

BIOTECHNOLOGY INDUSTRIAL PROPERTY PROBLEMS AND THEIR IMPACT ON PRODUCT DEVELOPMENT

NIGHTMARE IN DNA

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MAIN TRENDS IN INDUSTRIAL PROPERTY/BIOTECHNOLOGY

- Upsurge in patent applications
- More complex and sophisticated patent applications
- More upstream contracts - research tools
- More diverse contracts - MTA
- Everyone wants to profit from biotechnology
 - . inventors
 - . various contributors, countries and people

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CONSEQUENCES

- ♦ **A complex situation in patent matter for :**
 - . evaluating the patentability of inventions
 - . evaluating the exploitation risks of projects (FTO)
- ♦ **An obligation to sign**
 - . more difficult-to-manage contracts
 - . contracts on « reach through » research
 - . contracts with « pools »
 - . with more royalties

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THE UPSURGE IN PATENTS

- ◆ **Project : « Expression of haemoglobin in maize » (see Meristem table)**
 - 13 relevant patents have been identified**
 - . on technology for transforming plant
 - . general tools or process
 - . specific DNA for expression
- ◆ **Project : « DNA biochips »**
 - . Affymetrix
 - . its litigation with Oxford Gene Technology (Southern, Incyte)
 - . more than 600 publications on Affymetrix (patents, litigations)
 - ! Use of industrial property advertisement for raising funds

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MORE COMPLEX PATENTS

- ◆ **Ordinary patents :**
 - . Product : gene - relaxine - IL2
 - . Process : production of EPO
 - . Application : use of a gene for treatment
- ◆ **Upstream patents**
 - . Screening method: biological model (Cox II)
computer modelling (US 6 083 711, WO 01/54045)
 - . Research tools : 2D array (OGS) - Cre-Lox
 - . Monster patents : full genome: up to 100 000 pages
patent with 5 000 sequences (WO 96/40893)
sophisticated definition (US 5 756 466)

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CLAIMS AT THE EPO

Ex 1: Methods of screening GPCR (EP 1 078 040, Millennium)

A method of identifying a compound which binds to a protein comprising the amino acid sequence of SEQ ID No 2 comprising the steps of i) contacting the protein with a test compound and ii) determining whether the protein binds to the test compound.

Ex 2: Swiss-style claim (EP 702 555 B1, Pfizer)

The use of a cGMP PDE inhibitor, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic oral treatment of erectile dysfunction in man.

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Drug design claim using a virtual receptor in SKB's US PATENT 6 083 711

- A method of identifying a candidate inhibitor compound capable of binding to, and inhibiting the proteolytic activity of, an alpha or beta herpes protease, said method comprising:
 - a) introducing into a computer program information derived from atomic coordinate defining an active site conformation of a herpes protease molecule based upon three-dimensional structure determination comprising a catalytically active site formed by at least the interaction of three amino acids Serine, Histidine and Histidine, wherein said program utilises or displays the three-dimensional structure thereof
 - b) generating a three-dimensional representation of the active site cavity of said protease in said computer program
 - c) superimposing a model of the inhibitor test compound on the model of said site of said protease
 - d) assessing whether said test compound model fits spatially into the active site of said protease
 - e) incorporating said test compound in a protease activity assay for a protease characterised by said active site of said protease, or an antiviral assay for an alpha or beta herpes virus
 - f) determining whether said test compound inhibits proteolytic activity, or the herpes virus in said assay

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WO 01/54045 LION BIOSCIENCE

- 1) An analysis method for large and/or complex biological data sets from molecular biology experiments, the method comprising:
 - (a) importing data in a table data structure;
 - (b) comparing data points;
 - (c) calculating an optimized data representation; and
 - (c) displaying the representation.

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Organic chemical claimed by reference to its receptor in Vertex's US 5 756 466

- An ICE inhibitor comprising:
 - a) a first and second hydrogen binding moiety, each of said moieties being capable of forming a hydrogen bond with a different backbone atom of ICE, said backbone atom being selected from the group consisting of the carbonyl oxygen of Arg-341, the amide-NH- group of Arg-341, the carbonyl oxygen of Ser-339 and the amide -NH- group of Ser-339
 - 1) the distance from the centre of mass of the moderately hydrophobic moiety (of the inhibitor) in the P2 binding pocket to the carbonyl oxygen of Arg-341 of ICE is between about 7.1 ANG, and about 12.5 ANG; 2) the distance from the centre of mass of the moderately hydrophobic moiety (of the inhibitor) in the P2 binding pocket to the amide nitrogen of Arg-341 of ICE is between about 6.0 ANG, and about 12 ANG; etc.

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CONTRACTS

- ◆ **R&D agreement with start-up which are very aggressive: (down payment, milestones)**
- ◆ **MTA with clauses of non commercial use**
- ◆ **Need to sign agreement for research with PhD, PostDoc**
(in France, 50% of the royalties are returned to inventors in public organizations)
- ◆ **Need to sign with people giving the biological samples** (Kanavan's in USA)
- ◆ **Need to sign agreement with countries in case of Rio Convention**

PROBLEM OF REACH THROUGH ROYALTIES

- ◆ In case of an application dealing with a model of pathology X, patentee is willing to obtain royalties on chemical product Y obtained by using the screening model
- ◆ In his patent often no example of chemical product
- ◆ But, licensee agrees, for not taking any risks in the future
- ◆ The same for research tools (Cre-Lox technic) or combinational library in chemistry

IN ADDITION

- ◆ All of these discussions take place on non granted patent application with the risks of proceeding :
 - . divisional application / continuation application
 - . opposition (EPO - Kirin-Amgen) EP 148 605 filed on 1984, back to first instance, granted on March 1998 (T636/97)
 - . length of proceeding before the judges
- ◆ No clear european view on the infringement during research

CONSEQUENCES ON THE DEVELOPMENT

- ◆ Money - royalties stacking/milestones payment
- ◆ The visibility of a project is not clear (analysis of FTO in view of prior art but also in view of the signed contracts)
- ◆ Money : cost of proceedings both for patents and agreement's negotiations

BUT

- ◆ Creation of 1 500 start-up in Europe
- ◆ Development of hundred of new products. Since 1995, 20 marketing authorization by year for biotechnologic compounds - biotechnologic drugs are a reality
 - . Epogen + Neupogen (Amgen) CA/an: 3,2 Mds\$
 - . Enbrel (Immunex) : 0,7 Mds\$
 - . Herceptin (Genentech) : 1,7 Mds\$
 - . Rituxan (Genentech) : 1,7 Mds\$
- ◆ Industrial property is a very powerfull engine in biotechnology but is it necessary to try to have a better control of this engine

SUGGESTIONS

- ◆ Speed up the proceeding both in EPO but also before national judges
- ◆ Have better interpretation rules and jurisprudence, which will limits the number of patent applications filed (see the EST case)
- ◆ Clear up the problem of scope of reach through claims but also the definition of non infringement for research
- ◆ Not to provide new laws or additional laws, Biotechnology Directive is enough with Munchen Convention.