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**FINAL PROJECT REPORT**

**The Patenting of Human DNA: Global Trends in  
Public and Private Sector Activity  
(The PATGEN Project)**

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## Abbreviations

DNA	Deoxyribonucleic Acid
EPO	European Patent Office
ESTs	Expressed Sequence Tags
HGP	Human Genome Project
IP	Intellectual Property
IPR	Intellectual Property Rights
JPO	Japanese Patent Office
NIH	National Institutes of Health
PCT	Patent Cooperation Treaty
PCR	Polymerase Chain Reaction
PO	Patent Office
RNA	Ribonucleic Acid
RNAi	Ribononucleic Acid interference
SiRNA	Short interfering Ribonucleic Acid
SNPs	Single Nucleotide Polymorphisms
USPTO	United States Patent and Trademark Office

## Executive Summary

### Background

An upsurge in DNA patenting activity over the past 15 years has raised concerns over potential negative consequences of intensive intellectual property protection surrounding the human genome. Such concerns include inhibitory effects on research, innovation and access to healthcare. However it may be too soon to expect such negative effects to be apparent. Nevertheless sufficient time has now elapsed to allow an important prior question to be addressed: how many of the filed patents have actually been granted at the world's leading patent offices? The PATGEN project was initiated to investigate this and other related questions regarding patents claiming human DNA using published records from the major patent offices (EPO, JPO, USPTO). Interviews with 30 patent owning organisations (including charities, universities, biotechnology companies and pharmaceutical companies) were also conducted to identify current and future challenges for assignees and patent offices.

### Regional variation in DNA patent granting

Our research identified over 15,000 patent families seeking to claim human DNA between 1980 and 2003. By 2005, just under 6,000 of these families contained one or more patents granted at the main patent offices. There were significant differences between patent offices, with 94% of these families containing a USPTO patent grant, as compared to just 13% at the EPO, and less than 9% at the JPO. These data reflect the popularity of the USPTO due to the size of the US market and relatively low cost of gaining a US patent. However, they also may reflect more stringent patent examination at the EPO and JPO in the field of DNA patenting. The slower rate of processing applications at the JPO and the EPO may also have contributed to this gap, as the majority of EPO patents and JPO patents take more than 60 months to process, while most USPTO patents are processed in 30-60 months.

### Exploitation of granted patents

Once granted, DNA patents at the USPTO and EPO are generally maintained, although a significant proportion (30%) of US patents granted in the 1990s had already been abandoned by 2005 mainly due to commercial or technical reasons (eg. lack of commercial interest, cost cutting, scope of claims awarded too narrow).

Assignees indicated that their granted patents are primarily on research tools, diagnostics and therapeutics, with the majority suggesting research tools made up the largest proportion of their portfolios. The majority of assignees were yet to develop or commercialise most of their DNA patent portfolio. A large minority of private sector assignees held a significant number of patents to ensure freedom to operate. Licensing activity was undertaken most significantly by public sector organisations, although such organizations had relatively smaller portfolios than the biotechnology and pharmaceutical firms in our sample. The majority of organisations did not expect licensing activity to increase in the short term. Although most assignees did not expect to participate in patent pools in the short term, those from the public sector were more willing to consider such arrangements than those from commercial organisations, in general terms.

## **Fate of patent applications not granted**

Analysis of more than 8,000 EPO applications between 1981-2003 showed that more than half remained under examination and just over 10% had been granted by September 2005. In addition, approximately one third had been withdrawn. Of patent applications filed in the 1980s, 45% had been granted, compared to only 14% of those filed in the 1990s, although these figures will increase as ongoing examination processes draw to a close. Of the patent applications filed at the EPO in the 1990s, 44% of have already been withdrawn, with 36% still under examination.

Interviewees suggested that applications are withdrawn most often because of difficulties in demonstrating utility (industrial applicability) or novelty, or because of cost-cutting measures or a change in the business case for the invention. A minority of pharmaceutical assignees suggested that freedom to operate had been a significant motivation for filing many of their patent applications. In some cases these could be abandoned after publication, having served their purpose.

## **Trends in the ownership of patents over time**

The majority of granted DNA patents at the USPTO and EPO were held by US-based assignees. Conversely Japanese and EU-25 assignees had very small shares of the patents awarded at the USPTO. US firms increased their share from just over 20% of USPTO patents granted in the early 1980s to over 50% in the period 2000-2003. The share of Japanese and EU-25 firms did not change significantly, but the relative importance of public sector institutions from all regions declined.

The top ten public sector organisations in DNA patenting were exclusively US-based, with the exception of the Ludwig Institute of Cancer Research. The top ten firms were mainly US based, with GSK and Roche being the only non-US representatives (the latter being in the top ten due to its large equity stake in the US biotechnology firm Genentech). In general US assignees failed to replicate the same degree of success in obtaining US patents at the EPO and JPO, although assignees long established in the field of biotechnology patenting such as Amgen, Genentech, and the NIH enjoyed some success.

## **Assignee perspectives on patent offices**

Assignees highlighted problems that the new field of DNA patenting had presented for patent offices. These included difficulties in conducting examinations in complex cases, keeping up with the volume of work created by large numbers of patent applications, and public opposition to granted patents on human DNA. However some assignees considered that patent offices had worked well in concert through the trilateral discussions. Nevertheless a majority of assignees had faced increasing challenges in obtaining patents claiming DNA, and suggested that the bar to patentability had been raised across patent offices, for example through the new utility guidelines (from 2001) at the USPTO. It was also suggested that the inventive step requirement had become more difficult to meet at the EPO. Reluctance by patent offices to accept patents claiming large numbers of DNA sequences also led to some assignees facing problems with 'unity of invention' in their applications. Furthermore,

a number of assignees noted that the claims awarded in DNA patents had narrowed in scope and that future applications were likely to be required to provide greater detail in terms of biological data to obtain these claims.

### **Future trends**

The vast majority of assignees who shared their future strategies confirmed their intention to continue filing patent applications claiming DNA. While there was an expectation that novel sequences would be more difficult to find, Single Nucleotide Polymorphisms (SNPs) and splice variants were expected to be patentable. New uses for known sequences, particularly biomarkers and gene expression profiles, were also thought to be important areas of interest as were new therapeutic approaches such as RNAi. However there were concerns that as patentability guidelines became more stringent, some genuine inventions might not be granted protection at the EPO.

There was little comment from assignees on legal trends in Europe. However it was suggested that case law in the USA had already devalued DNA patents on research tools, by reducing the likelihood that Expressed Sequence Tags would be patentable in future, and reducing the enforceability of others, such as patents on drug targets. There was an expectation that assignees would move away from patenting DNA-related research tools in favour of patenting downstream inventions such as drugs.

### **Policy conclusions**

Debates on the patenting of human DNA need to reflect the disparities between patenting activity in the US and elsewhere. Moreover, with the number of patent applications in decline, more stringent examination procedures, and the likely restriction of the scope of granted patents by case law, suggest that the negative impact of DNA patenting may turn out to be more limited than some had feared. Finally, the increase in the thresholds for patentability perceived by interviewees suggests that patent offices are focused on providing due rewards.

## 1. Introduction

This report sets out the findings of a research project undertaken to analyse key trends in the filing, granting and exploitation of patents claiming human DNA sequences in Europe, Japan and the USA. Section 1 sets out the background to DNA patenting; current issues arising from the increased propensity to file DNA patents over recent years; previous research on trends in DNA patenting; and the objectives of the research project.

### 1.1 Background

Intellectual property (IP) protection is widely recognised as a crucially important component of public policy to promote innovation in the development of the life sciences and biotechnology. If research is to lead to new commercial products and processes, some form of IP protection will generally be required. In the life sciences and biotechnology, patents have proved to be a particularly important form of protection for new medicines, some diagnostics, as well as for research tools, including cell lines, antibodies, and processes such as polymerase chain reaction (PCR).

One notable feature of IP protection in the life sciences and biotechnology has been the extension of subject matter considered to be patentable. Over the past 30 years, as these fields have developed, IP protection through patents has been successfully sought for plants, animals, cell lines and biological molecules, including DNA. The patenting of human DNA sequences has been eagerly pursued by companies as well as public sector organisations, including hospitals, universities, research institutes, and governments. Viewed as chemical compounds by patent offices, DNA molecules *per se* were seen as eligible for patenting although there has been vigorous debate about the merits of this policy (see section 1.3).<sup>1</sup> A feature of the changing technical field and corresponding extension of intellectual property rights (IPRs) has been the complex interplay between interested parties. These have included legislating bodies, patent offices, assignees and other groups such as the scientific community. Together they have strived to achieve a balance between rewarding inventors and preventing undue monopolies or other undesirable social outcomes such as the inhibition of research. However to date there has been little by way of comprehensive comparison between patent systems on the extent to which this has been achieved (see section 1.5 for a review of previous work). In the meanwhile the activities of organisations seeking IPRs have raised a number of concerns.

### 1.2 Private and public sector policies in IPRs

Patents provide incentives for investments in R&D by excluding all those but the assignees or their licensees from commercially exploiting the claimed invention. This is a particularly important form of market protection in the biotechnology and pharmaceutical industries where therapeutic products incur particularly high development costs.<sup>2</sup> They have also been a critical driver for the formation of biotechnology companies whose IP is often an asset necessary to secure early stage

<sup>1</sup> Nuffield Council on Bioethics (2002) The Ethics of Patenting DNA: A Discussion Paper (London).

<sup>2</sup> M. Stott, J. Valentine (2004) Gene patenting and medical research: a view from a pharmaceutical company Nature Reviews Drug Discovery 3 (4) p.364-368.

funding.<sup>3</sup> Firms may seek protection on many aspects of their inventions to protect their markets, including the stages of any processes by which the invention is reached. For example, where an invention is a therapeutic molecule that acts on a given protein, the DNA sequence that describes the protein is sometimes claimed even where the therapeutic molecule itself is not related to that DNA. There has been a massive expansion of the biotechnology sector as the complexity of applying new genetic knowledge has necessitated a new division of labour between drug/diagnostics developers and developers of research tools.<sup>4</sup> Many of these tool developers have sought to protect their products and processes with patents on DNA. Although the resulting proliferation of patents in the field has led to concern (see section 1.4 below), the disclosure of these inventions and the availability of such tools is seen by some as beneficial to the long term health of the industry.<sup>5</sup>

Researchers in the life sciences and biotechnology who work in the public sector have also increasingly sought to protect their inventions by patents in recent decades. The US led the way with the introduction of the Bayh Dole Act which allows universities to seek patent ownership for inventions arising from federally-funded research.<sup>6</sup> Governments across Europe now encourage researchers in the public sector to protect their inventions to better facilitate the commercial exploitation of basic research.<sup>7</sup> Few public sector institutes seek to commercialise their inventions alone and therefore exploitation of their research relies on licensing of IP to private sector organisations. However such agreements are increasingly influenced by policies that seek to ensure the maximisation of social benefit from not-for-profit research efforts – such as the NIH guidelines on licensing.<sup>8</sup>

### 1.3 Perceptions of DNA patenting in the scientific community and the general public

The granting of patents claiming DNA appears to have been initially uncontroversial and attracted little attention in the 1970s and 1980s. This was despite the preceding international controversy surrounding the Diamond v. Chakrabarty decision on “living” subject matter.<sup>9</sup> This began to change with the filing of patents claiming ESTs by the NIH, which were opposed by the scientific community and some European governments from 1991 onwards because it was feared their claims could impinge on downstream inventions, and because they were thought to not meet the patentability criterion for utility (industrial applicability).<sup>10,11</sup> Furthermore as private

<sup>3</sup> Ernst and Young (2002) Beyond Borders: the Global Biotechnology Report.

<sup>4</sup> M. M. Hopkins, A. Kraft, P. A. Martin, P. Nightingale, S. Mahdi, (2006) Is the Biotechnology Revolution a Myth? In *Comprehensive Medicinal Chemistry* (2nd Ed) Taylor & Triggle (eds.)Elsevier.

<sup>5</sup> M. Stott, J. Valentine (2004) Gene patenting and medical research: a view from a pharmaceutical company *Nature Reviews Drug Discovery* 3 (4) pp.364-368.

<sup>6</sup> S Boettiger & A Bennett (2006) Bayh-Dole: if we knew then what we know now *Nature Biotechnology* Vol. 24 (3) March pp320-323.

<sup>7</sup> The European Commission (2004) Efficiency of innovation policies in high technology sectors in Europe (EPOHITE). EUR 20904. Luxembourg. p.47.

<sup>8</sup> L. Pressman, R. Burgess, R. M. Cook-Deegan, S. J. McCormack, I. Nami-Wolk, M. Soucy, L. Walters (2006) The licensing of DNA patents by US academic institutions: an empirical survey *Nature Biotechnology* 24 (Jan), pp31-39

<sup>9</sup> R. S. Eisenberg (2006) *Nature Biotechnology* 24 (3) 317-319.

<sup>10</sup> Editorial (1994) Ownership of the human genome *Nature* 29<sup>th</sup> September

<sup>11</sup> HUGO (1995) Hugo statement on patenting DNA sequences *Genome Digest* (April) pp6-9.

sector sequencing efforts appeared to outstrip the pace of the publicly funded Human Genome Project in the early 1990s, concerns grew further within the scientific community (including some in industry). A race developed between those seeking to patent and publish and those seeking merely to publish human genetic code.<sup>12</sup> It was at this time, with the private sector delaying the publication of their sequence data to the clamouring scientific community, that the issue appears to have attained widespread public recognition. The notion that scientific fields could become fragmented by IP rights leading to sub-optimal exploitation gained further notoriety following Heller and Eisenberg's publications on 'the tragedy of the anti-commons'.<sup>13</sup> Such concerns spiralled as relationships between those supporting the Human Genome Project and private sector groups became antagonistic - culminating in the Blair-Clinton statement of 2000 that called for greater freedom of access to raw genetic code.<sup>14</sup> Some industry figures with experience of commercialising DNA-based patents suggest the resulting public opposition to DNA patenting has been greater in the Europe than in the USA, with distinct concerns arising over time around ethical issues and the stifling of research.<sup>15</sup>

These concerns have led to widespread opposition of DNA patenting,<sup>16</sup> ultimately leading to delays in ratification of the 'Biotechnology Directive' and the passing of additional legislation by some states to satisfy national concerns (see section 4.5).

#### 1.4 Previous and remaining concerns

Arguments raised by opponents include suggestions that the practice of DNA patenting may be:

- (i) inhibiting the free exchange of information between researchers;
- (ii) involving unsuspecting parties in extensive and costly legal battles
- (iii) limiting access to healthcare by increasing the cost of diagnostics and treatment for certain diseases;
- (iv) preventing or hindering development of new or improved medicines and treatments;
- (v) skewing research towards commercially attractive science<sup>17</sup>

These claims have been systematically investigated in a series of reports and studies.<sup>18,19,20,21,22, 23</sup> In general these studies support more strict interpretation and

<sup>12</sup> K. Kliener (1994) There's no such thing as a free gene *New Scientist* 15<sup>th</sup> October, p.10

<sup>13</sup> M. A. Heller and R. S. Eisenberg (1998) Can patents deter innovation: the anticommons in biomedical research *Science* 280 pp.698-701

<sup>14</sup> R. S. J. Fox (2000) Human genome bombshell *Nature Biotechnology* 18 (April) p.365

<sup>15</sup> M. Stott, J. Valentine (2004) Gene patenting and medical research: a view from a pharmaceutical company *Nature Reviews Drug Discovery* 3 (4) pp.364-368.

<sup>16</sup> For example of opposition groups see 'Patenting genes – stifling research and jeopardising healthcare' [http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Patenting\\_Genes\\_A4\\_Version.pdf](http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Patenting_Genes_A4_Version.pdf)

<sup>17</sup> See Genewatch - [http://www.genewatch.org/sub.shtml?als\[cid\]=531144](http://www.genewatch.org/sub.shtml?als[cid]=531144) (accessed 12/06/06)

<sup>18</sup> Nuffield Council on bioethics (2002) *The ethics of patenting DNA: a discussion paper*, London. Available at: [http://www.nuffieldbioethics.org/publications/pp\\_000000014.asp](http://www.nuffieldbioethics.org/publications/pp_000000014.asp)

<sup>19</sup> National Academy of Sciences (2005) *Reaping the benefits of genomic and proteomic research: intellectual property rights, innovation and public health*, National Academies Press, Washington D.C. Available at: [www.nap.edu/catalog/11487.html](http://www.nap.edu/catalog/11487.html)

<sup>20</sup> S. Hansen, A. Brewster, J. Asher (2005) *Intellectual property in the AAAS scientific community*, AAAS.

enforcement of patentability criteria to reduce the number and scope of patents claiming DNA. They also make a number of specific points on the concerns above:

In regard to (i) and (ii) the findings of these investigations indicates a relatively low impact on research from DNA patenting at present. Recent studies suggests few research projects are reported as being abandoned or delayed due to IP issues, and the citation of patented work is only marginally diminished. However the possibility remains that existing impacts might grow over time. Concerns about limitations to the research exemption in the US in particular continue to be raised, and an OECD review of policy on best practice in different regions is currently ongoing.<sup>24</sup> In the meanwhile, more limited use of exclusive agreements in licensing arrangements or the incorporation of research exemptions by leading public sector institutions may signal another way to protect 'fair use' research from potential inhibitory effects of patenting on research.<sup>25</sup>

In relation to (iii) above on the availability of diagnostics, commentators highlight the difficulties faced by inventors in inventing around diagnostic patents claiming DNA which are thought to present higher hurdles than in other technical fields.<sup>26</sup> Studies also suggest some licensors have set terms and conditions on licensing that have prevented others from providing tests, such as in the case of BRCA1 and Haemochromatosis.<sup>27</sup> Generalisations from the BRCA1 case (which remains one of the few cited examples more than ten years after initial concerns appear to have surfaced) may however be inappropriate. BRCA1 is one of the most heavily patented genes in the genome, suggesting it might be an atypical case.<sup>28</sup> Furthermore key patent claims for BRCA1 have been revoked at the EPO, diminishing the likely impact on healthcare of even this notorious example.<sup>29</sup> Nonetheless, evidence does suggest that patents are restricting the numbers of laboratories offering tests, increasing costs and reducing scope for test improvements.<sup>30, 31</sup>

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<sup>21</sup> S. Stern and F. E. Murray, "Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge? An Empirical Test of the Anti-Commons Hypothesis" (July 2005). NBER Working Paper No. W11465. Available at SSRN: <http://ssrn.com/abstract=755701>

<sup>22</sup> J. P. Walsh, C. Cho, W. M. Cohen (2005) View from the Bench: Patents and Material Transfers. *Science* 309 23 September 2002-2003.

<sup>23</sup> Intellectual Property Institute (2004) Patents for Genetic Sequences: the competitiveness of current UK Law and Practice, London: DTI.

<sup>24</sup> C. Dent, P. Jensen, S. Waller and B. Webster (2006) Research Use of Patented Knowledge: A Review (OECD Directorate for Science, Technology and Industry Working Paper).

<sup>25</sup> National Academy of Sciences. *Reaping the benefits of genomic and proteomic research: intellectual property rights, innovation and public health*, National Academies Press, Washington D.C. (2005) Available at: [www.nap.edu/catalog/11487.html](http://www.nap.edu/catalog/11487.html)

<sup>26</sup> See also G. Matthijs (2004) Patenting genes BMJ 329 pp1358-1360

<sup>27</sup> M. K. Cho, S. Illangasekare , M. A. Weaver, D. G. B. Leonard, and J. F. Merz (2003) Effects of patents and licenses on the provision of clinical genetic testing services *Journal of Molecular Diagnostics* 5 (1) February 2003 pp.3-8.

<sup>28</sup> K. Jensen and Fiona Murray Intellectual property landscape of the human genome *Science* 310. 14<sup>th</sup> October 2005. pp.239-240

<sup>29</sup> A. Coghlan (2004) Europe revokes controversial gene patent, *New Scientist*, 19 May.

<sup>30</sup> M. K. Cho, S. Illangasekare , M. A. Weaver, D. G. B. Leonard, and J. F. Merz (2003) Effects of patents and licenses on the provision of clinical genetic testing services *Journal of Molecular Diagnostics* 5 (1) February 2003 pp.3-8.

<sup>31</sup> Merz J. F., Kriss, A.G., Leonard, D.G.B. and Cho, M. K. (2002) Diagnostic testing fails the test Nature Vol.415 7<sup>th</sup> February pp.577-579.

Provisions already exist in the US and Europe that could reduce the impact of diagnostic patents on public health use. The TRIPS agreement allows governments to issue compulsory licenses where there is a case for the protection of public health, and in the US courts may deny injunctive relief to assignees where health and safety issues prevail.<sup>32</sup> A bill named the ‘Genomic Research and Diagnostic Accessibility Act of 2002’, which may have addressed some of these concerns languished after its introduction to the US House of Representatives.<sup>33</sup> In Europe, Article 52 (4) of the 1973 European Patent Convention allows the EPO to refuse patents on ‘diagnostic methods, practiced on the human body’ although the circumstances under which this might be applied are not clear.<sup>34</sup> Others suggest that the problem is not so much with the patent system, but with the behaviour of specific licensors or the legal advice received by the laboratories they ask to desist from infringement.<sup>35, 36</sup> The solution to these problems therefore may not lie in change to the patent system. Patent licensing/clearing houses have been suggested as potential measures that might reduce difficulties in this area.<sup>37</sup>

In relation to (iv) and (v) above, there is still a need for evidence to support or counter the suggestion that DNA patenting is stifling the development of new medicines or skewing the selection of projects. Some in the pharmaceutical industry have highlighted the value of such licensing deals (which need not be exclusive) while at the same time emphasising that the cost of owning a patent provides a commercial imperative to overcome licensing difficulties.<sup>38</sup> However this is clearly an area that remains to be studied in greater detail.

The research referred to above provides some evidence that DNA patents may not be causing as many problems as had been feared by some commentators. However neither does this evidence suggest this state of affairs will remain the case. DNA patenting remains a relatively young field. Some consider that the patenting system is taking a long time to deal with key legal issues such as the patentability of ESTs (introduced in section 1.2 as one of the initial causes of concern) only recently being decided in court.<sup>39</sup>

Given the importance of the field, the monitoring of policies such as the ‘European Biotechnology directive’, which establish the framework for patenting of DNA-based inventions, continues to be vital. An important element of such monitoring is an examination of trends on the patenting of DNA.

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<sup>32</sup> National Academy of Sciences (2005) *Reaping the benefits of genomic and proteomic research: intellectual property rights, innovation and public health*, National Academies Press, Washington D.C. Available at: [www.nap.edu/catalog/11487.html](http://www.nap.edu/catalog/11487.html)

<sup>33</sup> <http://thomas.loc.gov/cgi-bin/bdquery/?d107:h.r.03967>: (accessed 12/06/06)

<sup>34</sup> G. Matthijs (2004) Patenting genes BMJ 329 pp1358-1360.

<sup>35</sup> OECD (2002) Genetic Inventions, Intellectual Property Rights and Licensing Practices

<sup>36</sup> M. Stott, J. Valentine (2004) Gene patenting and medical research: a view from a pharmaceutical company Nature Reviews Drug Discovery 3 (4) p.364-368.

<sup>37</sup> OECD (2002) Genetic Inventions, Intellectual Property Rights and Licensing Practices

<sup>38</sup> M. Stott, J. Valentine (2004) Gene patenting and medical research: a view from a pharmaceutical company Nature Reviews Drug Discovery 3 (4) p.364-368

<sup>39</sup> R. S. Eisenberg (2006) Nature Biotechnology 24 (3) 317-319.

## 1.5 Review of previous work monitoring DNA-patenting activity

Patents are often a useful indicator for addressing the question of whether balanced policy in science and technology has been achieved. Granted patents are published by all patent offices and the majority also publish information on applications. These data provide a wealth of information of interest to policy makers such as the type of organisations producing economically valuable research, their nationality, and the nature of the inventions being developed. Over time, trends in annual patenting statistics provide insights into the pace of innovation and competitiveness. Changes may also reveal the impact of policies or other events influencing the commercial environment.

Studies of patenting in relation to biotechnology, especially genetic subject matter such as DNA, have provided useful snap shots of activity.<sup>40, 41</sup> However such studies have been criticised as over estimating the numbers of patents on human genetic information by relying on methods that do not distinguish between patents claiming or merely describing DNA or between patent applications and granted patents.<sup>42</sup>

Although studies are available that have counted patents that claim sequences, they have focused only on the USPTO and in some cases are not limited to human DNA.<sup>43,44</sup> Further studies seeking an international perspective of trends over time have been hampered by difficulties in searching publicly available datasets.<sup>45</sup> Thus a need was identified for a study that combined more flexible commercial database formats with robust methods to generate well-bounded and comparable statistics from different patent offices.

## 1.6 Objectives of the research

The main objective of the PATGEN project is to provide a global and comprehensive quantitative and qualitative analysis of patents, filed and/or granted during the period 1981 – 2003, which claim human DNA sequences. This unique dataset forms the basis for four streams of evidence that provides a sound basis for policy making:

- A comprehensive analysis of patent applications and grants by public and private sector organisations. This provides systematic evidence on the extent

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<sup>40</sup> For example see Thomas, Hopkins, Brady Shares in the human genome – the future of patenting DNA *Nature Biotechnology* 20 pp.1185-1188.

<sup>41</sup> Finnegan, Henderson, Farabow, Garrett & Dunne, LLP (2005) Biotechnology Innovation Report 2005. (June) Washington, DC: USA.

<sup>42</sup> M. Stott and J. Valentine Impact of gene patenting on R&D and commerce July 2003 *Nature Biotechnology* 21 (7) pp.729-731.

<sup>43</sup> Kyle Jensen and Fiona Murray Intellectual property landscape of the human genome *Science* Vol. 310, 14<sup>th</sup> October 2005.

<sup>44</sup> L. Pressman, R. Burgess, R. M. Cook-Deegan, S. J. McCormack, I. Nami-Wolk, M. Soucy, L. Walters (2006) The licensing of DNA patents by US academic institutions: an empirical survey *Nature Biotechnology* 24 (Jan), pp31-39

<sup>45</sup> P. Oldham (2005) *Global status and trends in intellectual property claims: genomics, proteomics and biotechnology* Submission to the executive secretary of the convention on biological diversity available at: <http://www.cesagen.lancs.ac.uk/resources/docs/genomics-final.doc>

to which companies, universities, and research institutes from across the world seek to protect their DNA-based inventions by means of patents.

- A systematic analysis of the patent applications identified above to determine those that have been granted by the EPO and JPO during the period 1981-2003.<sup>46</sup>
- Data from patent offices and assignees illuminating the extent to which patent applications that have not been granted are actively being pursued; and the extent to which granted patents are subsequently allowed to lapse.
- Qualitative data from assignees on their experiences and strategies and to provide an assessment of emerging issues and future trends, as well as insights into the consequences of legal changes/patent office policies (such as the tightening of USPTO utility guidelines).

Section 2 sets out in more detail the methodology for the PATGEN project, while the results are described in Section 3. Section 4 places the results in a broader analytical context and draws conclusions and policy recommendations.

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<sup>46</sup> Until recently (since November 2000), the US Patent and Trademark Office (USPTO), has not published data on patent applications that have not been granted, unlike the European Patent Officer (EPO) and the Japanese Patent and Trademark Office (JPTO).

## 2. Methodology

The overall aim of the PATGEN project was to provide an analysis of the dynamics of patent applications and grants claiming human DNA sequences. This required the assembling of two datasets. The first dataset comprises information on patent documents filed at the EPO, USPTO and JPO, and the second from interviews of senior personnel at 30 organisations with the largest volume of patenting. This section describes the main elements of the methodology employed in assembling these data.<sup>47</sup>

### 2.1 Construction of the database on patenting activity

The first task in the construction of the PATGEN database was to isolate the patents of interest, i.e. only those claiming human DNA sequences. This is not a straightforward task as there is no specific Patent Classification (either USPC or IPC) that can be associated directly with human DNA. In this project we used an indirect approach by starting with the *GENESEQ* database produced by *Thomson-Derwent* and kindly provided by *GlaxoSmithKline (GSK)*. This database identifies patents containing a reference to a particular genetic invention, including DNA Sequences. A similar approach was employed in a previous study on human DNA patenting (see Thomas *et. al.*, 2002). One significant advantage of this database is that each record contains a unique identifier that provides a direct link to the *Derwent World Patent Index (DWPI)*, which has detailed information on all related patents (i.e. members of a particular patent family).

From the vast array of information in *GENESEQ* we isolated all patents containing gene sequences related to *human* DNA within their *claims*. This yielded 21,831 patent families ‘claiming’ 1,948,023 sequences in the period January 1980 to June 2004. The next step in the process was to obtain information on all the individual patents within these families. This was facilitated by a collaboration with *Thomson-Derwent*, the producers of the *World Patent Index* database.

For each patent family we obtained the following information:

- EPO, JPO and USPTO patent numbers associated with the invention.
- The application/filing date of each of these patents
- The publication/granting date of each of these patents
- All assignees associated with a particular family
- The address of each patent assignee

From the initial 21,830 patent families identified, 15,603 had at least one patent application filed at the EPO, JPO or USPTO. These 15,603 families contain 33,601 individual patent numbers (granted or published) distributed as follows amongst the 3 patent offices: 17,080 USPTO, 8278 EPO and 8243 JPO.

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<sup>47</sup> For further details see Interim Reports 1-3.

The next steps in the analysis involved establishing the legal status of the identified patents and cleaning and consolidating assignee names.

### 2.1.1 Establishing legal status of the patent families at the different patent offices

#### *EPO patents*

To establish the status of EPO patent applications we relied on two sources of information. Firstly the patent number where, in accordance with PCT (Patent Cooperation Treaty) conventions, the EPO indicates the progress of an application by adding a suffix to the original patent application number, known as *Patent Kind* (usually an alpha numeric such as A1, A2, B1, B2 etc.). Thus by examining the suffix of the patent number we determined some information on the latest status of the application. All patents with the letter A in the *Patent Kind* correspond to published applications while those with the letter B correspond to granted patents. This exercise was performed on the latest *Patent Kind* as a single *DWPI* record for a patent family contains information on all *Patent Kinds*. Of the 8,278 EPO patent numbers in our database, 774 are categorized as granted patents (as they have a suffix B) while the remaining 7,504 numbers are categorized as published applications (as they have a suffix A). This information is of course valid as of March 2005 when we obtained the patent data from *Thomson-Derwent*.

However, *DWPI* does not indicate whether a granted patent is still in force or whether a patent application has been abandoned. Such information can be obtained by examining the history of a particular patent provided by the *INPADOC* Patent Registration Service (PRS), which “describes all significant steps in the lifetime of an invention, from first publication (in some cases even from the filing) to the end of term of the patent, and includes data such as change of owner, examination request, grant, revocation etc.”. *Espacenet INPADOC* compiles all PRS information of majority of applications published by the various patent systems.

To ascertain the latest legal status of a particular EPO patent, we downloaded the whole PRS record for that patent from the *Espacenet INPADOC* web pages and reorganized this information in a database. This download occurred during August and September 2005, and thus the status of the EPO patents analysed below reflects the situation at that time.

For published patent applications (determined by Patent Kind as described above), we checked whether the application had been withdrawn, refused or had lapsed (e.g. due to non-payment of patent fees) in the 3 main EU countries (France, Germany and the UK).<sup>48</sup> If this was the case then we deemed that application to be ‘abandoned’, otherwise we categorized it as ‘still in force’. During this process we also discovered that some published applications identified through *Patent Kind* had now been granted. This occurred as a result of the time that had elapsed between the *DWPI* download in March 2005 and our web searching in August/September 2005.

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<sup>48</sup> In each of these cases we also checked if there had been an attempt to restore the application.

### *JPO Patents*

As in the case of EPO, to determine the status of a JPO patent we examined the latest *Patent Kind* from the *DWPI* database. All patent numbers with *Patent Kind* letter “B” were categorized as *granted* patents while all others (such as “A”, “T”, “W”, “X” and “Y”) are categorized as *published* applications. In the cases where there was no *Patent Kind Letter* from the original *DWPI* database, we examined the *Espacenet INPADOC* webpage for this information. Of the 8,243 JPO patent numbers we were able to determine the status of 8,237.

### *USPTO Patents*

The USPTO began to publish patent applications in late 2000. Prior to this, it only published information on those applications that were successful. Thus it was only possible to analyse the rate of patent filing or the proportion of applications that are granted in the short period from 2001-2003.

We determined the status of the granted US patents by examining whether they were being *maintained* with information obtained from the USPTO website.<sup>49</sup> In order to maintain a patent assignees have to pay a rising scale of fees beginning in year 3.5 from the date of grant. The searches were undertaken in March 2006, giving us information on the proportion of granted patents that were being maintained.

#### 2.1.2 Cleaning and consolidating assignee names

The consolidation and cleaning of assignee names is conducted *at the level of the patent family*. The main reasons for undertaking this exercise were that many patents are awarded under the names of subsidiaries and divisions of large firms and that the same firm may appear under many different names, including in some cases typing and spelling mistakes. Thus assignee names (excluding private individuals) were cleaned and standardized and firms were grouped in terms of their ultimate owner, according to the ownership structure in the year 2003. For this consolidation process, we examined the history of each assignee in *Hoovers Online* or using *Google*. We began with a list total of 2,057 original assignees which were consolidated into 1,260 Ultimate Assignees.<sup>50</sup>

At the same time we obtained the following information for each assignee: (a) country location of the headquarters; (b) whether the assignee is a Private or Public institution; and (c) in the case of firms, the sectoral (product group) designation, and (d) in the case of public institutions, whether this is a university or not. This information is obtained by examining the ‘homepage’ of the institution as well as the references contained in *Google*.

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<sup>49</sup> <http://portal.uspto.gov/external/portal/pair>

<sup>50</sup> This was done in the period March to September 2005 and thus reflects the company as it existed then.

## 2.2 Developing the assignee questionnaire

The original PATGEN project methodology proposed three surveys (based on email or telephone interviews) that were intended to reveal:

- (i) The fate of 350 filed patent applications not granted to date
- (ii) The exploitation of 350 granted patent applications
- (iii) The experiences of 30 assignees holding a significant proportion of the total patents in our cohort (as captured by the PATGEN v2 database)

After consultation with the PATGEN advisory board, a combined survey tool was developed to extend interviews for (iii) to encompass (i) and (ii) and provide insights into the fate of a much larger number of patents by focusing interview questions on the assignee's portfolio as a whole, rather than enquiring on the fate of a relatively small number of specific patents (not least because questions relating to 700 patent families would describe the fate of <5% of the identified cohort – judged not to provide robust results).

The questionnaire used for the interviews is in Appendix A. It was administered to 30 assignees collectively responsible for more than 29% of patent families seeking to claim human DNA sequences that are held in the PATGEN v2 database. The survey obtained quantitative and qualitative answers to a range of questions related to assignees' patent portfolios. However it should be noted that some assignees (mainly those where DNA sequences were a small focus in a broad portfolio) could not provide quantitative responses. Hence in Section 3 many figures presenting quantitative interview data are based on the answers of interviewees from 25 assignee organisations rather than 30.

The survey was complemented by objective data collection directly from the USPTO and EPO giving an insight into the legal status of a much larger proportion of the patents (as described above) - not thought to be feasible at the start of the project.

## 2.3 Interviewee selection

Interviewees were selected to provide expert opinions on developments in the field of DNA patenting and, where appropriate, nucleotide sequencing patenting more generally. To ensure adequate expertise, interviewees at the most active assignees in the field were sought. Therefore the experiences reported represent the perspective of those from assignee organisations that hold a large proportion of patents in the field.

The mission of an institution was judged to be the most influential guide to its patenting behaviour (above economic size or geographical location). Therefore to gain broad insights into trends in nucleotide patenting, interviewees were selected to reflect the range of missions of those groups holding the largest numbers of patent families claiming DNA sequences (whether these were applications or issued patents). Based on the findings of our database work, the institutions most active in the field of DNA patenting can be divided into three groups:

- Public sector organisations - including universities, hospitals, charities, government research institutions

- Small/ medium sized biotechnology firms
- Large pharmaceutical firms

Institutions were approached for interview, starting with the assignees in each group with the largest portfolios of published patents. Once assignees holding more than 25% of the patents in the cohort had been interviewed, the focus of interviewee selection was broadened to include a number of institutions with less prolific patenting activity, to allow exploration of different views. However due to the greater focus on high-patenting institutions, comparisons between the two sets of institutions can only be indicative.

Interviews were conducted with 38 individuals working for 30 assignees (see Table 1 for characteristics of the sample). Interviewees were often senior members of patent departments, including heads of Intellectual Property (IP) departments/ technology transfer offices, or their deputies. Interviews lasted between 30 and 90 minutes.

Table 2.1. Characteristics assignees in the survey sample

No. of published DNA patent applications filed between 1980 and 2003	Geographic HQ	Sector
Between 1-10 = 2	Europe = 13	Biotechnology firms = 10
Between 11-50 = 8	Japan = 3	Large Pharmaceutical firms = 10
Between 51-100 = 4	USA = 18	Not-for-profit = 10
Over 100 = 16	Other = 0	Other = 0

## 2.4 Limits of reporting

All interviews were conducted on the condition of strict anonymity and so results are reported here in a manner that protects the identity of the participants and reduces the chance of details of strategies and performance being linked to their employer. Furthermore, the views expressed by interviewees should be considered to be the views of individuals and may not represent the views of their employer.

Parts of Section 3 are based on qualitative responses to semi-structured questions where divergent themes have been explored with interviewees according to their experiences. For this reason evidence is often reported that appears supported by a relatively low number of interviewees. This does not necessarily reflect broader disinterest in those topics, but rather limitations in the breadth of discussion in the time available (although all interviewees gave generous amounts of time in answering the survey).

While every effort has been made to ensure the findings reported are the views of more than one individual, this has not been possible in all cases, and efforts have been made during data analysis not to exclude important view points because only a single interviewee raised them.

The authors cannot reasonably be responsible for ascertaining the accuracy of all interviewee statements made about third parties at interview.

### 3. Main Results

The key findings of the PATGEN project are summarised in this section. Section 3.1 reviews findings based on published patent records based on the database methodology described in section 2.1. Section 3.2 summarises the experiences of assignees seeking DNA patents, based on the interview programme described in section 2.3.

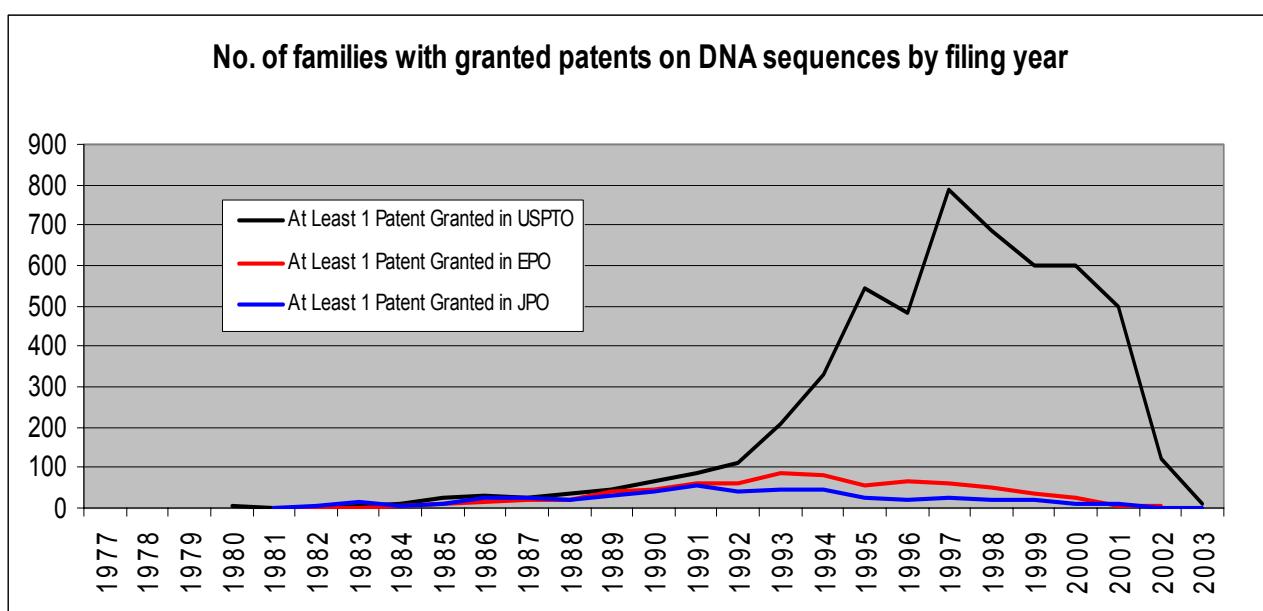
#### 3.1 Patent statistics on DNA patenting

##### 3.1.1 Trends in Granting

Our analysis identified a total of 15,603 patent families claiming human DNA sequences which were published between January 1980 and December 2003. Of these only one third (5,669) contain one or more patents granted by September 2005 at one of the three leading patent offices: the USPTO, EPO or JPO. Most of this subset (94% of those families) contains at least one granted US patent, with the numbers rising sharply during the 1990s (See Figure 1). By September 2005, of the 15,603 patent families only 750 contained granted EPO patents (just under 5% of all families, and 13% of families with granted patents), and only 494 families contained granted JPO granted patents (3% of all families, and 9% of families with granted patents).

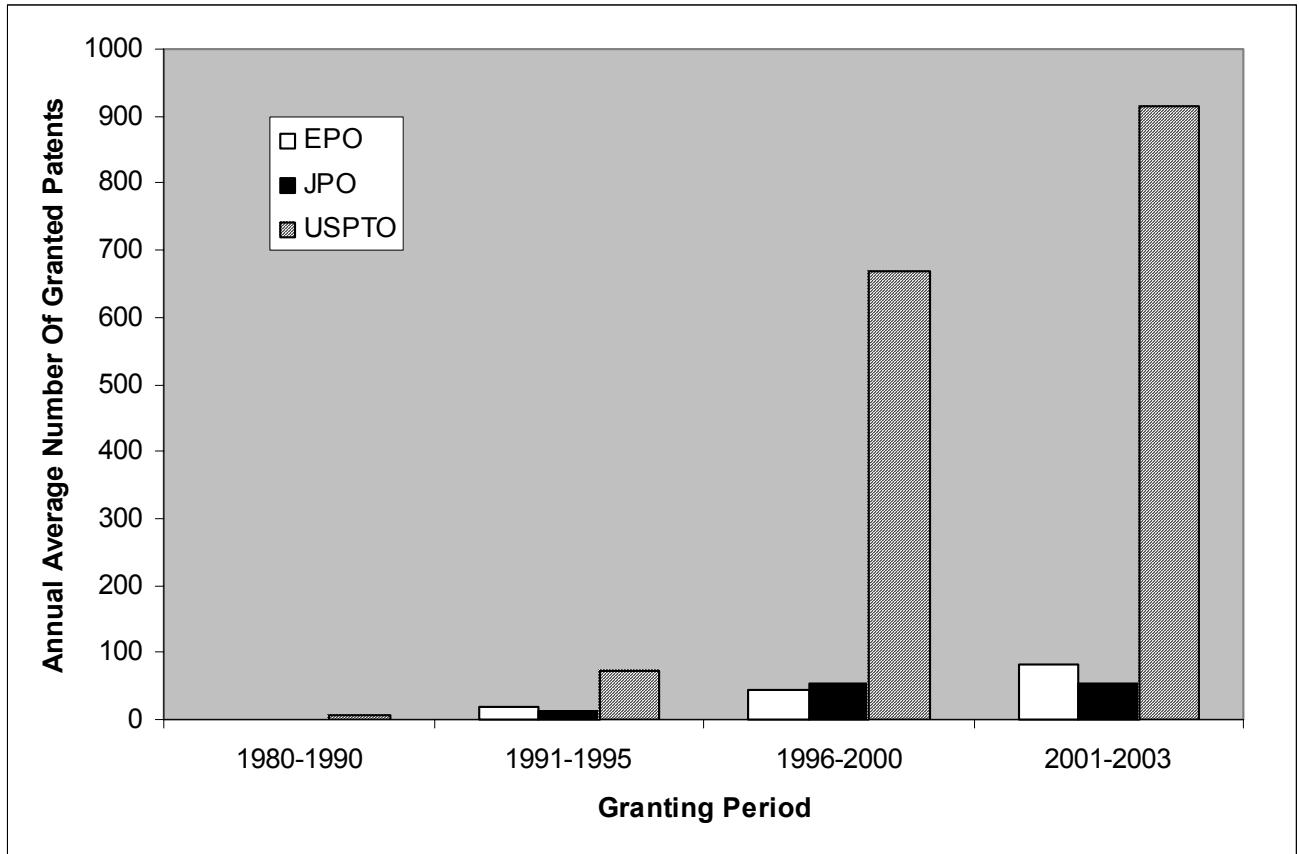
Figure 1 illustrates granting patterns have been broadly similar at the EPO and JPO for patents filed in the 1980s. However the EPO has to date granted more patent applications filed in the 1990s. By contrast to the relatively small numbers of patents granted by the EPO and JPO, the USPTO has granted many times more (even reaching x10 more at times) since the 1990s. Figure 1 also shows the low numbers of patents being granted on applications filed in the period since 2000, as examinations are ongoing.

Figure 1. Trends in granting by the EPO, USPTO, and JPO



The dominance of the USPTO in terms of DNA patent grants is further illustrated in Figure 2 which reports the annual average number of patents granted at each individual patent office per year in the period 1980 to 2003.

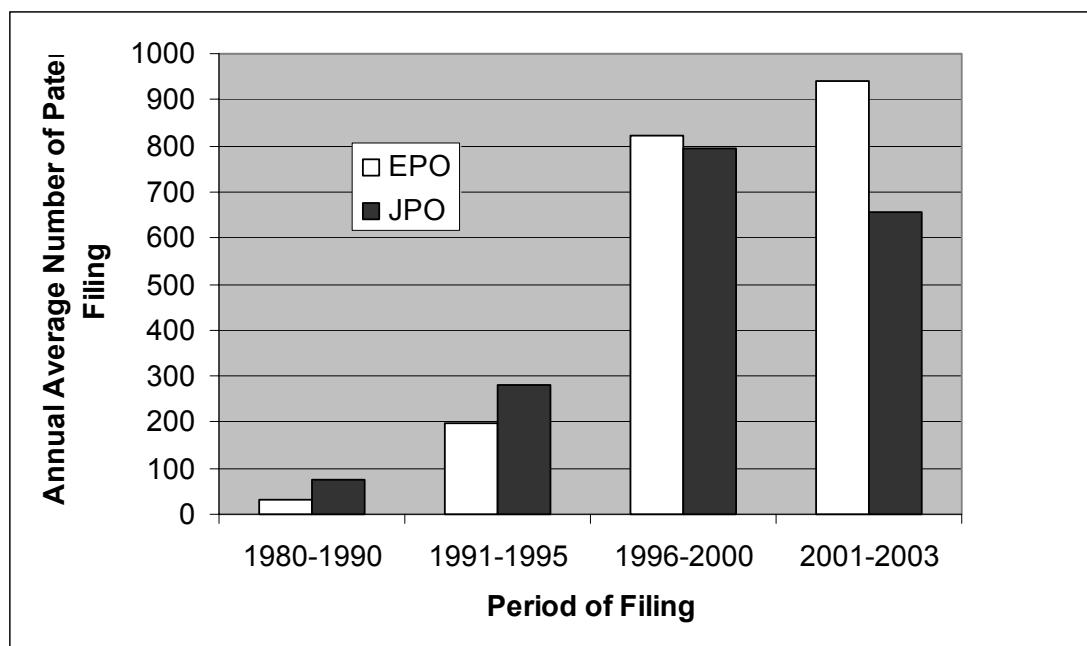
Figure 2. Trends in the granting of patents related to human DNA, by period of granting.



### 3.1.2 Trends in filing

The dynamics of filings at the EPO and JPO have been very similar (see Figure 3), with less than 100 patent applications filed per year in the 1980s, growing to around 800 per year in the second half of the 1990s. The period since 2000 has seen some divergence with increasing number of filings at the EPO but a slowdown at the JPO. For this last period (i.e. 2001 to 2003) we have comparable data for the USPTO showing that the average number of patent applications being filed in the US was just under 3000, compared to 941 at the EPO and 658 at the JPO.

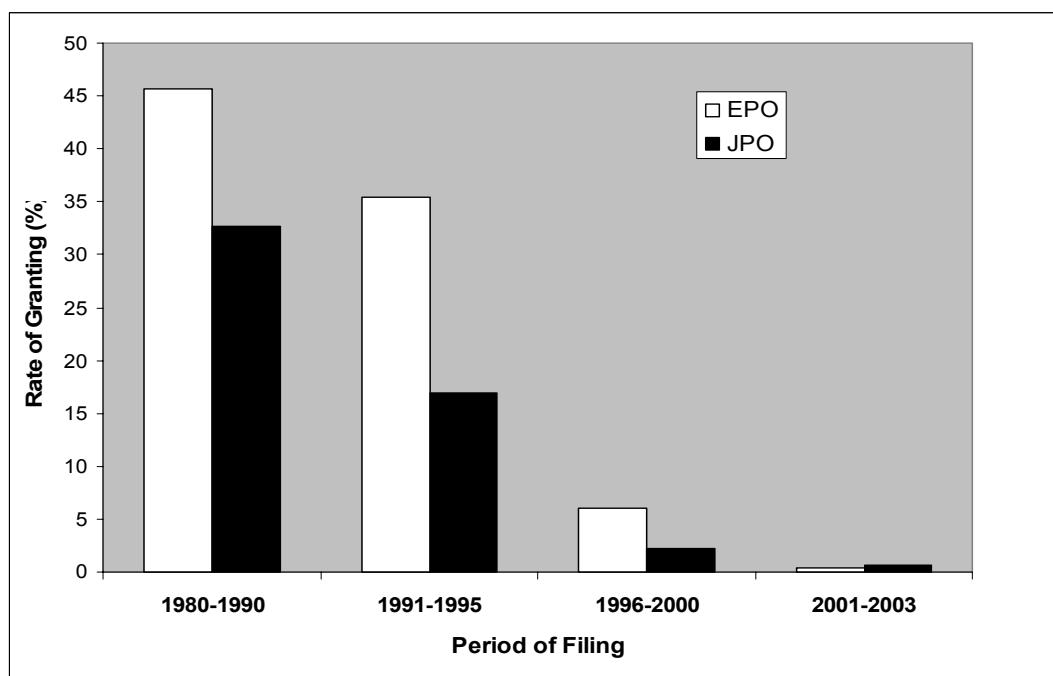
Figure 3. Trends in patent filings related to human DNA, by date of filing.



### 3.1.3 Trends in the rate of granting

Figure 4 shows that there has been a sharp decline in the rate of grant at both the EPO and the JPO. Moreover as of September 2005, patent applications filed during the period 1980-2003 had been granted at differing rates at these two patent offices. The EPO granted around 45% of applications filed in the years 1980-1989 inclusive (128 out of 282 filed) but only 8% of those filed in 1996-2000 (315 out of 4104 filings). The proportions for the JPO were 33% and 2% in the same two time periods.

Figure 4. Rate of granting of patents related to human DNA, by date of filing



For the period 2001 to 2003 we can make comparisons of the rate of granting between the EPO, JPO and the USPTO. This shows that as of September 2005 both the EPO and the JPO had granted less than 1% of patent applications filed in this period, but the USPTO had granted nearly 10% of such applications. However it should be noted these rates will increase as many applications in examination at present will be granted. These granting rates may rise as remaining patents filed in these periods complete their examinations.

### 3.1.4 Legal status of EPO patents that have not been granted

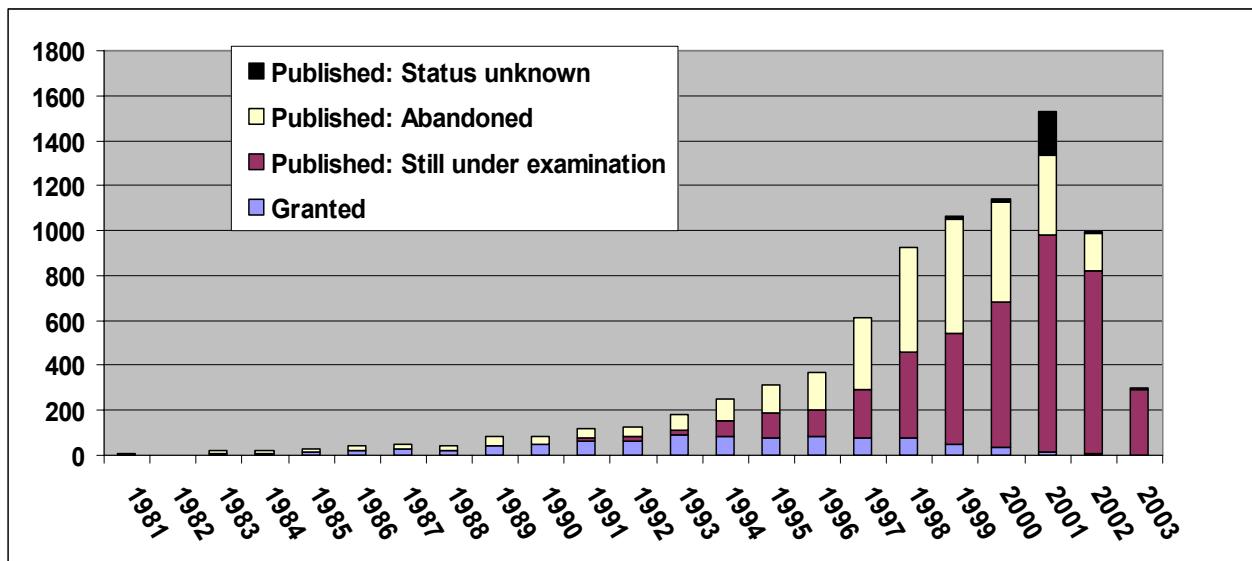
This section explores the fate of individual patent applications at the EPO that were not yet granted in September 2005. It is based on information gathered from INPADOC records as found on Espacenet.<sup>51</sup> Comparative information for USPTO and JPO patents was not available. This analysis complements the information gathered from interviews (see section 3.2.5 below) where assignees were asked to discuss the fate of the applications that had been filed but not granted.

Figure 5 shows the legal status of the 8,278 individual patent applications claiming DNA sequences and filed prior to the end of 2003 at the EPO. The status of the applications is current as of September 2005. Published patent applications are categorised according to whether they were *abandoned* or they were *still under examination*. The former include those that had *expired* (numbering 9 in the whole period 1981-2003), *lapsed* (1), been *refused*, with no further action at the time of analysis (112), and those withdrawn by assignees (2,849). The largest single category is applications that were *still under examination*, numbering 4,179 in September 2005.

<sup>51</sup> [http://ep.espacenet.com/search97cgi/s97\\_cgi.exe?Action=FormGen&Template=ep/en/number.fts](http://ep.espacenet.com/search97cgi/s97_cgi.exe?Action=FormGen&Template=ep/en/number.fts)

Detailed data show that around 250 of these were filed before 1996, i.e. have been under examination for around 10 years or more. Additionally there were 237 patent applications where the status was unknown.

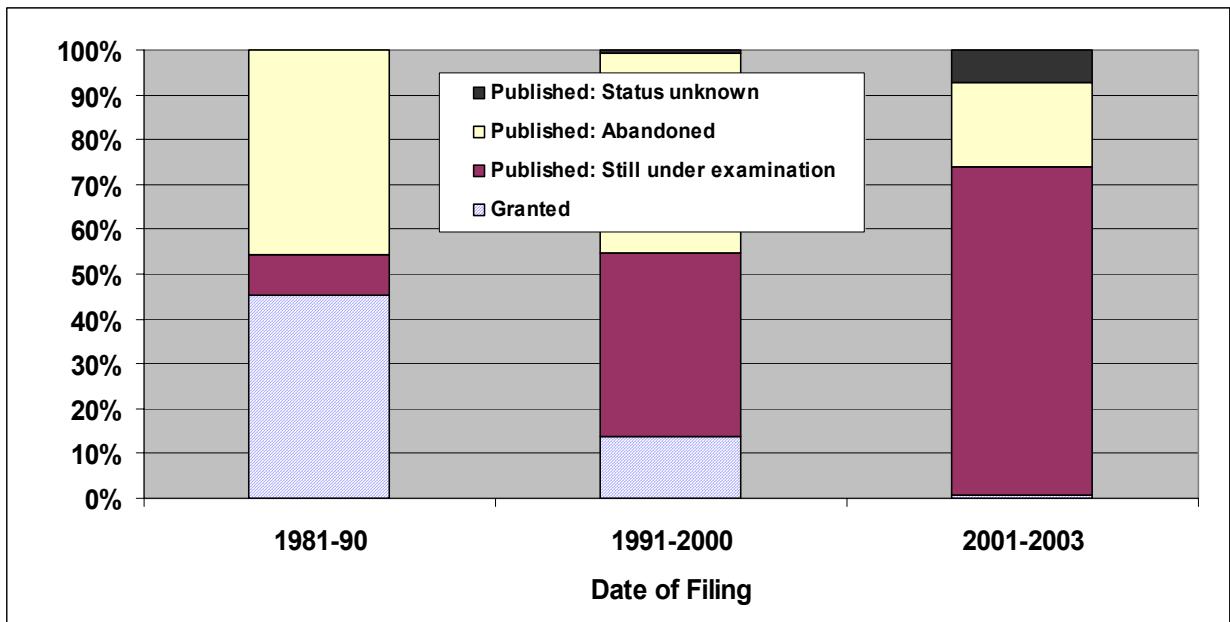
Figure 5: Status of patent applications filed at the EPO between 1981-2003 (as of Sept 2005)



Note: *Abandoned* includes *withdrawn, refused, expired or lapsed*

Figure 6 uses the same data as Figure 5, but expresses the status of patent applications by proportion in for each cohort of filings. It shows that 45% of the 282 patent applications filed during the 1980s had been granted by September 2005, with 25 applications (9%) still open for examination. For applications filed during the 1990s, 14% had been granted and 44% had been withdrawn. The balance of 36% (or 1445 applications) were still under examination. This figure is likely to rise as ongoing examination procedures reach their outcomes.

Figure 6: Status of patent applications filed at the EPO between 1981-2003 (as of Sep 2005): Distribution



### 3.1.5 Legal status of granted patents

The data on the legal status of granted patents comes from two different sources. Information for EPO patents was obtained via the searches of the INPADOC database in Espacenet (already described above) in September 2006. The status of USPTO patents was obtained from the maintenance fee records at the USPTO website through manual searching in early 2006.<sup>52</sup> Comparative data for JPO patents were not available.

The USPTO data in Table 3.1 shows that, unsurprisingly, half of granted DNA patents held in the PATGEN v2 database that had been granted during the 1980s are no longer in force. In part this is because the earliest patents issued on human DNA have reached the end of their term. Of the patents granted in the first half of the 1990s around 70% remain in force, while 90% of those granted in the late 1990s remain in force. In the most recent period covering the early 2000s, over 96% of granted patents remain in force.

<sup>52</sup> Espacenet holds data on the status of EPO patents. These data are available from: [http://ep.espacenet.com/search97cgi/s97\\_cgi.exe?Action=FormGen&Template=ep/en/number.htm](http://ep.espacenet.com/search97cgi/s97_cgi.exe?Action=FormGen&Template=ep/en/number.htm) accessed 23/06/06.

The USPTO holds data for US patents. These data are available from: <http://portal.uspto.gov/external/portal/pair> accessed 23/06/06

Table 3.1: Legal status of DNA patents granted by USPTO

Status (in 2006)	Granting Period			
	1983-1990	1991-1995	1996-2000	2001-2004
In force	34	253	3008	3423
Not maintained	32	104	325	122
Unknown	2	3	8	6
Total patents granted	68	360	3341	3551
% still in force	50.0	70.3	90.0	96.4

The fee structure for maintenance fees in the USA (see Table 3.2) provides some explanation for the attrition rate of older patents as assignees have a financial incentive to abandon granted patents that are not generating significant revenues.<sup>53</sup>

Table 3.2: Schedule of USPTO maintenance fees<sup>54</sup>

Renewal	Cost (\$)
Due at 3.5 years	900
Due at 7.5 years	2300
Due at 11.5 years	3800

Table 3.3 indicates the status of patents granted at the EPO. It shows that a vast majority of such patents were still in force as of September 2005. The proportion of patents granted but currently in opposition is quite small (around 5%). However this gives no indication of the total number of patents that have been opposed in the past as our methodology was focused on current status.

Table 3.3: The legal status of patents granted by the EPO (as of Sep 2005)

	Status of granted patents (by filing period)			
	1980-1990	1991-1995	1996-2000	2001-2003
Expired	12	1		
Lapsed	5	4	1	
Revoked	4	4		
Under opposition at present	2	28	17	
Unknown			2	
Total still in force	153	342	295	20
Total patents granted	176	379	315	20
% still in force	86.9	90.2	93.7	100.0

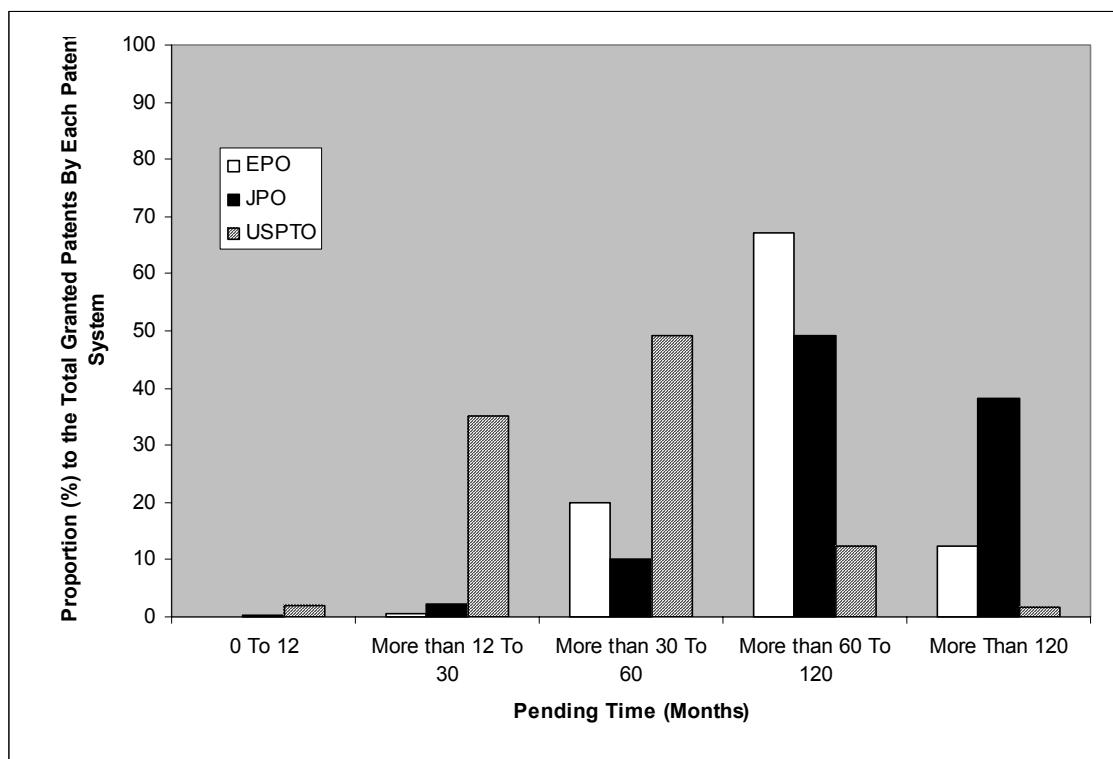
<sup>53</sup> The fees stated in Table 3.2 are indicative, as late fees, reduced charges for smaller entities and attorney fees may all affect the cost of maintaining a patent.

<sup>54</sup> <http://www.uspto.gov/web/offices/ac/qs/ope/fee2004dec08.htm> accessed 23/06/06

### 3.1.6 Time taken to patent grant

Figure 7 shows the time taken from the date of filing to the date of granting (in months) by the three patent offices for all the granted patents in the database. The main point to emerge from this analysis is that the USPTO processes DNA-based inventions at a much faster rate than the EPO or the JPO. Around 50% of granted USPTO patents have been in the system for between 30-60 months, while close to 70% of EPO patents and more than 45% of JPO patents have pending times of 60-120 months. A further 10% of EPO patents and almost 40% of JPO patents have pending times greater than 120 months. However it should be noted that in fact, these could have filing dates that are older than the current form of the patent that is 'open for examination'. This counterintuitive situation arises when patent applications are challenged by examiners for not showing unity of invention and claims subsequently are divided into more than one patent application. Nonetheless, some patent applications genuinely do languish for more than 10 years as prosecutions may be protracted in some cases.<sup>55</sup>

Figure 7. Distribution of pending time\* of granted patents.



Note \*Pending time is the time from the date of filing to the date of granting.

### 3.1.7 Analysis of assignee ownership

Our database showed that over 1200 assignees were involved in filing DNA patent applications in the period 1980-2003. Of these just under two-thirds were firms and

<sup>55</sup> However in some cases these extended periods may reflect assignee decisions to delay responses to PTO enquires or indeed, in Japan, examination may be delayed at the request of the applicant for several years.

over one-third were public sector organisations. The overwhelming majority of these organisations were based in Europe the USA and Japan, with 40% of assignees from the USA, and 26% based in the EU25, with Germany, the UK and France hosting more than half of the EU-25 assignees.

Table 3.4 shows the distribution of patents granted in the three patent systems according to the institutional affiliation of the assignee. It shows that US assignees from the public and private sector are dominant across all patent offices, together accounting for 76% at the USPTO, 55% at the EPO and 39% at the JPO. Conversely both Japanese and EU assignees have captured very small shares of the patents awarded at the USPTO.

Table 3.4 Ownership of DNA-based patent grants at the USPTO, EPO and JPO, relating to patents filed between 1980 and 2003

	USPTO		EPO		JPO	
	Number	%	Number	%	Number	%
<b>US firms</b>	3483	46.0	245	31.7	156	25.3
<b>EU25 firms</b>	729	9.6	128	16.5	50	8.1
<b>Japanese firms</b>	332	4.4	81	10.5	210	34.0
<b>Rest of the world firms</b>	517	6.8	96	12.4	72	11.7
<b>US public sector</b>	2343	31.0	184	23.8	86	13.9
<b>EU25 public sector</b>	312	4.1	76	9.8	28	4.5
<b>Japanese public sector</b>	70	0.9	12	1.6	45	7.3
<b>Rest of the world public sector</b>	376	5.0	49	6.3	30	4.9
<b>Unknown</b>	133	1.8	18	2.3	20	3.2

Figure 8 shows the same data as Table 3.4, divided into time periods to demonstrate trends in ownership over time of USPTO granted patents. This shows that the US private sector have extended its dominance over time, while the share of other groups, particularly the US public sector and the EU-25 public sector has weakened. The chart also shows the decreasing relative strength of the Japanese private sector as compared to the EU-25 private sector.

**Figure 8. Assignee share of granted patents by year at the USPTO**

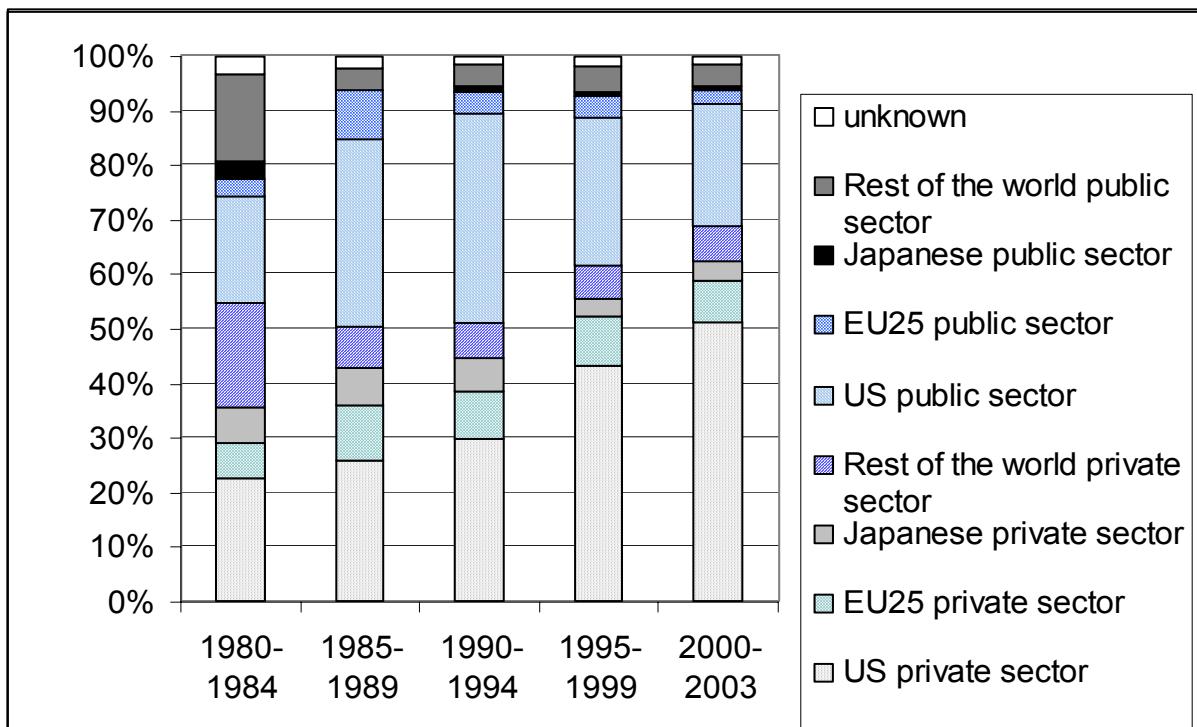


Table 3.5 shows that US biotechnology firms have been the most prolific in terms of ownership of DNA-based patent grants. Three European pharmaceutical firms also appear in the top ten, although for two of them (Roche and Novartis) this is in large part due to their acquisition of US biotech firms. While it is clear that the genomics firms (HGS, Incyte, Millennium and Celera) have filed large numbers of patents and enjoyed substantial success in obtaining granted patents at the USPTO, they have been less successful at the other patent offices. In part this may be due to their young portfolios. However even older biotechnology firms with longer experience in the field such as Amgen have substantially lower numbers of patent grants at the EPO compared to the USPTO. This pattern also appears to be replicated in the experiences of the large pharmaceutical firms. For example, GSK had 162 families with granted patents at the USPTO, while the number of families with granted patents at the EPO was only 15 out of 356 families containing an EPO application. The situation at the JPO is very similar to that at the EPO, with GSK having 298 families with JPO applications, but only one containing a granted patent.

Table 3.6 shows that the top ten public sector assignees with granted patents in this field are all based in the US, with the exception of the Ludwig Inst. for Cancer Research, an international charity with its financial HQ in Switzerland. The pattern of grants for public sector assignees shows the same trend as for the private sector, with far fewer granted patents in the EPO and JPO. However, public sector assignees have achieved notably higher proportions of granted to filed patents at the EPO and JPO compared to firms. Thus for example the top-ten public sector assignees had on average nearly 20% of all patent families with at least one granted patent at the EPO,

against around 6% for the top 10 firms (in Table 3.5). These results need to be interpreted with caution. Biotechnology firms have often been filing patents for a shorter period of time than universities, and so their portfolios may be less mature. Furthermore, because firms file defensive patents to ensure freedom to operate (see section 3.2.4), a greater proportion of their portfolios may be abandoned after filing. Therefore these results do not necessarily indicate that public sector patents are of higher quality (i.e. more likely to be granted) than those filed by the private sector.

Table 3.5. Top ten most active firms according to patent families with granted patents filed between 1980-2003.

Assignee	No. families with GRANTED patents at the USPTO, JPO or EPO	No. families containing GRANTED patents at the USPTO	No. families containing GRANTED patents at the EPO (number of applications)	No. families containing GRANTED patents at the JPO (number of applications)
INCYTE CORP	442	442	4 (513)	2 (485)
HUMAN GENOME SCIENCES	229	219	19 (471)	0 (378)
ISIS PHARM INC	217	217	2 (131)	5 (72)
AMGEN INC	181	165	44 (195)	28 (172)
GLAXOSMITHKLINE	170	162	15 (356)	1 (298)
MILLENNIUM PHARM INC	168	167	3 (286)	0 (94)
ROCHE (including Genentech)	159	140	37 (243)	35 (238)
APPLERA CORP (including Celera)	132	131	1 (178)	0 (70)
WYETH	111	107	16 (184)	10 (163)
NOVARTIS (including Chiron)	103	95	27 (160)	12 (130)

Table 3.6. Top ten public sector assignees by patent families with granted patents filed between 1980-2003.

Assignee	Families with GRANTED patents in the USPTO, JPO or EPO	Number of families containing GRANTED patents in the USPTO	Number of Families containing GRANTED patents in the EPO (number of families filed)	Number of families containing GRANTED patents in the JPO (number of families filed)
UNIV CALIFORNIA	130	125	11 (84)	7 (62)
US DEPT HEALTH & HUMAN SERVICES (including NIH)	111	107	20 (64)	8 (47)
UNIV JOHNS HOPKINS	80	79	9 (66)	5 (53)
LUDWIG INST CANCER RES	79	79	19 (93)	12 (78)
GEN HOSPITAL CORP	60	54	13 (52)	6 (40)
UNIV WASHINGTON	57	55	12 (33)	3 (30)
UNIV TEXAS SYSTEM	49	48	3 (44)	1 (28)
DANA FARBER CANCER INST	47	44	8 (39)	4 (28)
HARVARD COLLEGE	47	46	3 (26)	2 (22)
PARTNERS HEALTHCARE SYSTEM	43	40	5 (27)	2 (21)

### 3.2 Assignees experiences of the exploitation of human DNA patents

In this section we explore assignee responses to questions on the exploitation of human DNA sequences as claimed in patent families. The data in this section was gathered through interviews with 38 individuals from 30 assignees (see section 2.3).

#### 3.2.1 The nature of inventions described in granted patents

To gain an understanding of the types of utility nucleotide sequence patents may provide, assignees were asked to estimate the proportion of their patent portfolios that contained inventions with applications as research tools, diagnostics, therapeutics or ‘other’ applications.<sup>56</sup> All responding assignees reported the utility of some of their inventions as research tools and the majority (14/26) of assignees reported that at least 60% of their patents had utility as research tools. This finding is broadly in agreement with previous research which suggested research tools had become the fastest expanding area of patenting activity in the 1990s.<sup>57</sup> Biotechs and pharma appear proportionately more focused on research tool patents than public sector organisations.<sup>58</sup> Interestingly a relatively low proportion of patents held by pharmaceutical firms were on therapeutics (less than 20% for 6/10 of pharma respondents), perhaps indicating the early stage of the exploitation of this field or their proportionately high focus on research tools. Interest in diagnostics patents varied considerably between assignees, reflecting the diverse range of business models captured by the sample. Few assignees (6/25) reported having any patents claiming DNA relating to inventions other than research tools, therapeutics and diagnostics. 4/6 of these were pharma, with bio-manufacturing of drugs being an important focus.

#### 3.2.2 Reasons for abandoning granted patents

As revealed by searches of patent status at POs (section 3.1.5), a fraction of patents are not maintained for the full duration of their allowable terms. Half (13/26) of those responding (roughly equal numbers across sectors) suggested they expected a proportional increase in the abandonment of DNA patents, while a sizable minority did not expect proportional change in abandonment rates. Table 3.7 shows the main reasons assignees gave at interview for abandoning granted DNA patents and illustrates some differences in their relevance for different assignee groups. A more detailed discussion of these is available in the WP3 project report.

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<sup>56</sup> Individual inventions may have application in multiple categories, indeed one biotech firm stated that their applications were all equally applicable to therapeutics, research tools and diagnostics (B9). However in general assignees were able to make distinctions.

<sup>57</sup> S. M. Thomas, M. M. Hopkins, and M. Brady (2002) ‘Shares in the Human Genome – the future of patenting DNA’ *Nature Biotechnology* 20 (Dec): 1185-1188.

<sup>58</sup> Several interviewees indicated that patenting activity in this area has dwindled over time due to lower market demand, higher utility requirements and reduced chances of claims extending protection from the target to drugs acting on the target (this is discussed in Section 5.4.6).

Table 3.7 Reasons for abandoning granted patents

Reason	Assignee groups
Lack of business case (no longer of internal/external interest)	The single most prevalent reason for pharmaceutical, biotech, and public sector assignees.
Cost cutting	Relevant for a minority of biotech firms and at least one pharmaceutical firm. In general public sector organisations maintain patents only until licensees are found. Licensors will then be responsible for meeting costs.
Scope of claims awarded insufficient	Small minority of pharmaceutical and biotech firms, but also a consideration for public sector firms when reviewing patents to determine future licensing prospects.

### 3.2.3 Disputes over granted patents

Almost all interviewees reported low levels of suspected infringement of their DNA patents, although the extent to which infringement was monitored differed, with the biotechs in the sample appearing to be more vigilant.<sup>59</sup> A small number of firms reported that they were not interested in rigorously enforcing patents against minor infringement such as research usages and that the majority of assignees would only enforce patents when a product of significant value was launched – due to the cost of litigation and the uncertainty of outcomes, particularly in the USA. One assignee suggested resolution was often via cross-licensing arrangements without recourse to financial exchange.

While one large public sector organisation noted that “litigation is a proxy for value” a biotech interviewee suggested that there had been few litigations over patents related to DNA sequence claims. In this context, the biotech interviewee put forward several thoughts, following from the observation that US courts were reigning in the ‘doctrine of equivalence’, meaning that claims were interpreted so narrowly in court that infringement was difficult to prove:

“absence of litigation tells you one of two things: that there really isn't a problem; or 2# there's not a case....it's somewhere in between there I would suspect. And the other important point is that a lot of the sequence information has basically come out in the last maybe eight years or so and, you know, with the product timelines involved in the pharmaceutical industry there's no money been made either way. And it's not until you make money that it is worth fighting over.” (Biotechnology Firm 4)

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<sup>59</sup> A number (5) of highly active public and private sector assignees responded that they did not undertake comprehensive programmes of patent infringement monitoring, with two public sector organisations adding that they are reliant on their licensees undertaking such duties.. Another public sector organisation suggested that their patents were mainly on research tools and that infringement of these was difficult for them to detect.

### *Developments in case law*

A small number of important DNA patent court cases were mentioned by interviewees as being potentially influential in terms of future strategy (see Table 3.8) Three of these are infringement cases from the US, the other an appeal against a USPTO decision. No relevant influential case law was reported from the EU.<sup>60</sup>

The case law in Table 3.8 relates to research tools and suggests that these may potentially allow assignees to appropriate revenues from the downstream products produced by others from upstream patents. However the opportunities to do so may be less than originally expected and appear to be narrowing.

Table 3.8: Important case law raised by interviewees<sup>61</sup>

Case	Details	Implication
<i>In re Fisher</i> Decided by the US Court of Appeals for the Federal Circuit in September 2005	Monsanto attempted to overturn the USPTO's rejection of a patent based on ESTs. The Federal Circuit upheld the USPTO's decision to reject Monsanto's patent for lacking utility and enablement.	Millions of ESTs filed at the USPTO have been withdrawn on the basis of rulings that put their patentability in doubt. This case was the first test of the strengthened utility requirements put in place by the USPTO in 2001.
Merck KgaA v. Integra Decided by the US Supreme court in June 2005	Merck KgaA claims safe harbour against patent infringement - an exemption for those conducting research related to testing of new drugs. US supreme court supports Merck KgaA, overturning a previous ruling by the Court of Appeals for the Federal Circuit (CAFC) in Integra's Favour.	Increased uncertainty for biotechnology firms attempting to enforce IP related to research tools for drug discovery and development work
Pfizer v. University of Rochester Decided by the United States Court of Appeals for the Federal Circuit in February 2004.	The University of Rochester failed to overturn a trial court decision in favour of Pfizer, in their attempt to sue Pfizer for infringing the University of Rochester's patent on the Cox-2 receptor. The patent was invalidated for not inventing or disclosing inhibitor molecules.	This case reinforced USPTO policy that patent claims on research tools do not extend from a drug target to the product unless the assignee has demonstrated these credibly and specifically. The extension of claims from target molecules to exclusive commercialisation of drugs acting on those targets is known as 'reach-through'.
Ariad v. Lilly Decided by the United States District Court for the District of Massachusetts in May 2006	Ariad successfully sued Lilly for launching drugs acting on the NF-κB pathway without licensing Ariad's patent on NF-κB. The court awarded Ariad a royalty of 2.3% of Lilly's revenues from the infringing products.	Research tool patent claims <u>can</u> extend (reach-through) to encompass the exclusion of small molecules if sufficient disclosure has been made by the assignee in their patent.

<sup>60</sup> At present the only case of note by interviewees brought before a court in Europe (heard in the UK) was Kirin-Amgen Inc and others (Appellants) v. Hoechst Marion Roussel Limited and others. However in this case the key points of the case were not thought to be as relevant with regard to DNA patenting as the US cases described in Table 3.8.

<sup>61</sup> Synthesis in 'case' and 'details' based on accounts of cases at <http://patentlaw.typepad.com> Synthesis in 'implications' based on discussions with assignees.

### 3.2.4 Modes of exploitation of patent families seeking to claim DNA sequences

The exploitation of claimed inventions may take several forms, and does not necessarily rely on patents being granted. To explore the prevalence of strategies utilising different modes of exploitation, interviewees were asked to estimate the proportion of their relevant patent families that had undergone particular forms of exploitation.<sup>62</sup>

#### *Development/commercialisation of products/services*

The majority (16 of 25) of respondents were yet to develop or commercialise most of their DNA patent families. Assignees with large portfolios (those above the median) were just as likely as those with small portfolios to report low rates of exploitation. Only five assignees (2 biotechs, 2 public sector groups and one pharma) had begun to commercialise the majority of their portfolio (>60%). A small majority (14 of 25 assignees) expected the proportion of their patents supporting products or services to rise in the next five years.

#### *Use of patents to ensure freedom to operate*

Filing patents to ensure ‘freedom to operate’ involves making patent applications to spoil competitors’ chances of excluding others from commercialisation opportunities, without necessarily wishing to enforce the resulting patent. The majority (15/26) of respondents held very few patent families for this purpose (i.e. <20%). While public sector respondents did not engage in this strategy a minority of biotech firms and five of the nine pharmaceutical firms that gave answers suggested this was a very significant part of their motivation to file. Thus freedom to operate is probably an important motivation in a sizable proportion of DNA patent filings, but the exact magnitude of its importance is impossible to quantify from the data gathered here. Respondents made a number of important points suggesting: that such applications are viewed as having served their purpose as soon as they are published by the patent office and therefore can be abandoned before granting (see Section 5.4.2); that patent applications were no longer the only trusted route to achieving that aim; and that, biopharmaceuticals might become an increasing area of freedom to operate patenting. Most (15/25) expected no change in their freedom to operate filing policies in the future, although four pharma firms indicated a decrease in such activity, a number of assignees (including 3 biotechs, a pharmaceutical firm and a public sector organisation) expected freedom to operate to become a more prominent strategy for their organisation.

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<sup>62</sup> In almost all interviews, interviewees were provided with advance notice of the quantitative questions. Due to time constraints interviewees were asked to estimate rather than calculate their responses where these related to a percentage. Of the 27 respondents 22 indicated that they felt their responses were confident estimates, while five were less confident (two public sector organisations, two biotech firms, and one pharmaceutical firm). Three of the 30 assignees did not provide data in answer to quantitative questions.

### *Out-licensing (exclusively or non-exclusively)*

Licensing of DNA patents appears to be more successfully pursued by the public sector than by firms (although all but one of the not-for-profit assignees had portfolios below the median size for the sample of assignees overall). Nearly all responding pharmaceutical firms had licensed less than 20% of their DNA patents. Biotech firms had quite variable rates of licensing, presumably as a function of their diverse business models. A large minority of assignees (12/27) reported that they would undertake more licensing in the next five years, and a similar proportion reported that there would be no change. Biotech firms were more likely than pharmaceutical firms to expect increases in out-licensing.

### *Assignment of patents*

Assignees indicated that assigning patents to other organisations is something that most organisations, regardless of mission, do very rarely in this field. 13/27 had not assigned patents, and 13/27 had assigned in less than 19% of cases (with several interviewees commenting that it was low numbers). More generally, US public sector organisations noted that where inventions derived from federal funding, in whole or in part, the conditions of such funding under the Bayh-Dole Act meant that the patent could not be assigned to third parties (only exclusively licensed) as the state retains 'march-in rights'.<sup>63</sup> The overwhelming majority (21/27) of assignees did not expect the rate of assignment to change significantly in the short term.

### *Collective exploitation of IP via patent pools*

Concern has been expressed in recent years over the fragmentation of potentially valuable research fields due to the patenting of inventions of mutual interest by different assignees.<sup>64</sup> One solution to such problems successfully applied in other industries (such as electronics) is the patent pool.<sup>65</sup> Of those responding, 25 out of 27 assignees had no pooled DNA patents and the majority (15/26) did not anticipate this changing in the next five years, although six (mainly public sector organisations) did expect to undertake patent pooling in the future. A number of interviewees raised a range of barriers to patent pooling, such as previous licensing agreements, the need to raise significant revenues to justify maintaining patents, and scepticism over the

<sup>63</sup> The relevant text of the Bayh-Dole Act is available from:

<http://www.cptech.org/ip/health/bd/35usc203.html> accessed 23/05/06

<sup>64</sup> T. J. Ebersole, M. C. Guthrie & J. A. Goldstein (2005) 'Licensing problems with diagnostic genetic testing' *Genetic Engineering News* 25 (9) May 1

<sup>65</sup> Ebersole et al (2005) define as follows: 'A patent pool is an arrangement in which two or more patent owners agree to license certain patents to one another and/or third parties.....The pool members should issue nonexclusive licenses to the pooled patents at reasonable non-discriminatory royalties and allow pool members to offer licenses to one or more of their own pooled patents outside of the pool structure.' Several interviewees requested a definition of the term patent pool and were given a less precise definition such as 'a consortium whose members share patents'. Further clarifications excluded simple unilateral licensing of multiple patents to the same party and simple bilateral (cross-licensing) agreements, whilst emphasising multi-party schemes.

workability/suitability of pools in molecular genetics, bar key techniques such as PCR.

### 3.2.5 The fate of patent applications not granted to date

Interviewees were asked to estimate the proportions of their patent portfolio that had not been granted to date in the field of nucleotide sequence patenting that fell into the categories: withdrawn/ abandoned, awaiting examination, at examination or passed examination/awaiting grant. These questions (Section C of the questionnaire in Appendix A), which focused on the proportion of the sum of individual patent applications at the USPTO, EPO and JPO posed significant difficulty for a number of assignees, and indeed it was suggested by more than one assignee that they implied a linearity in the patent prosecution system that did not reflect reality. As a result only 15 interviewees could respond to questions in Section C with confident estimates, while 10 gave uncertain estimates (four pharmaceutical firms, four biotechs and two public sector organisations). From the answers of those responding, no apparent difference between the public sectors', biotechs' or pharmaceutical firms' propensity to withdraw applications emerged – however, half (13/26) of respondents suggested that at least 40% of their DNA patent applications had been withdrawn.

Assignees were asked to state the most common reasons for their patents to be abandoned/ withdrawn. It is clear that there are a broad range of reasons for the abandonment of DNA patents after application, especially in those firms that have been highly active in this field, perhaps most notably the pharmaceutical firms. These include the full range of rejections based on patentability issues from patent offices (i.e. novelty, enablement, utility etc.). Nonetheless assignee responses cluster around a number of themes, summarised in Table 3.9. These themes are more fully discussed in the WP3 project report.

Table 3.9 Dominant reasons for abandonment of pending patents

Difficulty in demonstrating utility/ industrial applicability	Common reason, given by around a third of assignees. Affects a minority of assignees interviewed across sectors.
Lack of business case (e.g. the invention was not as promising as expected, could not be licensed, failed in development)	Common reason, given by around a third of assignees. More commonly cited by public sector organisations, but affecting all sectors.
Cost cutting – especially for non-US patent applications	Common reason, given by around a third of assignees. More commonly cited by public sector organisations and biotech firms.
Invention rejected by patent office due to lack of novelty	Affecting a minority (5/20) of private sector assignees
Freedom to operate – achieving a granted patent was not essential to protect the assignee's interests.	A minority (4/10) of pharmaceutical firms suggested this was the most significant motivation for withdrawing filings.

### 3.2.6 Assignees' perspectives on the challenges faced by patent offices

Assignees identified a number of historical problems faced by patent offices following the emergence and subsequent growth of DNA patenting activity. Some problems remain to be fully addressed, as discussed below, but around a third of assignees suggested there had been improvements or that these issues had been “mainly resolved”, or “removed”, with the exception of political pressures not to grant DNA patent applications.

#### *Patent office funding and dynamics of new fields of IP*

The response of patent offices to nucleotide sequence patenting, has to be set against their institutional context including the funding environment. A wide range of interviewees raised particular challenges associated with the emergence of new fields and DNA patenting in particular. These included: insufficiency of funding at the USPTO; having to keep pace with an advancing state of the art; the environment for hiring/training new staff; and providing an appropriate patentability bar while learning particular details of an emerging field.

#### *Volume of filings*

The volume of applications was cited by a fifth of assignees as a challenge for the patent offices. The rate of patent filing in the 1990s was described by more than one assignee as a “flood” and “overwhelming”. However, in general there was no consensus amongst interviewees as to whether the problem posed by this rise in volume had passed or was passing. Interviewees reported backlogs at the EPO, USPTO and JPO. Many of these applications were seen as frivolous by both private sector and public sector interviewees.

#### *Complexity of cases*

Patents claiming DNA sequences were thought by several (4) interviewees to pose particular problems of complexity for examiners, placing a “tremendous amount of work” on patent office staff. Firstly, the sheer amount of material examiners needed to read for each application was seen as being arduous, and different assignees described how a hard copy of some applications could fill several large crates, or how the prior art relevant to a single sequence might be a stack of paper “half a metre off the desk”. Attempts to resolve such difficulties have been ongoing since the start of the 1990s.

#### *Political pressure against granting DNA patent applications*

Public debate was noted to be continuing around DNA patenting and, some suggested that poorly informed debate was having an adverse effect on the field. Over a third of private sector interviewees mentioned their suspicions that political rather than technical factors were influencing the examining outcomes for DNA patents at the USPTO and EPO. In Europe the EPO and national governments such as in France, Switzerland and Germany were all suggested as instituting their own discriminatory practices affecting the interpretation and enforcement of patents related to human genetic material by a number (3) of assignees. As a result, there was concern that the

criteria for patentability were being judged too tightly at the EPO or that European patents will not be enforced nationally in some countries. A common view amongst a minority of private sector respondents is reflected in the quote from one pharmaceutical executive: “It is much easier to get a use claim for a chemical compound than for a cDNA” (Pharmaceutical Firm 6)

#### *Co-ordination between the Triad patent offices*

A small number noted that initial differences between the way in which the USPTO, EPO and JPO would judge similar cases had been problematic because it was difficult to tailor the scope of inventions for different patent offices if the same application was to be filed internationally (for example by those assignees using the PCT system). However a larger number suggested these problems had largely been resolved. Assignees had followed tri-partite discussions between patent offices (for example in areas such as the inventiveness of automated/ computer generated inventions from sequence analysis) and this allowed them to understand the different offices’ stance more clearly. Nonetheless one public sector interviewee did suggest that an undesirable aspect of close ties seemed to be the adoption of measures that were not accompanied in their new context by the checks and balances found in the old. For example, the EPO was noted to be making more unity objections in the style of the USPTO, whilst at the same time not facilitating ‘continuation in part’.

#### 3.2.7 Challenges for assignees in obtaining patents

The task of the examiner is to question the assignee’s claims and to help the assignee to make clear where there is justification for their claims (the criteria applied are broadly similar between the US, European and Japanese patent offices). In doing so the examiner seeks to ensure the patent meets the criteria for patentability (US term in brackets):

- The invention is not disclosed in the prior art (novelty)
- There is an inventive step (non-obvious)
- The invention has an industrial application (~ utility)
- The inventor has shown sufficiency in their disclosure (enablement/ written description)

The challenges faced by assignees are therefore mainly related to these criteria are summarised in Table 3.10. A more detailed review of assignee perspectives is available in the WP3 project report. Overall, it was noted by some assignees that the more strict approach of the patent system in DNA patenting that Table 3.10 outlines was suggested to be less of a disadvantage to the established drug developers than for other assignees, particularly biotech firms.

Table 3.10. Main challenges for assignees in obtaining DNA patents<sup>66</sup>

Theme	Key issues
Unity of invention	Approximately a third of assignees were concerned that unity of invention objections were increasing. Some thought this a patent office reaction to 'bulk filing' applications containing many sequences, however with the emergence of biomarker/ gene expression profiling patents there is a feeling that legitimate inventions are being affected.
Industrial applicability/ Utility	A minority of assignees noted the utility/ industrial applicability bar had been raised since 2001. Although this was welcomed, some felt retrospective application had unfairly affected high-filing assignees that were active in the early genomics era.
Sufficiency/ enablement	Assignees noted that patent offices now required more data to support claims and that speculation was no longer sufficient. A quarter of interviewees noted the scope of claims awarded was narrowing, with more room for new applicants to invent around prior inventions.
No prior art/ Novelty	A quarter of assignees reported difficulties in achieving novelty as the body of prior art in the field grows.
Inventive step	A quarter of private sector of assignees suggested that the inventive step at the EPO has been raised. In some cases it is felt that the contribution of inventions is going unrewarded.

### 3.2.8 Assignees' views on overall trends in nucleotide sequence patenting

This section describes trends in the patenting of subject matter related to nucleotide sequences and trends relating to prosecution. Assignees were asked to identify emerging or future trends and were encouraged to interpret the question as broadly as they wished. Given the size of some of the organisations interviewed and the diversity of activities of the sampled assignees, it is perhaps not surprising that little overall consensus emerges on trends in subject matter, nonetheless a clustering of views formed around a small number of issues. These are summarised in Table 3.11, where they are divided into technical and legal trends. A more detailed discussion of future trends may be found in the WP3 project report.

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<sup>66</sup> The discussion is focused more on the USPTO than on the EPO or JPO because many assignees had more experience of the USPTO because 1) US organisations dominate DNA patent filing and they file in the USA first 2) the US is the largest market for DNA inventions 3) EPO and JPO patents take longer to each examination.

Table 3.11. Key trends in nucleotide sequence patenting

Trends in technical subject matter patented	<p>A quarter of assignees suggested that in future there would be a reduced volume of nucleotide related filings, but patenting is expected to continue in a number of areas.</p> <p>Several (5) respondents suggested that patents claiming new applications for known sequences would replace patents on novel sequences to a large extent.</p> <p>A third of respondents expected increasing patenting of SNPs and other sequence variations, often with diagnostic utility and especially in the field of pharmacogenomics/ pharmacogenetics.</p> <p>Several (7) assignees discussed the recent emergence of patents claiming biomarkers using gene expression profiling. There was concern that these might not be allowed by patent offices, due to challenges on unity of invention or sufficiency.</p> <p>Increases in patents claiming new bio-therapeutic modalities such as RNAi and gene therapy were discussed by a number of respondents (5). There were concerns that assignees might not obtain sufficiently broad claims to support investment.</p>
Trends in legal matters	<p>Some assignees (5) have noted a greater requirement for biological data to support patent claims by patent offices</p> <p>Some assignees (6) are receiving narrower claims and expect to receive more narrow claims in the future</p> <p>Assignees could not give a firm indication of trends in litigation, especially in Europe.</p>

### 3.2.9 Assignee strategies

As the field of DNA patenting has developed a range of commercially valuable applications were pursued by assignees including:

1. DNA sequences encoding proteins with therapeutic application (e.g. tissue plasminogen activator)
2. DNA sequences encoding proteins that could be targeted by monoclonal antibodies (e.g. Her-2 and Herceptin)
3. DNA sequences encoding proteins that could be targeted by small molecule drugs (e.g. receptors such as Cox-2 or NF- $\kappa$ B)
4. DNA sequences associated with diseases or drug metabolism where diagnostic/ prognostic tests could be developed (e.g. the enzyme Thiopurine Methyltransferase)
5. Nucleotides that could inhibit gene expression (RNAi, antisense)
6. Sequences that could be replaced/ inserted to correct/ improve disease conditions (gene therapy)

Options 1-4 were widely pursued by assignees participating in the PATGEN study, while option 5 was discussed as an emerging area by a handful of assignees. Option 6

was mentioned only briefly by three assignees and viewed as a more distant prospect. Of the more widely pursued commercial options, options 2 and 3 attracted the most discussion. These also appear to be the areas where strategies have changed most in recent years. Option 1 remains an area of high interest, although the exploitation of “druggable” proteins is seen as highly competitive. Option 4 is an area of continued interest as hopes of discovering diagnostically valuable genes have joined with hopes of finding diagnostic and prognostic biomarkers based on multiple SNPs or gene expression profiles.

It is interesting to note that older integrated biotechnology firms and younger genomics firms have extended their focus from options 1 and 2 to include option 3 – thus competing more directly with pharmaceutical firms.<sup>67</sup> Table 3.12 highlights key themes around assignee strategy. A more detailed discussion of assignee strategies is available in the WP3 project report.

Table 3.12 Key themes in assignee strategy

In the genome rush (from the late 1990s onwards) a race to file patents while their subject matter remained novel resulted in many premature applications by both public and private sector assignees.
The genome rush provoked filing to ensure freedom to operate on drug targets by established drug developers, but this is no longer a prime motivation to file as alternative approaches to publication have become established.
The filing of DNA patents has reduced, especially in the area of research tools as patent office restrictions on patentability and claims have reduced the value of many DNA patents, for example by limiting reach-through claims from drug targets to therapies acting on those targets to molecules disclosed in the patent application. <sup>68</sup>
The vast majority (13 vs 3) of those assignees who gave information about their future strategies revealed they would continue to file patents in this field.
The balance of costs and benefits, as well as the challenges of examination have led assignees to pursue fewer applications at the EPO and JPO than at the USPTO. Therapeutics are also more likely to be pursued than diagnostics and research tools.

<sup>67</sup> H. Rothman and A. Kraft (2006) ‘Downstream and into deep biology: Evolving business models in ‘top tier’ genomics companies’ *Journal of Commercial Biotechnology* 12(2) January, pp86-98.

<sup>68</sup> See trilateral study on research through claims at [http://www.trilateral.net/projects/biotechnology/reach\\_through\\_claims/](http://www.trilateral.net/projects/biotechnology/reach_through_claims/)

#### 4. Policy conclusions and recommendations

Encouraged by the success of early patents protecting drugs produced using recombinant DNA technology (e.g. erythropoietin for the treatment of anaemia) researchers have filed thousands of patent applications claiming human DNA over the past two decades. There has been wide speculation about the potential impact of these filings on research, innovation and access to healthcare. In particular, concerns about possible restrictions on the free exchange of information between researchers, increases in the cost of diagnostics and treatments, and hindering of the development of new or improved medicines have attracted the most attention in recent years.<sup>69, 70, 71</sup> A small number of specific studies have provided some insights into the extent of these impacts.<sup>72, 73, 74, 75, 76, 77</sup> Nonetheless it may be too early to fully address these questions, and further studies will be required to assess these impacts as patent grants increase. However sufficient time has now elapsed to allow us to address an important prior question relating to the scale of impact of these filings, using a methodology that allows a comparative approach between the granting of DNA patents on human sequences at the USPTO, EPO and JPTO.

As set out in section 3, this report provides an overview of key trends in the filing, granting and ownership of DNA patents over time, as well as detailed assignee perspectives. In this section (4) the implications of these findings are explored.

##### 4.1 Rationale for Patenting DNA

The data in section 3.1 shows the dynamics of DNA patenting since 1980. There was substantial interest from early commercial success in the 1980s, with JPO and EPO patent filings doubling every two to three years during the 1990s, until the time when the Human Genome Project and other efforts put substantial amounts of sequence data in the public domain. Inventions claiming DNA *per se* and applications as therapeutics (including vaccines) were joined rapidly by inventions based on the diagnostic or research uses of DNA (research tools), particularly as the 1990s progressed.

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<sup>69</sup> M. A. Heller & R. S. Eisenberg (1998) Can patents deter innovation? The anticommons in biomedical research. *Science* **280**, pp. 698–701

<sup>70</sup> Nuffield Council on bioethics (2002) The ethics of patenting DNA: a discussion paper, London. Available at: [http://www.nuffieldbioethics.org/publications/pp\\_000000014.asp](http://www.nuffieldbioethics.org/publications/pp_000000014.asp)

<sup>71</sup> G. Matthijs (2004) Patenting genes BMJ 329 pp.1358-1360

<sup>72</sup> J. Merz, A. Kriss, et al (2002) Diagnostic testing fails the test. *Nature* 415. pp.577-579.

<sup>73</sup> M. K. Cho, S. Illangasekare, M. A. Weaver, D. G. Leonard, & J. F. Merz, Effects of patents and licenses on the provision of clinical genetic testing services. *J. Molec. Diagn.* **5**, 3–8 (2003).

<sup>74</sup> J. P. Walsh, C. Cho, and W.M. Cohen (2005) View from the bench: patents and material transfers, *Science* 309 23 September. Pp. 2002-2003.

<sup>75</sup> National Academy of Sciences (2005) Reaping the benefits of genomic and proteomic research: intellectual property rights, innovation and public health, National Academies Press, Washington D.C. Available at: [www.nap.edu/catalog/11487.html](http://www.nap.edu/catalog/11487.html)

<sup>76</sup> S. Hansen, A. Brewster, J. Asher (2005) Intellectual property in the AAAS scientific community, AAAS.

<sup>77</sup> S. Stern, and F. E. Murray "Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge? An Empirical Test of the Anti-Commons Hypothesis" (July 2005). NBER Working Paper No. W11465. Available at SSRN: <http://ssrn.com/abstract=755701>

The surge of patents in the 1990s reflects the business models of the time, including those focusing on the commercial value of DNA sequences for diagnostics or as novel drug targets. Research tools, often related to drug targets appear to have provided a motivation to file a large proportion of patent applications in the field. These were filed by firms seeking to license such tools to drug developers or filed by drug developers to ensure freedom to operate. In response to concerns that patents on drug targets might prohibit downstream exploitation without a license, this study suggests some drug developers hastened to patent targets to ensure they could maintain their freedom to operate. This in turn has contributed to the inflation in patenting that has caused alarm in some constituencies.

Attempts by researchers to obtain rights on speculative claims led to calls for the thresholds for patentability to be raised.<sup>78</sup> Data in section 3.2.7 suggests that since 2001, when the USPTO issued new guidance,<sup>79</sup> utility, enablement and sufficiency have been more stringently enforced by patent examiners at the USPTO, with similar approaches adopted elsewhere.<sup>80</sup> According to assignees, this guidance has had an impact both on their propensity to file applications and on their rate of success at examination, as a result patenting strategies to secure freedom-to-operate, and protect research tools both were reported to be on the decline by interviewees. Nonetheless DNA patent applications are widely expected to continue to be filed. In particular new areas such as pharmacogenetics, RNAi and gene expression profiling are emerging. However the nature of these filings can be expected to be different from early patents on DNA *per se*. Claims sought and awarded are likely to be narrower, inventors will be expected to provide more supporting data, and often the DNA claimed will be a supporting part of an invention rather than the main focus (e.g. demonstrating reduction to practice).

We note that the biotechnology directive (EC 98/44) requires Member States and the EC to promote international dialogue and cooperation to encourage a level playing field with industrialised countries in patent protection on biotechnology inventions. In practical terms this means that continued collaboration between the patent offices through trilateral meetings is necessary to ensure that new forms of DNA-based inventions receive consistent examination in different regions in areas such as gene expression profiling and RNAi.

While interest in research tools may be diminishing, the emphasis on patenting therapeutics remains strong. However the commercial rationale for patenting diagnostics is less clear. Certainly there is continued interest in diagnostic applications as SNPs and gene expression profiles open up new prospects on previously-described genes. However, in general there are few models of commercial success for DNA-based diagnostics and one case, BRCA, has dominated discussion in the field by focusing attention on the disadvantages of patents on DNA-based diagnostic inventions. The cost of developing genomics-based diagnostics is substantial, with

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<sup>78</sup> Nuffield Council on Bioethics (2002) The Ethics of Patenting DNA: A Discussion Paper (London).

<sup>79</sup> FR Doc 01-322, Federal Register Vol. 66 No. 4 Friday January 2001, Available at <http://www.uspto.gov/web/offices/com/sol/notices/utilexmguide.pdf>

<sup>80</sup> European Patent Office, Japanese Patent Office and US Patent and Trademark Office. Report of the Trilateral Project B3b from the European, Japanese and US Patent Offices. (Nov 2001) annex 2. p.43. Available at: [www.European-patent-office.org/tws/report\\_start\\_page.htm](http://www.European-patent-office.org/tws/report_start_page.htm)

more complex tests requiring large-scale trials.<sup>81</sup> While it is likely that development costs for diagnostics will remain below those of drugs, assignees must balance the costs of securing global IP protection and development costs against the expected revenues in a sector where the evidence base and new markets can be slow to develop.

We accept that diagnostic patents should continue to be awarded where these meet the criteria for patentability. The credible threat of courts denying injunctive relief to infringed parties or granting a compulsory license needs to be explored as an incentive to encourage reasonable licensing practice and research use.<sup>82</sup> However these sanctions should not be used without regard for the costs of development and scientific contribution of the disclosed invention, as more complex and costly diagnostic tools may arise from current avenues of research.

#### 4.2 The impact of patenting DNA on research

The extent to which research is impeded by DNA patenting might be expected to vary regionally according to local exemptions to patent holder's monopoly that allow research on the subject matter in disclosed inventions. Japan has a statutory research exemption as part of its patent law. Australia, Canada, New Zealand and USA have no research exemption in statute. In the EU, Article 27(b) of the Community Patent Convention provides a research exemption that is statutory in most EU member states, although the interpretation varies nationally.<sup>83</sup> At present there is little evidence on the nature or scale of deleterious effects that the absence of a research exemption brings nor the optimal mode of provision for such exemptions.<sup>84</sup> Commentators have suggested that with no research exemption and higher levels of DNA patenting, the impact of DNA patenting should be most notable in the USA.<sup>85</sup> However, recent studies have concluded that there has been little impact on academic research from patenting in the biotechnology field.<sup>86,87</sup> This may be in part because researchers ignore existing patents as, despite the *Madey v Duke* decision that clarified academic research may be liable to infringement, surveyed academics often did not search for patents that their research might infringe.<sup>88,89</sup> Where researchers do explore licensing

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<sup>81</sup> M Baker (2006) New-wave diagnostics *Nature Biotechnology* Vol. 24 no.8 August pp.931-938.

<sup>82</sup> National Academy of Sciences (2005) Reaping the benefits of genomic and proteomic research: intellectual property rights, innovation and public health, National Academies Press, Washington D.C. Available at: [www.nap.edu/catalog/11487.html](http://www.nap.edu/catalog/11487.html)

<sup>83</sup> C. Dent, P. Jensen, S. Waller and B. Webster (2006) Research Use of Patented Knowledge: A Review (OECD Directorate for Science, Technology and Industry Working Paper)

<sup>84</sup> C. Dent, P. Jensen, S. Waller and B. Webster (2006) Research Use of Patented Knowledge: A Review (OECD Directorate for Science, Technology and Industry Working Paper)

<sup>85</sup> M. Stott, J. Valentine (2004) Gene patenting and medical research: a view from a pharmaceutical company *Nature Reviews Drug Discovery* 3 (4) p.364-368.

<sup>86</sup> J. P. Walsh, C. Cho, W. M. Cohen (2005) View from the Bench: Patents and Material Transfers. *Science* 309 23 September 2002-2003.

<sup>87</sup> National Academy of Sciences (2005) Reaping the benefits of genomic and proteomic research: intellectual property rights, innovation and public health, National Academies Press, Washington D.C. Available at: [www.nap.edu/catalog/11487.html](http://www.nap.edu/catalog/11487.html)

<sup>88</sup> C. Dent, P. Jensen, S. Waller and B. Webster (2006) Research Use of Patented Knowledge: A Review (OECD Directorate for Science, Technology and Industry Working Paper)

<sup>89</sup> J. P. Walsh, C. Cho, W. M. Cohen (2005) View from the Bench: Patents and Material Transfers. *Science* 309 23 September 2002-2003.

opportunities, more negative effects are reported although industrial researchers rather than academic researchers reported a greater disruption to their activities from IP.<sup>90</sup>

However any inhibitory effects of DNA patenting on industrial drug discovery may be reduced as a result of the ‘safe harbour’ use supported by the US Supreme Court in *Merck v Integra* in 2005. It may be that in general Material Transfer Agreements (MTAs) and scientific competition will have a greater impact on scientific progress than patenting.<sup>91, 92</sup> This is not to deny that DNA patenting may have some negative effects if levels of enforcement are increased. Indeed working around DNA-based inventions may be less practical than in other fields, and so an adequate research exemption may be more important in the biosciences than elsewhere.<sup>93</sup> Some interviewees suggested that patent enforcement could grow as revenues expand, suggesting these negative impacts may become more of a concern in the future. However the costs of litigation and uncertainties surrounding court decisions mean that assignees are unlikely to enforce their patents against infringement for research use where a marketed product is not threatened.

There is little evidence suggesting research is adversely affected by DNA patenting at present, although the evolution of case law and growth in patent numbers may change this over time. This situation should continue to be monitored especially in regions where the research exemption is poorly defined or not established.

#### 4.3 The impact of patenting DNA on innovation

The perceived importance in recent years of patents on DNA is evident from the broad range of private sector assignees identified in this study as being engaged in DNA-patenting (to a greater or lesser extent). These included 92 pharmaceutical firms, 572 biotechnology firms and 126 firms from other sectors such as food and beverages, and electronics/equipment. The scale of DNA patent applications pursued through to patent granting amongst biotechnology and pharmaceutical firms in particular demonstrates the importance they have placed on this field. The presence of such IP is viewed by industry as essential to promote investment in biotechnology, particularly in drug development where costs are high.<sup>94</sup> However interviews revealed that initial optimism has been followed by re-appraisal of value and a scaling back of inventions pursued. This is in part due to the complexity of genes and their interactions in disease processes; the more rigorous enforcement of patentability criteria by patent offices; and limitation, by case law and patent office guidelines, of reach through claims.<sup>95</sup> It would appear that in the future, the value of DNA- related

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<sup>90</sup> S. Hansen, A. Brewster, J. Asher (2005) *Intellectual property in the AAAS scientific community*, AAAS.

<sup>91</sup> S. Hansen, A. Brewster, J. Asher (2005) *Intellectual property in the AAAS scientific community*, AAAS.

<sup>92</sup> J. P. Walsh, C. Cho, W. M. Cohen (2005) View from the Bench: Patents and Material Transfers. *Science* 309 23 September 2002-2003.

<sup>93</sup> K. N. Cukier (2006) Navigating the future(s) of biotech intellectual property *Nature Biotechnology* 24 (3) March pp.249-251.

<sup>94</sup> M. Stott, J. Valentine (2004) Gene patenting and medical research: a view from a pharmaceutical company *Nature Reviews Drug Discovery* 3 (4) p.364-368.

<sup>95</sup> See Table 3.8 for discussion of case law and the following link for trilateral discussion by patent offices on reach through claims:

[http://www.trilateral.net/projects/biotechnology/reach\\_through\\_claims/](http://www.trilateral.net/projects/biotechnology/reach_through_claims/)

claims will be more often as an element of a product, rather than the product itself with regard to therapeutics (with some notable exceptions). Nonetheless some respondents suggested that the majority of their DNA patents supported products/services either in development or being marketed. Many assignees expected their current levels of exploitation to increase. This high level of perceived utility suggests DNA-patents are likely to support a significant volume of innovative products and services in the future.

Patterns of ownership suggest that by far the largest share of any innovative new products or services will be captured by the US public and private sectors in the USA and in the EU, although the Japanese private sector has thus far maintained dominance in Japan. By contrast the EU25 share of ownership in all three major patent offices is low (for example the EU-25 private sector holds less than 10% of the JPO and USPTO patents, and only 16.5% of EPO patents).

In the USA where DNA patents are granted in large numbers, the impact of these patents on inhibiting innovation might be a concern. However such concerns were not raised by assignees as an issue for their activities. This re-enforces views expressed elsewhere that the model of pharmaceutical innovation has fundamentally changed in recent years as the complexity of drug discovery and the division of labour within the sector have increased.<sup>96</sup> As such, it is envisaged that any short term gain to drug developers from not having to pay for externally developed research tools (were IP restrictions to make research tools unprofitable) would be at the cost of the longer term benefits these are expected to bring to internal efforts in R&D.

The data in section 3.1.1 has shown that the EPO and JPO have granted far fewer patents than the USPTO in this field. The need to patent biological molecules such as DNA has long been assumed as important to support innovation in biotechnology by the European Commission and others.<sup>97,98</sup> It is therefore reasonable to ask what the impact on innovation would be if DNA-patenting were not available or what the effect on innovation might be if patents could not be obtained for particular forms of DNA-based invention (e.g. research tools or diagnostics) in one region whilst continuing to be available in others. While a detailed analysis of this kind is beyond the scope of this report, it is clear that organisations such as universities might be able to use MTAs to generate some revenue from their research although if others can replicate the material, there would be no chance to enforce monopoly rights. Furthermore, the exclusivity over clinical data provided by drugs regulators in Europe does provide a period of market protection for drug developers (although for a shorter period than patents may allow) during which time competitors would not be able to launch a product without generating their own trial data. Thus anecdotal evidence suggests the non-availability of a patent on a drug in a market such as the EU might therefore not end the prospects for a product to be launched by a large pharmaceutical firm - if IP was available in other important markets such as the USA. However, under the same conditions a domestic biotechnology firm might be less able to launch a product as the

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<sup>96</sup> M. Stott, J. Valentine (2004) Gene patenting and medical research: a view from a pharmaceutical company *Nature Reviews Drug Discovery* 3 (4) p.364-368.

<sup>97</sup> S. L. Meltzer (2002) Intellectual property as a foundation for funding *Nature Biotechnology Bioentrepreneur Supplement* Vol.20 pp.47-50.

<sup>98</sup> E. R. Gold, A. Gallochat (2001) The European Biotechnology Directive: past as prologue *European Law Journal* Vol. 7 No. 3 September. pp.331-366.

financial uncertainties are relatively larger. Thus while a lack of DNA-patents in the EPO would be unlikely to prevent US biotechnology firms thriving in their domestic market and risking product competition in the EU, it would be far more difficult for EU-based firms with no domestic protection to provide a spring board to wider markets.

The EPO is granting far fewer DNA patents than the USPTO. Further analysis of granted patents in both regions would be necessary to determine whether there is a systematic effect that makes particular types of invention more difficult to patent at the EPO. This would require detailed examination of individual patent records in a manner that has not been possible in this study.

#### 4.4 The impact of patenting DNA on Healthcare

The patentability of DNA and other nucleotide sequences has spurred investment in healthcare-related R&D efforts globally and has facilitated the development of an impressive array of tools, tests and drugs. Patents on DNA support some of the most successful biotechnology drugs of the 1980s, such as Amgen's erythropoietin, and Genentech's tissue plasminogen activator. Although comparatively few health-related products from 1990s genomics have reached the market successfully to date, firms based primarily on a business model of patenting genes and developing therapeutics have rapidly established drug pipelines in recent years.<sup>99, 100</sup> The creation of such pipelines in itself can be argued to be a favourable impact. As noted in section 4.2 and 4.3 above, concerns that research tool patents might inhibit drug development have not been supported. The lack of reach-through claims and the general shift away from research tool patents revealed by this study may in part reduce these concerns.

This study also reveals that some assignees perceive the scope of claims issued in relation to DNA inventions is shrinking. The narrowing of patent claims is an important part of the cycle of maturation in an IP field. This stimulates follow-on innovations such as drugs with improved characteristics.<sup>101</sup> The main concern remains in areas such as diagnostics where those seeking alternative methods may less readily be able to invent around an initial invention.<sup>102</sup> Other concerns have been raised following the diminishing availability of testing, and increase in costs for a number of genetic diagnostics following patent issuances.<sup>103</sup>

A follow up study based on the PATGEN dataset could identify diagnostic patents, their ownership, coverage and the licensing intentions of their assignees through a survey. This might be useful in determining the extent to which more cases like that

<sup>99</sup> M. M. Hopkins, A. Kraft, P. A. Martin, P. Nightingale and S. Mahdi. (2006). Is the biotechnology revolution a myth? in *Comprehensive Medicinal Chemistry* (2<sup>nd</sup> Ed) Vol 1. Taylor and Triggle (Eds.) Elsevier.

<sup>100</sup> H. Rothman and A. Kraft (2006) 'Downstream and into deep biology: Evolving business models in 'top tier' genomics companies,' *Journal of Commercial Biotechnology* 12(2): 86-98.

<sup>101</sup> R. P. Merges, R. R. Nelson (1994) 'On limiting or encouraging rivalry in technical progress: the effect of patent scope decisions' *Journal of Economic Behavior and Organization* 25: 1-24.

<sup>102</sup> G. Matthijs (2004) Patenting genes BMJ 329 pp. 1358-1360

<sup>103</sup> M. K. Cho, S. Illangasekare, M. A. Weaver, D. G. B. Leonard, and J. F. Merz (2003) Effects of patents and licenses on the provision of clinical genetic testing services *Journal of Molecular Diagnostics* 5 (1) February pp.3-8.

of Myriad and the BRCA 1 gene may emerge and whether this may become a substantial problem for European Healthcare systems.

#### 4.5 Implications for Policy Framework in Europe

In the EU, member states are required to permit the patenting of DNA as part of their implementation of the directive on the legal protection of biotechnological inventions (EC directive 98/44). However, the European Parliament accepted EC98/44 only after vigorous ethical debate.<sup>104</sup> Even after this approval, resolution of remaining ethical issues led to the late transposition of the directive into national law by a number of Member States. These member states, including Italy, Germany and France have subsequently introduced modified clauses further limiting the scope of claims relating to DNA sequences, disrupting the intended harmonisation the directive.<sup>105, 106, 107</sup>

The data in section 3.1.1 clearly illustrate that the EPO has issued far fewer patents claiming DNA than the USPTO, and that in particular those filing claims insufficiently supported by biological data have not been able to achieve granted patents in the EU to the extent that they have enjoyed in the US. Consequently although patent applications seeking to claim human DNA have increased in recent years, around 40% of these have already been withdrawn in Europe. This number is likely to rise further as many of these patents are yet to enter examination. These data suggest the EPO is applying rigorous standards in their examination. The role of the EPO is crucial in implementing this policy as the wording of the EC98/44 is ambiguous and allows for a more generous interpretation. It is not the EC98/44 but the EPO that has focused on the eligibility of applications.

The evidence in this report suggests that countries taking steps beyond the Biotechnology Directive to ensure robust standards of patentability to prevent deleterious impacts on research, innovation and access to medicine may not have need to do so on account of EPO granted patents, although the remaining activities of national offices may in some cases be felt to warrant such protections.

This report provides empirical evidence of the extent of DNA patenting and is intended to contribute to the implementation of Action 5 on the Exploitation of intellectual property (particularly 5c).<sup>108</sup> It is important to communicate to policy makers, other stakeholders and the public, the extent of the difference between the pattern and context for DNA patenting in the US, (i.e. no research exemption) and the standards and protections upheld in the EU.

It is possible that the effects of uncertainty around the availability of IP protection in different Member States will have a disproportionate effect on EU-based assignees,

<sup>104</sup> E. R. Gold, A. Gallochat (2001) The European Biotechnology Directive: past as prologue *European Law Journal* Vol. 7 No. 3 September. pp.331-366.

<sup>105</sup> C. Nargolwalla (2003) France tackles EU biotechnology directive. June. [www.managingIP.com](http://www.managingIP.com)

<sup>106</sup> M. Huenges (2005) Biotech directive implemented (Germany) April. [www.managingIP.com](http://www.managingIP.com)

<sup>107</sup> M. N. Modiano (2006) New law on biotech inventions (Italy) May. [www.managingIP.com](http://www.managingIP.com)

<sup>108</sup> This Action requires Member States and the EC to clarify rules on ownership of intellectual property stemming from public research and to monitor the effect of implementation of patent legislation on research and innovation.

who cannot secure domestic market as a springboard overseas. Equally, such policies may be little more than an inconvenience to large firms attempting to expand their market following US product/service launches. Further research is needed to determine the extent of these potential difficulties and whether they create a playing field that disproportionately effects the competitiveness of particular groups of assignees, such as start-up firms based in the EU.

#### 4.6 Implications for policy framework in the USA

The USA has no specific legislation equivalent to EC 98/44. The Patent Act (35 U.S.C.) is used to enforce similar criteria to that in Europe (i.e. utility, inventiveness, novelty). However the US policy framework has been perceived as being more liberal than the EU in recent years. For example the threshold for inventive step is lower in the US.<sup>109,110</sup> Indeed there remains a perception that some patents are being granted with unduly broad claims, particularly those where the awarding of claims concerns speculative applications with insufficient enablement.<sup>111</sup> Refinements to patent examiner guidelines have recently been tested and upheld in the case of *In Re Fisher*.<sup>112</sup> Evidence from interviewees in the PATGEN study suggests these guidelines are being applied, with a significant proportion of assignees commenting on the more robust approach. It is difficult to quantify the impact of these guidelines as the US did not publish applications in the period prior to the change, so ratios of filings to grants cannot be calculated. However, data in this study and elsewhere indicate a marked decrease in patent filings, with some indications that a change in business models and more strict examining has led to a decrease in the patenting of research tools.<sup>113</sup>

In the years prior to 2001, the well developed SME sector in the USA was particularly well positioned to secure IP rights on human DNA on a significant scale. Early case law suggests that the scope of some of these, particularly research tool patents demonstrating limited enablement (after *Pfizer v Rochester*), may diminish in the future, although the extent of such weakness is not yet apparent.

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<sup>109</sup>Based on *In re Bell* 991 F2d 781 26 USPQ2d 1529 Fed.Cir. 1993 in the US, describing sequences that code for proteins is regarded as inventive because of the redundancy of the genetic code - see Nuffield Council on Bioethics (2002) *The Ethics of Patenting DNA: A Discussion Paper* (London).

<sup>110</sup> FR Doc 01-322, Federal Register Vol. 66 No. 4 Friday January 2001, Available at <http://www.uspto.gov/web/offices/com/sol/notices/utilexmguide.pdf>

<sup>111</sup> Paradise, J., Andrews, L., Holbrook T. (2005) Patents on Human Genes: An Analysis of Scope and Claims *Science* 11 March Vol.307 no.5715 pp.1566-1567.

<sup>112</sup> *In re Fisher*, Fed. Cir., No. 04-1465, 5/3/05 oral argument.

<sup>113</sup> Finnegan, Henderson, Farabow, Garrett & Dunne, LLP (2005) Biotechnology Innovation Report 2005. (June) Washington, DC: USA.

**APPENDIX A: CONFIDENTIAL QUESTIONNAIRE****SECTION A: ASSIGNEE'S VIEWS ON PATENTING POLICY**

1. *How has your organisation's strategy towards nucleotide sequence patenting (i.e. DNA, cDNA, mRNA etc.) changed in recent years?*
2. *What problems are you encountering in pursuit of your DNA-based inventions?*
3. *What problems do you think the main patent offices are facing in respect to DNA based inventions?*
4. *What do you think will be the next important trends in nucleotide sequence patenting?*
5. *How has your organisation exploited its existing human DNA patent families?*

(Please note: a given patent family may be counted more than once in your answers to a-e below)

**a) Assigned to others**

0%    1-19%    20-39%    40-59%    60-79%    80%-99%    100%

How do you anticipate this proportion will change in the next 5 years?

Increase    Decrease    No significant change    Unsure

**b) Licensed to others**

0%    1-19%    20-39%    40-59%    60-79%    80%-99%    100%

How do you anticipate this proportion will change in the next 5 years?

Increase    Decrease    No significant change    Unsure

**c) Held only for defensive use (i.e. freedom to operate not commercialisation)**

0%    1-19%    20-39%    40-59%    60-79%    80%-99%    100%

How do you anticipate this proportion will change in the next 5 years?

Increase    Decrease    No significant change    Unsure

**d) Used to directly support products/ services**

0%  1-19%  20-39%  40-59%  60-79%  80%-99%  100%

How do you anticipate this proportion will change in the next 5 years?

Increase  Decrease  No significant change  Unsure

**e) Made available in pools**

0%  1-19%  20-39%  40-59%  60-79%  80%-99%  100%

How do you anticipate this proportion will change in the next 5 years?

Increase  Decrease  No significant change  Unsure

Please indicate if your answers for Section A Question 5 are:

based on audit  based on confident estimates  based on uncertain estimates

## SECTION B: ON PATENTS GRANTED

This section relates to whole patent families (as opposed to individual patent applications at national offices) held by your organisation that meet the following conditions:

- i) a family with one or more granted patents in the USPTO or JPO or EPO
- ii) that claims one or more human DNA sequences

### *1. Of the patents your organisation holds that claim human DNA:*

Please note patent families may be counted more than once in categories a) to d)

#### *a) What proportion are research tools?*

- 0%    1-19%    20-39%    40-59%    60-79%    80%-99%    100%

#### *b) What proportion are therapeutics?*

- 0%    1-19%    20-39%    40-59%    60-79%    80%-99%    100%

#### *c) What proportion are diagnostics?*

- 0%    1-19%    20-39%    40-59%    60-79%    80%-99%    100%

#### *d) What proportion are for other purposes (please specify)*

- 0%    1-19%    20-39%    40-59%    60-79%    80%-99%    100%

*Other purposes:*

### *2. What proportion of your granted DNA patents are being maintained?*

- 0%    1-19%    20-39%    40-59%    60-79%    80%-99%    100%

### *3. What proportion of your granted DNA patents have been abandoned/ withdrawn?*

- 0%    1-19%    20-39%    40-59%    60-79%    80%-99%    100%

#### **3. (i) What is the main reason for abandoning/ withdrawing DNA patents in your organisation?**

#### **3. (ii) How do you anticipate this proportion will change in the next 5 years?**

- Increase       Decrease       No significant change       Unsure

**4. What proportion of your granted DNA patents at the EPO are in opposition?**

0%  1-19%  20-39%  40-59%  60-79%  80%-99%  100%

**5. What proportion of your granted DNA patents have been infringed or have been the subject of litigation?**

0%  1-19%  20-39%  40-59%  60-79%  80%-99%  100%

***Please indicate if your answers for Section B are:***

based on audit  based on confident estimates  based on uncertain estimates

## SECTION C: ON PATENTS PENDING

The questions in this section relate to the current status of patent applications that agree with the following conditions:

- i) applications seeking to claim human DNA sequences
- ii) filed at the USPTO, or the JPO, or the EPO
- iii) at any time since DNA patenting commenced by your organisation
- iv) not granted to date/ not published as granted

Answers are intended to be proportions of the sum of applications at the EPO, USPTO and JPO (e.g. if 10 patents were filed in each of the three regions, answers would be based on a percentage of 30).

**1. What proportion of your applications have been withdrawn/ abandoned (at any stage of proceedings after they have been filed)?**

0%  1-19%  20-39%  40-59%  60-79%  80%-99%  100%

***How does this proportion differ between patent offices?***

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**What are the most common reasons for patents to be withdrawn by your organisation and at what stage are they withdrawn?**

**2. What proportion of filed patents are yet to be examined?**

0%  1-19%  20-39%  40-59%  60-79%  80%-99%  100%

**3. What proportion of filed patents are still at examination?**

0%  1-19%  20-39%  40-59%  60-79%  80%-99%  100%

**What is the most common reason for your organisation's patents to be rejected by examiners?**

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**4. What proportion of filed patents are awaiting publication following grant?**

0%  1-19%  20-39%  40-59%  60-79%  80%-99%  100%

***Please indicate your answers for Section C are:***

based on audit  based on confident estimate  based on uncertain estimate