Intellectual Property In Bio-Technology: Relevance And Strategy In The Pharmaceutical Industry

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Protecting results from the research in the biotechnology field is an important issue for the pharmaceutical industry. Different strategies are pursued for research tools on the one hand and for biotechnological products on the other hand. For the development of new chemical entities as small molecules, biotechnological patents are relevant in defined stages, for example in the early discovery for the target identification and in the assay development.

1. Patenting in Biotechnology for the pharmaceutical industry

In the last decade, the biotechnology field evolved very fast and entered in an new phase in which:

- The first biotechnological products have proved their profitability in the pharmaceutical market (Epo, Betaferon, humanized insulin).

- The biotechnological tools became a standard in developing assays for HTS. This evolution can be observed also in the filed of intellectual property.

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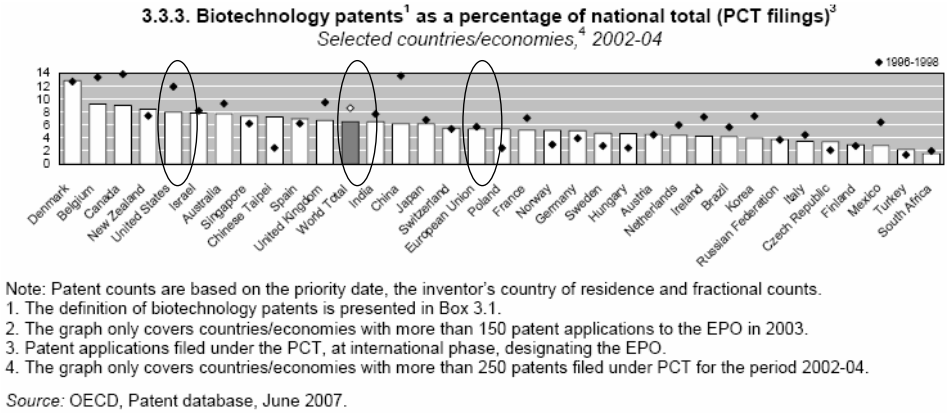

Note: Patent counts are based on the priority date, the inventor's country of residence and fractional counts.
1. The definition of biotechnology patents is presented in Box 3.1.
2. The graph only covers countries/economies with more than 150 patent applications to the EPO in 2003.
3. Patent applications filed under the PCT, at international phase, designating the EPO.
4. The graph only covers countries/economies with more than 250 patents filed under PCT for the period 2002-04.

Source: OECD, Patent database, June 2007.

Fig. 1 Source OECD (Organisation For Economic Co-operation And Development), 2007 – Biotechnology patents as a percentage of national total (PCT Filings).

With reference to international application from 2002 to 2004, biotechnology represented 6.5% of total PCT filings, compared to 8.6% in the late 1990s. This share reached more than 12% of all PCT applications in Denmark, Belgium and Canada to follow with around 9%. The relative weight of biotechnology in all international patent filings decreased between the mid-1990s and the early 2000s in most countries.

With reference to the EPO biotechnology patents applications grew by 5.8% a year between 1995 and 2003. However, the number of biotechnology patents started to decrease from 2000 (-6% on average over 2000-03, compared to +13% between 1995-2000).

A dramatically increase of applications was registered in the late 1990s in relation to the decoding of the human genome, while the reduction in the 2000s is often explained by patent offices' more stringent criteria for granting patents on genetic material.

C12 Biochemistry; Genetic engineering	1995	1996	1997	1998	1999	2000
	1613	1877	2313	2736	2860	3572
	2001	2002	2003	2004	2005	2006
	4248	4429	4163	3975	4040	3847

Fig. 2 European Application filed from 1995 to 2007 (Data obtained from the Business Report of the European Patent Office)

In the development of a pharmaceutical product based on a small molecule, the biotechnological IP situation has to be evaluated at the early stage of the target identification. A freedom to operate analysis on the target as well as on related research tools is essential. The outcome of the early research on the target offers a first opportunity to secure the exclusive right on the same.

During the prove of concept (Poc) phase, biotechnology plays again a major role. The possibility to identify biomarker which are relevant during clinical studies as well as for the development of diagnostic tools is a new area of high importance for the pharmaceutical industry.

The major pharmaceutical industries are still based on the development of small molecules and the patent strategy in relation to biotechnology invention differs between different companies. Several companies invested a lot in patenting the results of the genetic research. An other approach was the selective filing on the subject matter strictly required for the developing of the project and opting to publish the remaining results.

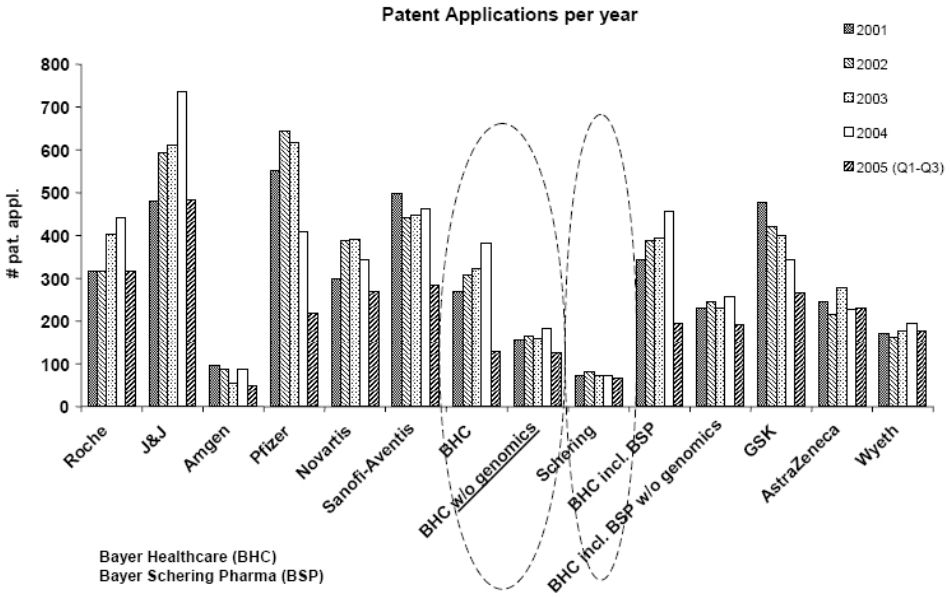

Fig. 3. Patent application per year for the major pharmaceutical companies. Comparison of applications at BHC with and without genomics (Information obtained from public available databases).

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A broad patent protection of biotechnological products is essential to the pharmaceutical industry in order to get a return of the high investments necessary for the development of a product. Here, claims e.g. on nucleic acids, proteins, the production process and uses may be granted. However, depending on the national law applied, the scope of protection may differ from country to country.

The jurisprudence and the national patent offices have defined the field of protection for biotechnology inventions. In the United States of America for example the decision *Madey v. Duke University*, 307 F.3d 1351 (Fed. Cir. 2002) signed the first milestone to defined the use of Research Exemption. In particular, the court found that the fact that research is conducted in a university setting does not make it devoid of commercial implication; "(Duke University) like other major research institutions of higher learning, is not shy about pursuing an aggressive patent licensing program from which it derives a not insubstantial revenue stream". This decision defined the filed for several research tools based on biotechnological inventions.

In the US again, with the decision *Merck v. Integra* 125 S.Ct. 2372 (U.S. 2005), the Supreme Court has defined the criteria for § 271(e)(1) Research Exemption: a) a reasonable basis for believing that a drug would produce a physiological effect; b) the intent to submit data to an entity, for example, the FDA, pursuant to a Federal law that regulates the manufacture, use or sale or drugs; c) the exempted act must coincide with

a Federal law that allows for development and submission of information to the entity, and finally d) the act must relatively directly contribute to the generation of information relating to the Federal law.

Another milestone in the US jurisprudence related to biotechnological inventions, particularly with reference to Research Tools, is *University of Rochester v. Searle* 358 F.3d 916 (Fed. Cir. 2004). According to US law the patent application should contain three separate requirements: written description, enablement, and best mode. Since the Rochester team did not take the "last, critical step" of synthesizing a specific compound, the court found, " the inventors could no more be said to have possessed the complete invention claimed by the (Rochester) patent than the alchemists possessed a method of turning base metals into gold". Adequate written description for chemical and biotechnology inventions requires a precise definition, such as by structure, formula, chemical name, or physical properties.

In Europe, according to the European Patent Office, claims aiming to protect: downstream developments, for example the development of a new drug, ligands, agonists/antagonists identified merely by a screening method, and use of ligands in medicine are not allowable.

According to the decision T609/02 of the Board of Appeal of the European Patent Office, if the description of a patent specification provides no more than a vague indication of a possible medical use for a chemical compound yet to be identified, later more detailed evidence cannot be used to remedy the fundamental insufficiency of disclosure of such subject-matter. On the same line the decision T669/04 has further stated that when "Claim 1 fails to define - functionally and structurally - the inhibitors used (…). The absence of these features leads - for the reasons given hereinafter - to a lack of clarity in the sense of Article 84 EPC in combination with an insufficiency of disclosure under Article 83 EPC".

Finally, EU Directive 98/44 /EC, also known as the „Bio-Patent Directive", had the goal to provide the harmonization of rules for the patenting of biological materials within the European Union and supply clear regulations for non-patentable matter. The directive was first produced in 1998 and was introduced in several countries only in 2006, after a troubled course. The directive was also incorporated in the European Patent Convention (EPC).

The directive (Art. 3(1) and EPC Rule 26) provides for the general patentability of biological materials, isolated from their natural surroundings or produced by means of a technical method, even if they already exist in nature; as well as isolated parts (of the human body), including sequences or partial sequences of genes if their commercial applicability (function) has been specifically described in the patent application, and if the other preconditions for patentability are fulfilled.

According to the directive, processes for the cloning of human beings, processes for modifying the genetic identity of the human beings' germ lines, use of human embryos for industrial and commercial purposes; and processes for modifying the genetic identity of animals, which are likely to cause these animals to suffer without any substantial benefit for man or animal, as well as the animal resulting from such processes, are not patentable.

Unfortunately, the purpose to give a common frame to the patentability of biological materials, in part failed during the nationalization process since the single states (i.e. Germany) modified and amended certain specific aspects of the directive under internal ethical and political reasons.

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EU Directive 98/44 /EC.