

# Behind the footnote in Merck KGaA v Integra

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The Supreme Court's recent decision in *Merck KGaA v Integra Lifesciences I, Ltd (Merck v Integra)*<sup>1</sup> expanding the statutory FDA research use exemption from patent infringement liability to allow unlicensed use of patented compounds during preclinical work does not authorise the unlicensed use of patented research tools. Faced with briefs from various *amici curiae* arguing that research tools are not covered by the exemption, as well as a brief of the US similarly suggesting that Congress may not have intended to include research tools in the exemption, the Court expressly stated in a footnote that its opinion does not address research tools. This article examines the arguments made to the Supreme Court regarding research tools and the FDA exemption in order to gain insight into the arguments that apparently persuaded the Supreme Court's to leave research tool patents untouched.<sup>2</sup>

Prior to *Merck v Integra*, members of the scientific community, the biotechnology industry and researchers, including those at major pharmaceutical companies, generally understood that licensing is required for use of patented research tools in drug development work.<sup>3</sup> Indeed, that view supported the development of a robust, nationwide research tool industry over the past few decades.<sup>4</sup> That view is based on the belief that 35 USC s271(e)(1) does not apply to patented research tools, because research tools typically do not go through the FDA pre-market approval process and none of the delay-related problems that gave rise to the enactment of s271(e)(1) apply to research tools. Nevertheless, when the Supreme Court granted *certiorari* in *Merck v Integra*, there were concerns that the Court might broadly interpret the statutory exemption, perhaps unintentionally, to encompass research tools used in the biotechnology and pharmaceutical researches.

To forestall such an interpretation, various *amici* submitted briefs to the Court explaining the importance of research tools

in the drug discovery process and arguing against application of the FDA exemption. The Solicitor General's brief supported this position, arguing that Congress may not have intended for the FDA exemption to cover research tools.<sup>5</sup> Even Merck acknowledged in its brief that 'it is not at all clear that use of the research tool would be exempt' from infringement, and provided several possible bases on which research tools could be excluded from the scope of s271(e)(1).<sup>6</sup> These arguments were not lost on the Supreme Court. By expressly refusing to address research tools in its otherwise broad opinion, the Court's decision leaves research tool patents untouched and maintains for the present the general consensus that research tool patents present valuable licensing opportunities in drug research and development. Unfortunately, however, the Court's decision provides little guidance on how this issue will be resolved prospectively.

## Background of the research tool issue in Merck v Integra

*Merck v Integra* involves a short tripeptide segment of fibronectin (the RGD peptide) that mediates interaction between fibronectin and a cell surface receptor integrin during angiogenesis which is a process essential for tumor growth. In 1995 Merck KGaA (Merck, a German company unrelated to Merck & Co in the US) entered into an agreement with Scripps Research Institute (Scripps) to conduct several *in vivo* and *in vitro* experiments on three cyclic RGD peptides. The experiments measured the efficacy, specificity, and toxicity of the cyclic RGD peptides as angiogenesis inhibitors, and evaluated their mechanism of action and pharmacokinetics in animals. Integra Life Sciences I, Ltd (Integra), owner of several patents on RGD peptides, sued Merck for patent infringement. Merck responded that its work with Scripps fell under the s271(e)(1) safe harbour. At trial, the jury found Merck liable for patent infringement,

and further that Merck had failed to show that its post-1995 activities were exempt by s271(e)(1). In a post-trial motion, the district court denied Merck's motion for judgment as a matter of law, reasoning that there was sufficient evidence to support the jury's finding on the s271(e)(1) issue. Merck appealed.

A divided panel of the Federal Circuit affirmed.<sup>7</sup> The Court found that the experiments done at Scripps were 'not clinical testing to supply information to the FDA, but only general biomedical research to identify new pharmaceutical compounds'.<sup>8</sup> One of the reasons provided by the Federal Circuit was that if the safe harbour exemption were expanded to include Merck's activities, it would 'effectively vitiate the exclusive rights of patentees owning biotechnology research tool patents'.<sup>9</sup> In a dissenting opinion, Newman J called the majority's reasoning based on research tools 'a misconception'.<sup>10</sup> She indicated that the RGD peptides at issue were not used by Merck as research tools. The Supreme Court granted *certiorari* to review the Federal Circuit's construction of s271(e)(1) to not apply to Merck's preclinical activities.<sup>11</sup>

On 13 June 2005 the Supreme Court issued a unanimous opinion in the case, broadly interpreting the scope of the safe harbour provision, s271(e)(1), which creates an exemption from patent infringement liability for use of a patented invention 'solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs'.<sup>12</sup> The Court held that the s271(e)(1) exemption extends to preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process.<sup>13</sup> This includes both preclinical data pertaining to drug safety in humans as well as preclinical studies related to a drug's efficacy, mechanism of action, pharmacokinetics, and pharmacology.<sup>14</sup>

The Court vacated the Federal Circuit's decision which had limited the s271(e)(1)

exemption to research activities that supply information for submission to the FDA. Confining its decision to correcting the Federal Circuit's erroneously narrow interpretation of the statute, the Court did not delineate the exact contours of the s271(e)(1) safe harbour. It did, however, explicitly decline to address 'whether, or to what extent, s271(e)(1) exempts from infringement the use of "research tools" in the development of information for the regulatory process'.<sup>15</sup>

### Review of the briefing on the research tool patent issue

The Supreme Court's discussion of the research tool patent issue in *Merck v Integra* is limited to just three sentences in a single footnote. Thus, to understand the Supreme Court's decision not to address research tools, it is helpful to review the briefing submitted to the Court by the parties, the Solicitor General and other *amici*. With a few exceptions, that briefing reflects a remarkable consensus of the importance of tool patents in the drug discovery process.

In its brief to the Supreme Court, Merck argued for a broad interpretation of s271(e)(1), and challenged the Federal Circuit's policy concern about research tools as misplaced. Merck did not, however, view s271(e)(1) to apply to research tools; rather, it noted that 'it bears emphasis that this case does not present the research tool question'.<sup>16</sup> Merck asserted that Integra had never argued in the lower court that the accused experiments constituted use of research tools. Merck added that the accused experiments used patented compounds, ie the cyclic RGD peptides, with a view toward bringing the compounds to market as drugs.

*In other words, in this case the patented inventions were the subject of the research, not just a tool used to study that subject. And that was the sole basis on which Integra litigated this case.*<sup>17</sup>

Moreover, Merck explicitly acknowledged that 'it is not at all clear that use of the research tool would be exempt', and provided several possible bases on which research tools could be excluded from the scope of s271(e)(1). It explained as follows:

*'A lower court could construe the language of the FDA exemption to apply only in circumstances where the "use" of "a patented invention ... develops ... information" for submission to the FDA about that patented invention, but not in situations where the use of the patented invention (the research tool) develops information but about something else (an unpatented drug candidate). Or a court might conclude that the use of a patented research tool is not "reasonably related" to the development of information for the FDA where equivalent data about the drug or the disease in question could easily be developed through other means, or perhaps where the research tool has no relationship to the disease under study.'*<sup>18</sup>

Merck concluded that the universe of research tools is so diverse and practices are changing so dramatically that the legal issue of how the FDA exemption relates to research tools could not be answered in *Merck v Integra* in the abstract.

The Solicitor General, in a brief on behalf of the US as *amicus curiae*, also urged the Court not to consider the issue of research tools. The US argued that 'Congress may well not have intended to include tool patents in the scope of affected inventions'.<sup>19</sup> The brief emphasised that 'it is unclear whether Section 271(e)(1) even applies to true research tools'.<sup>20</sup> It explained that Congress enacted the exemption to prevent the effective extension of patent terms due to delays that were occurring in the FDA pre-marketing approval process for competitors of patented drug products. But because research tools are not typically subject to those requirements, and are not typically included in final products that are subject to FDA approval, there is no patent term extension problem with research tools. The Solicitor General further pointed out that Congress had expected that s271(e)(1) would 'not have any adverse economic impact on a patent owner's exclusivity during life of the patent', because it permits only 'experimental activity'. But including research tools within the scope of s271(e)(1) would clearly diminish the value of those patents because research tools are used only at the experimentation stage and there is no subsequent consumer market

for them as there is in the case of drug products.<sup>21</sup>

Notwithstanding this apparent consensus of opinion between petitioner and the US, some *amici* who filed briefs in support of Merck went beyond Merck's argument and urged the Court to hold that the use of research tool patents is exempt under s271(e)(1).<sup>22</sup> There were various other *amici* in support of Integra, however, who argued that s271(e)(1) does not apply to research tools.<sup>23</sup>

The Supreme Court was apparently persuaded that the case does not involve use of patented research tools. In its opinion, the Court concluded that Integra had never argued that the RGD peptides were used at Scripps as research tools. The Court further found it 'apparent' from the record that they were not used as research tools.<sup>24</sup> Specifically, the Court cited Newman J's dissenting opinion at the Federal Circuit which states that '[u]se of an existing tool in one's research is quite different from study of the tool itself'.<sup>25</sup> Accordingly, the Court concluded that it 'need not – and [does] not – express a view about whether, or to what extent, s271(e)(1) exempts from infringement the use of "research tools" in the development of information for the regulatory process'.<sup>26</sup>

The Solicitor General's view that research tools may not be 'patented inventions' within the meaning of s271(e)(1).

In the US's *amicus* brief, the Solicitor General provided a detailed analysis of the tool patent issue which may prove instructive in future cases.<sup>27</sup> Specifically, by its terms, s271(e)(1) applies to the use of 'a patented invention'.<sup>28</sup> In 35 USC s100, Congress defined 'invention' generally to mean 'invention or discovery', but it also specified that that general definition does not govern if 'the context otherwise indicates'.<sup>29</sup> To ascertain whether the 'context' of a statute 'otherwise indicates' with regard to the definition of a particular term, one must take into account the statutory text surrounding the term at issue, the 'larger context of the whole statute and other laws relating to it', and whether the statute's purpose would be 'substantially frustrated' by the adoption of a particular definition.<sup>30</sup> The Solicitor General argued that the context of s271(e)(1) suggests that Congress indicated otherwise – that the term 'patented invention'

in s271(e)(1) does not include patented research tools.<sup>31</sup>

One contextual feature of s271(e)(1) on which the Solicitor General relied as an indication that the term ‘*patented invention*’ in s271(e)(1) does not include patented research tools is the fact that Congress meant for s271(e)(1) and another statute, 35 USC s156, ‘*generally to be complementary*’.<sup>32</sup> Sections 156 and 271(e)(1) were both enacted as part of the Drug Price Competition and Patent Term Act of 1984, popularly known as the Hatch-Waxman Act, in order to address unique problems caused by delays in the federal pre-market regulatory approval process for drugs. Section 156 allows for an extension of the patent term on certain products to address the problem that the FDA pre-market approval requirements reduced the effective patent term of some patented inventions.<sup>33</sup> Section 271(e)(1), on the other hand, allows certain unlicensed research use of patents to address the related problem of a patented invention gaining a *de facto* patent term extension because the FDA pre-market approval process for its competitor’s product cannot commence until the patent’s expiration.<sup>34</sup> The Hatch-Waxman Act thus balances the rights of the owners of patents on FDA-approved products and those who want to compete with the patent owner once the patent expires.

Congress further identified the product types eligible for s156 patent term extension, which include drug products, medical devices, food additives, and colour additives that are subject to regulation under the Food, Drug, and Cosmetic Act (FDCA).<sup>35</sup> Research tools, which are not subject to regulation under the FDCA, do not fall within those categories. Similarly, because competing research tools are not

delayed from getting to the market by the FDA premarket approval process, the *de facto* patent term extension problem addressed by s271(e)(1) does not arise. Because s271(e)(1) was enacted along with s156 as a ‘*roughly offsetting*’ measure so that the two provisions would address the ‘*dual distorting effects of regulatory approval requirements in this entire area*’,<sup>36</sup> the Solicitor General explained that including research tools within the scope of s271(e)(1) would destroy the symmetry between these two provisions.<sup>37</sup>

Another contextual feature on which the Solicitor General relied to indicate that the term ‘*patented invention*’ in s271(e)(1) does not encompass research tools is the statutory purpose.<sup>38</sup> Congress’s overall purpose in enacting s271(e)(1) was to ensure the continued development of new drugs for treatment of human diseases. Broadening the reach of s271(e)(1) to exempt research tools from patent protection for research use would not serve this goal because it would destroy the incentives for innovation in research tools that are critical to drug development. It would also undermine Congress’s efforts to narrowly tailor the statute to have a ‘*de minimis*’ effect on patent holders.<sup>39</sup> Unlike patented drug products whose value primarily resides in commercial sales to the general public after FDA approval, research tools derive their primary economic value from commercial sales to researchers and drug developers and have no market in the general public. Thus, to read s271(e)(1) to permit infringement of research tool patents for research uses would potentially destroy all economic value of research tool patents.

The *amici* from the research tool industry agreed with the Solicitor General’s position, arguing that the narrowness of the statutory

text of s271(e)(1) itself also supports the view that the term ‘*patented invention*’ in that provision does not include patented research tools.<sup>40</sup> They observed that s271(e)(1) includes a series of narrowing terms to tailor the exemption to the particular problem posed by the FDA pre-marketing approval process. Congress specified that, in order not to constitute infringement, the making, use or sale of the patented invention must be ‘*solely*’ for the uses described in s271(e)(1),<sup>41</sup> and that such uses must be ‘*reasonably related*’ to the ‘*development and submission of information under*’ particular federal laws. The *amici* concluded that these terms of limitation all suggest that the s271(e)(1) exemption was not intended to cover research tools because they were not affected by the problems created by the federal pre-market regulatory approval process.

Although the Supreme Court in *Merck v Integra* did not express an opinion on the meaning of ‘*patented invention*’ in s271(e)(1), it focused only on the situation where the patented invention used by the alleged infringer is the actual or potential subject of FDA regulatory review. That, according to Merck, was the sole basis of the litigation. Throughout its opinion, the Court referred repeatedly to use of ‘*patented compounds*’ in developing the compounds as drugs. For example, the Court stated that s271(e)(1) ‘*necessarily includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process*’.<sup>42</sup> It also stated that ‘[a]t least where a drugmaker has a reasonable basis for believing that a patented compound may work, ... that use is “reasonably related” to the “development and submission of information” under ... Federal law’.<sup>43</sup> This was contrasted with ‘[b]asic scientific research on a particular compound, performed without the intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect’ which does not fall under s271(e)(1).<sup>44</sup> Clearly, the Court’s opinion focused only on research ‘*on*’ a patented compound in clinical studies.

In contrast, research tools are used by pharmaceutical and biotechnology companies to find, refine, and otherwise design and identify a potential product or properties of a potential drug product.<sup>45</sup> Research tools include a wide range of

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devices, substances, and processes that are used to study other substances.<sup>46</sup> As the Supreme Court pointed out, the use of a research tool is different from the study of a tool itself. Accordingly, one can certainly argue that research tools are simply not the kind of ‘*patented invention*’ defined in the statute and not the kind of ‘*patented compounds*’ discussed in *Merck v Integra*.

### Policy arguments for and against application of s271(e)(1) to research tool patents

Some *amici* who urged the Supreme Court to broadly interpret s271(e)(1) argued that overly expansive patent rights would impede drug research or development and drive up the cost for prescription drugs.<sup>47</sup> Other *amici* pointed out, however, that with regard to research tools, the current patent system has been functioning very well.<sup>48</sup> They referred to a number of empirical studies for evidence of an efficient patent system. For example, a study funded by National Academies revealed that research tools are widely available through licences.<sup>49</sup> The study found that few worthwhile projects are being stopped because of the lack of access to intellectual property related to research tools.<sup>50</sup> Moreover, studies have shown that, instead of driving up the drug cost, discovery and development of new research tools actually leads directly to lower costs and time saving at every stage of the drug discovery process.<sup>51</sup>

Interestingly, Congress has specifically addressed the problem posed by recalcitrant patent holders in other statutes. For example, Congress authorised the US, under 28 USC s1498, to use and manufacture any federally patented invention, regardless of the patent owner’s consent, subject only to payment of the ‘*reasonable and entire compensation for such use and manufacture*’.<sup>52</sup> The US also wields a significant power over the right to use patented inventions under the Bayh-Dole Act 1980 as a result of the large role of federal funding in research, by reserving for the federal Government the right to practise, or to have practised for it or on its behalf, any invention developed with the use of federal funds.<sup>53</sup> Even these statutes, however, which were specifically enacted to address national health concerns, do not

create an unlimited right to patent infringement by the Government. Thus, the *amici* argued that Congress did not intend s271(e)(1) to be interpreted to allow private actors to have such a right.<sup>54</sup>

Some *amici* also expressed concerns that the line between tool and non-tool uses is difficult to draw.<sup>55</sup> The Supreme Court, however, did not seem to be particularly concerned about this problem. For example, the Court had no trouble deciding that it was ‘*apparent*’ that the RGD peptides were not used as research tools in this case but were, in fact, the drugs undergoing FDA review based on the record.<sup>56</sup> It indicated that there is an obvious difference between the use of a substance as a tool to study other substances, and the study of the substance itself. Indeed, even in cases where a patented invention has both tool and non-tool uses, the tool market usually has no difficulty in distinguishing between those two.<sup>57</sup> Thus, the mere fact that some inventions may have both tool and non-tool uses does not mandate an all-inclusive exemption from infringement liability for all patented inventions used during drug research and development.

Other *amici* argued that application of s271(e)(1) to patented research tools would have grave consequences for progress in research and development generally and particularly in the drug research field. They argued, for example, that because the patent system provides incentive for investment in innovative technologies, interpreting s271(e)(1) to authorise infringement of research tool patents would mean a one-time giveaway of drug discovery and development technology to the pharmaceutical industry, only to remove the incentive to develop and make available the next generation of drug research tools.<sup>58</sup>

It is possible that such policy arguments played a significant role in the Court’s decision to explicitly decline to address whether research tool patents are covered by the FDA exemption. The question going forward, however, is how will other courts interpret s271(e)(1), given the lack of guidance from the Supreme Court on the issue of research tools.

To date, the courts, as well as the patent and research community, have not viewed

s271(e)(1) as being so expansive as to cover research tool patents. The very existence of a large variety of companies that develop, create, and sell research tools attests to the widely recognised economic worth of the research tools and their underlying patents. Notably, as Merck pointed out in its brief, in the more than 20 years since the enactment of s271(e)(1), only one reported case has emerged in which a drug innovator invoked the exemption in order to claim the right to infringe a patent that ‘*could even arguably be called a research tool patent*’.<sup>59</sup> The absence of litigation in which s271(e)(1) has been invoked to defend against infringement claims involving research tools suggests a long-standing understanding among many members of the patent and scientific communities that s271(e)(1) does not authorise infringing uses of patented research tools. By declining to address the issue of whether uses of patented research tools are exempt under s271(e)(1), the Supreme Court left the *status quo* untouched but provided little guidance for the future.

### Conclusion

By explicitly declining to address the issue of research tools in *Merck v Integra*, the Court removed any doubts regarding the impact of its decision on research tool patents. Although it remains to be seen how future courts define the reach of s271(e)(1), the Supreme Court’s opinion left unchanged the general consensus that research tool patents are valuable in both basic research and research in drug development. ■

- 1 125 S Ct 2372 (2005).
- 2 The authors submitted an *amicus* brief in support of *Integra* on behalf of several companies and organisations in the research tool industry, including Invitrogen, ALSSA, BIOCROM, Affymetrix, Diversa, Quantum Dot Corp, Sangamo Biosciences and Symyx Technologies. In the brief, the research tool industry argued that the statutory exemption, 35 USC s271(e)(1), does not encompass research tool patents and specifically urged the Court to avoid issuing an opinion that could be interpreted as endorsing the efforts by some of the *amici* supporting Merck to expand the exemption to research tools.

- 3 See, for example, John P Walsh et al, *Research Tool Patenting and Licensing and Biomedical Innovation, in Patents in the Knowledge-Based Economy* 285, 322–8 (Wesley M Cohen and Stephen A Merrill eds 2004).
- 4 For example, it was estimated that the world market for life science and analytical products and services is more than US\$26bn. Brief of Invitrogen et al as *Amicus Curiae*, at 8.
- 5 Brief of US as *Amicus Curiae*, at 29.
- 6 Brief of Merck, at 41–3.
- 7 *Integra Lifesciences I, Ltd v Merck KGaA*, 331 F 3d 860 (Fed Cir 2003).
- 8 *Ibid* at 866.
- 9 *Ibid* at 867.
- 10 *Ibid* at 877–8 (Newman J, dissenting).
- 11 125 S Ct 823 (2005).
- 12 35 USC s271(e)(1).
- 13 125 S Ct at 2380.
- 14 *Ibid* at 2381–2.
- 15 125 S Ct at 2382 n 7.
- 16 Brief of Merck, at 41–2.
- 17 *Ibid* at 42.
- 18 *Ibid* at 43.
- 19 Brief of US as *Amicus Curiae*, at 29.
- 20 *Ibid*.
- 21 *Ibid*.
- 22 See generally, for example, Brief of Eli Lilly et al as *Amicus Curiae*.
- 23 See, for example, Brief of Invitrogen et al as *Amicus Curiae*; Brief of Applera Corp et al as *Amicus Curiae*; Brief of Vaccinex et al as *Amicus Curiae*; Brief of Wisconsin Alumni Research Foundation et al as *Amicus Curiae*; cf Brief of San Diego Intellectual Property Law Association as *Amicus Curiae* (supporting neither party).
- 24 125 S Ct at 2382 n 7 (citing 331 F 3d at 878 (Newman J, dissenting)).
- 25 *Ibid*.
- 26 *Ibid*.
- 27 Brief of US as *Amicus Curiae*, at 29.
- 28 35 USC s271(e)(1).
- 29 35 USC s100.
- 30 *Rowland v California Men's Colony*, 506 US 194, 199, 209, 210 (1993) (interpreting phrase 'context indicates otherwise' as used in the Dictionary Act).
- 31 Brief of US as *Amicus Curiae*, at 29.
- 32 *Ibid* at 29 n 12 (citing *Eli Lilly & Co v Medtronic, Inc*, 496 US 661, 673 (1990)).
- 33 *Eli Lilly & Co*, 496 US at 669–71.
- 34 *Ibid*.
- 35 35 USC s156(f).
- 36 *Eli Lilly & Co*, 496 US at 672.
- 37 Research tools are unlike the medical devices at issue in *Eli Lilly & Co v Medtronic, Inc*, 496 US 661 (1990) that the Court found subject to s271(e)(1) exemption. Those medical devices were 'products' within the scope of s156.
- 38 Brief of the US as *Amicus Curiae*, at 29.
- 39 HR Rep No 98-857, pt II at 30 (1984) (stating that Congress intended to tailor the statute to have a 'de minimis' effect on patent holders).
- 40 Brief of Invitrogen et al as *Amicus Curiae*, at 26.
- 41 Some amici in support of Integra specifically argued that the term 'solely' in the statute takes use of research tools out of the safe harbour protection. See, for example, Brief of Applera Corp et al as *Amicus Curiae*; Brief of Vaccinex et al as *Amicus Curiae*; Brief of Wisconsin Alumni Research Foundation et al as *Amicus Curiae*.
- 42 125 S Ct at 2380.
- 43 *Ibid* at 2383.
- 44 *Ibid* at 2382.
- 45 Federal Trade Commission, *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy*, Ch 3 at 18 (2003) (providing definition of 'research tools').
- 46 Brief of US as *Amicus Curiae*, at 28.
- 47 See, for example, Brief of AARP as *Amicus Curiae*, at 3.
- 48 See, for example, Brief of Invitrogen et al as *Amicus Curiae*, at 9–15.
- 49 Walsh, *supra*, 286 n 3.
- 50 *Ibid*. Other recent systemic studies have reached similar conclusions. See *National Research Council, A Patent System for the 21st Century* 111 (Stephen A Merrill et al eds 2004) ('Obtaining licences to use such technologies may entail an immediate cost in licensing fees ..., but being denied access to the technologies is not usually a problem because their sole or principal market is research applications.'). *Organisation of Economic Cooperation and Development, Genetic Inventions, Intellectual Property Rights and Licensing Practices: Evidence and Policies* 50 (2002) ('There is in fact little evidence so far of breakdowns in negotiations over IP rights or evidence that biomedical research has slowed.'). *Ibid* ('Most of these "general tools" ... are licensed broadly.').
- 51 See Walsh, *supra*, at 301 (survey respondents believed costs of research tools 'to be within reason largely because the productivity gains conferred by the licensed research tools were thought to be worth the price'); Joseph A Dimasi et al, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 *Journal of Health Economics* 151, 181 (2003) (noting that costs of 'discovery and preclinical development' were growing, 'but much more slowly than in the past,' and hypothesised that '[t]he widespread use of discovery technologies ... may have created enough efficiency gains to slow down the ... cost').
- 52 28 USC s1498(a).
- 53 See 35 USC s202(c)(4).
- 54 Brief of Invitrogen et al as *Amicus Curiae*, at 16–8.
- 55 See, for example, Brief of Eli Lilly et al as *Amicus Curiae*, at 17–8.
- 56 125 S Ct at 2382 n 7.
- 57 One such example is erythropoietin (EPO), which was developed by Amgen as a drug for the treatment of anaemia and, when studied as a drug, was subject to s271(e)(1). See *Amgen, Inc v Hoeschst Marion Roussel, Inc*, 3 F Supp 2d 104 (D Mass 1998). In the meantime, Amgen also sold non-therapeutic forms of EPO in the tool market – a highly concentrated form known as 'Ultrapure EPO' and a less concentrated, tissue culture grade form known as 'TC EPO'. See *Techno Corp v Amgen, Inc*, No CIV-00-2157, 2001 WL 1690062 (D Minn 7 January 2001). Thus, the EPO used for therapeutic use is easily distinguishable from the EPO used for non-therapeutic purpose because of different concentrations and tissue culture grades, as well as by the licensing arrangements.
- 58 Brief of Invitrogen et al as *Amicus Curiae*, at 12.
- 59 Brief of Merck, at 42–3 (citing *Bristol-Myers Squibb Co v Rhone-Poulenc Rorer, Inc*, 2001 WL 1512597 (SDNY 28 November 2001)). See also Jian Xiao, *Carving Out a Biotechnology Research Tool Exception to the Safe Harbor Provision of 35 USC s271(e)(1)*, 12 *Texas Intellectual Property Law Journal* 23 (2003) (reviewing s271(e)(1) cases prior to *Merck v Integra*).