Patenting of Genes and Exploiting as Well as Enforcing such Patents in Europe as Compared with the US

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Secretary's Advisory Committee on Genetics, Health and Society

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Overview

- Statutory vs. Case Law Approach
- Patent granting practice – Statistics
- Exploitation & Enforcement
- Summary

Patentable Subject Matter – EU Directive 98/44/EC

- **Not patentable: The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, incl. the sequence or partial sequence of a gene [Art. 5 (1)].**

- **Gene sequences – patentable - if isolated from the human body or technically produced (e.g. through synthesis) – sequences or partial sequences of a gene – patentable inventions – even if structurally identical to that of a natural element [Art. 5 (2)]. However**

- **A mere DNA sequence without indication of a function – not a patentable invention [Recital 23] – thus „function“ [not necessarily biological function] integral part of the notion „invention“.**

Patentability Requirements – Europe - EPC

- **Novelty: „absolute“ – no „grace period“ – however, [product] patents available for first medical indication even for known products [covering all medical uses]**
- **Inventiveness: Non-obvious for expert in view of the relevant state of the art – could/would test – reasonable expectation of success**
- **Industrial applicability: DNA claimed for production of a protein or part of a protein, „industrially applicable“ only if the protein or part of the protein and its function[s] disclosed**

Patentability & Patentability Requirements under US Law

- Patentable “anything man-made under the sun”
- Narrow prior art [grace period; oral disclosures & public use abroad – not part of]
- Non-obviousness: Structural similarity approach adopted – very low yardstick – a partial amino acid sequence does not make the DNA sequence obvious – due to the degeneration of the genetic code
- Utility: Specific, substantial, credible [US PTO Utility Examination Guidelines]

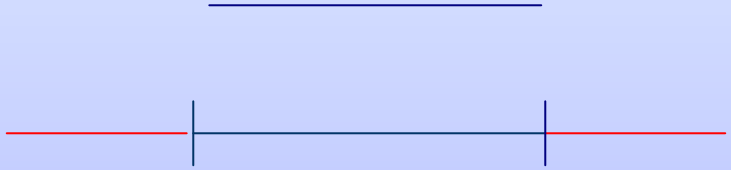
Effects of Patents on DNA Sequences

- **USA: No specific rules – no statutory research exemption [but: Merck vs. Integra Supreme Court]**

- **EU Directive: Product protection for product containing or consisting of genetic information extends to all materials – EXCEPT TO THE HUMAN BODY – „in which the product is incorporated and in which the genetic information is contained and PERFORMS ITS FUNCTION“ [Art. 9]**

- **EU-Member States: Statutory research exemption covers further developments, improvements, etc., even if for commercial purposes**

EU-Directive‘s Special dependency rule for patents on sequences which overlap only in part



- If the overlapping part not essential (subjectively/objectively?) for the invention – patents independent! [Recital 25]
- Multi-functional genes?
- Alternative splicing (40% of all genes)?

Germany: Sec. 1a Patent Act 2006

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(3) The industrial applicability of a sequence or a partial sequence of a gene must be concretely described in the application by indicating the function of the sequence or partial sequence

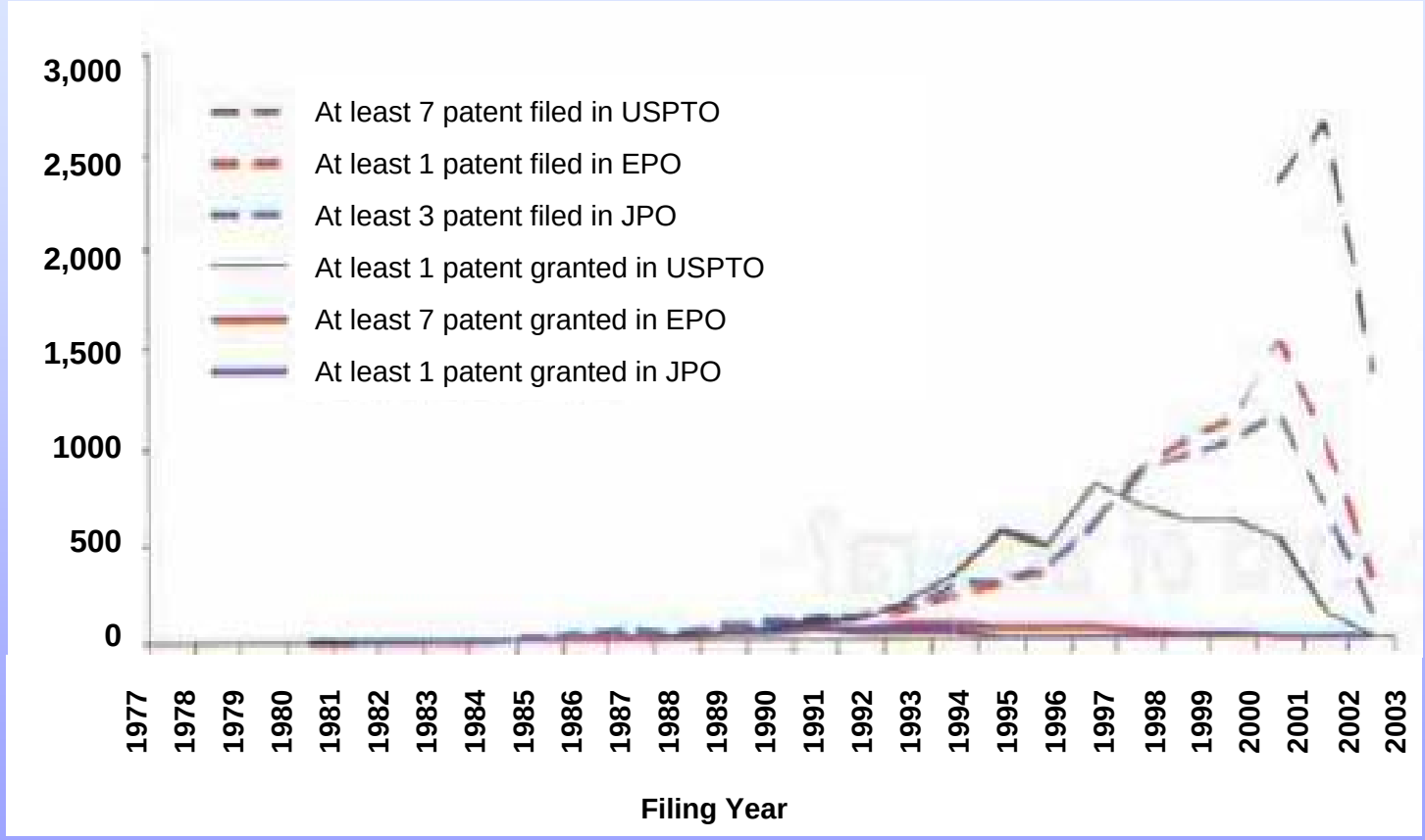
Germany: Sec. 1a Patent Act 2006

(4) In case the subject matter of an invention is a sequence or a partial sequence of a human gene, whose structure is identical to the natural sequence or partial sequence of a human gene, its use for the industrial application specifically described according to para. (3) must be incorporated into the claim.

Presumably no impact on EPO patents

Number of families containing filed/granted DNA patents

Filed applications and granted patents on patent families claiming human DNA sequences



Source: Nature Biotechnology, Vol. 25, Nr. 2, February 7, p. 186

Number of DNA-based U.S. Patents (as of June 30, 2005)

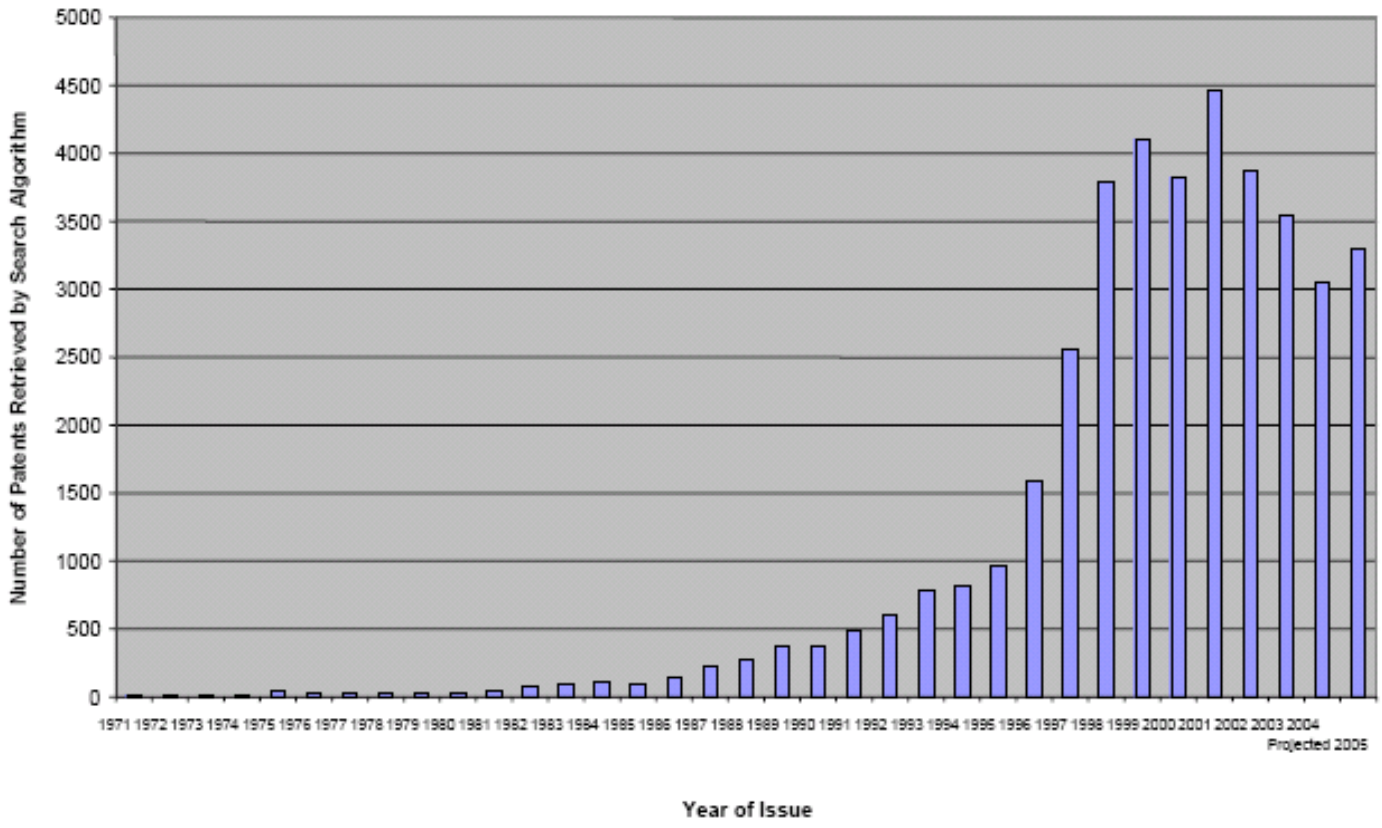
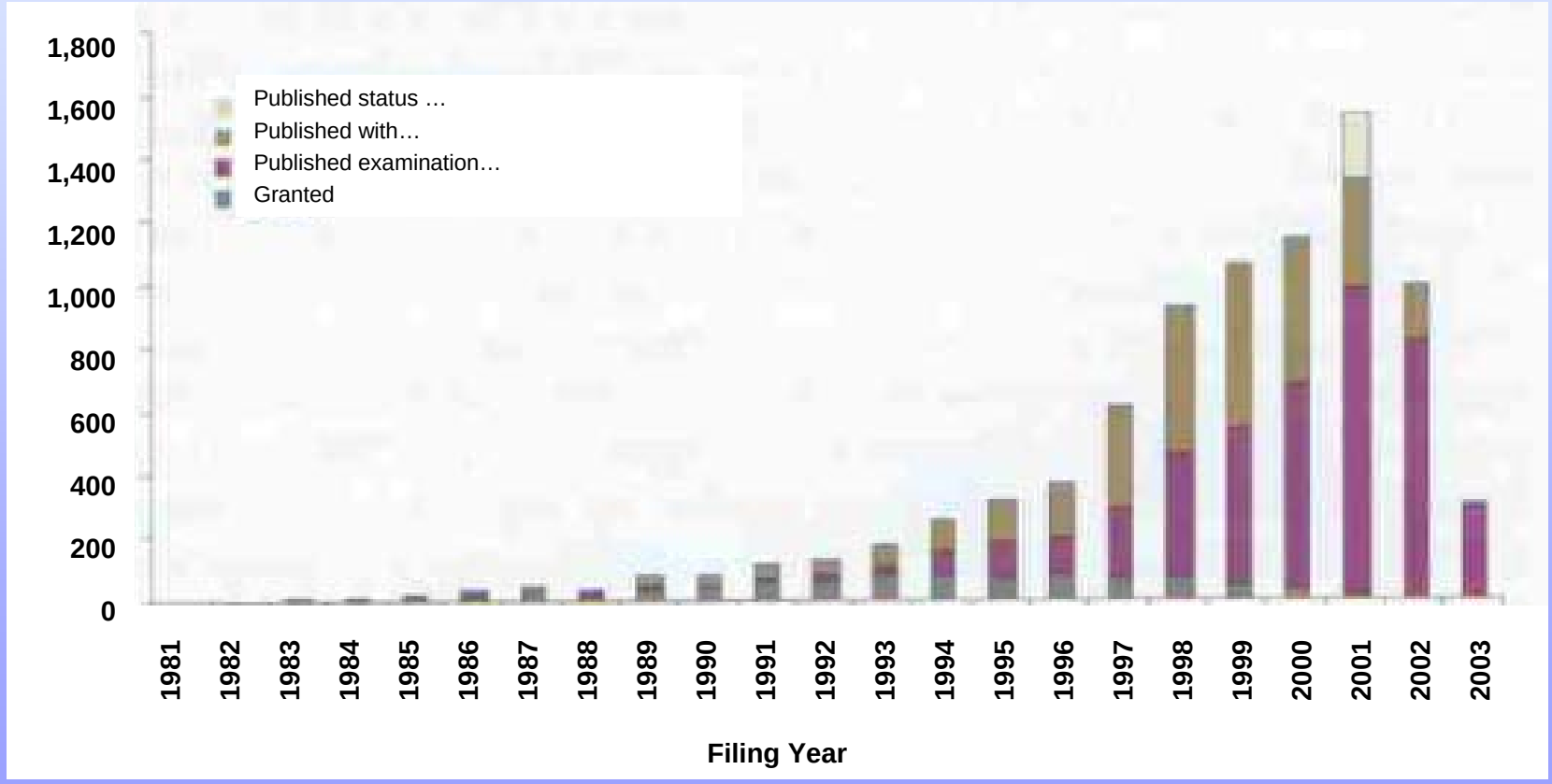


Figure 4-1 Number of DNA-based U.S. Patents (as of June 30, 2005)
2005 Projection is based on mid-year total
Source: Georgetown University Database

Source NRC 2005

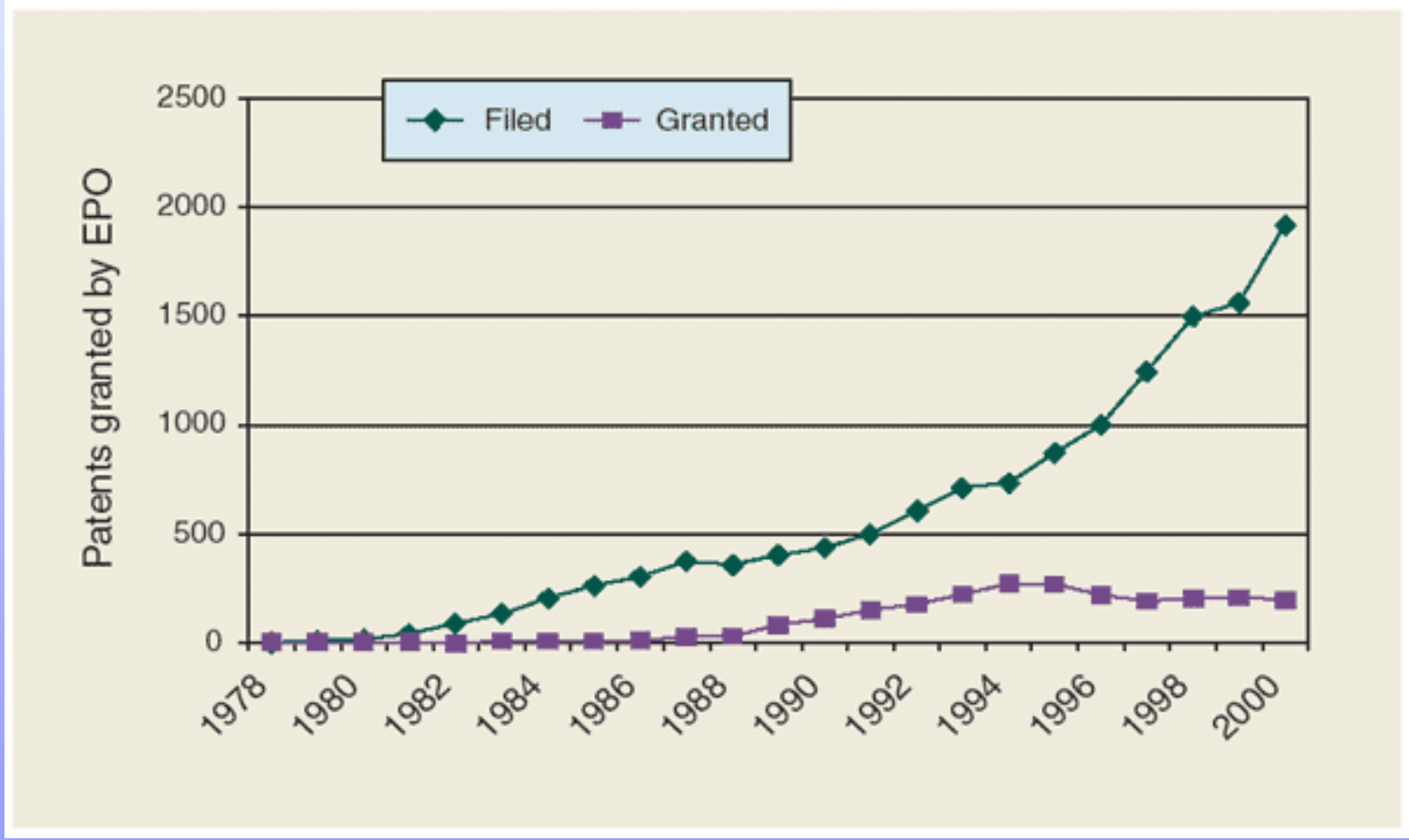
Number of DNA patent applications

Status in 2005 of patent applications claiming DNA sequences filed with the European Patent Office between January 1981 and December 2003



Source: Nature Biotechnology, Vol. 25, Nr. 2, February 7, p. 186

Applications filed & Patens Issued in EPO claiming DNA



European Bioindustry Landscape

Table 1 Selected European big pharma spinoffs and buyouts

Company (Location)	Parent	Focus	Year formed	Initial public offering (Year)
Basilea Pharmaceutica (Basel)	Roche (Basel)	Anti-infectives	2000	$161 million (2004)
Biovitrum (Stockholm)	Pharmacia, now Pfizer (New York)	Metabolic disease	2001	Listed, no cash raised (2006)
BioXell (Milan)	Roche	Urology	2002	$46 million (2006)
Elbion (Dresden, Germany)	Degussa (Düsseldorf, Germany)	Inflammation	2002	Private
LifeCycle Pharma (Hørsholm, Denmark)	Lundbeck	Cardiovascular, immunology	2002	Private
Medivir (Stockholm)	Astra, now AstraZeneca (London)	Antivirals	1988	SEK150 ($15) million (1996)
Nabriva (Vienna)	Sandoz (Holtzkirchen, Germany)	Anti-infectives	2006	Private
Newron (Milan)	Pharmacia and Upjohn, now (Pfizer)	CNS disease	1998	Private
Novexel (Paris)	Aventis	Anti-infectives	2004	Private
NovusPharma (Milan), acquired by Cell Therapeutics (Seattle) in 2004	Roche	Oncology	1999	$150 million (2000)
ProSkelia (Paris), now merged with Strakan Pharmaceuticals to form ProStrakan (Galashiels, Scotland).	Aventis, now Sanofi-Aventis (Paris)	Bone disease, hormonal disorders	2002	$76 million (2005)

Source: Companies web sites. *CS*

Source: Nature Biotechnology, 12/2006

European Myriad Genetics Patents

- **EP 0699754 – "Method for Diagnosing a Predisposition for Breast and Ovarian Cancer"**
  - **Issued January 10, 2001 – revoked in opposition May 17, 2004 – appeal pending – no hearing yet**

- **EP 0705903 – "Mutation in the 17q-Linked Breast and Ovarian Cancer Susceptibility Gene"**
  - **Issued May 23, 2001 – upheld in opposition with amended claims – appeals pending – no hearing yet**

European Myriad Genetics Patents

- **EP 0705902 – "17q-Linked Breast and Ovarian Cancer Susceptibility Gene"**
  - **Issued November 28, 2001 – upheld in opposition with amended claims – appeals pending – no hearing yet**

- **EP 0785216 – "Chromosome 13-Linked Breast Cancer Susceptibility Gene BRCA 2"**
  - **Issued January 8, 2003 – upheld in opposition with amended claims – no appeal filed**

Reactions on Myriad Patents in Europe

- Greenpeace and the German Federal Chamber of Medical Doctors – requested withdrawal
- Patients' organisations protested
- European Parliament, in October 2001, adopted a resolution against BRCA 1 patents

Reactions on Myriad Patents in Europe

- European Parliament requested the Council, Commission and Member States to ensure the availability of the human genome for research purposes
- High cost of testing because of patents
- Concerns based on possible negative impact concerning improvements of diagnostic methods

Overall Status Quo of Myriad Patents

- No request for compulsory license filed
- No court cases pending
- 1996 – 2004: Myriad allowed the “German Cancer Aid” BRCA 1 & BRCA 2 mutation testing in 12 centers (more than 3,000 gene tests – predominantly by DHPLC method)

MPI/BMBF/OECD Empirical Study (2002)
Testing Public Concerns

- Interviews in 25 Institutions: Pharmaceutical Companies, Start-Ups, Research Institutes, Clinics
- No proof for public concerns
- Majority in favour of product protection for DNA-sequences
- Critical point: No or little search for further functions of patented genes
- Results not entirely representative – still only few products on the market
- No single request for a grant of a compulsory license filed

Summary

USA

- More applications filed [ESTs!]
- More patents issued – valid?
- No excessive litigation activities
- Negative impact on R & D?

Europe

- Less applications filed [none for ESTs]
- Less patents issued [more stringent examination]
- Litigation activity relatively comparable
- No negative impact on R & D

Questions?