Abstract

This article centres on pan-European litigation concerning a patent for a newly discovered human protein and its encoding gene sequence. Parallel revocation proceedings were instituted at the European Patent Office (EPO) and in the High Court on the basis that the invention was not patentable. Although the patent was eventually maintained in both jurisdictions, the Supreme Court overlooked CJEU jurisprudence concerning the standard for industrial application under the Biotechnology Directive and instead followed inconsistent EPO jurisprudence (for example, relating to the admissibility of 'post published evidence' in substantive examination) even though the EPO Technical Boards are themselves not so bound. The result is a doctrinally muddled, 'sliding-scale' standard for inventions arising in biotechnology. The ramification of a patent policy that supports early-research inventions in biotechnology necessitates that the standard for industrial applicability be brought into line with that set by the CJEU in *Monsanto,* and a consistent jurisprudence at the EPO established.

Keywords: Patents, biotechnology, industrial application, insufficiency, inventive step, *HGS v Eli Lilly, Monsanto v Cefetra*

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Has the commodore steered the fleet onto the rocks?[1] Biotechnology and the requirement for industrial applicability

'[I]f you allow the patenting of chemicals whose use you do not really know you will subvert the patent system and be likely to stultify research by others rather than encourage it'.[2]

1. Introduction

In the European Union, the Biotechnology Directive[3] came into force at a time when researchers involved in the Human Genome Project were beginning to produce DNA sequences and identify a number of important genes.[4] Proliferate patent applications were filed internationally over DNA fragments[5] and newly identified human gene sequences,[6] frequently with unknown or speculative function. In response the US Patent and Trademark Office tightened its utility practice guidelines[7] inventions in an

[1] *Eli Lilly v Human Genome Sciences Inc* [2010] EWCA Civ 33 at [39], citing *Actavis v Merck* [2008] EWCA Civ 444, 48.
[2] *Eli Lilly v Human Genome Sciences Inc* [2010] EWCA Civ 33 at [67-68].
[3] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the Legal Protection of Biotechnological Inventions.
[4] For example, the *BRCA2* gene, associated with increased risk of breast cancer; the *MSH2* gene, which increases the risk of colon cancer for carriers and the *FAD* gene variants, which together confer an almost 100 per cent risk of developing Alzheimer's disease: http://www.sanger.ac.uk/about/history/hgp/ (last visited January 2013).
[5] For example, express sequence tags used in research.
[6] It is estimated that between 70,000-100,000 genes are distributed within 3 billion base pairs within the human genome, which is organised into 23 pairs of chromosomes consisting of DNA and other proteins. Sequencing of the human genome has been equated in importance with the discovery of germ theory: American Medical Association (CSA) Report 9 of the Council on Scientific Affairs (I-00).
[7] In December 1999, USPTO published the Revised 'Utility' Guidelines in the Federal Register (64 FR 71440, Dec 21, 1999) and public comment invited. The Guidelines, which govern internal practice, came into force in 2001. See: http://www.uspto.gov/web/menu/utility.pdf.; included in Annex D in the *Examination Guidelines for patent applications relating to biotechnological inventions in the UK Patent Office* (2003).

attempt to stem a stream of inadequate filings over biological material and in response to concerns about the effect of patents over genetic material, and on health care and research more generally. By 2003 the whole human DNA sequence containing some 3 billion letters of genetic code was mapped and sequenced to 99.99 per cent accuracy.[8] An astonishing feat, yet the quest to understand genetic nature still remains a long way from completion, with 'unknowns abounding'.[9]

This article is concerned with the proper standard for industrial application for newly discovered human protein and encoding gene sequences. It is a question of law upon which the Supreme Court delivered judgment, apparently without recourse to the standard provided by the Court of Justice of the European Union (CJEU) 16 months earlier. This is problematic as the EU standard (to which English courts are bound) is higher and more robust than the mere 'plausibility' threshold in operation at the EPO. The Supreme Court followed a line of demanding EPO jurisprudence from which an extraordinary list of principles were extracted that overtly support the patentability of 'early-research' findings. All three strata into which the principles are grouped are challenged, for the primary reason that a decreasing standard for inventions using human biological material, based on ad hoc, fact-specific case law which is in conflict with EU principle for industrial application in biotechnology, is not a *legitimate* direction in which to take English patent law.

[8] International Human Genome Sequencing Consortium. (2004) Finishing the euchromatic sequence of the human genome. *Nature* 431:931-945.
[9] Welcome Trust Sanger Institute, available at http://www.sanger.ac.uk/about/history/hgp/ (last visited January 2013).

Admittedly a technically difficult field, their Lordships seemed most impressed by the Bioindustry Association's (BIA) unilateral intervention in the proceedings. Yet, the ramification of a policy that promotes the patentability of speculative inventions requires a more *balanced* consideration. Industrial application should be brought into line with the standard set by the CJEU for three reasons; because English courts are legally bound by such decisions; to avoid the risk of the patent system being 'subverted,' and to promote its functioning in a way that is seen to support the public interest. A greater consistency in certain aspects of EPO biotech case law (discussed below) would make it easier for the national courts of contracting parties to follow their expert lead in this challenging field.

A. Setting the Context

Industrial application[10] is one element of international[11] trinity criteria[12] for patentability. It hitherto enjoyed a relatively innocuous existence in patent law, rarely featuring in patent litigation. In most cases industrial application is clear from the nature of the invention but in the context of biotechnology, the requirement to explain how an invention can be made or used in industry may not be abundantly apparent. The evaluation of industrial application is particularly important in respect to patent applications that lay claim to new gene or protein sequences identified through homology

[10] Synonymous with 'usefulness' (FN 5 to the TRIPS Agreement, n 11).
[11] Pursuant to Article 27 of the 'Trade Related Aspects of Intellectual Property' (TRIPS) Agreement, Annex 1C of the Agreement establishing the World Trade Organisation, approved by Council Decision 94/800/EC of 22 December 1994 concerning the conclusion on behalf of the European Community as regards matters within its competence.
[12] With novelty and inventive step (non-obviousness).

(comparison) studies. This is because sequence data[13] does not decode the gene or protein's function, knowledge about which is required to fulfill industrial application. That must be elucidated by some other method, to support industrial applicability. The HGS litigation involved a patent for a newly discovered human protein and its encoding gene sequence (owned by Human Genome Sciences), opposed by Eli Lilly (who were working on the same gene) in proceedings at the European Patent Organisation and in England. The disputed patent (EP (UK) 0,939,804) claimed a gene sequence,[14] encoding neutrokine-α[15] (the gene), neutrokine-α (the protein), anti-neutrokine-α antibodies and their use in diagnostic and pharmaceutical compositions.[16] HGS had discovered neutrokine-α using bioinformatics; high through-put computational studies which enable researchers to identify genes (and encoded proteins) by comparing their sequences with previously identified and characterised genes. The function of sequences and efficacy of their putative therapeutic effect must be determined by other methods (eg by conducting assays).[17] HGS worked out the protein belonged to a known 'superfamily' of which many members shared properties useful in a vast array of methods of diagnosis and therapy. HGS' guess was that neutrokine-a might have similar functions (and therefore applications) in the medical field, so claimed them all. Eli Lilly challenged the patent

[13] That is, nucleic acid sequence (DNA) or amino acid sequence (protein).

[14] Genes are lengths of DNA made up of 4 nucleic acid base, that encode proteins made up of amino acids ('building blocks').In patent documents, gene and protein inventions are identified by their nucleic acid or amino acid sequences, respectively. Both nucleic and amino acid molecules are treated as chemical compounds.

[15] The Patent discloses the nucleotide and amino acid sequence of a novel member of the TNF ligand superfamily which it calls Neutrokine-a.

[16] Claim 20: A pharmaceutical composition comprising the nucleic acid molecule of any one of claims 1 to 4, the polypeptide of any one of claims 11 to 14, or the antibody or portion thereof of any one of claims 15 to 19 and optionally, a pharmaceutically acceptable carrier. Claim 21: A diagnostic composition comprising the nucleic acid molecule of any one of claims 1 to 4, the polypeptide of any one of claims 11 to 14, or the antibody or portion thereof of any one of claims 20 to 25.

[17] *Eli Lilly v HGS Inc* [2008] EWHC 1903 (Pat) [75].

partly on the allegation that HGS' invention was not industrially applicable, alleging that nobody – including HGS, knew what function 'neutrokine-α' *actually* performed at the time the patent was filed.

Although other grounds were argued, the patent was invalidated in the English High Court because the claimed inventions were not susceptible of industrial application *at the date of the patent*.[18] The trial Judge (Kitchin J) considered it was no answer to say that subsequent research, so-called 'post patent evidence,' had shown the inventions may be useful to treat particular diseases.[19] Kitchin J found the skilled addressee would understand the commercial applications listed in the patent to be entirely speculative, containing '*an astonishing range of diseases and conditions which Neutrokine-α and antibodies to Neutrokine-α may be used to diagnose and treat*', claims that he found were unsupported by data of any kind.[20]

HGS sought leave to appeal. As there were parallel proceedings at the EPO, an acceleration request was made by the national court to expedite proceedings before the Boards of Appeal. In the meantime, it was agreed that the English appeal would be stayed until the TBA had issued their decision.

[18] A patent application undergoes substantive examination according to the date the application was filed. This is highly relevant, as the EPO has developed a line of case law that permits 'post published' evidence to support industrial application with retrospective effect.
[19] Associated with particular B cell disorders; n 17 above, 237.
[20] n 17 above, 231.

In a central attack at the EPO, Eli Lilly successfully instituted opposition proceedings against the patent but on appeal, the Technical Board of Appeal (TBA)[21] reached a different conclusion again, holding the HGS patent to be validly granted. Therefore, the appeal in the English Court went ahead.[22]

The Court of Appeal upheld the findings and judgment of Kitchin J, but the Supreme Court overruled both lower courts on the basis that EPO jurisprudence was 'tolerably clear' and should therefore be followed.[23] A central issue analysed in this paper is whether that assessment was in fact correct. While it is the case that any principle of law clearly laid down by the Technical Boards will be followed by British courts, this must be subject to the caveat: *'... unless we are sure that the commodore is steering the fleet on to the rocks.''*[24]

16 months earlier, in a reference for a preliminary ruling concerning the Biotechnology Directive the CJEU was called upon to clarify points of law in the context of a gene patent. A key purpose of this type of proceeding is to prevent divergent interpretations of European Union legislation. The declaration concerning the primacy of EU law and cornerstone principle of EU Law[25] appears at the end of the Treaty of

[21] T 0018/09 - 3.3.08. *Neutrokine/* HUMAN GENOME SCIENCES (21 October 2009).
[22] n 2 above, 33.

[23] *Eli Lilly v Human Genome Sciences Inc* [2011] UKSC 51.
[24] Jacob LJ at [39].
[25] Case 6/64, *Falminio Costa v ENEL* [1964] ECR 585, 593; C-213/89 *Factortame I* [1990] ECR I-2433; C-106/77, *Simmenthal II* [1978] ECR 629; Case C-106/89 *Marleasing* [1991] 1 ECR 4135.

Lisbon.[26] The UK recognises the primacy of the Court of Justice of the European Union for areas of law in which the EU has competency; the patenting of biotechnology representing one such area.[27]

Kitchin J considered the fact that Articles 1 to 11 of the Biotechnology Directive were not implemented into the Patents Act 1977 until 2000[28] meant that the rules did '*not strictly apply*' to the case, which concerned an application filed in 1996. Yet the absence of transitional provisions to protect the position of pre-existing biotech patents before the entry into force of the Biotechnology Directive suggests this might not be correct. The CJEU has consistently held the commitment to interpret national law in conformity with the law of the European Union which applies to provisions of national law that pre-date the relevant EU provisions.[29] The following excerpt from *Marleasing* serves to remind that, '… *in applying national law, whether the provisions in question were adopted before or after the directive, the national court called upon to interpret it is required to*

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[26] Declaration 17 concerning Primacy: Consolidated protocols, annexes and declarations attached to the treaties of the European Union. Declarations annexed to the Final Act of the Intergovernmental Conference which adopted the Treaty of Lisbon, signed on 13 December 2007. Available at http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2008:115:0001:01:EN:HTML (last visited Dec 2012).

[27] n 3 above. It was intended to harmonize the laws of Member States regarding the patentability of biotechnological inventions, including plant varieties (as legally defined) and human genes.

[28] Articles 1-11 of the Directive implemented in the UK by the Patents Regulations 2000 (into force on 28 July 2000).

[29]; C-106/89 *Marleasing* [1991] 1 ECR 4135, [para 8]discussed by AG Mengozzi in *Monsanto v Cefetra* 9 Mar 2010 at [66].

do so, as far as possible, in the light of the wording and the purpose of the directive in order to achieve the result pursued by the latter.' [30]

It is for this reason that *Monsanto*, a judgment of the CJEU which (in part) interprets the requirement for industrial application for gene sequences under Directive 98/44/EC, should have been taken into account by the Supreme Court in *HGS*. Failure to do so has resulted in inconsistency with the approach taken by the CJEU creating a divergent jurisprudence in England.

B. Industrial Application: the Legislative Matrix

(i) European Union law

Pursuant to international obligations incumbent on the European Union[31], patent protection must be guaranteed for products and processes in all areas of technology.[32] Therefore the Biotechnology Directive[33] requires Member States to protect biotechnological inventions under national patent law.[34] The main objective of the Directive is to promote the internal market and competition[35] by preventing differences in national laws exerting a negative effect on trade within the European Union.

[30] ibid 29, 8.
[31] Annex 1C of the Agreement establishing the World Trade Organisation, (the TRIPS Agreement 1994), approved by Council Decision 94/800/EC of 22 December 1994 concerning the conclusion on behalf of the European Community as regards matters within its competence.
[32] Article 27(1) TRIPS;
[33] n 3 above.
[34] Recital 12 of Directive 98/44/EC, n 3 above.
[35] Recital 5.

Although there is no definition of a biotechnological invention, the Directive provides for the patentability of inventions that are novel, inventive and industrially applicable, '*even if they contain a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used*'.[36]

The first (and so far, only) time the CJEU has been called upon to interpret the Biotechnology Directive was in *Monsanto v Cefetra* .[37] The referral broadly involved questions concerning (1) whether the Directive denies absolute (product 'per se') protection for gene sequences, and (2) whether protection for gene sequences is contingent upon the gene performing the function for which it was patented. The importance of the case for present purposes concerns the question of patent protection for a DNA sequence *as such,* which is not linked to the performance of a specific function;[38] an argument that was rejected outright by the CJEU.[39]

Interpreting the import of Recitals 23 and 24 in conjunction with Article 5(3) of the Directive[40] which is concerned with industrial application, it was observed that the Directive makes the patentability of a DNA sequence, 'subject to indication of the function it performs'.[41] As such, the court stated that the Directive must be regarded as not according any protection to a patented DNA sequence *which is not able to perform*

[36] n 3 above, Article 3. Also, inventions concerning a microbiological or other technical process or a product obtained by means of such a process: Article 4(3).
[37] *Monsanto v Cefetra* [2011] All E.R. (EC) 209.
[38] ibid, 41.
[39] n 37 above, 42 *et seq*.
[40] n 3 above, Article 5(3) *The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application.*
[41] n 37 above, 45.

the specific function for which it is patented.[42] Protection *as such* only extend to material of which the DNA sequence forms a part 'as long as that situation continues'.[43] But where a patented DNA sequence is unable to perform its claimed function, it enjoys no patent protection under any provision of the Directive.[44]

The upshot is that EU law requires real and present function (industrial application) to be recited in the patent – and the claimed sequence *must* be presently capable of performing *that* function. If the sequence can not perform the function so claimed, the patent claim is unenforceable.

(ii) The European Patent Convention

The European Patent Convention (EPC)[45] comprises the legal instrument that defines the grant of EPO patents in European states.[46] Incorporating the provisions of the Biotechnology Directive[47], the EPC is applied by patent examiners dealing with patent applications in all technical fields, including biotechnology and the Directive is to be used as a supplementary means of interpretation of those rules The legal system established under the EPC does not treat either the EPC Guidelines or established

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[42] n 37 above, 45.

[43] n 37 above, 47.

[44] n 37 above, 49.

[45] An international treaty ratified by 38 European states.

[46] The 14th edition of the European Patent Convention contains the text of the Convention on the Grant of European Patents (EPC) applicable since 13 December 2007, as amended by the EPC Revision Act of 29 November 2000.

[47] In biotechnology cases, the relevant provisions of the EPC are to be applied and interpreted in accordance with Chapter V of the Implementing Regulations (Rules 26 to 34 to the EPC) and the Directive is to be used as a supplementary means of interpretation.

jurisprudence of the Technical Boards as binding,[48] and it is possible for two Technical Boards to deliver different decisions on a point of law.[49] Although the European Patent Organization and its tribunals are not bound by EU law, most contracting parties to the EPC are in fact members of the EU.[50]

It is a requirement of patentability that a claimed invention is susceptible of industrial application, pursuant to Article 52(1)[51] and Article 57 EPC. The former requires the invention to be 'susceptible of industrial application' and the latter defines such susceptibility by reference to whether the invention 'can be made or used in any kind of industry, including agriculture'.[52] The language for Article 57 EPC was directly carried over, unchanged, from Article 3 of the Strasbourg Convention of 1963.[53] During the *HGS v Eli Lilly* litigation no reference was made to the *travaux* to that Convention, rightly dismissed as superfluous by Jacob LJ on the basis that a contemporary meaning in respect to biotechnology is called for. The Article 52(1) EPC test and Article 57 EPC test are separate and independent.[54] Although an invention might be considered industrially applicable, this factor does not overcome deficiency under Article 52(1) EPC.

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[48] The absence of any general obligation to treat earlier decisions as binding follows from Article 112(1)(b) EPC and Articles 15 and 16 of the Rules of Procedure of the Boards of Appeal. The EPC only comprises two provisions giving a decision of a Board of Appeal or the Enlarged Board of Appeal a binding effect, namely those of Articles 111(2) and 112(3) EPC, respectively: T 740/98 at point 2.3 of the reasons.
[49] Article 112(1)(b)EPC.

[50] Croatia, Iceland, Serbia, Former Yugoslav Republic of Macedonia, Turkey and Albania are all contracting parties to EPC but are not EU member states. Montenegro and Bosnia & Herzegovina are states that 'recognize EU patents upon request' (November 2012).

[51] *European patents shall be granted for any inventions, in all fields of technology, provided that they are new, involve an inventive step and are susceptible of industrial application*.
[52] *Chiron* v *Murex* [1996] FSR 153, 177.
53 Article 3, Council of Europe, *Convention on the unification of certain points of substantive law of patents for invention* European Treaty series no. 47, (27 Nov 1963).
[54] UKIPO (2011) Manual of Practice: Patents, 4.03.

Reflecting the text of the Directive[55], the EPO Practice Guidelines provide that sequences and partial sequences of genes are *not* patentable inventions absent identification of at least one function, which conveys the necessary technical information.[56] The EPO Practice Guidelines also provide that where a gene sequence is used to produce a protein, it is necessary to specify which protein is produced and what function this protein performs.[57]

2. Meaning of 'Industrial Application' for Bioscience Inventions: an Overview

Industrial application was originally interpreted by the Technical Boards to mean 'financial gain' or 'profitable use', '*.. the notion of the concept 'industry' implies that an activity is carried out continuously, independently and for financial gain*.'[58]

In *Max-Planck* the question was whether the patent application disclosed how properties of a newly isolated protein called 'Brain Derived Phosphatase 1' (BDP1) might be exploited in the pharmaceutical industry. The Board applied the standard established in previous case law that industrial application should be geared to financial

[55] n 3 above, recital 23: a mere DNA sequence without indication of a function does not contain any technical inf*ormation and is therefore not a patentable invention.*
[56] EPO Guidelines for Examination Part G - Chapter III-2 June 2012: Part 4 *Sequences and partial sequences of genes.*
[57] EPO Guidelines for Examination Part G - Chapter III-2 June 2012: Part 4 *Sequences and partial sequences of genes.* Alternatively, when a nucleotide sequence is not used to produce a protein or part of a protein the function to be indicated could eg be that the sequence exhibits a certain transcription promoter activity.
[58] T 144/83 - 3.3.01 *Appetite suppressant*/ DU PONT (March 1986), point 5.

gain[59], judging the speculative indication of possible objectives that might or might not be achievable insufficient to fulfill the requirement Article 57 EPC.[60]

An interpretation geared to 'financial gain' was rejected by the Board in *ZymoGenetics* because the meaning of industrial application had to be wider than commercial interest or economic profit:[61] Profitable use was redefined in the following way,

'… *[profitable use] must be understood in the wider sense that the invention claimed must have such a sound and concrete technical basis that the skilled person can recognize that its contribution to the art could lead to practical exploitation in industry*.'[62]

The Board re-interpreted 'profit' to mean some 'benefit' rather than financial reward and the expression 'profitable use' to mean 'immediate concrete benefit'.[63] 'Concrete benefit' requires that the purported exploitation is real, not merely theoretical and imposes the need to disclose:

'… *in definite technical terms the purpose of the invention and how it can be used in industrial practice to solve a given technical problem, this being the actual benefit or advantage of exploiting the invention*.'[64] 'Immediate' conveys that this should be derivable directly from the description, if not already obvious from the nature of the invention or the background art.[65]

[59] T 870/04 – 3.3.8 *BDP1 Phosphatase*/MAX-PLANCK (May 2005), point 19.
[60] ibid point 21.
[61] T 898/05 – 3.3.08 *Hematopoietic receptor*/ZYMOGENETICS (July 2006), point 5.
[62] ibid point 5.
[63] n 61 above, point 6.
[64] n 61 above, point 6.
[65] n 61 above, point 6.

In England, Section 1(1)(c) Patents Act 1977 requires that a patentable invention must be capable of industrial application. This is defined in section 4(1) as meaning it can be, 'made or used in any kind of industry, including agriculture'. The provisions were new in 1977, having been introduced because of the European Patent Convention, and are required by section 130(7) to be construed and applied so far as possible to produce uniformity.

The requirement is aimed at ensuring that a patentable invention has a real practical application, a use for which it can be employed. In *Chiron v Murex* (No 12) the Court of Appeal interpreted the sections as requiring that an invention can be made or used 'in any kind of industry' so as to be 'capable' or 'susceptible of industrial application', the connotation being that of trade or manufacture in its widest sense and whether or not for profit, concluding that, '*industry does not exist in that sense to make or use that which is useless for any known purpose*.'[66] It is, however, settled law that inventions alleged to operate in a manner which is clearly contrary to well-established laws of physics are regarded as not having industrial application.[67] The requirement has been rarely problematic in practice.[68]

[66] *Chiron Corp v Murex Diagnostics Ltd* [1996] RPC 535
[67] BL O/086/08 *Application of Joe Spiteri-Sargent* (March 2008).
[68] Hon Judge Fysh, A Roughton, P Johnson & T Cook (eds), The Modern Law of Patents (London: Lexis-Nexis, 2010).

In *Icos*,[69] the EPO Opposition Division imported US criteria for 'utility'[70] finding that *potential* functional uses of the claimed protein were, '… *speculative ie are not specific, substantial and credible and as such are not considered industrial applications.'*[71]

US patent law serves to ensure that patents are only granted for inventions that are 'useful.'[72] This has a Constitutional footing — Article I, Section 8 of the Constitution authorises Congress to provide exclusive rights to inventors to promote the 'useful arts.' In *Icos*, disclosure of the claimed gene and protein without industrial applicability was not a patentable invention as it lacked technical character, pursuant to Article 52(1) EPC[73] *and* Recital 23 of the Directive, '*Whereas a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention*'.

The Opposition Division interpreted the requirement for an 'indication of a function' to be one which amounts to 'more than speculation' which under the *Directive*, does not confer technical character.[74]

In *Chiron Corp* the Court of Appeal observed that section 4(1) Patents Act 1977[75] is not satisfied if the product made is 'useless'.[76] The US standard was explicitly adopted

[69] ICOS Corp/Novel V28 seven transmembrane receptor [2002] 6 OJ EPO 293.
[70] For comment see S. Thambisetty, 'Legal transplants in patent law: why utility is the new industrial applicability', (2008) LSE Law, Society and Economy Working Paper, available at Social Sciences Research Network electronic library at: http://ssrn.com/abstract=1111966 (last last visited February 2013).
[71] n 69 above, point 9.
[72] See *Carl Zeiss Stiftungv.Renishaw PLC*, 945 F.2d 1173, 20 USPQ2d 1094 (Fed. Cir. 1991).
[73] n 69 above, point 10.
[74] n 69 above, point 11(ii).

in interpreting industrial application by the UK intellectual property office (UKIPO) in *Aeomica Application*.[77]

Later, in the English High Court, Kitchin J considered US principles on 'utility' in his analysis of Article 57 EPC jurisprudence, '… The application must show that the invention is useful to the public as disclosed, not at some future date after the research. The utility must be significant and presently available. It must also disclose a use which is well defined and not so vague as to be meaningless'.[78]

A series of comparative studies were reported on biotechnology patent practice at the three major granting offices (USPTO[79], JPO[80] and EPO) in 2001. It is instructive to consider one of these which concerned the evaluation of industrial applicability (and inventive step) for nucleic acid (DNA) molecule-related inventions whose functions are inferred based on homology search (as was neutrokine-a, HGS' invention). [81]

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[75] Patents Act 1977 s. 4 (1) Subject to subsection (2) below, an invention shall be taken to be capable of industrial application if it can be made or used in any kind of industry, including agriculture…
[76] n 66 above, 607.
[77] *Aeomica's Application* BL O/286/05, Oct 25, 2005.
[78] n 17 above, [222].
[79] 35 U.S.C. § 101: Utility, requires that an invention must have at least one specific, substantial and credible utility asserted in the specification, or well established in the art. There is no requirement at the USPTO for evidential function or utility of the invention. Both nucleic and amino acid molecules are treated as chemical compounds.
[80] The JPO also treats nucleic acid molecules as chemical compounds. Japanese Patent Law, Section 29 (first sentence) requires that inventions should be industrially applicable and that utility (specific function) must be described or able to be inferred from the specification. Like the EPO, where this is not evident, the JPO may request experimental evidence of such. Section 36(4) requires that: '*the detailed description of the invention shall be stated … in such a manner that is sufficiently clear and complete for the invention to be carried out by a person having ordinary skill in the art to which the invention pertains'*. The claims must have clear scope so that the invention is readily identifiable on the basis of the statement of each claim (Section 36(6)). See also the JPO Guidelines Part VII, Chapter 2.
[81] Trilateral B3b report: Comparative study on biotechnology patent practices: *Nucleic acid molecule related inventions whose functions are inferred based on homology search.*
See http://www.uspto.gov/web/tws/sr-3-b3b_bio_search.htm (Last visited November 2012).

On the question of the kind of function to be described in a specification to show industrial applicability and the types of information needed, the following responses of the EPO illuminates the prevailing standard,

'... the function performed by a claimed sequence and the protein it encodes should be certain to the degree that a specific utility for the sequence becomes apparent beyond the realm of speculation[82] *... in cases where the (encoded) protein and its specific function serve as a basis for the assessment of inventive step, industrial applicability, and sufficiency of disclosure, the application as filed should provide an example showing how said protein had been expressed, and indicate the specific function of the protein'.* [83]

Some 9 years later Jacob LJ put it like this,

'You can patent an isolated gene sequence but only if you disclose the industrial application of the protein for which it encodes. However clever and inventive you may have been in discovering a gene sequence , you cannot have a patent for it or for the protein for which it encodes if you do not disclose how it can be used'.[84]

Yet it is on this point of law that the UK Supreme Court chose to part company with the learned Judge on the basis that it was a 'more exacting' standard than that required by the EPO Technical Boards. The Supreme Court noted that US cases on utility

[82] Nucleic acid molecule-related inventions whose functions are inferred based on homology search http://www.trilateral.net/projects/biotechnology/mutual.pdf, 16 (last visited November 2012) *'If the alleged function of a claimed nucleic acid molecule is not credible beyond mere speculation the EPO will request experimental evidence demonstrating the function* **…** *Such evidence, although not formally part of the description, will be taken into account when assessing patentability. Experimental evidence normally is a prerequisite for second medical use claims* Trilateral B3b report *(ibid*) – at point 4 etc, on page 17-18 of the report.
[83] Ibid 8.
[84] n 2 above, [57].

'deserve great respect.'[85] To circumvent this standard and follow the more relaxed, generous policy of the EPO Lord Neuberger said that delineating boundaries of patentability on the basis of industrial application in the UK cannot be attempted by reference to US jurisprudence because of 'fundamental differences'.[86] Be that as it may, it was a serious oversight that recent CJEU jurisprudence on the patentability of isolated DNA in *Monsanto v Cefetra*, was not taken into account. The following section shows how this jurisprudence was (mis)interpreted and applied by the TBA in respect to HGS patent.

3. At the Technical Board of Appeal: *Neutrokine/ HGS*[87]

As indicated earlier, initial opposition instituted by *Eli Lilly* at the EPO found HGS' patent invalid on grounds of obviousness and added matter. The Technical Board was required to deal *inter alia*, with allegations of lack of industrial application and insufficiency.

In respect to industrial application the TBA found that the 'boiler-plate'[88] which occupied numerous pages covering the many purposes to which the invention might (but not necessarily could) be put, did not lead to invalidity because the skilled person would distinguish '*positive*' technical data from all the other contradictory and over-broad statements. The skilled person would realise the list was merely 'an enumeration of

[85] n 23 above, [39].
[86] n 23 above, [40].
[87] n 21 above.
[88] The practice of filing patents with long lists of conditions and activities and subsequently relying on the few that are confirmed or demonstrated: referred to at point 27.

general properties of the superfamily to which the gene belonged'.[89] The TBA found the skilled person to be imputed with knowledge about boiler-plate practice, which it held to be common (though not necessarily '*proper*') so that the skilled addressee would be, '… *able to differentiate mere boiler-plate from positive technical information*'. [90] The TBA interpreted the structural identification linking the new protein to a particular superfamily, together with '*post published*'[91] data supporting the assumption relied on by HGS at filing, as technical information[92] sufficient to warrant a finding of industrial applicability.[93]

So the TBA watered down the industrial application requirement by transplanting an approach deployed in the assessment of inventive step to industrial applicability. In this, the EPO employs a 'problem-solution' approach. Having identified the 'problem', starting from the closest prior art, the technical contribution of the invention is identified. The question then becomes whether that contribution (solution) is inventive.

The TBA in *Neutrokine/* HGS considered the technical problem to be the provision of a further member of the TNF ligand superfamily.[94] In the biotechnology field, the 'problem' is usually framed as 'the provision of a further family member'; the 'solution' the newly characterised gene or protein – though this is contingent on evidence of technical character, pursuant to Recital 23 Directive 98/44.[95] But the TBA in *Neutrokine/* HGS relying on *ZymoGenetics* formulated the question under Art 57EPC to

[89] n 21 above, point 26.
[90] n 21 above, point 26.
[91] Data to support (best-guessed) function after the patent application is filed.
[92] Regarding effect on T cells and tissue distribution.
[93] n 21 above, point 27.
[94] n 21 above, point 36.
[95] For example, n 21 above, 36; T1329/04 – 3.3.8. *Factor-9*/ JOHN HOPKINS (June 2005), points 4 and 5.

enquire whether the 'solution' itself (ie the gene and amino acid sequence for neutrokine-a) sufficed to suggest a practical exploitation, which could be considered an immediate concrete benefit.[96]

The TBA considered that allocating a newly found protein to a superfamily meant that a specific function could be assigned where it was established that all members shared (at least) one function that was well characterised and understood. This would provide the requisite one 'immediate concrete benefit',[97] a scenario considered to be one end of the spectrum. At the other was one where family members do not share even one function. Therefore, experimental evidence demonstrating function is required.[98] HGS' case was one which the TBA, rather generously said, fell somewhere in-between as the specification provided structural identification of neutrokine-α with *plausible* (not demonstrated) technical data such as expression distribution in tissue and activated T cells.

Eli Lilly argued that lack of experimental data to support the claimed effect (on T cells) would mean the skilled person could not work[99] the invention without the undue burden of undertaking a research programme.[100] In rejecting this line of argument the TBA found the post-published evidence convincing and that the claimed activities '*may*' represent a valid basis for a possible industrial application and '*might*' be relevant to

[96] n 21 above, 21.
[97] n 21 above, point 22.
[98] n 21 above, point 22.
[99] Requirement of Article 83EPC.
[100] And that no industrial application could be derived from co-stimulation of T cells: n 21 above, point 28.

certain immune diseases.[101] However, they were more persuaded that expression in B and T cell lymphomas provided a solid basis for an industrial application.[102]

The standard to show a patent as not complying with the requirement for sufficient disclosure under Article 83 EPC ('serious doubt, substantiated by verifiable fact') set in *Onco-Mouse*[103] was applied by the TBA in *Neutrokine/* HGS although curiously, not in respect to the insufficiency allegation but industrial application. Another standard was therefore crossed over so that the Article 57EPC objection could only be sustained if serious doubts existed substantiated by verifiable facts.[104] The TBA said the standard of proof had to be the same as for Article 83EPC because of their 'close relationship'; the application of a different standard, 'unfair'. The allegations asserted by Eli Lilly concerning industrial application were rejected as unsupported assumptions. Post-published evidence relating to the possible application of Neutrokine-α in therapy and diagnostics provided the plausibility of the patent's disclosure and basis for exploitation in industry. Furthermore, the TBA found this same plausibility offered 'positive reflections' on the evaluation of sufficiency, contributing to a finding of sufficient disclosure under Article 83EPC.[105] 'Plausibility' therefore bridged the evidential gap without '*concrete experimental data*' to support putative function, on the basis of *ZymoGenentics*. Finally the TBA accepted post-published evidence going beyond speculation for the first time to reinforce the predicted function.[106]

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[101] n 21 above, point 29.
[102] n 21 above, point 30.
[103] T 19/90 – 3.3.02. *Onco-Mouse* [October 1990], point 3.3; T 292/85 – 3.3.02. *Polypeptide Expression* (January 1988) a biological invention was considered sufficiently disclosed if it clearly indicated at least one way in which the skilled person could carry it out.
[104] n 21 above, point 32.
[105] n 21 above, point 20.
[106] n 21 above, point 24.

(i). The TBAs re-interpretation of 'sufficiency' in respect to HGS' claims to therapeutic applications

It is a basic tenet of patent law that claims must be concise, clear and supported by the description,[107] militating against speculative claims going beyond the actual technical contribution. The Article 83 EPC 'sufficiency' requirement serves to ensure that a patent specification discloses enough for the invention to be carried out by someone skilled in the art.[108] The invention must *work* [109] – it must do, 'what it says on the tin', so to speak. Of the sufficiency test in the UK, Lord Hoffmann said

'*Whether the specification is sufficient or not is highly sensitive to the nature of the invention. The first step is to identify the invention and decide what it claims to enable the skilled man to do. Then one can ask whether the specification enables him to do it'.*[110]

Article 83 EPC is aimed at the subject matter of a particular claim[111] rather than what may be perceived to be the invention as discerned from the specification; or what is considered to be the contribution to the art. Therefore, sufficiency of disclosure must be made in relation to the whole subject matter of individual claims.[112] The requirement for sufficiency in respect to gene or protein sequences means the skilled person must be able to reproduce the invention and put it to work in the field claimed under Article 57 EPC. It

[107] Article 84 EPC.
[108] Article 83EPC and Rule 42(1)(e): *The description shall - describe in detail at least one way of carrying out the invention claimed, using examples where appropriate and referring to the drawings, if any.*
[109] Per Lord Hoffmann, *Conor Medsystems Inc v Angiotech* [2008] UKHL 49, 37.

[110] Lord Hoffmann in *Kirin Amgen Inc and others v Hoechst Marion Roussel Ltd and others* [2005] 1 All ER 667 at [112].

[111] T 792/00 – 3.3.04. *Varied binding proteins*/DYAX (July 2002), point 2
[112] T 601/05 – 3.3.04. *Anti-TNF alpha human monoclonal antibodies*/BAYER III (December 2009), point 33.

is usual for 'reproducibility' to be assessed at examination of the application and examples are usually most appropriate to fulfill the requirement.[113]

For inventions based on biological material to be claimed as therapeutic compositions or treatment, the patent must provide some information, such as experimental data, to show that the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease[114], this mechanism being known either from the prior art, or demonstrated in the patent *per se*. [115] The Technical Boards have consistently held that, where a therapeutic application is claimed – whether in the form of a first or further medical use – this has the consequence under Article 83 EPC, that unless this is already known to the skilled person at the priority date, the patent must *disclose the suitability of the product for the claimed therapeutic application*.[116]

As to the standard of proof required to show that a patent does *not* disclose the suitability of a product for the claimed therapeutic application, EPO jurisprudence has developed a principle that a insufficiency objection can only succeed where 'serious doubts are substantiated by verifiable facts' exist.[117]

In *Neutrokine/* HGS there seemed no way around a conclusion that a skilled addressee must embark on a program of research to elucidate a pharmaceutical effect *and*

[113] Rule 27(e) EPC.
[114] n 112 above, point 91.
[115] Disclosing a pharmaceutical effect *in vitro* is only sufficient if the skilled addressee considers the observed effect directly and unambiguously reflects such a therapeutic application: n 112 above, point 91, citing T 609/02 – 3.3.08. *AP-1 complex*/ SALT INSTITUTE (October 2004), point 9.
[116] Ibid, point 9 in relation to a claim to a second medical use; T 219/01 – 3.3.04. *HIV Vaccine*/GENENTECH, (December 2004) point 4, in relation to a first medical use; n 112 above, point 90.
[117] n 21 above, point 32 ; n 112 above, point 94.

suitability for therapeutic application, to work HGS' pharmaceutical and diagnostic inventions.

Yet although the insufficiency attack mounted on HGS' patent succeeded at first instance in the UK and would have likely succeeded at the Court of Appeal[118], none of the allegations against HGS' claims to therapeutic and diagnostic compositions[119] succeeded at the TBA because the claims were considered *plausible*, serving to extinguish any (serious) doubts that may have otherwise existed. It did so by averting from traditional doctrine, pointing to what it considered a *plausible* disclosure of a '*prospect of a real possibility of exploitation in the pharmaceutical and diagnostic fields'*.[120] In the Board's view, this conferred '*positive reflections*' [121] on the evaluation of sufficiency which meant the skilled addressee could work all that was claimed, 'without undue burden or inventive skill.'[122] The TBA arrived at its conclusion, apparently undeterred by the absence of experimental data to demonstrate therapeutic efficacy,[123] or the numerous contradictory, broad statements concerning the range of conditions and diseases, which the English lower Courts were convinced would have been dismissed by the skilled addressee as speculation with no actual relevance.

In adjudicating the insufficiency objection against HGS' patent the TBA emphasised a '*close inter-relationship*' between Article 83 (sufficiency) and Article 57

[118] n 17 above; the insufficiency and inventive step points were not considered by the Court of Appeal in light of the adverse finding on industrial application, though it was likely to have '… gone hand-in-hand with Article 57', n 2 above at[159].
[119] The patent did not disclose any *disease* in which the level of Neutrokine-α expression was increased or reduced.
[120] n 21 above, point 20.
[121] n 21 above, point 20.
[122] n 21 above, point 24.
[123] n 112 (Salt Institute) above, point 9 in relation to a claim to a second medical use; n 116 above, point 4 in relation to a first medical use; n 112 above, point 90.

(industrial applicability),[124] perceiving a common ground inasmuch as both demand sufficient description of the invention.[125] The TBA might have been expected to restrict itself to question whether, in light of common general knowledge, the patent provided an 'enabling disclosure' sufficient to work the invention across the full breadth of the claims, which is also the standard applied in English courts,[126] most recently in *Conor v Angiotech* (concerned with inventive contribution). It is instructive to the debate, to consider this case. The claims in issue were to a medical device, a stent coated with polymer loaded with the drug taxol. The invention was held by the lower courts to be obvious (non-inventive) but this finding was reversed by the House of Lords. The House considered the lower courts had erred by applying a test involving, '*an illegitimate amalgam'* of inventive step with either sufficiency, support, or both.[127] Lord Hoffmann emphasised that inventive step and sufficiency are separate requirements that should not be conflated. Counsel's argument that lack of evidence in the specification compromised inventiveness was rejected because *inventive step* does not call for experimental evidence to show that an invention *will* work. As noted it is enough if a specification passes a 'threshold test' of disclosing enough to make an invention *plausible*. Lord Hoffmann saw no reason why inventive step should be subject to a different standard to sufficiency. But if a claim turns out *not to be true* the patent is insufficient.[128]

In *Neutrokine/ HGS*, the question whether there was sufficient information *how* to work the claimed therapeutic and diagnostic inventions was subtly altered by the TBA to,

[124] n 21 above, points 16 and 18.
[125] n 21 above, point 18.
[126] *Biogen v Medeva plc* [1997] RPC 1.
[127] n 110 above at [17].
[128] n 110 above at [37].

in what industrial field? This is perplexing because one cannot exploit (within the meaning of Article 57EPC) a pharmaceutical composition if the instructions how to perform it *as a therapeutic* are inadequate. Even though the skilled addressee is able to make the composition, he is not able to *work* it. To grant a patent is not to 'reserve an unexplored field of research for an applicant'. [129] So, conventional sufficiency rules necessitating evidence of the product's suitability for the claimed therapeutic application were conflated with those for industrial application[130], resulting in (to coin Lord Hoffmann's expression) another 'illegitimate amalgam.'[131] The question became first, whether the specification disclosed the nature and purpose of Neutrokine-a (ie its biological, biochemical or cellular function); and second, how it can be used in industrial practice.[132] This allowed the '*how* to work it' (sufficiency) part to be evaded in preference to '*where* to work it'. So, 'exploitation in pharmaceutical and diagnostic fields,' amounted to plausible (therefore sufficient) disclosure in the absence of verified evidence to the contrary. [133]

Although some might regard, '*plausibility of a prospect of a real possibility'* as unfathomable imprecision; and that '*positive reflections'* must fall short of an acceptable standard of proof, without further ado the insufficiency point had been concluded. In sum, the TBA in *Neutrokine/* HGS put forward a conclusion about industrial applicability for inventions arising in proteomics and genomics through the application of what may be described as convoluted logic, arriving at a test that involves different standards -

[129] n 59 above, at [21].
[130] n 21 above, point 18.
[131] n110 above at [17].
[132] n 21 above, point 18.
[133] n 21 above, point 20.

'plausibility' on one hand and 'serious doubts substantiated by verifiable facts' on the other. The standard for a negative finding (akin to 'beyond reasonable doubt') is far higher than for a positive finding (mere plausibility), perpetuating the generosity to the patentee that the Board in *Max-Planck* stated 8 years before should be curtailed. [134]

Furthermore, the TBAs finding of industrial applicability for HGS' invention was only possible by application of a usurped concept ('plausibility') to bridge an otherwise fatal evidential-gap (relating to showing one real, actual function), bolstered inappropriately by post published data going beyond speculation for the first time (contrary to the ratio of *John Hopkins*), rendering the Board's finding of sufficiency[135] equally unconvincing as that of industrial applicability.

The EPO's reformulation of the sufficiency standard is unwarranted. A relationship between sufficiency and industrial application must (and does) exist.[136] However unusual it may be, failure of one does not *necessarily* entail failure of the other.[137] For example, an invention might be difficult to carry into practice because the patent's teaching is insufficient; whereas the industrial applicability might be clear from its nature coupled with common general knowledge. The criteria are distinct, assessed at different stages of examination. Furthermore, industrial applicability cannot 'fix' an insufficient patent, and vice versa. The effect of the TBAs 'illegitimate amalgam' serves to gloss over an insufficiency objection by avoiding the question whether *how* to perform the thing as claimed has been taught.

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[134] n 59 above.
[135] n 21 above, points 37-38.
[136] Objection arises under art 83 and art 52(1) EPC; T 005/86 – 3.5.01. Newman/ Perpetual Motion.(March 1988).
[137] See for example n 112 above; T 604/04 - 3.3.08. *PF4A receptors*/GENENTECH (March 2006).

The view in *Neutrokine/* HGS that unfairness is obviated by application of the same standard for industrial application as for sufficiency is difficult to comprehend where this results in biotech patents being granted and maintained, without at least one *actual* function and *practical use* being identified, contrary to its own guidelines for examinations.

4. *HGS v Eli Lilly* at the Supreme Court

It may be recalled that the central issue at the EPO and in the English lower Courts was whether, in light of common general knowledge, the patent satisfied Articles 52 and 57 EPC, allowing HGS to claim the encoding gene for Neutrokine-a.[138]

Kitchin J (affirmed by the Court if Appeal) determined the sum of the patent's teaching to be:

1. existence and structure of a gene HGS called 'neutrokine-a'
2. that neutrokine-a is a member of TNF ligand superfamily.

On appeal to the Supreme Court, HGS asserted this set too high a standard for industrial application in the context of a patent for biological material.[139] Yet even taking common general knowledge into account Kitchin J could find no teaching for a practical way to exploit neutrokine-a in industry.[140] That finding was corroborated by the fact that a number of years after the patent was filed HGS, Eli-Lilly and another company (Biogen)

[138] n 23 above, 27.
[139] n 23 above, 33.
[140] n 23 above, citing Kitchin J, 75.

were each engaged in research to discover where neutrokine-a was expressed, where its receptors were expressed and what its activities were. The research endeavor resulted in neutrokine-a being viewed as a therapeutic *target,* possibly in the treatment of B-cell disorders[141] but even then, specific function remained elusive.

Preferring the interpretation of the Technical Board in *Neutrokine/* HGS rather than (concomitant) findings[142] of the lower courts, the Supreme Court found the patent taught:

1. that neutrokine-a is a member of the TNF ligand superfamily,
2. tissue distribution of neutrokine-a,
3. expression of neutrokine-a in B and T cell lymphomas.[143]

Their Lordships' view of the patent's *teaching* undoubtedly assisted HGS, yet it should be borne in mind the patent contained nothing that showed function (2) and (3)[144]. Instead, the principle discerned from TBA jurisprudence more generally, was that it was enough if these functions were *plausible* (supported by post published evidence).[145] Similarly there was nothing to indicate the invention was useful for any of the diagnostic or therapeutic treatments listed in boiler-plate '*wide ranging and generalized suggestions as to uses which neutrokine-a and its antibodies might be put*'.[146] The fact that

[141] n 23 above, citing Kitchin J, 75.
[142] Where the Court of Appeal has upheld the trial judge's findings of fact and value judgments.
[143] n 23 above, 103.
[144] Expression in activated T cells and neutrokine-a activity on leucocytes, reported in the patent, 'although without concrete experimental data': n 21 above, point 24, cited in n 23 above, 77. Report that neutrokine-a expressed in B and T cell lymphoma reinforced speculative function: n 23 above, 111. Industrial applicability supported by interest in the pharmaceutical industry [111].
[145] n 23 above, [81].
[146] '… there is no experimental evidence to support any of those suggestions', per Lord Neuberger n 23 above at [8].

pharmaceutical companies were engaged in research to find out where neutrokine-a was expressed, where its receptors were expressed and what its activities were 2-3 years after the patent was filed confirmed (at least to the minds of the Kitchin J and those in the Court of Appeal) the findings of fact.[147] Another document, cited by Jacob LJ in the Court of Appeal indicated that even nine years post grant of HGS' patent, the significance of T cell activity remained elusive.[148]

The Supreme Court determined none of this mattered. It did not matter because EPO Article 57 EPC jurisprudence was 'tolerably clear' and should therefore be followed.[149] 15 principles were identified and grouped within 3 normative strata[150] formulating a reducing standard for Article 57EPC inventions arising in the biotechnology field.

The first stratum enumerates 'general principles' that are uncontroversial, with the following exception:

(iv) *The patent and common general knowledge must* ***enable*** *the skilled person 'to reproduce' or 'exploit' the claimed invention without 'undue burden', or having to carry out 'a research programme.'*

'Enablement' is not a standard typically applied to industrial application but rather novelty or sufficiency of disclosure. Case authority (*Genentech,* at point 22) for

[147] n 17 above at [235].
[148] n 2 above at [156].
[149] n 23 above at [123].
[150] (i) – (iv) general principles; (v) - (x) new protein and encoding gene; (xi) – (xv) new protein putative member of a family or superfamily, n 23 above, 107.

this principle does indeed concern *sufficiency* (Article 83EPC). General principle iv therefore confusingly recites a test for sufficiency of disclosure, which is misplaced in a list of principles for industrial application.

The second stratum applies to newly identified genes and proteins and is singularly problematic for the reason that the introduction of 'plausibility' as a standard for Article 57EPC to support principles (viii-ix) is part-based on a TBA decision in which Article 57EPC was neither pleaded, argued nor discussed (*John Hopkins).*[151] Each principle in this stratum draws authority from *ZymoGenentics,* analyzed below.[152]

The third stratum applies to new proteins that are putative family or superfamily members, authority for which is based on *John Hopkins, Genentech, Max-Planck, Bayer* (and *Schering Corp*). The most controversial of third stratum principles is principle xiii – '*If the disclosure is 'important to the pharmaceutical industry', the disclosure of the sequences of the protein and its gene may suffice, even though its role has not 'been clearly defined,'* [153] and is established on the basis of *Genentech* alone.

Although decisions of the Technical Boards on questions of law are of immense importance,[154] British courts should not simply follow *any* standard applied in a series of cases by the Technical Boards.[155] This is partly because decisions of the Technical Boards are often based on an 'ex parte' hearing where only one side is argued[156] – as was the case in *Max Planck, John Hopkins, Schering* and *Zymogenetics*. There are differences

[151] The case is discussed in a section of the Supreme Court's judgment that identifies TBA jurisprudence on Article 57EPC and biological material n 23 above, 48-50.
[152] n 61 above.
[153] n 137 at point [18].
[154] n 2 above, 38.
[155] n 2 above, 41.
[156] n 2 above, 84.

between procedural rules on admissibility of evidence and a limited ability to cross-examine, compared with the British common law tradition, the hallmarks of which are oral argument, disclosure (discovery) of documents, cross-examination of witnesses, and witnessing of experimental evidence.[157] As one commentator points out,

'The TBA decision should be seen for what it is – an appellate body of an organization whose job it is to grant patents … [it] will not look at a patent document and the evidence submitted by all parties in opposition and appeal proceedings with the same eyes as a national court … these factors combined could restrict the ability … to test the veracity of written evidence and so hamper the fact-finding mission of the tribunal.'[158]

A decreasing standard for inventions arising in biotechnology based on ad hoc, fact-specific case law in conflict with EU principle for industrial application in biotechnology is not a *legitimate* direction in which to take English patent law. The most controversial aspects of these principles are now examined in doctrinal context.

A. 'Plausibility' and 'Post-Published Evidence'

The 'threshold plausibility test' is a standard arising from the EPO's so-called, 'problem-solution' approach. Traditionally associated with the evaluation of inventive step[159] (ie

[157] World Intellectual Property Review, 'Inside the PCC: An interview with Colin Birss', March/April 2013, 22.
[158] G. Morgan, 'When the TBA just isn't enough' *CIPA Journal* (2010) (39) **4** 229, 231.

[159] As Lord Hoffmann pointed out in *Conor Medsystems* v *Angiotech,* there is no reason as a matter of principle why, if a specification passes a threshold test of disclosing enough to make the invention plausible, the question of obviousness should be subject to a different test. The standard at the EPO for sufficiency is negative, the burden on the respondent to demonstrate serious doubts based on verified facts.

the requirement to show a *plausible* solution to an identified problem), the TBA in *John Hopkins,* in relation to inventive step said,

'The definition of an invention as being a contribution to the art, ie as solving a technical problem and not merely putting forward one, requires that it is at least made plausible by the disclosure in the application that its teaching solves indeed the problem it purports to solve'.[160]

Inventive step requires the disclosure to go beyond that which is obvious.[161] There is no requirement in patent law that the patent application must demonstrate by experiment that the invention will work, or why, only that it is *plausible* that it will work.[162] Therefore, a 'theory'[163] put forward in a patent may meet the '*threshold test of disclosing enough to make the invention plausible*' despite absence of experimental data to support the hypothesis.[164] If 'post-published' evidence is taken into account, this must not provide the sole basis for demonstrating that the patent's teaching solves the problem identified.[165]

In contrast, at least one function that can be applied industrially must be documented in the patent, supplemented only by the common general knowledge of the skilled addressee at the time, as demanded under EU law.[166] 'Post-published evidence' can not include evidence that establishes something for the first time or adds to what the

[160] n 95 above at point [12].
[161] n 95 above.
[162] n 110 above, 23.
[163] n 110 above, 37.
[164] n 110 above at [37].
[165] n 95 above, 12.
[166] Article 5(3) Directive 98/44/EC [industrial application]; n 37 above.

potential industrial application of the patented subject matter might be,[167] '…*it is surely axiomatic that whatever the standard for susceptibility to industrial application may be, the information about it must be in the patent*' per Jacob LJ.[168]

The TBA in *Neutrokine/ HGS* crossed over 'plausibility' (from the assessment for inventive step) to the assessment of industrial application. Although speculation or an educated guess about gene or protein function may be plausible, can this be reconciled with the demands of Article 5(3) of the Biotechnology Directive upon which patentability rests? Jacob LJ insisted the meaning of 'plausible' in relation to industrial application, meant '*…more than 'not incredible' is required – there must be some real reason for supposing that the statement is true'.*[169] In what may be considered a key point of departure between the British lower courts and the Supreme Court, Jacob LJ said, '… *it is not good enough to say this protein or any antibody to it probably has a pharmaceutical use. Such a statement is indeed plausible, but is of no real practical use. You are left to find out what that use is.*'[170] The Supreme Court considered EPO jurisprudence did not require a use to be specific, or specified at anything less that a high level of generality. Moreover, it did not consider that principle to be bad.

Yet, can it really be good policy to permit a patentee to rely on research evidence (possibly derived from others' work) to prove a speculative function over which claims to gene products and processes may have been filed some years before, if validity is challenged? Should post published evidence be permitted to convert mere '*plausible*

[167] n 2 above at [92].
[168] n 2 above at 92.
[169] n 2 above at [111].
[170] n 2 above at [112].

function' at a high level of generality to a specific function, required under EU law? As the TBA in *John Hopkins* said, enumerating any and all putative functions of a given compound is not the same as providing technical evidence as regard a specific one.[171]

EPO jurisprudence is not consistent[172] in respect to the admissibility of 'post published evidence' in substantive examination or prosecution. For example, the Board in *John Hopkins* (cited by the Supreme Court both in *Conor v Angiotech* and *HGS v Eli Lilly*) determined that speculation as to how the encoding gene (GDF-9) and protein were *inventive,* did not meet the threshold test of plausibility - and post published evidence could not be relied on to remedy the defect:

'*This cannot be regarded as supportive of an evidence which would have been given in the application as filed since there was not any. The said post-published documents are indeed the first disclosures going beyond speculation. For this reason, the post-published evidence may not be considered at all. Indeed, to do otherwise would imply that the recognition of a claimed subject-matter as a solution to a particular problem could vary as time went by'*.[173]

The TBA continued that even if *supplementary* post-published evidence may in the proper circumstances be taken into consideration, it can not serve as the sole basis to

[171] n 95 above, point 10.
[172] 'Post published evidence' cannot support a *present* industrial application; thus the applicant in *Icos* (n 69 above) could not rely retrospectively on data of which it was unaware at the time the patent was sought, to later confirm function.
[173] n 95 at [point 12]

establish that an invention solves the problem identified.[174] If it is correct to say that 'threshold plausibility' may apply to show industrial application in the same way that it *may* apply to show inventive step, then *John Hopkins* establishes that speculative function that does not achieve threshold plausibility, but which is later confirmed by post published evidence going beyond speculation for the first time, *does not amount to industrial application.*

Post published evidence is a concept that has *no place* in substantive patent examination, being diametric to the principle that all criteria for patentability must be ascertained as from the effective date of the patent, engendering a policy in the biotech industry that supports patents for guesses – open to anyone, to claim anything yet to be substantiated. Neither is EPO jurisprudence settled as to whether so-called 'boiler-plate' drafting is correct practice,[175] being what:

'*… patentees without evidence of treatable conditions do when filing patent applications, namely include as 'boiler-plate' the disclosure of a long list of possible activities and conditions (including implausible, self-contradictory ones) from which they later 'cherry-pick' the very few which have been subsequently confirmed or demonstrated'.*[176] The skilled addressee must fathom from (boiler-plate) description what exactly the patent teaches. This raises the question about what attributes the average skilled worker in the biosciences must be considered to have.

[174] n 95 above, point 12.
[175] n 21 above, point 27.
[176] n 21 above at page 22 (respondent's argument).

In EPO (biotechnology) case law the skilled person is not only familiar with the common general knowledge in the technical field but also possesses the following characteristic: '… *is driven by its naturally present scientific curiosity*'.[177] This in turn poses the question – how *driven* is 'driven'? If one considers that, besides common general knowledge, it is necessary to take into account, *'the then prevalent attitude of the person skilled in the art',*[178] it is easy to see how these indeterminable qualities invite uncertainty about the level of drive, attitude and curiosity to be attributed to a skilled (hypothetical) person at the priority date for the assessment of industrial applicability, contributing to further obfuscate. This can be seen in *HGS v Eli Lilly* in the split view of what the skilled person would make of boiler-plate drafting, a question that must surely turn on how driven the skilled person is to work out which parts of the (long and contradictory) list in HGS' patent constituted positive technical data, as opposed to irrelevant boiler-plate. [179] As noted above, the British lower courts were convinced that the skilled worker would simply dismiss the lot;

'The skilled person would consider it totally far-fetched that Neutrokine-a could be used in relation to them all and … would be driven to the conclusion that the authors had no clear idea what the activities of the protein were and so included every possibility. To have included such a range of applications was no better than to have included none at all.'[180]

So, knowledge of attorney 'boiler-plate' drafting from which relevant technical information must be divined from copious amounts of dud – and the need to be cognisant

[177] n 191 above at [point 9].
[178] n 137 at [point 15].
[179] n 21 above, point 15.
[180] n 17 above at [232].

of patent language nuances (so-called 'patentese')[181] amounts to a good deal of specialist knowledge that must be imputed to the nominal skilled addressee over and above that which is reasonable, serving to diminish the principle that a patent is granted only where it provides a full and enabling disclosure, comprehensible to the skilled addressee, of the invention it claims.

Counsel for Eli Lilly submitted that the 'wordy and extravagant claims' should count against *HGS* as a matter of policy, a point which the UKSC said had '*some attraction*'.[182] But as the patent was not actually so confusing that it *diverted* the person skilled in the art from being able to understand the teaching, the point fell flat. It is submitted this cannot be a correct statement of the principle. It is untenable that the policy for disclosure in patent law should be negatively directed to avoiding actual diversion of the skilled addressee, rather than positively teaching how to perform the invention. It is further evidence that the UKSC judgment, based heavily on the TBA in *HGS*,[183] swings too far in favour of BIAs call for early patenting in biotechnology because of commercial pressures, contrary to the *quid pro quo* of the system; ie the requirement for a clear and full disclosure, comprehendible to the skilled addressee, in return for the monopoly.

A. Critical Analysis of Authority for Second Stratum Principles

[181] T. E. R. Singer & J. F. Smith, 'Patentese: a dialect of English?' *J. Chem. Educ.*, 1967, 44 (2), 111 (discussing word usage of patent attorneys); '… spoken in all European patent courts but, it appears, understood in very few of them'; http://ipkitten.blogspot.co.uk/search?q=patentese (last visited January 2013).
[182] n 23 above, 117.
[183] n 23 above, 117.

As noted, UKSC second stratum principles are based on authority derived from *ZymoGenentics*, a case which concerned a newly identified receptor (Zcytorl), a putative member of Haematopoeitin receptor family. The TBA clarified that where a nucleic acid sequence is given but its function is only vaguely understood, this can,

'*… prevent further research in that area, and/or give the patentee unjustified control over others who are actively investigating in that area and who might eventually find actual ways to exploit it*.'[184]

Having alluded to the problem caused by granting patents too early in the research process, the TBA embarked on a judgment of tortuous reasoning concerning three scenarios in respect to industrial application and new protein sequences.

1. The Board's first principle was that characterization of protein structure was not capable of industrial application if its function was undetermined, or obscure, or only vaguely indicated.[185]

2. Alternatively, if protein structure was characterised, and, in light of the common general knowledge, indicated the new protein was plausibly usable (as a result of the reinterpretation of 'profitable use' widely defined/concrete benefit), this could amount to industrial application.[186] Genesis of the role of 'plausibility' as the standard for industrial application in cases where a product is definitely described and plausibly

[184] n 61 above at [point 7].
[185] n 61 above, point 7.
[186] n 61, point 8

shown to be usable (eg to cure a rare or orphan disease) conferring a profitable use or 'immediate concrete benefits', was established. [187]

3. The third scenario was rather less straight-forward than the previous two. If a protein is structurally characterised and an educated guess about its function made, this should be assessed against the common general knowledge and prior art. If the assessment fails to raise 'significant or serious doubts'[188], the assumption or 'educated guess' is considered a *plausible* function to attribute to the molecule,[189] and post-published evidence can be considered.

But, plausibility alone does *not* suffice to show industrial application. One must establish whether the protein's function at one of three levels (biological[190], chemical or cellular) is too vaguely defined[191] that no practical application or profitable use can be envisaged'.[192] On the other hand, if it is not too vaguely defined, it must be ascertained whether there are indications (eg therapy) which are directly derivable from that level of function. If so, industrial application can be acknowledged.

The TBA applied this reasoning to the facts of the case. The applicant (ZymoGenentics Inc.) had recited an 'educated guess' in the specification that the newly identified receptor was a member of the 'Haematopoeitin Receptor' family**,** absent

[187] n 61, point 8
[188] n 61, point 27.
[189] n 61 above, point 31.
[190] n 61 above. Biological function may be elucidated via computer assisted methods: point 31.
[191] n 61 above. The Board said that none of the 3 levels - cellular, biochemical or biological (widely defined) are more 'specific' or less vague than the others.
[192] n 61 above, point 28.

experimental data to this effect. This educated guess was confirmed by post published evidence spanning 4-6 years after the priority date.[193] Biological function, identified by computer assisted methods implicated therapeutic function, which was more than 'vaguely defined'[194] upon which an industrial application in the pharmaceutical field (as a therapeutic) was directly derivable. It did not matter that nothing was known about other functional levels (cellular and chemical).[195] Instead industrial application depended on the extent of disclosure, background art and post published evidence.[196]

It is noteworthy that the Technical Board in *ZymoGenentics* accepted post published evidence going beyond speculation *for the first time* to corroborate the predicted function recited in the patent, to make a finding of industrial applicability. This practice was applied in *Schering*[197], where sequence similarity disclosed in the application suggested the encoded protein was a member of a superfamily. This was equated to plausible function (in immune response) and confirmed by post published evidence 4 years after the patent application was filed.[198] In yet another case (not considered by the UK Supreme Court) the TBA again accepted post published evidence for the first time going beyond speculation,[199] to reinforce putative function of the

[193] Post published documents dated 4-6 years after the priority date confirmed preliminary findings: n 61 above points 17-18 & 24.
[194] n 61 above, point 36. Compares T870/04 (n 59 above) – distinguishes on facts, as the claimed molecule had no clearly identified role.
[195] n 61 above, point 30. This principle was applied by the Board in T 641/05 *Pharmacia & Upjohn* (Nov 2006) at point 13 – no actual information regards function of the claimed clone – at any of the 3 particular levels of function referred to in 898/05 – can be directly derivable from the application or the prior art.

[196] n 61 above, point 20.
[197] T1165/06 – 3.3.08. *IL-17 related polypeptide*/SCHERING (July 2007).
[198] ibid [point 25]referring to document D5 dated 2004 (patent filed 2000).
[199] Concerning the relevance of a specific marker to detect *activated* T cells as opposed to T cells *at rest*: T 1540/07 - 3.3.08. *Cytokine receptor*/HUMAN GENOME SCIENCES (December 2008), point 11.

claimed protein and encoding gene, found to confer 'an immediate concrete benefit,' so complying with Article 57EPC.[200]

These cases may be contrasted to *Max-Planck* where the TBA found that speculation about the function of the BDP1 protein in issue could not amount to 'plausibility' and post published evidence served only to demonstrate that any influence of the claimed BDP1 polypeptide remained to be adduced by continuing research – which the Technical Board said, at 8 years after priority, was rather far away from an assertion supporting implicit disclosure.[201] The TBA in *Max-Planck* earnestly advocated that EPO practice should be aligned with the law to ensure that patents (or an application for one) relates to inventions that are capable of industrial exploitation. The TBA considered the munificence hitherto extended to applicants for speculative claims over newly identified genes and proteins should be reigned in;

'While the jurisprudence has tended to be generous to applicants there must be a borderline between what can be accepted, and what can only be categorized as an interesting research result which per se does not yet allow a practical industrial application to be identified'. [202]

Specifically, the Board sought to curtail patents for newly isolated naturally-occurring substances, where:

1. Function is unknown or incompletely understood, and

[200] ibid point 16-17 .
[201] n 59 above, point 17.
[202] n 59 above at [point 6].

2. No condition has yet been identified as being attributable to an excess of deficiency of the substance, and
3. No other practical use is suggested observing that research results may be a scientific achievement of considerable merit, but they are not necessarily *an invention* which can be applied industrially.[203]

This decision indicates the case law of the Technical Boards at the time of the HGS litigation could not be considered 'established' as suggested by the TBA in *Neutrokine/ HGS* even though subsequent TBAs have not followed *Max-Planck* in preference to the generous policy established in *ZymoGenentics*.

The TBA in *TGFα-HII/*HGS [204] was no exception. In contrast to the 15 principles identified by the UK Supreme Court, the TBA promulgated two *general* principles, applicable to *all* claims, to comply with Article 57EPC. The TBA emphasised that *putative* function must be disclosed, although experimental evidence was 'not always necessary'.[205] If an educated guess (i) is plausible to the skilled person based on information in the patent, and (ii) post published evidence provides a clear basis for an industrial application, this will suffice. Applying these principles the Technical Board found that putative function in conjunction with post published evidence indicating the

[203] n 59 above, point 6.
[204] T1450/07 – 3.3.08. *TGFα-HII*/HUMAN GENOME SCIENCES (February 2009)
[205] ibid point 5.

claimed protein '*may be said to be useful in the treatment of neurodegenerative disorders such as Parkinson's disease,*' meant that industrial application could be acknowledged.[206]

In *Myriad*[207], the appellant repeatedly invoked the principles recited in *Icos*[208] against the patent in suit, as did the appellant in *Neutrokine/ HGS*[209] 2 years later, (which both Boards rejected in preference to *ZymoGenentic*s). As the claimed gene probes were definitely described and plausibly shown in the patent to be useful in the diagnosis of cancer, particularly breast, industrial application was acknowledged.[210] The view of the Technical Board in *Neutrokine/ HGS* contrasts starkly with *Max-Planck* in that post published evidence was accepted to demonstrate implicit disclosure, notwithstanding some reservation about the 'correctness' of such evidence.[211]

B. Critical Analysis of Authority for Third Stratum Principles

As noted earlier, third stratum principles apply to new proteins that are putative family or superfamily members. The most contentious of these (principle xiii) is established on the basis of *Genentech* alone which introduced, '*if important to Pharma,*'[212] as a principle for industrial application. Although the decision in the earlier case of *Max Planck* nowhere implied that if a substance could be argued to be, 'of great interest to Pharma', that this

[206] n 196 above at [point 8].
[207] T 1213/05- 3.3.04. *Breast and ovarian cancer*/UNIVERSITY OF UTAH (Sep 2007).
[208] Decision of the Opposition Division published in the Official Journal of the EPO (2002, page 293).
[209] n 21 above.
[210] n 199 above, point 67.
[211] Reliance on post-published evidence should have no place in substantive patent examination, which may be viewed as tantamount to impermissible addition of matter.
[212] n 137 at [point 18].

could amount to industrial application, this is precisely the interpretation of the Technical Board in *Genentech* - which cited *Max Planck* in support of it.

The invention in *Genentech* concerned a newly isolated receptor which putatively belonged to the PF4AR superfamily.[213] The TBA decided the invention possessed industrial application absent any real functional information. The reasoning is as follows; at the priority date, F4-related proteins were considered 'attractive targets for the development of new therapeutic agents'.[214] This suggested the skilled addressee would have perceived chemokines (PF4-related proteins were chemokines) as being of great interest to the pharmaceutical industry, 'if only to investigate their potential as *targets* for drug development, *irrespective of what the end result might be*' (emphasis added).[215]

Leaving aside the criticism that investigating an invention's 'potential as a drug target' is difficult to meaningfully distinguish from merely using the thing to find out more about it, which does not amount to industrial applicability; the decision is most remarkable for the way in which it shifts the burden on the patentee to identify a *specific* function in respect to industrial application for gene or protein sequences, to a generalised footing – *a possible target.*[216]

On the sufficiency issue, the Board in *Genentech* considered its newly established ground ('*if important to Pharma*') could not support claims directed to use in therapy, or

[213] 'Claim 1 to an isolated PF4AR superfamily polypeptide receptor having at least an 85 per cent sequence homology with the translated amino acid sequence of Figure 4 or 5'.
[214] n 137 above at [point 17].
[215] n 137 above at points [17] and [27].
[216] n 137 above, point 27.

as a pharmaceutical composition.[217] A lingering doubt must remain that Genetech's disclosure should have failed for want of both sufficiency and industrial application but for the Board's interpretative wizardry, so that Article 57EPC was met by common general knowledge *alone* (that chemokines were of great interest to 'Pharma'), squeezing Genentech's claim past Article 57EPC (if not Article 83EPC) without recitation of any one specific function for the newly identified receptor upon which to base an industrial application.

'Of interest to Pharma' is not an established principle in TBA jurisprudence. All proteins have some sort of function. Therefore any protein and its antibodies could well have therapeutic potential and so be of interest to the pharmaceutical industry. Where an element is of interest to it, this does not mean that a practical (industrial) application is inevitable (or even possible). Therapeutic importance might not be realised, or it might only come to light years after the patent is granted, so the grant of a patent could well serve to close off areas of research, contrary to established patent policy. The extension ('*if important to Pharma'*) is unwarranted and unworkable, threatening doctrinal coherence, courting the well-known commodore-and-rocks metaphor of Jacob LJ[218].

So, the general principle that a patent should provide a use in industrial practice, derivable from the description coupled with common general knowledge,[219] is progressively dismantled by the Supreme Court in the second and third strata. If a claim to a gene and its protein fall into the second stratum, the patentee need only offer an *educated guess* about industrial applicability in return for their 20-year monopoly

[217] n 137 above, point 27.
[218] n 1 above at [39].
[219] n 23 above at [107] principle (ii).

because an educated guess (if it is reasonably credible[220]) is considered in some EPO case law to confer *threshold plausibility* (a concept filched from inventive step and sufficiency doctrine), that effects a lowered standard for industrial application in biotechnology, diminishing the demand on the patentee to provide a practical application in industry. If a gene and its protein are alleged to be a family or superfamily member, then the demand to show industrial applicability based on an identified function, is entirely obliterated[221] because it is enough if the claimed biological matter is '*important to the pharmaceutical industry', 'absent clear functional definition'*.[222]

The problem that 'plausibility' may involve *speculation* (notwithstanding the concepts are stated to be different)[223] was dismissed by their Lordships because it takes matters 'no further' as regards patentability; if the patent's predictions are plausible, a smattering of speculation matters not. This reasoning led to rejection of the assertion that the need for further work to see whether the invention actually had therapeutic benefits, '… *does not, at least without more, undermine the validity of the patent'*, according to EPO jurisprudence.[224]

In sum, the Supreme Court found the approach of the Court of Appeal, like that of Kitchin J, to be predicated on, '*a mistaken belief that it was not enough for the patent to satisfy the requirements of points (xi) to (xiii)*'.[225] Lord Neuberger and Lord Hope apparently derived considerable assistance from the approach set out by the TBA in

[220] n 23 above at [107] principle (viii).
[221] Unless evidence is available that calls the role or membership into question (xiv).
[222] n 23 above at [107] principle (xiii).
[223] n 23 above, 123.
[224] n 23 above at [120].
[225] n 23 above at [121].

Neutrokine/ HGS, which Lord Neuberger considered was 'entirely consistent with earlier jurisprudence,'[226] although it may be more accurate to say that some aspects of the reasoning were consistent with some aspects of (developing) EPO jurisprudence.

Jacob LJ pointed out that there is no British tradition of deference to the EPO Technical Boards concerning fact specific objections, in preference to the intense fact finding and evaluation process in English courts. It is not clear why the Supreme Court did not so think, particularly as the question before the lower courts in *Eli Lilly* v *HGS* concerned a question of degree turning on the facts rather than a pure question of law.[227] The exhortation that national courts follow 'settled EPO case law', when the Technical Boards themselves are not so bound, cannot be justified in the quest for interpretative uniformity, at the cost of doctrinal coherence.

Furthermore the point at which EPO case law may be considered to be established, particularly in a rapidly developing technological field where there is no decision of the Enlarged Board of Appeal is moot. This EPO case law cannot be considered settled. For example, *Genentech Inc* exists in isolation in determining that '*of interest to Pharma*' may amount to industrial application. Yet this has been adopted as a principle in English patent law, although it enjoys no such status at the EPO. The Supreme Court acknowledges that national courts should not regard the reasoning in each decision at the EPO as effectively binding because it may consider the decision to take the law in an

[226] n 23 above, [110].
[227] n 2 above, 70.

inappropriate direction, to misapply EPO jurisprudence or fail to take a relevant argument into account.[228]

Even if the 15 principles concerning industrial application are considered to be correctly predicated on the principles established for inventions in the biotechnology field by EPO jurisprudence, does EU law demand more?

The legitimacy of applying different standards in patent law for genes and proteins based on alleged membership of a 'family' or 'superfamily,'[229] is questionable. These terms are not used in the Biotechnology Directive and may mean different things to the skilled addressee[230], rendering neither sufficiently precise around which to craft legal principle. For example, (multigene) 'families' may be defined as groups of genes with sequence homology and shared overlapping functions.[231] Others assume the term to connote shared homology, but not necessarily shared function.[232] In other words, a 'multigene family' might include groups of genes that encode proteins with similar sequences either over their full lengths or just a partial match, so they are a family of related proteins encoded by a set of similar genes.[233] As regards 'superfamily', if a group of proteins or genes contains a domain of common origin with non-overlapping functions, it is considered a 'superfamily.'[234] Or it may be defined as a group that shares *the same*

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[228] n 23 above, 87.

[229] n 23 above, General Principles (xi)-(xv), at [107].

[230] 'The expression 'superfamily' does not appear to have a precise meaning': per Lord Hope n 23 above at 147 and Jacob LJ n 2 above at [73].

[231] T. Ohta (Mar 2008) Gene Families: Multigene Families and Superfamilies. In: eLS. John Wiley & Sons Ltd, Chichester. http://www.els.net [doi: 10.1002/9780470015902.a0005126.pub2], last visited July 2013.

[232] Department of Cardiovascular Science, University of Sheffield.

[233] Ibid.

[234] n 232 above.

function but not necessarily homology or structure;[235] rather it is the function that defines the family.[236] Furthermore, a protein or a gene may belong to two or more superfamilies.[237] Pondering the lack of precision attributed to the term 'superfamily', Lord Hope seemed to satisfy himself that whether or not an effect (function) can be assigned to an alleged new superfamily member, could be revealed by a detailed examination of the facts which may be enough to show a 'specific function' without experimental evidence.[238] On this point, note the view *supra* that superfamily members do not *necessarily* share homology; but the purported new member is putatively assigned on the basis of shared homology in cases where the sequence is identified by computerised homology studies. Without experimentation to demonstrate membership of a particular supergroup, the allocation is purely speculative. And that is not enough for the industrial application criterion under the Biotechnology Directive.

Why should the premature applicant who possesses no *functional* knowledge about a claimed gene sequence deserve the 20-year monopoly, over those who expend time, effort and resources to demonstrate actual function upon which a biotech invention might properly be based? The Bioindustry Association (BIA) interceded on behalf of its members in the UK bioscience sector by submitting a public interest intervention[239] pointing out the critical importance of a patent portfolio to secure investment for research and development into potential therapeutic value of newly discovered proteins or

[235] n 233 above.
[236] Although they may not share sequence homology now, they probably descended from the same ancestral gene generations ago.
[237] n 232 above.
[238] n 23 above at [148] per Lord Hope, referring to n 61 above, point 22.
[239] Rules 26(1)(a) Supreme Court Rules 2009 and 52.12A Civil Procedure Rules 1998.

antibodies.[240] Acquiring a portfolio was said to be contingent on legal certainty so that funders might be 'reasonably confident' that patents in the portfolio were safe from attack - and that pending applications were likely to be granted. Although the literature concerning the power of patents to attract initial venture capital investment is often anecdotal,[241] empirical studies exist to demonstrate that patents both attract[242] and increase the amount of venture capital funding received for a first round of financing.[243] Notably this power is reduced once information asymmetries between firm and venture capital investor decrease [244] and patenting activity ceases to increase the level of funds by the second round of financing.[245] So how can this policy be said to promote BIAs call for legal certainty, when claims to gene-related products, absent disclosure of specific function that can be industrially exploited, are inherently non-patentable inventions, therefore revocable? How can this engender legal certainty to assist young biotech firms to attract venture funding? In short, I do not believe it can.

The standard for industrial application enunciated at the CJEU in *Monsanto* is higher than the 'plausibility' threshold standard adopted by the EPO technical Boards.

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[240] n 23 above, 97-98.

[241] The Government agrees with Sir Ian Hargreaves Review that robust evidence should drive all IP policy, not generally the case in the past: Government Response to the Hargreaves Review of Intellectual Property and Growth, 2011, 3. Available at: http://www.ipo.gov.uk/ipresponse-full.pdf (last visited December 2012).

[242] Shedding new light on why and how patents provide sources of advantage by decoupling from the services they render, see: D. H. Hsu & R. H. Ziedonis (2012) 'Resources as dual sources of advantage: Implications for valuing entrepreneurial-firm patents' available at, http://www-management.wharton.upenn.edu/hsu/inc/doc/papers/david-hsu-signaling.pdf. See also, C. Häussler & H. M. Zademach (2007) 'Cluster performance reconsidered: Structure, linkages and paths in the German biotechnology industry, 1996-2003,' *Schmalenbach Business Review* 59(3) 261-281; R. J. Mann & T. W. Sager (2007) 'Patents, venture capital, and software start-ups' *Research Policy* 36(2) 193-208; D. H. Hsu (2007) 'Experienced entrepreneurial founders, organizational capital, and venture capital funding' *Research Policy* 36: 722–741.

[243] S. Hoenen, C. Kolympiris, W. Schoenmakers & N. Kalaitzandonakes (2012) 'Do patents increase venture capital investments between rounds of financing?' Manuscript presented to Patent Statistics for Decision Makers 2012 Knowledge Assets and Economic Growth, OECD, Paris, November 28 and 29, 2012 **http://www.oecd.org/site/stipatents/5-3-Patents-signal.pdf**

[244] Ibid.

[245] N 241 above, 34.

The requirement to identify a *specific function* calls for precision. It cannot be enough to theorise or best-guess function and to postulate some practical application at the highest level of generality. The European legislature has drafted the requirement for industrial applicability in biotechnology, as interpreted in *Monsanto.* Nowhere does Directive 98/44 provide latitude for such a low standard as that articulated by the UKSC in the assessment of industrial application for biotechnology.

5. Conclusion

The patent system must be seen to operate in the public interest. Whether it serves public policy to support the patenting of early-stage research in the biosciences or whether health care research will be '*stultified*',[246] merits sober consideration. That their Lordships did not give any weight when articulating policy to the possible upstream (and downstream[247]) effects of patenting at an early stage was regrettable, this being an issue that has dominated the bioscience patent literature[248] since Heller and Eisenberg's anticommons hypothesis was published in 1998.[249] *If* it is correct that an anticommons

[246] n 2 above.
[247] J. Powles (2012) Case comment: industrial applicability of bioscience inventions in the Supreme Court *C.L.J.* 71 (1), 50-52, allowing the patentee '*to claim beyond their actual technical contribution'.*
[248] See: Nuffield Council on Bioethics (2002) *The Ethics of Patenting DNA* London; W R Cornish, M Llewelyn & M Adcock (2003) *Intellectual Property Rights and Genetics*. Public Health Genetics Unit, Cambridge; Intellectual Property Institute (2004) *Patents for Genetic Sequences: The competitiveness of current UK law and practice.* A study on behalf of the DTI, London. Available at http://www.bis.gov.uk/files/file10475.pdf (last visited December 2012); R.A. Epstein & B.N. Kuhlik, (2004) 'Is there a biomedical anticommons?' *Regulation* 54-59. Available at: http://www.cato.org/pubs/regulation/regv27n2/v27n2-7.pdf (last visited December 2012); C. Arup & W. van Caenegem (eds) (2009) *Intellectual property policy reform: Fostering Innovation and Development*, Edward Elgar, UK.
[249] M. A. Heller & R. S. Eisenberg (1998) 'Can patents deter innovation? The anticommons in biomedical research' *Science* 208 (5364) 698 – 701; see also M.A. Heller (2013) 'The tragedy of the anticommons: a concise introduction and lexicon' MLR 76 (1), 6-25.

tragedy in bioscience does in fact exist,[250] the policy promoting early-research patenting promulgated by the Supreme Court is likely to exacerbate it. The early-research patent policy has been achieved by eroding the requirement to show industrial applicability to such an extent that patents may be granted over genes and proteins that offer little more than sequence data with an educated-guess about function (or indeed any practical use at all). Widespread uncertainty across Europe about patent validity generally in the sector will increasingly shift the remit of granting offices to maintain the quality of patents onto industry itself to regulate through litigation. Young, innovative firms, strategically important to the UK's innovation performance, are least capable of absorbing such costs.

The law concerning the patenting of biotechnology inventions is intended to be harmonised within the EU trade region. The Supreme Court has effected divergence with CJEU jurisprudence that could impede the functioning of the internal market, generating disincentive to trade in member states where the law is inconsistent with EU principle and therefore vulnerable to legal challenge.[251] The supremacy of EU law requires the present standard for industrial application in England to be brought into line with that set in *Monsanto* because it is *function* which confers technical character for inventions based on a newly isolated gene or protein sequence, upon which industrial application may rest. A policy that promulgates a falling standard for newly identified gene and protein sequences does not fulfill this requirement. Furthermore, the question whether protection should be extended for early innovation arising in the biosciences should not to be decided on the basis of EPO jurisprudence that conflicts with settled sufficiency doctrine

[250] Hargreaves Report – highlights the problem of patent thickets leading to 'market gridlock' (tragedy of the anticommons) at 6.15 and 6.30, although no data/analysis in regard to market effects is reported.
[251] n 3 above, recitals 5 and 7.

and EU principle for industrial application in biotechnology. Consistent EPO jurisprudence is needed in this technical area, which would no doubt be assisted by greater reliance on inventive step and sufficiency.[252]

[252] See *Eli Lilly v Janssen Alzheimer Immunotherapy* [2013] EWHC 1737 (Pat) concerning another speculative invention held to be insufficient because 'the focus was on the right issue' (Trevor Cook).