



Managing regulatory uncertainty in rapidly emerging areas: pharmacogenetics

European Medicines Agency Perspectives and strategies

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Presentation outline



General considerations



EMEA strategy


(<http://www.emea.eu.int/htms/general/direct/roadmap/roadmapintro.htm>)



Conclusions



Why venturing in uncertainties ?

- 
1. Large majority (>80%) of compounds entering clinical trials fails because of toxicity or unsatisfactory efficacy. (50% phase III fail for safety/efficacy reasons)
 - Risk of pipeline draught
 - ~30% failure of MAAs in the centralised procedure
 2. Significant labelling restriction at the time of approval and within the first two years after launch
 3. Two or more valuable medicines per year withdrawn because of serious ADRs (1991 and 2004)
 4. Current mortality and morbidity due to ADRs or insufficient efficacy

Impact on individual patients,
public health, industry

PG potential

- ★ ■ Greater understanding of patho-physiology and subtypes of diseases
- ★ ■ More efficient science-based drug design, prediction of efficacy and management of toxicity in drug development
 - **Better target identification and improved selection of candidate compounds**
 - **Higher POS in the pipeline**
- ★ ■ More appropriate drug and dose selection in a better defined population or individuals
 - **Improved benefit/risks balance**
 - **Less treatment failures and withdrawals**
- ★ ■ More vigorous and productive industry



Regulators' responsibilities



Protecting public health by assessing benefit/risk balance and risk management of drugs



Promoting strategies and technologies for optimal development of innovative medicines



Contributing to the societal debate providing independent information



for the attainment of both industrial and public health sector goals





Managing regulatory uncertainty in rapidly emerging areas



- **Ensure science-based regulatory environment and strengthen the regulatory processes**
- **Be proactive in facts finding and encourage innovation to come forwards in the Regulatory arena: create new structures and processes to adjust for complexity**
- **Discuss issues and solutions with stakeholders so to anticipate impact on current practices and policies**
- **Support international efforts to develop harmonised global understanding and standards**



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Managing regulatory uncertainty in rapidly emerging areas Structural adjustments

EMEA Innovation Task Force (ITF)

The screenshot shows a Microsoft Internet Explorer browser window displaying the EMEA website. The address bar shows the URL: <http://www.emea.eu.int/htms/human/itf/itfintro.htm>. The page title is "Emerging Therapies and Technologies: Introduction". The website header includes the EMEA logo and navigation links: Home, Site Map, Links, Help. The main navigation menu includes: About Us, What's New, Human Medicines, Veterinary Medicines, General Reporting, Inspections, and Search the Site... The main content area is titled "Emerging Therapies and Technologies" and contains an "Introduction" section. A sidebar on the left lists: Introduction, Areas of interest and available guidelines, How to get support from EMEA?, and Link to other EMEA webpages of interest. A "Contact Point..." box on the right provides contact information for Dr. Maria Papaluca-Amati and Dr. Constantinos Zogas. The footer contains copyright information for 1995-2005 EMEA and contact details for web content and functionality queries.

Emerging Therapies and Technologies: Introduction - Microsoft Internet Explorer

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Emerging Therapies and Technologies

Introduction

Areas of interest and available guidelines

How to get support from EMEA?

Link to other EMEA webpages of interest

Introduction

In this area of the EMEA web page you will find information on activities performed at the EMEA in the field of emerging therapies and technologies.

In consultation with the European Commission, scientific input of experts from all EU Members States as well as international cooperation, EMEA actively supports scientifically sound development of those therapies so that they might be made available for the benefit of public health.

A number of scientific committees, working parties and expert groups have been set up to contribute to the provision of scientific information in this field listed on these web pages. This includes the setting-up of EMEA Innovation Task Force (ITF), which will ensure EMEA-wide coordination of scientific and regulatory expertise in this field as well as a forum for early dialogue with applicants.

In addition, a number of procedures are available at the EMEA to support applicants in the development of new therapeutic approaches. These include designation of orphan medicinal products, EU-wide CHMP scientific advice on tests and trials to be conducted during development, as well as briefing meetings with EMEA and provision of advice on the classification as medicinal products (regulatory classification) prior to access to EMEA procedures, including scientific advice, orphan medicinal product designation and marketing authorisation application.

Contact Point...

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For further contact information see **Contact points**

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Send all queries regarding the Web content to: info@emea.eu.int
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CHMP PG Working Party

<http://www.emea.eu.int/pdfs/human/pharmacogenetics/10159204en.pdf>

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- A vertical grey bar on the left side of the slide, containing five white stars arranged vertically.
- **Share experience on issues arising from the integration of pharmacogenetics in drug development, assessment and information**
 - **Prepare, review and update guidelines**
 - **Support dossier evaluation and contribute to scientific advice**
 - **Advise on Pharmacogenetics related issues the European Commission**
 - **Liaise with interested parties**
 - **Support European and international cooperation**



PG Working Party: new structure

Chairperson E. Abadie
Vice-Chairperson: B. Flamion

50% academia scientists

50% regulatory scientists

**+ “area” specialists and industry’s scientists invited
for PG briefing**



PG briefing: new process

What is a PG briefing meeting?

A new way of submitting preliminary data

**A new informal dialogue among Regulators, Academia
and Industry scientists on emerging science**

**A new way to reduce uncertainties for further research,
development and decision making**

A tool for raising awareness and training

A good operational model for tackling innovation



PG briefing: a new process

What a PG briefing meeting IS NOT

A Scientific Advice pre-submission meeting

**A CHMP scientific advice on how to implement PG
in the development program**

A preliminary MAA data assessment



PGWP activities

Released documents:

Terminology in PG

Draft Guideline on briefing meetings: format and content

Concept paper on biobank issues relevant to pharmacogenetics

Upcoming public documents

Revised paper in lay language

“Understanding the terminology used in pharmacogenetics”

Concept paper on impact of PG on PK studies

Revised PGWP Workprogramme 2006 +.....

PGWP activities

Workshop 2003 on PG in clinical development (DIA plat.)

Workshop 2004: do we need further regulation

Seminar with Industry Dec 2005: biobanks issues

Eleven briefing sessions + 3 scheduled Dec 05

2 PG platforms sponsors + 12 Drug sponsors

Therapeutic areas

- Diabetes, Obesity
- Depression
- Rheumatoid arthritis, transplantation, asthma
- Cancer
- Hypertension, Myocardial Infarction



Examples of scenarios discussed at PG briefing meetings

- ★ **•Genomic expression signature as a biomarker bridging proof-of-concept from animal model to man**
- ★ **•Data from pre-collected samples. Potential regulatory value in conducting retrospective PG biomarkers analyses and impact on existing and new drugs**
- ★ **•Genomic markers in prospective studies. Methodological options.**
- ★ **• Determination of the PG clinical utility (clinical magnitude of the differential response, benefit in clinical outcomes using the PG test) and labelling implications**
- ★



Managing regulatory uncertainty in rapidly emerging areas



Support to European and international harmonisation



Support to european and international harmonisation



- **Contribution to relevant EU initiatives**



- **Contribution to international debate on PG (e.g.DIA workshops, CIOMS Expert group, OECD)**



- **Implementation of confidentiality arrangements with FDA**



- **ICH**



Challenges to PG potential development

- **Samples collections and data pooling**
- **PG Biomarker “validation” data requirements**
- **Population genetic ancestry impact**
- **Co-ordination of submission of drug and test data pre and post approval**
- **Clinical validity/utility**
- **Impact on the label and on risk management and minimization (including educational programmes)**



Challenges for PG development: biobanks

- **Concept paper released March 2005**

- maintenance in biobanks of identifiable samples for pharmacogenetics use, the duration of their availability versus the handling of anonymous or anonymized samples
- scientific needs and objectives of the regulatory oversight
- issues relevant to the scientific validity of pharmacogenetics studies





Challenges in EU for PGx products: biobanks

- **Points to consider in defining the procedures for collecting, storing, handling/curing and analysing samples and relevant data for pharmacogenetics purposes**
- **Implications of removing from samples and data identifying information in pre and post authorization assessment of medicinal products**
- **Systems of quality assurance and quality control**



Issues discussed on PG-driven co-development of test and drug in EU

- **IVDD classification**
 - Annex II-List B (high accuracy needed for medical practice e.g. other clinical biomarkers HLA, PSA)
 - Not listed in Annex II and not intended for self-testing (most current devices, used by trained personnel)
- **Location for testing**
 - Clinical chemistry laboratory
 - Reference testing laboratory
 - Genetic testing laboratory
- **Technology platforms validation**
 - Reagent and systems



Issues discussed on PG-driven co-development of test and drug in EU

- **Overlapping data required for regulatory oversight: IVD overarching requirements for risk analysis & risk management**
 - **Design, construction, clinical validation**
 - **Technical documentation, quality assurance**
 - **Intended use**
 - **Labelling and language**
 - **False positive &/or false negative rate**
 - **Impact of test results on medical practice**





Joint VGDS/ Briefing

- **May 17, 2005: first joint EMEA/FDA VGDS briefing**
- **Videoconference**
- **Preparation:**
 - sponsor submit **data**
 - EMEA/FDA scientific review of sponsor questions
- **Pre-meeting dialogue between FDA and EMEA**
- **Sponsor presentation for interactive discussion via videoconference**
- **Final meeting report back to sponsor and in the network**
- **Further 4 sessions planned in 2006**
- **Joint EMEA/FDA public paper to describe operations (in preparation)**



ICH Brainstorming Nov 2005

- Share experience
- Create basis for pro-active harmonization
- Identify areas of differences that are important for facilitating global drug development

ICH priorities yet to be identified

Possible topics

- ✓ Definitions of terms, including implications for PG samples collection, submission format and content, and common data standards for genomic expression
- ✓ General Principles of pharmacogenomic clinical trials

Conclusions

- **EMA road map: long term commitment in support of innovation in liaison with stakeholders**
- **New informal regulatory processes and expert panel established at the EMA**
- **Dialogue and international co-operation essential:**
 - Interaction with the European Commission**
 - FDA/EMA confidentiality arrangements**
 - ICH**





Thank you