, developing new regulatory frameworks and policies for instance in the field of nutrition. The EFSA is not involved in these management processes, but its independent advice gives them a solid scientific foundation.

Through its risk communications activities, the EFSA seeks to raise awareness and further explain the implications of its scientific work. The EFSA aims to provide appropriate, consistent, accurate and timely communications on food safety issues to all stakeholders and the public at large, based on the Authority's risk assessments and scientific expertise.

Notes

1. A full list of GMO Panel members can be found at: *http://www.efsa.europa.eu/EFSA/ScientificPanels/GMO/efsa_locale-1178620753812_PanelMembers453.htm*

2. A full list of scientific documents published can be found at: *http://www.efsa.europa.eu/EFSA/ScientificPanels/efsa_locale-1178620753812_GMO.htm*

3. "Cumulative long-term effects" refers to the accumulated effects of consents on human health and the environment, including flora and fauna, soil fertility, soil degradation of organic material, the feed/food chain, biological diversity, animal health and resistance problems in relation to antibiotics (EC, 2001c).

4. "Hazard" means a biological, chemical or physical agent in, or conditions of, food or feed with the potential to cause an adverse health effect.

   "Risk" means a function of the probability of an adverse health effect and the severity of that effect, consequential to a hazard.

   "Risk analysis" means a process consisting of three interconnected components: risk assessment, risk management and risk communication.

   "Risk assessment" means a scientifically based process consisting of four steps: hazard identification, hazard characterisation, exposure assessment and risk characterisation.

"Risk management" means the process, distinct from risk assessment, of weighing policy alternatives in consultation with interested parties, considering risk assessment and other legitimate factors, and, if need be, selecting appropriate prevention and control options.

"Risk communication" means the interactive exchange of information and opinions throughout the risk analysis process as regards hazards and risks, risk-related factors and risk perceptions, among risk assessors, risk managers, consumers, feed and food businesses, the academic community and other interested parties, including the explanation of risk assessment findings and the basis of risk management decisions.

5. "Direct effects" refer to primary effects which are a result of the GMO itself and which do not occur through a causal chain of events.

"Indirect effects" refer to effects occurring through a causal chain of events, through mechanisms such as interactions with other organisms, transfer of genetic material, or changes in use or management.

"Immediate effects" refer to effects which are observed during the period of the release of the GMO.

"Delayed effects" refer to effects which become apparent either at a later stage or after termination of the release.

Bibliography

EC (1990), "Council Directive 90/220/EEC of 23 April 1990 on the deliberate release into the environment of genetically modified organisms", *Official Journal of the European Communities* L117:15-27. *http://europe.eu.int/servlet/portail/RenderServlet?search=RefPub&lg=en&nb_docs=25&domain=&in_force=NO&year=1990&month=&day=&coll=JOL&nu_jo=117&page=15*

EC (2001), "Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC", *Official Journal of the European Communities* L106, 1-39. *http://eur-lex.europa.eu/smartapi/cgi/sga_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=EN&numdoc=32001L0018&model=guichett*

EC (2002a), "Commission Decision (2002/623/EC) of 24 July 2002 establishing guidance notes supplementing Annex II to Directive 2001/18/EC of the European Parliament and of the Council on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC", *Official Journal of the European Communities* L 200: 22-33. *http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2002:200:0022:0033:EN:PDF*

EC (2002b), "Council Decision of 3 October 2002 establishing guidance notes supplementing Annex VII to Directive 2001/18/EC of the European Parliament and of

the Council on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC", *Official Journal of the European Communities* L, 27-36.

EC (2002c), "Council Decision 2002/812/EC of 3 October 2002 establishing pursuant to Directive 2001/18/EC of the European Parliament and of the Council the summary information format relating to the placing on the market of genetically modified organisms as or in products", *Official Journal of the European Communities* L280: 37-61. *http://ec.europa.eu/environment/biotechnology/pdf/dec2002_812.pdf*

EC (2002d), "Council Directive 2002/53/EC of 13 June 2002on the common catalogue of varieties of agricultural plant species", *Official Journal of the European Communities* L 193: 1-11. *http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2002L0053:20040418:EN:PDF*

EC (2002e), "Council Directive 2002/55/EC of 13 June 2002 on the marketing of vegetable seed", *Official Journal of the European Communities* L 193: 33-59. *http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2002:193:0033:0059:EN:PDF*

EC (2003), "Guidance document for the risk assessment of genetically modified plants and derived food and feed", prepared by the Joint Working Group on Novel Foods and GMOs, 6-7 March 2003, *http://europa.eu.int/comm/food/fs/sc/ssc/out327_en.pdf*

EC (2004), "Directive 2004/35/CE of the European Parliament and of the council of 21 April 2004 on environmental liability with regard to the prevention and remedying of environmental damage", *Official Journal of the European Communities* L, 56-75.

EC, 2009. Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. Official Journal L 309, 24/11/2009 P. 0001 – 0050. *http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32009R1107:DE:NOT*

EFSA (2004), "Opinion of the Scientific Panel on Genetically Modified Organisms on the Use of Antibiotic Resistance Genes in Genetically Modified Plants", *The EFSA Journal* 48, 1-18.

EFSA (2006), "Opinion of the Scientific Panel on Genetically Modified Organisms on the Post Market Environmental Monitoring (PMEM) on Genetically Modified Plants", *The EFSA Journal* 319, 1-27.

EFSA (2007), "Statement of the Scientific Panel on Genetically Modified Organisms on the safe use of the nptII antibiotic resistance marker gene in genetically modified plants".

EFSA (2008a), Working document of the EFSA GMO Panel on "The Environmental Risk Assessment of Genetically Modified herbicide tolerant plants and the interplay between Directive 2001/18/EC and Directive 91/414/EEC", *http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902601039.htm*

EFSA (2008b), "Draft opinion of the Scientific Panel on Genetically Modified Organisms on the risk assessment of genetically modified plants used for non-food or non-feed purposes", *http://www.efsa.europa.eu/cs/BlobServer/DocumentSet/gmo_draftgd_nonfoodfeed_en.pdf?ssbinary=true*

EFSA, 2010. Draft guidance document for the environmental risk assessment of genetically modified plants. 100pp. *http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2010-00109*

OECD (1993a), Safety Considerations for Biotechnology: Scale-up of Crop Plants, OECD, *http://www.oecd.org/dataoecd/26/26/1958527.pdf?channelId=34537&homeChannelId=33703&fileTitle=Safety+Considerations+for+Biotechnology+Scale-up+of+Crop+Plants*

OECD (1993b), "Safety Evaluation of Foods Derived by Modern Biotechnology: Concept and Principles", OECD, *www.oecd.org/dataoecd/57/3/1946129.pdf?channelId=34537&homeChannelId=33703&fileTitle=Safety+Evaluation+of+Foods+Derived+by+Modern+Biotechnology+-+Concepts+and+Principles*

Pidgeon J.D., *et al.* (2007), "Mitigation of Indirect Environmental Effects of GM Crops", *Proceedings of the Royal Society B-Biological Sciences* 274, 1475-1479.

SSC (2000), "First Report of the Scientific Steering Committee on the Harmonisation of Risk Assessment Procedures, European Commission", Health and Consumer Protection Directorate-General, *http://europa.eu.int/comm/food/fs/sc/ssc/out83_en.pdf* Appendices: *http://europa.eu.int/comm/food/fs/sc/ssc/out84_en.pdf*

WHO/FAO (2000), "Safety Aspects of Genetically Modified Foods of Plant Origin", Report of a joint FAO/WHO expert consultation on foods derived from biotechnology, 29 WHO/FAO, 2000. *http://www.fao.org/es/ESN/food/pdf/gmreport.pdf* *http://www.fao.org/es/esn/food/risk_biotech_aspects_en.stm*

WHO/FAO (2001), "FAO/WHO expert consultation on foods derived from biotechnology, Evaluation of allergenicity of genetically modified foods", WHO/FAO, January 2001, Rome. *http://www.who.int/foodsafety/publications/biotech/en/ec_jan2001.pdf* *http://www.fao.org/es/esn/food/risk_biotech_allergen_en.stm*

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

The OECD is a unique forum where governments work together to address the economic, social and environmental challenges of globalisation. The OECD is also at the forefront of efforts to understand and to help governments respond to new developments and concerns, such as corporate governance, the information economy and the challenges of an ageing population. The Organisation provides a setting where governments can compare policy experiences, seek answers to common problems, identify good practice and work to co-ordinate domestic and international policies.

The OECD member countries are: Australia, Austria, Belgium, Canada, Chile, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Korea, Luxembourg, Mexico, the Netherlands, New Zealand, Norway, Poland, Portugal, the Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey, the United Kingdom and the United States. The European Commission takes part in the work of the OECD.

OECD Publishing disseminates widely the results of the Organisation's statistics gathering and research on economic, social and environmental issues, as well as the conventions, guidelines and standards agreed by its members.

OECD PUBLISHING, 2, rue André-Pascal, 75775 PARIS CEDEX 16
(51 2010 05 1 P) ISBN 978-92-64-09009-5 – No. 57785 2010

Challenges for Agricultural Research

As the world has changed during the past 50 years, so has agriculture. And so has agricultural research, which continues to confront new challenges, from food security to ecological concerns to land use issues. Indeed, as Guy Paillotin, the former president of the French National Institute for Agricultural Research (INRA) has noted, agricultural research "has reached new heights in biology and is exploring other disciplines. It is forever changing, as are the needs of the society".

The changing challenges faced by agricultural research were examined in depth at a conference organised by the OECD's Co-operative Research Programme on Biological Resource Management for Sustainable Agricultural Systems, together with the Czech Republic's Ministry of Agriculture. Participants came from all agricultural sectors and included farmers, industry, scientists and decision makers, as well as other stake holders.

This publication presents the twenty papers delivered at the conference. They highlight recent major progress in agricultural research outcomes and address the challenges that lie ahead.

www.oecd.org/agriculture/crp

Please cite this publication as:

OECD (2011), *Challenges for Agricultural Research*, OECD Publishing.
http://dx.doi.org/10.1787/9789264090101-en

This work is published on the *OECD iLibrary,* which gathers all OECD books, periodicals and statistical databases. Visit ***www.oecd-ilibrary.org***, and do not hesitate to contact us for more information.

OECD*publishing*
www.oecd.org/publishing

ISBN 978-92-64-09009-5
51 2010 05 1 P