Abel+Imray

Biosciences & Pharma Group Newsletter

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The Abel & Imray Biosciences & Pharma Group Newsletter is intended to keep clients and associates up to date with patent developments and news in the UK, Europe and beyond. We hope the items will interest you. In this edition:

Matthew Fletcher
Partner, Bath
matthew.fletcher@abelimray.com

EPO Adopts New Approach to Embryonic Stem Cells

The experience of Applicants and recent announcements by senior personnel at the EPO indicates that EPO examination practice regarding assessment of the patentability of subject matter including or *implying* the use of human embryonic stem (hES) cells has changed recently.

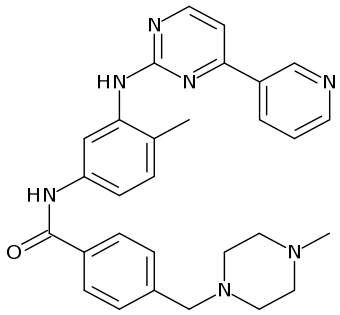
The previous approach of EPO Examiners was to follow the EPO's Enlarged Board of Appeal "WARF" decision G2/06, which interpreted the statutory exclusion of "use of human embryos for industrial or commercial purposes" as precluding protection for inventions which *necessarily involved* the use and destruction of a human embryo regardless of whether the patent claims themselves included a step using an embryo. In practice this effectively outlawed first generation ES cell applications but permitted, subject to suitable claim wording, those filed after May 2003 when hES cell lines began to be available from public depositories as an alternative to using human embryos as a direct source of starting material.

In October 2011 the Court of Justice of the EU issued an opinion (the Brüstle decision, C-34/10) which took a more restrictive approach to the issue. Although binding on the natural courts of EU member states the EPO has declined to *officially* adopt the CJEU's opinion as a matter of principle because the EPO is not an organ of the EU.

However, recently the EPO's Examining Divisions have informally started to adopt the CJEU's approach and will now refuse claims which relate to inventions using post-2003 deposited cell lines as their starting material because such cell lines of course ultimately did involve blastocyst destruction in their production.

Applicants do however still have some room for manoeuvre. Applications filed after the January 2008 publication of the single blastomere biopsy process, which provides a route to ES cells without necessary blastocyst destruction, might still be allowable subject to suitable claim wording. Inventions relating to ES cell culture media and/or apparatus and also relating to induced pluripotent stem (iPS) cells may also be patentable if appropriately claimed, as are inventions relating to non-human animals. We will keep you informed of any further developments and would be pleased to advise on claim strategy in his complex area of law.

Polymorphs in India and Europe – Gleevec and Beyond



Imatinib

Much has been said about the recent Gleevec decision of the Supreme Court of India (SCI), in which Novartis was refused a patent for a new crystalline form of a known compound (the β-crystalline form of imatinib mesylate). However, given India's strong generics industry, and its historic reluctance to grant patents for pharmaceuticals *per se*, the decision of the SCI cannot have been completely unexpected.

The β-crystalline form of imatinib mesylate fell foul of novelty and inventive step provisions, as well as the highly controversial section 3(d), which sets out restrictions on what is considered to be an invention. The relevant part of section 3(d) states that a "mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance is not an invention", setting an additional barrier for new forms of pharmaceutical compounds to be considered as inventions.

In the Gleevec case, the SCI interpreted the word "efficacy" in s. 3(d) very narrowly, holding that it meant improved therapeutic effect, and that improved physico-chemical performance (such as improved flow properties, thermodynamic stability, hygroscopicity) was not sufficient. Of course, the question arises as to what type of improvement in properties for a new form of a known chemical substance could be considered to meet the threshold? In that regard, the SCI refused to be drawn on whether reduced toxicity might constitute enhanced therapeutic efficacy, but indicated that improved bioavailability would not be sufficient, where it had not been demonstrated that the improved bioavailability led to an enhancement in therapeutic efficacy.

The SCI also appeared to take the view that since imatinib mesylate was covered by the claims of an earlier US patent, the non-crystalline form was known from that publication, even though not specifically disclosed. The SCI were reluctant to distinguish between what is protected by a patent (the scope of the claims) and what is disclosed in a patent specification, and that has caused concern to patent practitioners and users. Depending on how that aspect of the SCI's judgement is implemented by the Indian Patent Office, it may be that it will prove more difficult for patentees to obtain broad patent protection in India for applications covering ground-breaking inventions which open up new fields of research, but which do not necessarily specify every detail of all applications of the invention.

The decision of the SCI can be compared with the situation in Europe concerning patentability of new forms of pharmaceutical compounds. The EPO has no difficulty in recognising the novelty of specific salts or polymorphs in cases where the prior art discloses the parent compound in more general terms. The main issue in Europe is usually inventive step, and decision T777/08 (mentioned briefly in our March newsletter) is useful as an example that sets out the EPO's approach to consideration of inventive step for new pharmaceutical forms. In that case the EPO considered that, in the absence of technical prejudice or unexpected properties, mere provision of a crystalline form of a known compound (atorvastatin) was not inventive. In T777/08, the closest prior art was the amorphous form of the compound, and the Board of Appeal reasoned that there was an expectation that a crystalline form would have improved filterability and drying characteristics, and arbitrary selection of one polymorph from equally suitable candidates was not inventive.

Although that decision arguably raised the bar for inventive step for polymorph cases, the opportunities for obtaining patent protection do not appear to be as bleak in Europe as in India. T777/08 still leaves open the possibility of obtaining patent protection in Europe where a new polymorph is associated with an unexpected property. It may also still be possible to obtain protection in cases where routine experiments are unsuccessful in identifying polymorphs, and narrow/unusual sets of conditions are required to produce a particular crystalline form.

Clarity, Sufficiency, and the Importance of Data – A UK Perspective

The case of Generics ("Mylan") v. Yeda & Teva (2012 EWHC 1848 Pat) was decided in the UK High Court last year. It concerned a proposed generic version of the drug "Copaxone", used for treating multiple sclerosis, and has been widely quoted in relation to its comments regarding the level of technical data required to be included in patent specifications, and for its somewhat cryptic remarks regarding whether evidence filed after the date of filing can be used to support or deny the presence of an inventive step over the whole scope of the claim. Certainly the decision reinforces the importance of ensuring that, in chemical and biological cases, the specification as filed contains as much experimental data as possible illustrating that the invention actually works. However, the Court also addressed issues concerning clarity and sufficiency, which are of interest to anyone involved in drafting patent specifications.

The judge had to consider whether claim 1 was truly ambiguous (in which case the patent would have been bad for insufficiency) or whether it was just difficult to construe. Claim 1 reads:

"A copolymer-1 fraction, wherein said fraction contains less than 5% of species of copolymer-1 having a molecular weight over 40 kilodaltons and wherein over 75% of said fraction is within a molecular weight range from 2 kilodaltons to 20 kilodaltons."

At issue was the definition of "copolymer-1", which was defined in the description as being "…a synthetic polypeptide analog of myelin basic protein (MBP), which is a natural component of the myelin sheath….Copolymer-1 is a mixture of polypeptides composed of alanine, glutamic acid, lysine, and tyrosine in a molar ratio of approximately 6:2:5:1, respectively." The problematic term was the "fuzzy" boundary of "approximately 6:2:5:1". In finding that the patent was valid and infringed, the judge held that the skilled team would consider that the word "approximately" was intended to cater for variations in both amino acid analysis and synthesis of the polymer, but that such a "fuzzy" boundary did not render the claim ambiguous.

A further point at issue was whether the claim was ambiguous because the specification did not define whether the basis on which the molecular weight of the claimed copolymer-1 fraction (which was referred to in a number of the sub- claims as "average molecular weight") was to be understood. The judge concluded (with some reluctance) on the basis of the evidence that "molecular weight" and "average molecular weight" should be understood as meaning M_p (peak molecular weight), which was one of a number of possibilities. The interest in this point is in the judge's statement that: "…the skilled team is deemed to read the specification with a mind willing to understand it. It follows that they would not throw up their hands when confronted with the problem, but would consider the specification with care to see if it was possible to work out what was meant by "average molecular weight".

The judgement gives welcome encouragement to patentees that common sense will be applied in the interpretation of claims, while reinforcing the message that ambiguity in patent specifications should be avoided whenever possible.

If you have any questions about matters in the Newsletter, please get in touch with your usual Abel & Imray contact, or e-mail to ai@abelimray.com

London
20 Red Lion Street
WC1R 4PQ, UK
T +44(0)20 7242 9984
F +44(0)20 7242 9989

Cardiff
3 Assembly Square
Britannia Quay
CF10 4PL, UK
T +44(0)29 2089 4200
F +44(0)29 2089 4201

Bath
Westpoint Building
James Street West
BA1 2DA, UK
T +44(0)1225 469 914
F +44(0)1225 338 098