Standing on shaky ground: US patent-eligibility of isolated DNA and genetic diagnostics after *AMP v USPTO* – Part IV¹

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As discussed in the previous issues of QMJIP, the Federal Circuit's decisions in Myriad I² and II³ appear to provide considerable prospects for patentees, as clever claim drafting may still help to avoid most patent-eligibility traps set by the much debated US Supreme Court decision in Prometheus.⁴ Yet, the split opinions also contain elusive reasoning by each of the three judges. The questions left open by Prometheus and the remaining split at the Federal Circuit with regard to inter alia DNA-related product claims provide excellent fodder for another US Supreme Court review with potentially broad implications for biotech patents. Acknowledging the criticism of excessively broad upstream patent claims and referring briefly to corresponding European debates, Part IV of this series finally discusses the recent developments from a broader innovation-policy perspective. Highlighting the mitigating effects of additional factors, such as higher thresholds for other patentability

1. Part IV could not consider developments that occurred after 15 November, 2012. Recent developments occurring after completion of Parts IV up until the final editorial deadline will be addressed in a sequel.

2. *The Association for Molecular Pathology v United States Patent and Trademark Office*, 653 F.3d 1329 (Fed. Cir. 2011) ('*Myriad I*' – summarized in Part I of this four-part paper, cf. Timo Minssen and David Nilsson, 'Standing on Shaky Ground: US Patent-eligibility of Isolated DNA and Genetic Diagnostics after *AMP v USPTO* – Part I' (2011) 1(3) QMJIP 223–47.

3. *The Association for Molecular Pathology v United States Patent and Trademark Office*, 689 F.3d 1303 (Fed. Cir. 2012) ('*Myriad II*') (Decision on remand from grant of *certiorari*, vacatur and remand, *Association for Molecular Pathology v Myriad Genetics, Inc.*, _U.S._, 132 S. Ct. 1794, 182 L. Ed. 2d 613 (2012)). For a more detailed discussion of *Myriad II* cf. Timo Minssen and Robert M Schwartz, 'Myriad Reloaded and Ready for the Next Round?' (2013) 3(1) QMJIP 70–80. Note that the CAFC's prior decision in *Myriad I* (2011) had been remanded by the Supreme Court for examination in light of its March 2012 decision in *Prometheus*, cf. Timo Minssen and David Nilsson, 'The US Supreme Court in *Mayo v Prometheus* – Taking the fire from or to Biotechnology and Personalized Medicine' (2012) 2(4) QMJIP 376–88. The two freestanding case reviews mentioned above complement the four-part 'Standing on Shaky Ground' article series. This resulted in six interrelated papers on patent-eligibility all published in QMJIP from late 2011 to early 2013.

4. *Mayo Collaborative Services, dba Mayo Medical Laboratories, et al., Petitioners v Prometheus Laboratories, Inc.*, 132 S.Ct. 1289; cf. Minssen and Nilsson, *supra* n 3.

criteria, scientific advances, post-grant mechanisms and the dynamic qualities of biomedical innovation, the authors note that overly static eligibility doctrines entail considerable risks for technological progress. While it is essential that the Supreme Court further clarify its principles, the authors urge it not to categorically close the 'patent-eligibility door' to important emerging technologies.

Keywords: *biotechnology, US, DNA, Myriad, patent-eligibility, personalized medicine, genetic diagnostics*

This is the fourth of a four-part article discussing the US Federal Circuit decision in *Myriad* also known as the ACLU⁵/*Myriad* 'gene patenting' case. Part I⁶ commenced with a description of the legal framework and an explanation of how the decision relates to the recently invigorated US debate on patent eligibility, referring *inter alia* to the 2010 US Supreme Court decision in *Bilski v Kappos*⁷ and the then pending *certiorari* in *Prometheus v Mayo*⁸ (section 1). Against this background, Part I recited the complex procedural history of *Myriad I* (section 2) and summarized the underpinnings of the outcome, that is, the three different opinions of the Federal Circuit judges Lourie, Moore and Bryson who comprised the panel (section 3). Part II⁹ continued the tale with a detailed analysis of the decision's practical implications (section 4), which was followed by a closer look at the procedural chances for an ultimate Supreme Court review (section 5). Next, Part III¹⁰ clarified why further Supreme Court review for *Myriad I* that considered both method- and product-claims in DNA-related patenting was indeed necessary. This part elaborated on the myriad of unsolved questions raised by both *Myriad I* and a body of subsequent case law addressing the patent-eligibility of biological correlations and software-related 'inventions' (section 6). Following the subsequent Supreme Court decision in *Prometheus v Mayo*¹¹ and the resulting *Myriad II* decision,¹² which were summarized and analysed by two complementary case reviews in preceding issues of this journal,¹³ Part IV now offers a broader discussion of recent US patent-eligibility developments from an innovation policy perspective and including brief references to recent European developments (section 7). This article commences by briefly recapitulating the general context and different levels of debate in order to clarify

5. ACLU = American Civil Liberties Union.

6. Cf Minssen and Nilsson, *supra* n 2.

7. *Bilski v Kappos*, _U.S._, 130 S. Ct. 3218, 177 L.Ed.2d 792 (2010).

8. The patent challenger sought review of the recent CAFC decision in *Prometheus Laboratories, Inc. v Mayo Collaborative Services*, 628 F.3d 1347 (Fed. Cir. 2010) (per Lourie, J). In June 2011, the Supreme Court granted *certiorari*, and on 20 March 2012 reversed the Federal Circuit in a strong statement on the nature of patent ineligible subject matter, holding those method claims invalid as effectively claiming the underlying laws of nature themselves. *Mayo Collaborative Services v Prometheus Laboratories, Inc.*, _U.S._, 132 S. Ct. 1289, 182 L. Ed. 2d 321, 101 U.S.P.Q.2d 1961 (2012) ('Prometheus').

9. Cf Timo Minssen and David Nilsson, 'Standing on Shaky Ground – US Patent-eligibility of Isolated DNA and Genetic Diagnostics after *AMP v USPTO* – Part II' (2012) 2(2) QMJIP 136–57.

10. Cf Timo Minssen and David Nilsson, 'Standing on Shaky Ground – US Patent-eligibility of Isolated DNA and Genetic Diagnostics after *AMP v USPTO* – Part III' (2012) 2(3) QMJIP 225–49.

11. See *supra* n 4.

12. *Supra* n 3.

13. See Minssen and Schwartz and Minssen and Nilsson, *supra* n 3.

the main focus of the subsequent discussions. Taking into account most recent developments, a more specific analysis will then be delivered in sub-sections 7.1 to 7.3. This will provide the basis for summarizing conclusions (section 8).

As in the previous parts, recent developments occurring after completion of Parts IV up until the final editorial deadline will be addressed in a sequel.

7 DISCUSSION

Spurred by novel scientific advances and case law, the implications and applications of modern biotechnology continue to be at the centre of public debate on both sides of the Atlantic. As noted above, these discussions are particularly fierce over the question of whether it should be possible to patent the results of biotechnological research. In particular, product patents on DNA and protein sequences, whose functions have not been fully understood, are heavily disputed. Moreover, there is a long-standing debate in both Europe and the US concerning the patent-eligibility of inventions based on the methodical use of information, such as claims on computer- and software-related technology, or claims on the methodical use of biological phenomena and information, such as information encoded by DNA through the genetic code. Recent advances in personalized medicine and accompanying case-law developments merge these areas of patent-eligibility debate, rendering them highly significant in practice. Accordingly, they present an ideal testing ground for the development of a modern patent-eligibility doctrine. Discussing these issues, which might also properly be referred to as patent law's problem children,¹⁴ is an inherently complex and multifaceted endeavour. Any legislative or policy choices or positions require a balancing act that involves additional consideration of further patentability requirements during patent prosecution and litigation, as well as scientific, historical, political, religious, ethical and economic facts or arguments. When discussing these recent patent-eligibility developments it is important to acknowledge this complexity and be aware of the fact that a perfect legislative or judicial solution is probably impossible to agree on. It therefore seems appropriate to start by briefly sketching out the different levels of debate in order to clarify the main focus of the principal discussion.

Considering the often very emotionally charged debate over DNA and protein-related patenting, basically two diametrically conflicting schools of thought can be identified. Some people believe, for numerous ethical, scientific or religious reasons, that DNA, and in particular, human DNA, is much more than a mere chemical structure. They believe that any form of patenting of DNA, or of the natural processes involving it, is utterly wrong, since any DNA and the information it contains is the embodiment of the code of life. This view emphasizes that DNA is a 'product of nature' whose functions depend on 'processes of nature', and that it should therefore be regarded as part of the common heritage of mankind.¹⁵ Some patent opponents go even further and argue for a complete prohibition of patents on proteins. Others, in particular the life science industry, argue that DNA and proteins are simply chemical compounds, albeit complex ones. They assert that it should be possible in principle to grant patents on isolated DNA sequences

14. Cf CIPIL Guest Lecture by Professor Dan Burk: 'Patent Law's Problem Children', 16 November 2010, see <<http://www.law.cam.ac.uk/press/events/2010/11/guest-lecture-by-professor-dan-burk-patent-laws-problem-children/1337>> (accessed 10 December 2011).

15. See also Sven JR Bostyn, 'Narrow Trousers and Narrow Patents, A Health Risk?' (2004/2005) 2 Bio-Sci. L.R. 89.

and the proteins that are encoded by it. In the past, US and European patent authorities have generally followed this line of thinking. Thus, the grant of patents on DNA-related technology became routine. It is this precedential doctrine that was defended by Judge Lourie in *Myriad I* and *II* for both cDNA and isolated genomic DNA, while Judge Moore expressed doubts in the case of genomic DNA and Judge Bryson directly opposed any patentability for isolated genomic DNA. It appears extremely difficult – if not impossible – to find a compromise between these fundamentally diverging views, which are bogged down in their own logic.¹⁶

Yet, it is also important to realize that the Judges' opinions on the product and method patents seem to have been very much influenced by a third area of debate. That focuses on the fierce discussions among those who principally support patents on DNA-related technology yet have concerns over particular threshold requirements for granting such patents, the appropriate scope/form of their protection, and their exclusionary effects. Among other things, they fear that excessively lenient standards for the grant of overly broad patent rights at a too early stage of development might have deleterious effects on beneficial research and downstream product development.¹⁷ In the following concluding discussion we will predominately address this third area of debate.

7.1 The importance of a better articulated pre-emption standard

Turning *first* to the patent-eligibility assessment biotechnological method claims, it is clear that the earlier Federal Circuit decisions that were rendered before the Supreme Court handed down its much criticized *Prometheus* ruling required a much more specific articulation of the limits of method and process claims in biotechnology and in particular DNA- and protein-related storage mechanisms of biological information. As demonstrated by our previous analysis of the abovementioned Federal Circuit decisions in *Myriad*, *Prometheus* and *Classen*,¹⁸ a central challenge to the analysis of life

16. See also Timo Minssen, *Assessing the Inventiveness of Bio-Pharmaceuticals under European and US Patent Law – A Comparative Analysis with a Special Focus on DNA and Protein Related Technology* (Lund University, 2012), 430 pp, at pp IV–VII.

17. This is often discussed in the context of the so-called 'Tragedy of the Anticommons', see Michael A Heller and Rebecca S Eisenberg, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research' (1998) 280 *Science*, 698–701; Frederic M Scherer, 'The Economics of Human Gene Patents' (2002) 77 *Academic Medicine* 1363 (arguing that this problem is analogous to conditions on the Rhine River during the eighteenth century). The extent to which such tragedies are real-world occurrences is, however, very much a matter of dispute. See eg, Christopher M Holman, 'The Impact of Human Gene Patents on Innovation and Access: a Survey of Human Gene Patent Litigation' (2007) 76 *UMKC L. Rev.* 295 (warning 'Without more compelling evidence of an overwhelming negative impact in contexts that are critical to the public good, there is no adequate justification for rushing into a radical legislative fix that might have substantial ... negative consequences'). See also id, 'Gene Patents Under Fire: Weighing the Costs and Benefits', in Emanuela Arezzo and Gustavo Ghidini (eds), *Biotechnology and Software Patent Law: A Comparative Review of New Developments* (Cheltenham, Edward Elgar Publishing Ltd, 2008), pp 260 ff; id, 'Human Gene Patent Litigation' (2008) 322 *Science* 198 (2008); Timothy Caulfield, Robert M Cook-Deegan, F Scott Kieff and John P Walsh, 'Evidence and Anecdotes: an Analysis of Human Gene Patenting Controversies' (2006) 24 *Nature Biotechnology*, 1091.

18. *Classen Immunotherapies, Inc. v. Biogen IDEC*, 659 F.3d 1057 (Fed. Cir. 2011) (On remand from *_U.S._*, 130 S. Ct. 3541, 177 L.Ed.2d 1119 (2010) reh'g en banc denied

science *method* claims arose from the fact that the dominant analytic tests have been derived from computer and business method patent controversies where §101 has been deemed to be merely a ‘threshold test’.¹⁹

The underlying problem was that the Supreme Court in *Bilski v Kappos* merely confirmed old patent-eligibility precedent using the same linguistic rubrics and thus essentially reset the focus of the patent-eligibility assessment to where the patent-eligibility doctrine stood before *In re Bilski* was decided.²⁰ Consequently, the essential question remained whether or not the patent claims encompass a ‘fundamental principle’, such as principles of nature, natural phenomena, abstract ideas or mental processes.²¹ However, in deciding the case rather narrowly, the Supreme Court unfortunately gave insufficient direction concerning the crucial determination of whether a patent claims a fundamental principle or precisely the boundary lines between principle and method.²² More specifically, the Court gave no proper hint regarding the central question of how exactly to proceed where the claim is asserted to be a fundamental principle in the form of a *biological* natural phenomenon, such as natural relationships claimed in diagnostic patents or product patents on isolated genes, and what exactly it entailed for a patent claim to pre-empt such a phenomenon.²³ While the majority of the US Supreme Court held the business method patent at issue to be unpatentable as claiming an ‘abstract idea’,²⁴ it provided completely insufficient guidelines on what would be understood to constitute an abstract idea.²⁵ This explains why *Bilski v Kappos* would not succeed in resolving the long-standing division of opinions in US courts as to what it means to claim an

30 November 2011, Petition for *certiorari* filed, _S. Ct._, 2012 WL 2368671 (U.S.) 80 USLW 3518 (Feb 28, 2012)(No. 11-1078) *sub nom Glaxosmithkline v Classen Immunotherapies, Inc.*, S.Ct. Invitation to Solicitor General to file a brief expressing the views of the United States, _S.Ct._, 2012 WL 2368671 (U.S.), 80 USLW 3707 (June 25, 2012).

19. *Bilski v Kappos*, 130 S.Ct. at 3225, *Classen* 659 F.3d at 1063–65, *Ultramercial, LLC v Hulu, LLC*, 657 F.3d 1323, 1326 (2011) (‘By directing attention to these substantive criteria for patentability, the language of § 101 makes clear that the categories of patent-eligible subject matter are no more than a “coarse eligibility filter.” ... In other words, the expansive categories – process, machine, article of manufacture, and composition of matter – are certainly not substitutes for the substantive patentability requirements set forth in § 102, § 103 and § 112 and invoked expressly by § 101 itself’) (citations omitted). Cf Kane, *infra* n 77, at 102.

20. Since the Supreme Court stressed the effect of other patentability criteria and affirmed the Federal Circuit’s abrogation of *State Street*, it may, however, also be argued that *Bilski* did not completely turn back the clock. See Timo Minssen and Robert M Schwartz, ‘US Patent Eligibility in the Wake of *Bilski v. Kappos*: Business as Usual in an Age of new Technologies?’ (2011) 30(1) *Biotech. L. Rep.* 3–58.

21. As described in Part I at pp 1–3 the Supreme Court developed this patent-eligibility test in its 1980 decision *Diamond v Chakrabarty*, 447 U.S. 303, 309 (1980).

22. See also Christopher M Holman, ‘The Impact of *Bilski* on Biotechnology’, on Holman’s Biotech IP Blog, available at <<http://holmansbiotechblog.blogspot.com/2010/07/impact-of-bilski-on-biotechnology.html>> (accessed 15 August 2010).

23. *Ibid.*

24. *Bilski v Kappos*, 130 S.Ct. 3218 (2010).

25. Cf Justice Stevens in *Bilski v Kappos* 130 S.Ct 3218 (2010), at 3226 (‘The Court, in sum, never provides a satisfying account of what constitutes an unpatentable abstract idea. Indeed, the Court does not even explain if it is using the machine-or-transformation criteria. The Court essentially asserts its conclusion that petitioners’ application claims an abstract idea. This mode of analysis (or lack thereof) may have led to the correct outcome in this case, but it also means that the Court’s musings on the issue stand for very little’).

‘abstract idea’,²⁶ a problem which parallels the European debate over the meaning of the ‘as such’ provision in EPC Article 52(3).²⁷

As discussed in the previous parts of this article, one group of Federal Circuit judges interpreted the US Supreme Court decisions in *Benson*²⁸ and *Flook*²⁹ as comprising a wide-ranging bar to patenting abstract ideas or algorithms. Referring to *Benson* they emphasized that a claim is invalid if it would ‘wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself’,³⁰ and referring to *Flook* they generally stressed that ‘limiting an abstract idea to one field of use ... does not make the concept patentable’.³¹

The other faction of Federal Circuit judges followed a very narrow interpretation of the exclusion from patent-eligibility of fundamental principles and applied it only to completely ‘abstract’ ideas. As long as the idea or formula is claimed in the form of a practical application, they considered it to be patentable. Notwithstanding *Benson* and *Flook*, the Federal Circuit Court of Appeals has followed the approach of *In re Alappat*³² where it held that a ‘useful, concrete, and tangible result’ is sufficient to qualify for patent-eligibility. This approach was also followed in *State Street*,³³ where the court established a low water mark for the patent-eligibility requirement and found that ‘a practical application of a mathematical algorithm’ is sufficient to establish patent-eligibility. As articulated in *Diehr*, the rationale for this approach was that a substantive objection to patenting of ideas ‘if carried to its extreme, makes all inventions unpatentable because all inventions can be reduced to underlying principles of nature which, once known, make their implementation obvious’.³⁴

The divergent post-Bilski decisions of the Federal Circuit described in the previous parts of this paper, such as *Myriad I*, *Prometheus* and *Classen* in the biotechnological field, as well as *Cybersource*, *Ultramercial v Hulu*, and *Dealertrack v Huber* concerning computer-aided methods, reflected these diverging opinions and demonstrated how this split had led to different results in arguably similar cases. As a result, the patent-eligibility doctrine had become ‘as clear as mud’. Moreover, due to the general technical neutrality of patent law this morass threatened, and in many respects – as

26. As Judge Rader noted in *Ultramercial*, ‘[b]oth members of the Supreme Court and this court have recognized the difficulty of providing a precise formula or definition for the judge-made ineligible category of abstractness’, *Ultramercial, LLC v Hulu, LLC*, 657 F.3d 1323, 1327 (2011) (internal citations omitted).

27. Cf Norman Siebrasse, ‘Post-Bilski Split on Patentable Subject Matter’, available at <<http://ipkitten.blogspot.com/2012/01/post-bilski-split-on-patentable-subject.html>> (accessed 23 October 2012). For a much more detailed critique cf id, ‘The Rule Against Abstract Claims: A Critical Perspective on US Jurisprudence’ (2010) 27(1) C.I.P.R. 3–4, available at SSRN: <<http://ssrn.com/abstract=1782747>>; id, ‘The Rule Against Abstract Claims: History and Principles’ (2011) 26(2) C.I.P.R. 2 205–29, 206, available at SSRN <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1782712> (accessed 25 January 2012).

28. *Gottschalk v Benson*, 409 U.S. 63 (1972).

29. *Parker v Flook*, 437 U.S. 584 (1978).

30. *Benson* at 72.

31. *Flook*, at 584, 591–2.

32. *In re Alappat*, 33 F.3d 1526, 1544 (Fed. Cir. 1994).

33. *State Street*, 149 F.3d 1368, 1373 (Fed. Cir. 1998).

34. See *Diehr*, 450 U.S. 175, 189 (1981), cf Siebrasse, ‘Post-Bilski Split on Patentable Subject Matter’, supra n 27 (adding, ‘As Laddie J said in *Fujitsu Ltd’s Application* [1996] RPC 511 at 523 (Pat), “most inventions are based on what would be viewed by many people as discoveries”’).

discussed in the previous issues by our *Prometheus* and *Myriad II* case reviews – still threatens to engulf a wide area of different technologies.

Since 20 March 2012 this morass has had to be navigated through by taking into account the much criticized, rather ambivalent guidelines provided by the Supreme Court in *Mayo v Prometheus*. In a somewhat surprisingly, *unanimous* decision, the Court held that the claims in *Mayo Collaborative Services v Prometheus Laboratories, Inc.* effectively claim a law of nature and are not patent-eligible under 35 U.S.C. § 101.³⁵ As discussed in the previous issues of this journal, the decision is based upon a comprehensive assessment of *Prometheus*' claims in light of the Court's precedents. The Court reiterated the traditional 'laws of nature, natural phenomena, and abstract ideas exceptions' to categories of patent-eligible subject matter under 35 U.S.C. § 101 as set forth by the US Supreme Court in *inter alia* *Bilski*, *Chakrabarty*, *Flook* and *Diehr*. The Court also addressed the 'machine-or-transformation' test considered in *Bilski* and confirms once more that it remains an 'important and useful clue' to patentability, but that it does not supersede the 'law of nature' exclusion. The Court underlined that a claim that is directed to a law of nature or natural correlation, with additional steps that involve well-understood, routine, conventional activity previously engaged in by researchers in the field is not patent-eligible, regardless of whether the steps result in a transformation (an issue that would of course also be significant in the obviousness assessment). On the contrary, the Court explained, a claimed process including not only a law of nature, such as the fact that hot air promotes ignition, but also several unconventional steps, such as involving a blast furnace, might still be patent-eligible, if it confines the claims to a particular, useful application of the principle.

Turning to the facts of the case, the Supreme Court held that since the laws of nature recited by *Prometheus*' patent claims – that is, the correlations between concentrations of certain metabolites in the blood and the likelihood that a thiopurine drug dosage will be ineffective or harmful – are not themselves patent-eligible, the claimed processes are likewise not patent-eligible unless they have additional features that provide practical evidence that the processes are true applications of those laws instead of rather being drafting efforts designed to monopolize the correlations. The Court also found that while the additional steps recited in the claimed processes in this case cannot be considered to be natural laws as such, the patent applicant would have been required to add more in order to transform the nature of the claims.

The Court has thus clarified that in order to transform an unpatentable law of nature into a patent-eligible application of such a law, it is not sufficient to simply state the law of nature and then add the phrase 'apply it'. Essentially, appending conventional steps specified at a high level of generality, to laws of nature, natural phenomena, and abstract ideas cannot render those laws, phenomena, and ideas patent-eligible.³⁶

Arriving at a debatable conclusion with regard to the particular claims at issue, the Court's approach appears to place more emphasis on the confinements of the claims and their pre-emptive effects. However, the decision also illustrates the dilemma found in the fact that the terms 'abstract idea' and 'natural phenomenon' are themselves general and very elusive and that they are therefore not always helpful to assess

35. *Mayo Collaborative Services v Prometheus Laboratories, Inc.*, U.S. ___, 132 S.Ct. 1289, 182 L.Ed.2d 321 (2012), argued December 7, 2011, decided March 20, 2012, available at <<http://www.supremecourt.gov/opinions/11pdf/10-1150.pdf>> (accessed 24 March 2012).

36. See the Memorandum by Andrew H Hirshfeld, Associate Commissioner For Patent Examination Policy (dated 21 March 2012), available at <http://www.uspto.gov/patents/law/exam/mayo_prelim_guidance.pdf> (accessed 31 March 2012).

patent-eligibility in the life science sector. This has also been recognized by several academics, such as Robin Feldman, who pointed out:

For example, LabCorp was a relatively simple application of personalized medicine. It involved one biomarker and a reasonably straightforward correlation for treatment. In contrast, most personalized-medicine diagnostics are developed using whole genome expression or sequencing arrays to identify hundreds or even thousands of biomarkers that can be used to diagnose a specific disease state. The machine learning algorithms used to identify these markers do not operate on statistical concepts as simple as linear correlation, which for some of us is complicated enough. Machine learning algorithms employ statistical models to identify different combinations or ‘patterns’ of markers that correlate with a specific disease state. Usually these markers are selected and statistically modeled to compensate for human genetic and environmental variation. Thus, most personalized-medicine programs are tremendously complex compared even to logistic regression and other simple forms of statistical analysis. They are not simply a reflection of a natural phenomenon; they are an interpretive model of nature. Nor are they analogous to or preemptive of human thought.³⁷

To us it appears inappropriate to invalidate claims on such inventions simply on the ground that they are patent-ineligible claims on natural phenomena, abstract ideas or mental steps, without a careful consideration of the claimed subject matter as a whole and in a wider context.

Similar arguments could be made for claims involving complex applications of computer programs.³⁸ At least so far, the view of Judge Rader, as expressed in for example *Ulramercial* and his unwillingness to invalidate such claims as being directed to ‘abstract ideas’ seems to be the correct approach.³⁹ We infer this also to be the

37. Robin Feldman, ‘Where do Processes of Nature End and Processes of Human Invention Begin?’, available at <<http://www.patentlyo.com/patent/2011/12/rethinking-patent-law.html>> (accessed 13 December 2011), featuring an excerpt from his forthcoming book *Rethinking Patent Law* (Harvard University Press 2012).

38. Ibid (‘The logic that appears to have been used is the following. Computer programs are mathematical formulas, and mathematical formulas are laws of nature. We know that laws of nature cannot be rendered patentable by limiting their application to a particular field of use. Computer programs, therefore, cannot be rendered patentable by limiting their application to a particular field of use. This sequence contains a number of logical errors. Computer programs may be expressed in a language that looks like math, and some do involve calculations, but they are not necessarily analogous to mathematical formulas. Most important, they are not analogous to natural laws just because both are expressed in formulaic languages. One must look to the content of the computer program and its potentially preemptive effect to determine patentability’).

39. Interestingly, this is also reflected in European case law. See eg the shift in German case law from the so-called ‘Kerntheorie’ and ‘Technizität’ approach (BGH, GRUR 1986, 531 ‘Flugkostenminimierung’), which had focused on the so-called ‘technical character’, to the so-called ‘Gesamtcharakter der Erfindung’ approach (BGH GRUR 2000, 498 ‘Logikverifikation’ and BGH GUR 1992, 430 ‘Tauchcomputer’), which considers the ‘entire character of the invention’. Part of the problem is that it could never be sufficiently defined what exactly a ‘technical character’ entails, although several attempts were made by the BGH, see eg ‘Rote Taube’, GRUR, 1969, 672 and ‘Dispositionsprogramm’, GRUR 1977, 96 (defining the word ‘technical’ as a teaching for an action according to a method by using controllable forces of nature for the causally surveyable achievement of a result which is without intermediary activity of the human mind the direct consequence of the use of controllable forces of nature). But see Peter S Menell, ‘Forty Years of Wondering in the Wilderness and No Closer to the Promised Land: Bilski’s Superficial Textualism and the Missed Opportunity to Return Patent Law to its Technology

approach of the Federal Circuit in the pending CLS Banking case⁴⁰ which will be heard later this year. That *en banc* panel will decide the following questions which may result in greater clarity:

- (a) What test should the court adopt to determine whether a computer-implemented invention is a patent ineligible 'abstract idea'; and when, if ever, does the presence of a computer in a claim lend patent eligibility to an otherwise patent-ineligible idea?
- (b) In assessing patent eligibility under 35 U.S.C. § 101 of a computer-implemented invention, should it matter whether the invention is claimed as a method, system, or storage medium; and should such claims at times be considered equivalent for § 101 purposes?⁴¹

Considering these questions, it would, however, also appear unreasonable if claims could always be rendered patent-eligible simply because they also claim a complex application of a natural principle, correlation or abstract idea that cannot be carried out by using 'pen and paper'.⁴²

In that regard we also refer to Norman Siebrasse's notions. He has (prior to the US Supreme Court decision in *Prometheus*) argued that '[b]y consistently addressing subject matter exclusions in terms of the rule against abstract claims, the U.S. Supreme Court has used the wrong tool for the job and consequently, it has damaged the tool, and done a poor job'.⁴³ He notes that this was also pointed out in the lengthy concurrence by former Supreme Court Justice Stevens⁴⁴ in *Bilski v Kappos*.⁴⁵ Consequently, he asserts that the rule against fundamental principles, such as abstract claims, is an inadequate tool to determine patent-eligibility and that the patent-eligibility doctrine needs to be supplemented by additional exclusions of particular subject matter fields that are distinct.⁴⁶ Elaborating further on this approach, this would imply that claims on a biotechnological method which depends on biological correlations or business methods might very well withstand patent-eligibility challenges based on for example the

Mooring' 63 Stan. L. Rev. 1289 1312–13 (2011) (urging that patents only be granted for 'technological arts' and that business models do not meet this criterion: 'There is no reason to believe that "business methods" have become a science or technology fitting the functional patent mold during the course of the past two centuries. Furthermore, the fact that business methods can be implemented on computers does not mean that courts cannot distinguish between advances in computer technology and the business methods that they implement', internal citations omitted).

40. *CLS Bank International v Alice Corporation Pty. Ltd.*, 685 F.3d 1341 (Fed Cir. 2012), petition *en banc* granted, opinion vacated, appeal reinstated, 2012 WL 4784336 (Fed. Cir. October 9, 2012).

41. 2012 WL 4784336 (Fed. Cir. October 9, 2012).

42. Feldman, *supra* n 37 ('Thus, for example, an inventor could not save a claim to all uses of $E = MC^2$ by limiting the claim to 'all uses of $E = MC^2$ in the construction field. Sliding the analogy over to software, however, involves logical errors').

43. Norman Siebrasse, 'The Rule Against Abstract Claims: A Critical Perspective on U.S. Jurisprudence' (2010) 27(3) C.I.P.R. 27–28 (2010), available at <http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1782747> (after having criticized the various approaches taken in *Ultramercial* and *Dealertrack* as being wrong: 'While Chief Judge Rader is right in his approach to the rule against abstract claims, which was distorted beyond recognition by the US Supreme Court in *Benson* and *Flook*, the US courts generally have been wrong to refuse to identify any limits on subject matter patentability other than that imposed by that rule').

44. John Paul Stevens served as an Associate Justice of the US Supreme Court from 19 December 1975 until his retirement on 29 June 2010.

45. *Bilski v Kappos* 130 S.Ct. 3218, 3231–57 (2010).

46. *Ibid*, for a detailed discussion of Justice Steven's opinion see Minssen and Schwartz, *supra* n 20.

exclusion of abstract claims or mental steps, since they are directed to a practical application. Such claims might, however, still be invalidated on the basis that they fall within an additional, separate category of subject matter excluded from patent eligibility. Whether business methods or specific biotechnological methods and products should actually fall within the categories of exclusion is a distinct question which follows from this framework.⁴⁷

One approach following from this line of thinking could of course be to explicitly exclude certain types of invention categories from patentability through congressional action as it was considered by Judge Moore. This might include business methods, genetic diagnostics or claims on isolated DNA sequences.⁴⁸ However, such static, technology specific exclusions would, in our view, pose considerable danger to the advances of emerging technologies and they should therefore be considered only if absolutely necessary and in the most extreme cases.⁴⁹ Moreover, the continuing debates concerning the explicit European exclusions from patentable subject matter⁵⁰ and the continuing discussion concerning Article 3, 5 and 6 of the Biotech Directives⁵¹ demonstrate that legislative codifications alone do not solve these problems. We therefore believe that the future patent-eligibility doctrines should predominantly be based on a more flexible approach.

One of the more flexible tools that should be further elaborated to identify additional categories of patent-(in)eligible subject matter in compliance with the guidelines set forth by the Supreme Court in *Prometheus* requires a clarified and better articulated pre-emption inquiry. If carefully and plausibly applied, such a test could help to establish a reasonable patent-eligibility standard.⁵² Ideally it should take effect in cases where a proper application of the basic patentability requirements would nevertheless

47. Cf Siebrasse, *supra* n 27.

48. Justice Stevens, eg, would have explicitly excluded business methods. Moreover, in 2007 Michael Crichton teamed up with Lori B Andrews, from the Chicago-Kent College of Law, and found support in Representatives Xavier Becerra and Dave Weldon, who unsuccessfully introduced a Bipartisan Bill (H.R. 977) in the 110th Congress to restrict future patenting of genes and proteins.

49. Until recently, nuclear weapons were the only invention category completely excluded from patent-eligibility (albeit not from a prize system), albeit this exclusion is not codified in the Patent Act, but in the Atomic Energy Act, 42 U.S.C. § 2181(a) (2000). The ‘America Invents Act’ (AIA) (H.R. Res. 1249, 112th Cong. (2010) (enacted)), however, has now introduced an immediately effective ban on patents covering tax strategies and/or claims ‘directed to or encompassing’ human organisms (Dr Frankenstein must now rely on trade secrets). Future exclusions might also be based on moral concerns. Exclusions based on ‘morality’ or ‘ordre public’ have been codified in European patent law but are only addressed sparsely in the US under the ‘utility’ doctrine, cf Margo A Bagley, *Patent First, Ask Questions Later: Morality and Biotechnology in Patent Law*, Emory Public Law Research Paper No. 03-13 (2004), available at <<http://ssrn.com/abstract=448940>> (accessed 10 December 2011). Another questions is of course if patents, which are after all negative exclusionary rights, should be concerned with moral concerns that should be predominantly addressed by distinct legislation. Note finally that under Section 27 of the AIA, the USPTO is required to study effective ways to provide independent, confirming genetic diagnostic test activity where gene patents and exclusive licensing for primary genetic diagnostic tests exist.

50. See *infra* nn 109–112.

51. *Ibid*.

52. Compare also Mark A Lemley, Michael Risch, Ted Sichelman and R Polk Wagner, *Life after Bilski* (2011), 63 *Stanford L. Rev* 1315, available at <<http://ssrn.com/abstract=1725009>> (accessed 15 December 2011).

lead to inappropriate results. The primary goal of such an inquiry should be to guarantee an appropriate scope of protection for patents that involve the application of natural phenomena or abstract ideas.

The conundrum for identifying appropriate areas for protection lies in the reality that '[t]echnology is always and everywhere about utilizing natural phenomena and regularities to extract from Nature something which she does not willingly give us'.⁵³ Such an inquiry should revolve around the following question: 'How may a process or method *involving* a natural phenomenon, fundamental principle or abstract idea be claimed in order to comply with §101?'

Here we also note the different evidentiary standards for granting and invalidating claims. While patent claim construction is exclusively within the Court's competence,⁵⁴ an issued patent is entitled to a statutory⁵⁵ presumption of validity which may only be overcome by 'clear and convincing evidence'.⁵⁶ Where, as in the case of new technology, the claims are highly technical, expert testimony should be presented to explain them.⁵⁷ But where a patentee seeks to overturn a USPTO rejection she continues to shoulder the burden of proving and explaining her claim and the Court may construe the language using only the evidence proffered at the PTO. Indeed, most of the Supreme Court precedents for patent-ineligible subject matter concern appeals from PTO rejections.⁵⁸ In our view, the failure in the *Myriad I* and *II* cases to hold proper claim construction hearings contributed substantially to the three judges' clearly differing views of the technology before them and just what the claims actually comprised.⁵⁹ To us it is

53. Joel Mokyr, *The Enlightened Economy: An Economic History of Britain 1700–1850* (New Haven, Yale University Press, 2009), p. 12.

54. *Markman v Westview Instruments, Inc.*, 517 U.S. 370 (1996).

55. 35 U.S.C. § 282.

56. *Microsoft Corp. v i4i Limited Partnership*, _U.S._, 131 S.Ct. 2238 (2011), see also Guyan Liang, *Molecules or Carriers of Information: A Chemist's Perspective on the Patentability of Isolated Genes*, (2012) 22 Alb. L.J. Sci. & Tech. 133, 146–7 (2012).

57. *Daubert v Merrell Dow Pharmaceuticals*, 509 U.S. 579 (1993) (for a scientific assertion to qualify as 'scientific knowledge', an inference or assertion must be derived by the scientific method), *Kumho Tire Co. v Carmichael*, 526 U.S. 137 (1999) (the principles of *Daubert* apply broadly to scientific, technical, or other specialized knowledge); see also *Pharmastem Therapeutics, Inc. v Viacell, Inc.*, 491 F.3d 1342, 1379 (2007).

58. See eg *Gottschalk v Bensen*, 409 U.S. 63 (1972); *Parker v Flook*, 437 U.S. 584 (1978); *Diamond v Chakrabarty*, 447 U.S. 303 (1980); *Diamond v Diehr*, 450 U.S. 175 (1981); *Bilski v Kappos*, _U.S._, 130 S.Ct. 3218 (2010). Of the cases post the 1952 Patent Act only *Funk Brothers Seed Co. v Kalo Inoculant Co.*, 338 U.S. 127 (1948) and *Prometheus* involved issued patents. *Le Roy v Tatham*, 55 U.S. (How.) 156 (1852) and *O'Reilly v Morse*, 56 U.S. (56 How.) 62 (1853) were decided before the 1870 Patent Act substituted the focus from central claiming for the prior acts' 'specifications'. See *Markman*, 517 U.S. at 378 ('[t]he idea that the claim is just as important if not more important than the description and drawings did not develop until the Act of 1870 or thereabouts' (quoting 1 A Deller, *Patent Claims*, 2d edn (1971) § 4, p 9). See Andrew P Morris and Craig Allen Nard, 'Institutional Choice & Interest Groups in the Development of American Patent Law: 1790–1865' (2011) 19 S. Ct. Econ. Rev. 143, 153–9 (describing the invention of 'claims' by lawyers as a device to clarify the 'specifications' of the 1793 Patent Act and the 1836 Patent Act's distillation of practice into patent law). See also David J Brennan, 'The Evolution of English Patent Claims as Property Definers' (2005) 4 Int. Prop. Q. 361, 365–6.

59. See *Brief of Amicus Curiae Law Professor Christopher M. Holman in Support of Neither Party*, 2012 WL 2884112 (Fed. Cir. 8 June 2012) *2–3. (This is how the three judges in *Myriad I* and *II* were able to describe those claims so differently and opine on their speculative effects on future research.)

thus evident that proper solutions concerning the assessment of patent-eligibility under substantive law can only be achieved if the assessment is conducted within a proper procedural framework.

Be that as it may, where the abovementioned pre-emptive effects of the relevant claims would have to be delineated within such a proper framework, the answer would be quite straightforward in the two most extreme cases, that is, either (1) if any invention would have to be automatically made patent ineligible merely because it involved a practical application of a natural phenomenon, *or* (2) if the prohibition of patents on natural phenomena is interpreted narrowly to only encompass patents on natural phenomena or abstract ideas *per se* such as the genetic code, magnetism, photosynthesis or – returning to the examples used in *Bensen* and *Chakrabarty* – Newton’s law of gravity and Einstein’s famous $E = mc^2$.

However, considering the general history of the patent-eligibility debate, as well as the Supreme Court’s formulations in *Bilski v Kappos*,⁶⁰ *Metabolite*⁶¹ and *Prometheus*,⁶² it appears that the Supreme Court favours a patent-eligibility doctrine placed somewhere in between those extreme positions. This implies that the explicit prohibition of patents claiming natural phenomena must presumably include more than the mere patenting of natural phenomena *per se*, which would make it rather easy to circumvent the exclusions, but at the same time are less than categorical prohibitions of patents involving a well-defined practical utilization of a natural phenomenon, which would deny patents to most useful technologies.⁶³

The decisive question is therefore how to define the metes and bounds of this ‘middle-position’. One main criterion that would point towards patent-ineligibility of an asserted invention seems to be where the claims at issue *effectively pre-empt all practical uses of a natural phenomenon or abstract idea*. As described above, the District Courts, the Federal Circuit and the Supreme Court have regularly referred to this criterion to invalidate overly broad patent claims under § 101. In essence, it seems thus that at least two conditions would have to be fulfilled before patent claims can be rejected or successfully challenged under § 101 based on the argument that the claims encompass a natural phenomenon. *First*, the claims would have to involve a natural phenomenon or abstract idea, and, *second*, the claims would have to *effectively pre-empt all practical applications* of the identified natural phenomenon or abstract idea it relates to.⁶⁴

Since it appears extremely difficult to clearly define ‘fundamental principles’, such as principles of nature, natural phenomena, abstract ideas or mental processes,⁶⁵ the

60. *Bilski v Kappos*, 130 S.Ct. 3218, 3231–57 (2010).

61. *Laboratory Corporation of America Holdings v Metabolite Laboratories*, 548 U.S. 124 (2006) (dismissing writ of *certiorari per curiam*, see the dissent by Justice Breyer, joined by Justices Stevens and Souter).

62. *Mayo Collaborative Services, dba Mayo Medical Laboratories, et al., Petitioners v Prometheus Laboratories, Inc.*, 132 S.Ct. 1289.

63. Cf Christopher M Holman, ‘The Impact of *Bilski* on Biotechnology’, supra n 22 (stating ‘Clearly Justice Breyer and the other dissenting justices in *LabCorp* saw its reach in much broader terms. The claim at issue in *LabCorp* was not directed towards the physiological correlation *per se*, but rather to a method that involves assaying the blood for total homocysteine level and using that information to diagnose the vitamin B deficiency. ... Nonetheless, the court concluded that this process amounted to an impermissible attempt to claim the natural phenomenon itself’).

64. *Ibid*.

65. Due to lack of guidance in *Bilski v Kappos* and *Prometheus* and the split in *Myriad I* and *II* it is still not completely clear what exactly will constitute a true natural phenomenon in the context of patent-eligibility exclusions. Is it enough for eligibility that a natural process occurs as a

particular effect of the patent-eligibility doctrine as articulated by the Supreme Court very much depends upon how the term 'effective pre-emption' is interpreted and applied by the courts.⁶⁶ The Supreme Court decision in *Prometheus*, as well as *Myriad II* provide some further guidelines for the pre-emption standard but eventually come back to the same place *Bilski* left us.

In any case, the lower courts will most likely continue to consider whether or not the claims at issue are limited to a particular use or transformation of a particular compound or sample. Under the *Bilski* and *Prometheus* principles (which will certainly soon be complemented by another Supreme Court decision in *Myriad II*) it can be presumed that claims including a well-defined limitation directed to the testing or transformation of a particular sample will be held patent-eligible, while claims broadly directed to pure diagnosis or analysis of data, in particular relating to what are basically mere data-gathering or post-solution steps, will *not* be patent-eligible.

In light of such an interpretation, we believe that the correctness of the Supreme Court's decision to invalidate the relevant claims in *Prometheus* is debatable. After all, it could still be claimed that the administering step in *Prometheus* was not simply data-gathering but an essential transformative element of *Prometheus*' claimed methods of a particular treatment sufficiently definite to confine the patent monopoly within rather definite bounds. Notwithstanding the Supreme Court's conclusions on the facts of the case, we believe there were good arguments for the view that *Prometheus*' claims do not 'wholly pre-empt' the use of correlations between metabolites of thio-purine drugs and their toxicity and efficacy. Instead, the claims utilize, not pre-empt, the correlations of natural processes in a series of specific steps that are arguably patent-eligible subject matter according to the statute.⁶⁷ Likewise, *Myriad*'s claim 20 would also pass the 'pre-emption' test, since it was limited to a specific use in combination with a cell recombinantly engineered and modified by human intervention to express BRCA1. Thus, the claim cannot broadly prohibit scientists from screening for cancer therapeutics or from exploiting the 'scientific method' as such, and would thus not wholly pre-empt a natural phenomenon.⁶⁸

result of human intervention or should a natural process only be regarded as a true, and thus a patent-ineligible natural phenomenon if it occurs without any human intervention? In other words can a certain degree of human intervention and/or modification render a naturally occurring compound or process patentable? And, if so, exactly what level of human intervention is required to render a compound sufficiently distinct from its naturally occurring form and thus patentable?

66. Holman, *supra* n 63.

67. *Ibid.*

68. As a matter of fact one could also argue that the *Prometheus* claim and *Myriad*'s limited claim 20 actually do not encompass a *true* natural phenomenon, see also Christopher M Holman, 'Brief of Amici Curiae Interested Patent Law Professors in Support of Neither Party in *Prometheus v. Mayo*' (18 January 2009, concerning Appeal No. 2008-1403), available at <<http://ssrn.com/abstract=1504925>> (accessed 10 September 2011), pointing out that characterizing the interaction of a non-naturally occurring molecule with the human body as a natural phenomenon simply because the interaction is governed by natural principles of chemistry and physiology is analogous to characterizing the interaction of an airplane with the atmosphere as a natural phenomenon just because the interaction of airplane with the air is governed by fundamental scientific principles (at 12). Holman also argues that if the interaction of a drug metabolite with the human body were to be treated as a natural phenomenon, this would logically mean that the interaction of drugs with the human body are generally natural phenomena, which would cast substantial doubt on the validity of many important drug patents (at 13 ff). Similarly, *Myriad*'s claim 20 seems more to encompass a specific natural process that occurs as the result

In contrast, the extremely broad claims in *Myriad*, *Metabolite* and *Classen* clearly do not withstand the pre-emption test. For example, Myriad's gene patent method claims broadly directed to the identification and comparative analysis of natural mutations in the BRCA genes failed the pre-emption test and were declared patent-ineligible, since they pre-empted any diagnostic use of the information regarding the mutations.⁶⁹ Similar arguments could be made in cases where a doctor has allegedly infringed patent claims by simply recognizing and thinking about a claimed biological correlation, such as in the *LabCorp v Metabolite* saga and in *Classen*. The claims at issue in *LabCorp v Metabolite* would fail the test since they would effectively pre-empt any practical method of exploiting a natural phenomenon, that is, the correlation between total homocysteine levels and vitamin B deficiency, and the claims in *Classen* since they sought to monopolize the process of discovery itself. In that context it seems important to note that although *Classen*'s claims were limited to a single field, that is, immune disorders, they were, unlike *Prometheus*' claims, not confined to any more specific transformative treatment steps, drugs or even any specific chronic immune disorder.⁷⁰ In that regard, it could further be argued that the transformative steps in *Classen*'s claims were indeed merely data gathering steps or insignificant post-solution activities that were not central to the real purpose of the claims, that is, to completely pre-empt and keep others from exploring the fundamental principle of the correlation between vaccination schedules and incidence of chronic immune diseases.⁷¹

of human intervention and consequently it might be argued that is not a true natural phenomenon occurring absent human intervention. Moreover, if particular methods using cells modified by human intervention to screen for potential cancer treatment become unpatentable many other patent claims relating to biotechnology would be invalidated. It seems unlikely that a potential Supreme Court decision would so limit the protection of biotechnological inventions.

69. These claims improperly pre-empt the mental process of observing the existence of the mutation. One can compare two gene sequences without isolating DNA, for example, if the DNA sequencing and analysis had been accomplished and reported by someone else and this sequence is compared to another. Myriad obtained overly broad method claims, unlimited by any physical analysis step, and the decision to hold them being patent-ineligible was therefore correct, cf *Holman*, supra n 63 (stressing that Myriad's unsuccessful argument for a narrower interpretation was an ex post litigation argument in an attempt to save them, adding: 'Whether or not this is the right outcome, I think it is consistent with current Federal Circuit case law, particularly *Prometheus* and *Bilski*, although perhaps this will change after the Supreme Court decides *Bilski*. In *Prometheus*, the Federal Circuit stated that the "mental step" of observing a level of drug metabolites indicating a need to adjust the amount of drug subsequently administered is patent ineligible, which I think implies that a claim that would be infringed by merely "comparing" two DNA sequences would likewise be patent ineligible').

70. The '139 and '739 claims in *Classen* were – unlike the claims in *Prometheus* – broadly directed to general methods for scheduling and conducting all types of immunizations without more precise specifications. The '283 claim was even broader since it did not include the subsequent step of selecting an immunization schedule. See also Judge Moore in *Classen Immunotherapies, Inc. v Biogen IDEC*, 659 F.3d 1057, 1076 (Fed. Cir. 2011) (noting that 'the *Prometheus* court concluded that the claims, which were drawn to the administration of specific drugs providing 6-thioguanine to a subject and then measuring specific metabolites, do not pre-empt broadly the use of any natural correlation, but rather recite specific treatment steps with specific drugs. 628 F.3d at 1355. None of this analysis exists in the majority opinion here in *Classen*. There is no consideration of the extent of preemption by these staggeringly broad and abstract claims').

71. *Ibid*.

A specific challenge to the eligibility question for genes is whether the courts should utilize a general or specific patentable subject matter theory for product claims on isolated DNA and proteins. The choice will determine whether a decision has implications for general patenting in biotechnology.⁷² It is evident that the Supreme Court in *Prometheus* could not provide sufficient answers to that question, since it focused on method claims. For *Myriad I* and *II*, perhaps one of the most essential additional issues will be to determine how far biological substances would have to be modified through human intervention to warrant product claims. As we have analysed above, the current split at the Federal Circuit leaves many questions unresolved and could potentially have a great impact on biopharmaceutical patenting. A potential Supreme Court review would require further explanation of the ‘unfortunate’ language in *Myriad II* that distinguishes between ‘isolated’ and ‘purified’ products.

Moreover, it must be clarified to what extent isolated DNA corresponding to a naturally occurring gene, or even ‘synthesized’ DNA molecules, must be modified in order for it to become patent eligible under § 101.⁷³ In particular, it seems extremely difficult to define the precise meaning of ‘markedly different characteristics’ and what exactly this entails for multifunctional biotechnological inventions.⁷⁴ If a strict test is adopted this would probably mean that to be patentable an invention must have acquired a ‘markedly different utility’ from naturally occurring sequences through human intervention. This would probably only permit the patenting of either isolated cDNA that can be used for a different purpose than the corresponding genomic sequence, or of other synthetic DNA or protein molecules that have been modified to such an extent that they have a different (or improved?) utility. Due to patent law’s general neutrality, and depending on how ‘different’ is interpreted (are improved qualities enough?), this might also imply that many pharmaceutical patents could be called into question. A more lenient test would simply require a ‘markedly different chemical structure’. Strictly applied it might mean that both genomic and cDNA will not be considered to be sufficiently different from naturally occurring DNA to warrant patent protection, yet it could also mean that only isolated genomic DNA would be excluded or – considering Judge Lourie’s very permissive covalent bond test – that both isolated genomic and cDNA would pass the test.

To sum up, it is evident that many details concerning the necessary level of human intervention or the precise interpretation of the pre-emption standard will still have to

72. Eileen Kane, *infra* n 77 (adding that this ‘illustrates how the technological neutrality of patent law causes doctrines that originate from one technical field to influence judicial review in an unrelated field’).

73. Cf Andrew W Torrance, ‘Synthesizing Law for Synthetic Biology’ (2010) 11 Minn. J. L. Sci. & Tech. 629, 641–2 (adding: ‘What is certain is that this stunning court decision has focused intense interest on the potential synthetic biology holds for designing genes unlike those “found in nature”. The promise of synthetic biology represents an important new pathway to obtaining patent rights that successfully claim DNA’).

74. Cf Christopher M Holman, ‘In Case Challenging Myriad Gene Patents, ACLU and Public Patent Foundation Prevail in District Court’, in Holman’s Biotech IP Blog, 30 March 2010, available at <<http://holmansbiotechipblog.blogspot.com/2010/03/in-case-challenging-myriad-gene-patents.html>> (accessed 10 November 2012) (asking: ‘Would a labelled probe, designed to recognize a naturally occurring mutation, be patent eligible? What about a recombinant construct comprising a DNA sequence encoding a naturally occurring protein coupled with a non-naturally occurring regulator of transcription like a promoter? How about genetically engineered cells, or chimeric sequences formed by combining two or more naturally occurring protein coding sequences? A DNA-based vaccine?’).

be clarified and it is equally clear that, ultimately, much will depend on how the lower courts and the Supreme Court – hopefully in *Myriad II* – will carry out these inquiries. However, it appears as if a reasonable application of the human intervention standard enunciated by *Chakrabarty*, distinguishing between phenomena that occur as the result of human intervention and natural phenomena that occur absent human intervention might, in combination with a properly applied pre-emption standard, lead to fairly balanced results. In particular, it provides the courts with a convenient doctrine with which claims covering specific diagnostic methods and targeted applications of more effective (personalized) drugs, which most stakeholders would accept as deserving patent protection, may be held valid.⁷⁵ On the other hand, courts would also have the means to invalidate overly broad claims that stray from claiming the effects of inventive human intervention into pre-empting the realm of naturally occurring biological phenomena.⁷⁶ For good reason such claims have been the main source of public policy concerns. Their invalidation would most likely increase the public understanding of what protecting specifically useful inventions is all about and thus hopefully strengthen public trust in the patent system.

75. Cf Holman, *supra* n 63 (adding that patent ineligibility based on pre-emption of a natural phenomenon could either have little impact on such patent claims, or if interpreted more restrictively, could constitute a new substantial obstacle to broad patent claims such as those at issue in *Prometheus*, and *Classen* in the ACLU patent lawsuit. In that context he notes with regard to the *LabCorp v Metabolite* claims that ‘one could alternatively find that since the claim has no impact on the correlation as it exists and functions naturally in the human body, the phenomenon is not entirely preempted by the claim’. He further points out that a court that applies a less restrictive interpretation of the pre-emption might stress that *Myriad*’s gene patent method claims do not cover the mutations as they exist in nature nor the effect of changes in the BRCA sequence on human physiology, and might thus conclude that the claim does not preempt the natural phenomenon).

76. Once again, similar arguments could be made in the computer and software context, see Feldman, *supra* n 37 (‘As described earlier, the term “algorithm” in computer science means a series of steps performed on input data by a computer. This process may or may not raise pre-emption concerns. Some computer ‘algorithms’ are based on properties inherent in types of input and output data. Such broad, generic algorithms, which can be used on a variety of types of input data, may raise threats of preemption. In other words, if an inventor asks for a patent on a software program that works with whole sets of numbers or entire types of data, such a patent would not be patentable subject matter. Particularly in light of the bargaining potential that would come with such a grant, the patent would risk tying up entire types of data rather than constituting something applied. This does not mean that all software is unpatentable. Claims to programs that are applied to a specific type of data in the pursuit of particular types of outputs do not present the same level of preemption threat. For example, a personalized medicine algorithm (i.e., series of steps) that employs a specific type of statistical model using a fixed set of markers to produce a very specific diagnosis would not threaten to preempt other methods of performing the same diagnosis that use different markers or novel types of statistical models. Such an invention should be patentable. Computer programs may be many things, including methods of creating useful models of the world around us, methods of providing interpretations of information, and methods of sorting information. When methods of creating a particular type of model are described at a very general level, they may threaten to preempt the broad activity of exploration. However, when claimed at the level of a specific method of sorting a particular type of information for a particular pursuit, they should constitute an applied invention. Such specificity is the hallmark of what separates unpatentable abstractions from applications of those abstractions in the useful arts in a way that is worthy of patent protection’).

7.2 Mitigating effects of strictly applied patentability requirements, technological advances and post-grant mechanisms

The US Supreme Court and the Federal Circuit now have an opportunity to refine the set of legal instruments for addressing this debate and assessing the patent-eligibility of cutting-edge biotechnological and genetic sciences. Ideally this might resolve some of the eligibility controversies for the benefit of scientific progress, without losing sight of scientists, medical practitioners and patients who wish to use isolated genes and genetic correlations in research and medical care.⁷⁷ The resolution of eligibility for genes has implications for the patenting of other bio-molecules, while the resolution of the eligibility of genetic testing methods has implications for the contours of the pre-emption analysis as applied to subject matter in the life and physical sciences, including such scientific sectors as nanotechnology.⁷⁸

While it is important that the patent-eligibility doctrine be further clarified in order to establish reasonable legal certainty, it is also clear that any future Supreme Court judgment should take great care not to categorically close the patent-eligibility door. Although patent-eligibility should not be conflated with patentability requirements, we believe that a sound policy decision can only be achieved if the Supreme Court and lower courts sufficiently consider the checks and balances that have been incorporated into the patent system on both the post and pre-grant level. This includes *inter alia* the mitigating effects of other patentability requirements, such as novelty, obviousness, utility and sufficient disclosure.

Recent developments demonstrate that a more restrictive application of these criteria contributes either directly or indirectly to limiting the scope of protection for many biotechnological inventions. This, in turn, helps to avoid patent claims effectively pre-empting *any* application of ‘fundamental principles’ or ‘natural phenomena’.⁷⁹ The completion of the Human Genome Project and the rapid growth of similar databases focusing on DNA/protein structures and functions have, for example, made it much more difficult for many biotechnological inventions to meet the novelty requirement. Moreover, the increasing predictability of some scientific steps involved in molecular biology, in combination with the establishment of a lower threshold for obviousness by *KSR v Teleflex*, has led to a situation where it is often not enough for a patent to simply isolate naturally occurring biological sequences, such as in the form of cDNA.⁸⁰ The improved predictability of these processes, especially in the field of synthetic biology,⁸¹ employs standardized techniques and processes, many of which are

77. Cf Eileen Kane, ‘Patenting Genes and Genetic Methods: What’s at Stake?’ (2010) 16 J. Bus. & Tech. L., 1 available at <<http://ssrn.com/abstract=1747191>> (accessed 8 December 2011).

78. Ibid.

79. Cf James R Farrand, ‘Patent Reform Arrives – Without Congressional Action’ (2010) Express O, available at <http://works.bepress.com/james_farrand/1> (accessed 10 August 2012).

80. The specific effect of *KSR* on DNA patents became evident in *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009); cf Timo Minssen, ‘The U.S. Examination of Nonobviousness After *KSR v Teleflex* with Special Emphasis on DNA-Related Inventions’, (2008) 39(8) IIC 886.

81. Synthetic biology is commonly understood as the synthesis of DNA molecules and the design and implementation of genetic circuits utilizing engineering principals. See ‘Synthetic Biology Standards and Intellectual Property’, Commissioned Paper by Andrew W Torrance and Linda J Kahl, presented at the Board on Science, Technology, and Economic Policy’s Symposium on Management of Intellectual Property in Standard-Setting Processes, 3–4 October 2012, Washington, DC.

maintained by standard-setting institutions⁸² to create these ‘made to order’ DNA molecules and processes.

The focus of patent activity is thus steadily shifting to truly inventive modifications and applications that are limited to claims on various unexpected functions⁸³ and methodological uses of biological subject matter.⁸⁴ Stricter application of the utility requirement guarantees that these functions must be truly understood and elucidated and that they should have a specific, substantial and credible ‘real-world’ use.⁸⁵ Inventions that meet those criteria must also be sufficiently disclosed in accordance with 35 U.S.C. § 112’s criteria which require *inter alia* that the claims point out and distinctly claim the invention’s subject matter and specify the limitation of such subject matter.⁸⁶

Further, the increasing sophistication of techniques used in modern biotechnology has now made it possible to efficiently and more accurately modify DNA and protein

82. These include, *inter alia*, ‘Open Source’ institutions such as the BioBricks Foundation (‘BBF’), the International Genetically Engineered Machine Foundation (‘iGEM’), the Registry of Standard Biological Parts (‘Registry’), the Synthetic Biology Engineering Research Center (‘SynBERC’), BIOFAB: International Open Facility Advancing Biotechnology (‘BIOFAB’), and the Synthetic Biology Open Language (‘SBOL’) Team. See also Torrance and Kahl, *supra* n 81, and Andrew W Torrance, ‘Planted Obsolescence: Synagriculture and the Law’ (2012) 48 Idaho L. Rev. 321, 341–5 (discussion of open synthetic biology institutions).

83. Since the inventiveness of full product claims might still be based on unexpected functions, it will be important to establish a rather high threshold for ‘truly’ unexpected functions. Only then will the patent protection correspond to the inventor’s actual contribution to the state of the art. Technical developments increasing predictability would guarantee that it will become more difficult to prove truly unexpected functions. Also the threshold for accepting evidence for such functions after the filing date should be set at a high level.

84. Cf. Michael M Hopkins, Surya Mahdi, Pari Patel and Sandy M. Thomas, ‘DNA Patenting: the End of an Era?’ (2007) 25 Nature Biotechnology 185, 187 (noting that both in the US and Europe it has become more difficult to patent research tools including DNA fragments such as ESTs and adding: ‘On future strategies, some interviewees indicated that they will now focus on new uses for known rather than novel sequences, with applications now likely to require greater preparation and more biological data to support narrower claims. Diagnostic/prognostic tests based on gene expression profiling or single nucleotide polymorphisms (SNPs), and therapeutics based on RNA interference were identified as new areas for patenting, although doubts were expressed by a minority over the likelihood of such inventions obtaining satisfactory patent protection ...’). Thus it can be argued that the focus seems to shift from upstream research tools to downstream applications). Yet, many of these functions might be old or obvious due to the increasing predictability of molecular biology, cf Benjamin Roin, ‘Unpatentable Drugs and the Standards of Patentability’ (2009) 87 Tex. L. Rev. 503–70 (discussing alternative forms of protection for old or obvious compounds with a high pharmaceutical potential).

85. *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005) (the Federal Circuit held that any invention must have both a *substantial* (‘an asserted use must show that the claimed invention has a significant and presently available benefit to the public’) and *specific* utility (‘an application must disclose a use which is not so vague to be meaningless’ and ‘an asserted use must [] show that the claimed invention can be used to provide a well-defined and particular benefit to the public’). Cf 2001 USPTO examination Guidelines. In Europe the use must ‘merely’ be plausible at the time of the application, cf Minssen and Nilsson, *infra* n 111.

86. As for biotechnology cf *Ariad Pharmaceuticals, Inc. v Eli Lilly and Co.*, 598 F.3d 1336 (Fed. Cir. 2010) *en banc* (sufficiency); note further that the claims in *Dealertrack, Inc. v Huber*, 674 F.3d 1315 (Fed. Cir. 2012) (Linn, J) would also have been invalidated under 35 U.S.C. § 112, since the computer-keyed process was not supported by disclosure of a specific supporting algorithm. (This was also noted in *CLS* 685 F.3d at 1351 which is now for *en banc* consideration.)

sequences through human intervention and adapt their structure to very specific uses. The creation of synthetically produced DNA using standardized processes clearly affects their patentability without the same recourse to philosophical analyses of products of nature or natural phenomena. Since these modifications are rather different from naturally occurring sequences and involve more human intervention than the mere isolation of cDNA, such synthetic compounds would probably meet the majority standard set in *Myriad I* and *II*.⁸⁷ It is not entirely clear, however, exactly what level of human intervention and difference from naturally occurring sequences is required under the current *Myriad* standard.

Another factor that will presumably contribute to the diminished relevance of first-generation product patents on isolated cDNA sequences, such as *Myriad*'s early BRCA patents, relates to the increasing understanding of epigenetic mechanisms, such as DNA methylation, histone modification, or related mechanisms, such as RNA interference.⁸⁸ Recent research has led to a much better understanding of how these mechanisms control the interplay of genetic information and activate or deactivate specific DNA sequences at various stages. Of particular interest is that epigenetic changes can be inherited, *but* unlike mutations of the base structure in DNA sequences, epigenetic changes of gene expression can also be more easily reversed through medication. It is therefore widely believed that epigenetic science will provide the key for many new individualized pharmaceuticals. Moreover, these new insights imply that singular isolated DNA sequences are only of very limited value to finding cures for many diseases.⁸⁹ More important is discovering how the genome and the genetic code are orchestrated and to what extent environmental factors can influence gene expression. The research focus of the industry is therefore shifting from the study of single DNA sequence mutations towards elucidating how epigenetic mechanisms work and may be manipulated.⁹⁰ As a result the new science of pharmaco-epigenomics is flourishing.⁹¹

While advances in epigenetics and the increasing insights about the complex interaction of genes and the environment will create new legal challenges and many

87. See Torrance, *Synthesizing Law for Synthetic Biology*, supra n 73, 641–2, 649 (pointing out that the recent uncertainty regarding the patentability of isolated human genes is likely to raise the prospective value of synthetic genes. He also highlights the suitability and increasing importance of alternative forms of protection for such sequences such as 'synthetic gene copyrights' and 'synthetic gene trademarks').

88. Influenced by environmental factors, some DNA in the body may undergo chemical modifications, such as methylation, which can affect the level of activity of a gene, but does not affect the nucleotide sequence of the gene. Note further that many patent applications involve RNA interference. For an overview of recent patent applications, see 'Recent Patent Applications in RNA Interference' (2009) 27 *Nature Biotechnology* 249.

89. See eg Cinthia Briseno, 'Wettlauf um die Gen-Zauberformel' in *Spiegel Online*, 9 August 2010 (in German), available at <<http://www.spiegel.de/wissenschaft/natur/0,1518,710603,00.html>> (accessed 10 August 2010) (referring to J Sweet in *AMP v USPTO* and describing how epigenetics and pharmaco-epigenomics diminish the practical relevance of the debate over product patents on isolated gene sequences. Single DNA sequences will mostly be useful for diagnosis while epigenetics holds the key for treatment).

90. Interestingly, the analysis of epigenetic processes and mechanisms has been much facilitated through the development of microarrays that can analyse DNA methylation patterns on DNA, cf. LM Butcher and S Beck, 'Future Impact of Integrated High-throughput Methylation Analyses on Human Health and Disease' (2008) 35 *J. Genetics & Genomics* 391–401.

91. Antonei B Csoka and Moshe Szyf, 'Epigenetic Side-effects of Common Pharmaceuticals: A Potential New Field in Medicine and Pharmacology' (2009) 73 *Medical Hypotheses* 770–80.

mysteries relating to genes or proteins might not necessarily be solved nor explained by epigenetics,⁹² it can nevertheless be assumed that most DNA or protein-related patents of the second or third generation do not pose the same difficulties in separating patentable subject matter from mere discoveries of natural phenomena.⁹³ Although most of these technologies will still rely on the utilization of natural processes, such as the genetic code, the focus will most likely be on specific functions of subject matter manipulated by human intervention that will *not* essentially pre-empt all applications of a fundamental principle.

Last but not least, it should be remembered that most of the perhaps overly broad patents that were granted in the early days of the biotechnological revolution have now expired or are about to expire. Due to legislative and procedural changes it has also become easier to attack overly broad product claims during patent litigation. As a result many (bio-) pharmaceutical inventions have fallen – or will soon fall – from the ‘patent cliff’. This forces the pharmaceutical industry to seek new business models. Since the necessary activities should, ideally, not be merely restricted to ‘re-inventing’ essentially old products and concepts, it will be important to provide appropriate incentives⁹⁴ for both upstream inventions and downstream innovation. Particularly in the complex field of biopharmaceutical innovation, which is not always easy to ‘reproduce’ (eg in the case of ‘biosimilars’) and depends on a very particular know-how, this would also require a closer look at the pre-emptive effects of alternative forms of protection that could *inter alia* be provided by regulatory data- or market-exclusivities periods, a prize system or trade secrets.

Concerning trade secrets, it has been pointed out that ‘the confidentiality of information deserves to be recognized as one of the key legal problems of our age’,⁹⁵ and in the foreword to the second edition of *Gurry on Breach of Confidence*,⁹⁶ Francis Gurry points out that conflicts over confidential information are increasing in a wide

92. For a good overview on current epigenetic research, cf Bryan M Turner, ‘Defining an Epigenetic Code’ (2007) 9 *Nature Cell Biology* 2–6, and id, ‘Simplifying a Complex Code’ (2008) 15 *Nature Structural & Molecular Biology* 542–4; as for legal issues see also Mark A Rothstein, Yu Cai and Gary E Marchant, ‘The Ghost in Our Genes: Legal and Ethical Implications of Epigenetics’ (2009) 19 *Health Matrix* 1; M Rothstein et al., ‘Ethical Implications of Epigenetics Research’ (2009) 10 *Nature Reviews Genetics* 224.

93. Judge Dyke recently examined the history of the patent statutes’ term ‘discovery’ holding that it has long had an established meaning in the sense that it required the use of some form of inventive facility in addition to its being new, ie that the shape or form in which it is produced shall not have been known previously, in addition to the requirement that it be useful. *In re Beineke*, 690 F.3d 1344, 1349 (2012) (citing and quoting *Thompson v Boisselier*, 114 U.S. 1, 11 (1885)).

94. These are arguably not only dependent on patents but also on trade secrets, regulatory exclusivities, better approval pathways and more efficient clinical trials, new models of public–private co-operation, etc. Moreover, one could discuss more governmental involvement. These factors will presumably become more significant. Yet, it can still be assumed that patents will remain the life-blood of the (bio)pharmaceutical industry.

95. As pointed out by Sundara Rajan on IPKat, available at <<http://ipkitten.blogspot.se/2012/12/gurry-on-breach-of-confidence-review.html>> (accessed 19 December 2012).

96. See, *Gurry on Breach of Confidence: The Protection of Confidential Information*, Second Edition, by Tanya Aplin, Lionel Bently, Phillip Johnson and Simon Malynicz (Oxford University Press, Oxford 2012). See also the recent EU study conducted by Hogan Lovells International LLP, *Study on Trade Secrets and Parasitic Copying (Look-alikes) MARKT/2010/20/D – Report on Trade Secrets for the European Commission*, available at <http://ec.europa.eu/internal_market/iprenforcement/docs/trade/Study_Trade_Secrets_en.pdf> (accessed 10 December 2012).

range of areas since ‘technology has made information precarious’. In their introductory remarks, the co-authors emphasize the far-reaching consequences of rules on confidence, noting that:

... confidentiality is a legal concept which is of serious, and almost certainly increasing, importance. Confidentiality is a critical tool in the regulation of the dissemination of ideas and information, and as such plays a key role in determining the boundary between ‘openness’ and ‘secrecy’. The work of the law of confidentiality thus has an impact upon personal autonomy, economic mobility, political transparency (and thus accountability), open justice, as well as innovation, competition, and economic prosperity.⁹⁷

Interestingly, the body of knowledge already in Myriad’s proprietary database of clinical information is probably protectable as a trade secret,⁹⁸ or, at least in Europe, under the EU Database Directive.⁹⁹ While Myriad’s method claims were held patent-ineligible and are accordingly in the public domain, its clinical database obtained while the claim remained valid is not, despite calls and recommendations for its release.¹⁰⁰

This is just another indicator of the increasing importance of the protection of confidential information and demonstrates how this form of protection may influence biomedical innovation. In that context it seems important to consider that a decrease of biomedical compounds and methods that may be protected by patents as patentable subject matter, could very well lead to greater protection of confidential information and secrecy in private business with potentially negative effects on innovation.

7.3 A remaining need for coherent and predictable principles in Europe and the US

In light of the above described developments, any further Supreme Court review addressing patent-eligibility should complement its *Prometheus* judgment with clarifications that ‘leave the door open’ for emerging technologies. The Court would be well advised *not* to establish an overly restrictive patent-eligibility doctrine that *categorically* excludes otherwise patentable inventions involving certain biotechnological products and diagnostic methods. Although a better articulated rationale for patent exclusions is needed and the concerns of the scientific community concerning overly

97. *Gurry on Breach of Confidence*, supra n 96, para 124. See also Sundara Rajan, supra n 95 (adding that: ‘Yet, as this book demonstrates, the law on breach of confidence is far from straightforward. The complexity of this area of the law owes itself to at least two important factors. First, the legal rules on breach of confidence are derived from diverse sources, both ancient and modern, leading to challenges in locating, articulating, and applying the law. Secondly, the fact that confidential information arises in so many contexts leads to an overlap between the legal principles on confidence and a wide variety of related legal regimes. Accordingly, an understanding of confidence may depend on the ability to work simultaneously within different legal and conceptual frameworks. For example, confidentiality in the context of intellectual property rights can mean something quite different from the confidentiality of state secrets’).

98. See Robert Cook-Deegan, John M Conley, James P Evans and Daniel Vorhaus, ‘The Next Controversy in Genetic Testing: Clinical Data as Trade Secrets?’ (2012) *Eur. J. Hum. Genet.* 1, 2, advance online publication 14 November 2012 (doi: 10.1038/ejhg.2012.217).

99. Directive 96/9/EC of the European Parliament and of the Council of 11 March 1996 on the legal protection of databases OJ 1996 L 77/20. See also, Case C-304/07, *Directmedia Publishing GmbH v Albert-Ludwigs-Universität Freiburg*, 9 October 2008 [2008] ECR I-7565.

100. Robert Cook-Deegan, supra n 98 at p 2, noting *inter alia* recommendations in two reports to the National Academies.

broad and too early granted product or method patents that might impede scientific progress must be taken seriously, it seems indeed a better way forward to focus on a strict application of the other patentability criteria and to further develop reasonable post grant mechanisms to alleviate potential conflicts that might still occur.¹⁰¹ Moreover, if one focuses *inter alia* on pre-emption of laws of nature and natural phenomena as the primary concern it seems as if extreme solutions for many patent-eligibility problems can be avoided.¹⁰² This, however, requires a wise elaboration of this doctrine, which should carefully take into account the complex mechanisms and factors that drive innovation.

Considering the technological advances and the specific impact of a strict application of patent criteria on the category of claims typically applied for and granted, it seems as if the open questions concerning the patentability of biotechnological *processes* and diagnostic *methods* present one of the most relevant issues. The trend to personalized medicine and the growing commercial value of biopharmaceutical process and method patents will most likely stir creative minds to challenge them as mere claims to natural phenomena or abstract ideas under the principles established by the Supreme Court in *Bilski* and *Prometheus*. Our study of the inconsistent post-*Bilski* Federal Circuit case law and the questions still left open by the subsequent Supreme Court decision in *Prometheus* demonstrates that it is now of uttermost importance how the Federal Circuit elaborates, refines and applies the patent-eligibility inquires to various field of technology. Without a workable rationale, lower courts will continue to feel like Alice down the rabbit hole when presented with a fountain of challenges to the subject matter patentability of method claims that depend upon the utilization of natural phenomena, such as the genetic code or principles of metabolic transformation.¹⁰³

Concerning DNA-related products claims, *Prometheus* has simply kicked these cans down the road and it remains to be seen whether or not a Supreme Court decision in *Myriad II* will introduce further fundamental changes to patent law and the patent-eligibility of biotech-related product claims. In any case the Court will have to think about how to harmonize exceptions to patent-eligibility under the Patent Statute with the rationale set forth in the Patent Clause of the US Constitution: 'To promote the Progress of Science and useful Arts ...'. Particularly for the US, this remains mostly

101. As for post-grant mechanisms this might include research exemptions, compulsory licensing or a more stringent application of concepts relating to competition law. Concerning further post-grant alternatives for dealing with gene patents cf. Geertrui Van Overwalle (ed), *Gene Patents and Collaborative Licensing Models: Patent Pools, Clearinghouses, Open Source Models and Liability Regimes* (Cambridge University Press, Cambridge 2009) (a collection of articles of more than 30 contributors focusing on striking the right balance between the positive and negative aspects of both the patent monopoly and the weapons that are developed to combat it). But see Allen Yu, 'Subject Matter Eligibility – the Disease and the Cure' (2010) Blog Express O, available at <http://works.bepress.com/allen_yu/1> (arguing that it is insufficient to rely on further patentability criteria).

102. Cf. Feldman, supra n. 37 (noting '[t]he Federal Circuit's decision in *Prometheus* seemed to suggest that most life science inventions would satisfy the requirements of patentable subject matter, while the PTO's application of *Prometheus* could lead to the rejection of numerous inventions in this arena. Neither extreme is necessary if one focuses on preemption of laws of nature and natural phenomena as the primary concern').

103. See Minssen and Schwartz, supra n 20, at 55–8 (citing Lewis Carroll, *Alice in Wonderland*, Chapter I, 'Down the Rabbit Hole' (Samuel Gabriel & Sons, New York 1916), p 1.

an economic question.¹⁰⁴ The decisive significance of economic analysis has been very well demonstrated in Judge Moore's concurring opinion in *Myriad I* and *II*. This and the diverging views on the economic and innovation policy aspects of DNA-related patenting indicate how important further economic studies and evidence are in this area.¹⁰⁵ One question that will have to be addressed with hindsight is, would the biotechnological revolution that we have experienced during the last 30 years predominantly in the US, Europe and Japan have taken place with the same speed and efficiency without the initial grant of rather broad DNA- and protein-related patent claims?¹⁰⁶ Another much more tricky questions is, what effect would a more restrictive patent eligibility threshold have for the development of emerging technologies?

Since intellectual property is a currency of the global economy these questions are not unique to the US legal system. In the face of the challenges posed by growing international economic competition and the broadening of the patentable subject matter doctrine by the US courts in *Chakrabarty* and subsequent cases,¹⁰⁷ their European and Japanese counterparts felt compelled to also gradually broaden the categories of patentable subject matter. In Europe this resulted in the patentability of computer implemented inventions 'as such'¹⁰⁸ and biotechnological methods and compounds, such as isolated DNA sequences.¹⁰⁹ Consequently, Europe is going through its own debates on the extent of patentable subject matter at the national, EU and the EPO level. As in the US, the European debate is *inter alia* greatly influenced by a general fear of overly broad upstream patents on natural products and processes that are granted at too early a stage. This has

104. Cf Minssen and Schwartz, *supra* n 20 (citing Li Lan Ren, 'US: Why Defining Patentable Inventions is an Economic Questions, MIP (July 1st, 2010) available at: <<http://www.managingip.com/>> (stressing the economic implications of patent eligibility)).

105. This is also reflected in § 27 of the new AIA, which requires the USPTO to prepare a report on the impact of patents on genetic diagnostic testing and second opinions, see <www.uspto.gov/aia_implementation/2012-1481_genetic-testing-hearing-notice.pdf> (accessed 29 June 2012).

106. Cf Terry Bradford, 'Biotechnology in the USA: Convergence of Scientific, Financial and Legal Practices' (2005) 2 *Tailoring Biotechnologies* 121, 130–31 ('[T]he... industry saw the 1980 ruling as the protection necessary to embark on the investment of billions of dollars that has taken us from the characterization of the DNA double helix to Dolly the sheep and to the development of scores of biotherapeutic drugs and diagnostics. Without [Chakrabarty], commercial biotechnology based on recombinant DNA technologies would not exist today'); for a different view cf Michael Heller, *The Gridlock Economy: How Too Much Ownership Wrecks Markets, Stops Innovation, and Costs Lives* (Basic Books, Philadelphia 2008).

107. See eg *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200 (Fed. Cir. 1991) and *Genetics, Institute Inc. v Amgen Inc.*, 502 U.S. 856 (1991) ('Amgen II') (confirming the patentability of isolated DNA).

108. Yet, what exactly this means appears to remain as unclear as the US exclusion of abstract ideas. A recent EPO Enlarged Board of Appeal decision in G 0003/08 (May 2, 2010 – computer implemented inventions) did not provide sufficient answers to significant questions. Cf Timo Minssen and Giovanni Gozzo, 'Obesvarade frågor rörande patent på datorrelaterade uppfinningar och affärsmetoder?' (Unanswered questions concerning patents on computer-related inventions and business methods?) (2007) 76(3) *NIR* 220–45.

109. EPO case law followed US precedent and held isolated, new, inventive and industrially useful human DNA to be patentable, see eg the final decision in T 272/95 *Relaxin/HOWARD FLOREY INSTITUTE* (2002). The European Biotech Directive 98/44/EC also affirmed this principle in its Articles 3(2) and 5(2), which have been incorporated into Rule 27(a) and Rule 29(2) EPC 2000. Yet, this did not quell the debate on exactly how the Directive should be interpreted, cf *infra* n 112.

not only led to numerous high-profile decisions on patent eligibility,¹¹⁰ but also to a heightened ‘plausibility’ threshold for demonstrating inventive step, industrial application and sufficient disclosure in patent applications.¹¹¹ In addition the European debates resulted in differing national implementations of the Biotech Directive.¹¹²

While it seems impossible to achieve static legal certainty in high-tech patenting and avoid all its inherent problems without risking technological progress, continual comparative study of developments on both sides of the Atlantic should aid in identifying reasonable utilitarian compromises that can narrow the parameters within which the patent pendulum will continue to swing. In any case it is evident that a Supreme Court review of *Myriad II* could have a significant influence on the ongoing European debate,¹¹³ in particular when considering the potential impact of future CJEU rulings,

110. The European discussion raises sometimes comparable but also slightly different issues. European patent law focuses *inter alia* on the term ‘invention’. Cf Articles 52(1) EPC and 52 (2) which identify certain subject matter, such as discoveries, scientific theories, aesthetic creations, presentations of information and computer programs *as such* (cf Article 52 (3) EPC) that shall not be regarded as inventions. Moreover, patents can be challenged on the grounds of morality and *ordre public* under both Article 53(a) EPC and Article 6 of the EU Biotech Directive (98/44), cf the Enl. BoA in G 2/06 (patent ineligibility of human embryonic stem cells under Article 53(a) EPC) and the CJEU’s decision in C-34/10 *Brüstle v Greenpeace* (patent-ineligibility of human embryonic stem cells under Article 6(2)(c) of the Biotech Directive). In addition, specific exceptions to patentability in Article 53(c) attempt to address socio-ethical and public health considerations. It excludes from patentability methods for treatment of the human body or animal body by surgery or therapy and diagnostic methods *practised on the human or animal body*, while products for use in any of these methods are expressly exempted from this exclusion. Yet, the interpretation of this provision, which had been designed to alleviate the ‘hands on’ work of medical practitioners and to protect their patients, is far from straightforward and is hotly debated, cf recent EPO Enlarged Board of Appeal decisions on Articles 52, 53 and 54 EPC in G 2/08 (2010 – dosage regime); G 1/07 (2010 – method for treatment by surgery); and G 1/04, OJ 5/2006, 334 (diagnostic methods). See also Eddy D. Ventose, ‘Patent Protection for Dosage Regimes in Europe: a Dissenting View’ (2011) 6(4) JIPLP 238–53, id, ‘Making Sense of the Enlarged Board of Appeal in *Cygnus/Diagnostic Method*’ (2008) EIPR 145–50. As for agricultural patents, cf G 2/07-Broccoli/PLANT BIOSCIENCE and G 1/08-Tomatoes/STATE OF ISRAEL (December 2010) (patent ineligibility of non-microbiological process under Article 53(b) EPC).

111. Yet, the UK Supreme Court recently rendered a more patent-friendly decision on the ‘plausibility’ of industrial applications in biotech, cf *HGS Inc v Eli Lilly & Co* [2011] UKSC 51. For a more general discussion, cf Timo Minssen and David Nilsson, ‘The Industrial Application Requirement for Biotech Inventions in Light of Recent EPO & UK Case Law: A Plausible “Hunting License”?’ (2012) 10 E.I.P.R. 689–703.

112. Some national legislation requires patent applicants to include the specifically identified function of (human) cDNA or even proteins into the claims, thereby restricting the scope of protection of patents to these functions. Other countries and the EPO still grant full product protection for such sequences, cf Timo Minssen, *Es bleibt dabei: Eine schwedische Stellungnahme zur europäischen Debatte über den absoluten Erzeugnisschutz bei der DNA Patentierung*, KLIFOR 3 & 4 at 93–120 (2008, in German). Cf the CJEU’s decision in C-428/08, *Monsanto Technology LLC v Cefetra BV* (6 July 2010). Due to the factual circumstances underlying the case and the focus of the decision on Art 9 of the Biotech Directive many questions remain unresolved, cf G. Van Overwalle, ‘The CJEU’s Monsanto Soybean Decision and Patent Scope – As Clear as Mud’ (2011) 42 IIC 1, at 1; MA Kock, ‘Court of Justice of the European Union Limits Patents on DNA Sequences: Much Ado About Nothing or the Beginning of Erosion for Biotech Patents?’ (2011) 11(1) BSLR 3–12.

113. As for the EPO decisions on *Myriad*’s BRCA patents and potential impacts of a US Supreme Court judgment, cf Isabelle Huys, Geertrui Van Overwalle and Gert Matthijs, ‘Gene and Genetic Diagnostic Method Patent Claims: a Comparison under Current European and

which is, like the US Supreme Court, a generalist court, within the framework of the emerging unitary patent system.

8 CONCLUSIONS

At first sight, the practical impact of the Federal Circuit's decisions in *Myriad I* and *II* seems moderate because clever claim drafting helps to avoid most patent-eligibility traps. Yet, the split decisions also contain elusive reasoning by each of the three judges, which have raised issues that could not be sufficiently addressed in the Supreme Court's *Prometheus* decision and therefore provide excellent fodder for potential US Supreme Court review. Such a review could have broad implications for the future of biotechnology, individualized medicine and tailored drug-research.

Any further high-profile decisions in both Europe and the US should take the criticism of excessively broad upstream patent claims very seriously. But courts should also carefully consider additional factors, such as higher thresholds for patentability criteria, scientific advances and post-grant mechanisms. The mitigating effects of such factors and the dynamic qualities of biomedical innovation will have to be balanced against the considerable risks that overly static eligibility doctrines might entail for technological progress. While it is essential that the US Supreme Court – as well as European courts – clarify its principles and develops a coherent eligibility doctrine that is not conflated with other patentability requirements, it would be well advised not to categorically close the 'patent eligibility door' to inventive, useful and sufficiently disclosed claims in emerging technologies with a well-delineated scope of protection. As the courts promote true innovative efforts through an accurate application of 35 U.S.C. § 101, creative applications of fundamental knowledge will emerge, deserving legal protection that corresponds to the inventor's actual contribution to the state of the art. At the same time, the intellectual foundations of genetic science should remain publicly accessible. Considering carefully the rationales for patent protection in combination with scientific and economic evidence, it should indeed be possible to reconcile the prohibitions on patenting laws of nature, natural phenomena, and abstract ideas with patenting practices that advance the application of genetics to medicine.¹¹⁴

Regardless of which position is taken in the debate, it is clear that further clarification of the eligibility doctrine in biotechnological patenting has both broad practical and theoretical implications. The scientific communities and the life science industries have every reason to demand a coherent and contemporary interpretation of the product of nature doctrine and its scope, as well as a modern case-by-case analysis of whether and how correlations in the life sciences are defined as laws of nature, natural phenomena or abstract ideas.¹¹⁵

US Patent Law', Eur. J. Hum. Genet. (June 2011) 1–4. See also Suleman Ali, 'Taking it Personally: Patents, Medicines and Genetic Markers', available on the IPKat weblog at <<http://ipkitten.blogspot.dk/2012/08/taking-it-personally-patents-medicines.html>> (accessed 17 August 2012) (commenting on a report of a meeting held on 10 November 2011 between the EPO and the biotech committee of the epi on *inter alia* 'inventions in the area of pharmacogenomics' and noting: 'it seems that EPO is taking a stricter view of the issue, and is probably looking for a test case to change the case law').

114. See also Kane, *supra* n 77, at 134.

115. *Ibid* at 102.

Sequel: Post 16 November 2012

Part IV of this series on patent-ineligible subject matter ended with *Myriad II* (or *AMP v PTO déjà vu*). On 25 September 2012, the Public Patent Foundation and the ACLU filed a petition with the US Supreme Court seeking a grant of *certiorari*.¹¹⁶ Petitioners sought review of three questions, to wit:

1. Are human genes patentable?
2. Did the court of appeals err in upholding a method claim by Myriad that is irreconcilable with this Court's ruling in *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012)?
3. Did the court of appeals err in adopting a new and inflexible rule, contrary to normal standing rules and this Court's decision in *MedImmune, Inc. v. Genentech, Inc.*, 549 U.S. 118 (2007), that petitioners who have been indisputably deterred by Myriad's 'active enforcement' of its patent rights nonetheless lack standing to challenge those patents absent evidence that they have been personally threatened with an infringement action?

On 30 November 2012 the US Supreme Court granted a writ of *certiorari sub nom. Association for Molecular Pathology v Myriad Genetics, Inc.* limited to question 1 presented by the petition.¹¹⁷ Before we address the import of the first question we note that the questions that didn't make it are interesting as an aid to understanding where the Supreme Court may go. A decision to address the '282 patent's claim for a method of using genetically modified cells to screen for drug candidates could have had serious consequences for innovation in health sciences.¹¹⁸ It would also have placed numerous existing patents into question, with many patentees holding their breath until the US Supreme Court explained just where it was going with question 2. The decision not to grant *certiorari* for the standing question means that NGOs like the ACLU and concerned scientists who are not directly impacted by a patent claim will find it difficult to file broad challenges concerning ethical, theoretical, or societal questions.

Question 1, as set forth in the petition could be addressed by the Court in many ways. *First*, question 1 is framed in a way that directs attention away from the focus of the decision below and suggests the petitioners' desired answer. After all, the Myriad patents only claim *isolated* DNA sequences outside of the human body which correspond to parts or segments of whole human genes, which are – however – not claimed *in vivo* and in their natural environment.¹¹⁹ So the question really concerns the patent eligibility of naturally occurring biomolecules as isolated strands, and that is how the Court should address the issue. *Second*, while it seems unlikely that the Supreme Court will address question 1 in the broad terms which the ACLU's language encourages, the Court could attempt to articulate a new theoretical definition of a 'product of nature'. The temptation is great for generalist judges whose job is to think in theoretical terms to establish universal rules for determining whether or not a claim encompasses a patent-ineligible product or compound. Such theoretical language,

116. *The Association for Molecular Pathology v Myriad Genetics, Inc.*, 2102 WL 45029 (U.S. September 25, 2012).

117. *Association for Molecular Pathology v Myriad Genetics, Inc.*, 81 U.S.L.W. 3199, 2012 WL 4508118 (U.S. November 30, 2012).

118. See also Christopher M Holman, 'Supreme Court Grants Certiorari in Myriad Gene Patent Case', 3 December 2012 on Holman's Biotech IP Blog, available at <<http://holmansbiotechip-blog.blogspot.com/>> (accessed 14 December 2012).

119. *Ibid*.

however, may create particular challenges for claims involving breakthroughs in life sciences absent the discipline provided by evidentiary inquiries into complex scientific new scientific areas and the special vocabulary used to delineate claims in a new field. *Third*, the Court may opt for the lighter touch of reformulating established principles through modifying existing linguistic rubrics. Unfortunately, that may not be sufficient to guide practitioners, the PTO and lower courts in how to apply old chestnuts to new, not well understood fields. Only the passage of time will reveal the Supreme Court's approach. We will closely follow these events in the next issues of this journal.