H. Lundbeck A/S

Submission to the Pharmaceutical Patents Review

21 January 2013

Introduction

This submission by H. Lundbeck A/S (Lundbeck), a global pharmaceutical company working on treatments for brain disorders, headquartered in Copenhagen, Denmark, responds to a number of the issues and questions raised in the Pharmaceutical Patents Review: Background and Suggested Issues Paper released in November 2012 (Issues Paper).

Lundbeck has had the opportunity to review a draft version of the submission made by Medicines Australia and the submission made by Michael Caine on 17 January 2012. Lundbeck supports the views advanced in each of those submissions.

For further information or queries, please contact John Meidahl, Divisional Director of Corporate Patents and Trademarks by email at jmp@lundbeck.com.

About Lundbeck

For more than 50 years Lundbeck has been providing innovative medicines to people who suffer from brain disorders.

Lundbeck is different from most other research-based pharmaceutical companies. It is 70% owned by the Lundbeck Foundation, which supports research at the highest level within biomedicine and the natural sciences through grants. Lundbeck is highly committed to improving the quality of life for people suffering from brain disorders; about 20% of Lundbeck’s revenue is invested in researching and developing new medicines.

Lundbeck employs about 6,000 people worldwide in 57 countries. It has production facilities in Italy, France and Denmark and research centres in Denmark, China and the United States.

In 1997, Lundbeck established a small presence in Australia. Lundbeck Australia’s first products were two conventional antipsychotics, FLUANXOL and CLOPIXOL. Today, Lundbeck Australia employs 44 people and markets products for the treatment of depression and anxiety, bipolar disorder, schizophrenia, Alzheimer’s disease, and Parkinson’s disease.

It is part of Lundbeck Australia’s philosophy that its role with the medical profession is to provide education and support. In the same year that Lundbeck established a presence in Australia, it introduced the Lundbeck Institute, a series of seminars and workshops that provide a unique opportunity for practising psychiatrists, neurologists and registrars...
to share experiences in treating patients. The Lundbeck Institute uses evidence-based medicine and international guidelines as the background material to the seminars in an effort to help the participants reach consensus on the optimal treatment and care of patients.

Since 2000, the Lundbeck Institute has completed more than 100 local seminars in Australia attended by more than 2,500 specialists and general practitioners. The continuing feedback is that these seminars are of an excellent quality and clinical relevance, with more than 25% of participants attending a second seminar.

Lundbeck Australia is actively involved in clinical research. Australian researchers were involved in clinical trials investigating a new, multimodal treatment for depression, vortioxetine, which was recently submitted for regulatory approval in the US, Europe and Australia. Two trials investigating novel agents for the treatment of Alzheimer’s disease and ischaemic stroke are currently ongoing in Australia.

The escitalopram case

1.1 Background

The Issues Paper refers to the escitalopram case\(^1\) in which Lundbeck sought to defend the validity of a patent term extension of its patent for the isolated (+)-enantiomer of citalopram, known as escitalopram, which was granted by IP Australia in 2003 on the basis of the first listing in the Australian Register of Therapeutic Goods (ARTG) of LEXAPRO (the first product sold comprising the patented isolated enantiomer). The validity of the extension of term was first challenged in 2005 by the generic pharmaceutical company, Alphapharm Pty Ltd (Alphapharm). In addition to challenging the validity of the extension of term, Alphapharm sought to revoke the escitalopram patent on the basis that the invention was not patentable.

Following decisions by IP Australia and a single judge of the Federal Court, Justice Lindgren, the matter was appealed to the Full Court.

As the Issues Paper observes, the Full Court found that Lundbeck’s extension of term application should have been based on the first listing on the ARTG of a different product, CIPRAMIL, which contains the racemate citalopram (a substance consisting of equal proportions of the (+)- and (-)-enantiomers). However, the Full Court found that the patent was valid as escitalopram was novel and inventive over the earlier disclosure of citalopram.

1.2 The Full Court’s interpretation

The escitalopram decision has been criticised because of the Full Court’s finding that the extension of term should have been based on the registration of a product (CIPRAMIL) which did not fall within the scope of the claims of the patent to be extended (CIPRAMIL is a racemate, not the isolated (+)-enantiomer). While the Full Court construed the claim in the patent to be a claim to escitalopram, which is, by definition, the isolated (+) enantiomer, and found that substance to be novel and inventive, when applying the extension of term provisions the Court proceeded to identify that escitalopram was contained in CIPRAMIL. The difficulty with the decision is that: while it

\(^1\) H. Lundbeck A/S v Alphapharm Pty Ltd [2009] FCAFC 70.
is true to say that both enantiomers of citalopram are present in CIPRAMIL, it is nonsensical to say that CIPRAMIL contains escitalopram when, by definition, escitalopram means the (+)-enantiomer without the (-)-enantiomer.

A problematic implication of the Full Court’s finding is that a substance upon which an extension of term should be based need not be a substance claimed in the patent that is the subject of the extension of term application. This follows from the Court’s failure to find that the reference to a “substance” in 70(3) of the *Patents Act 1990* necessarily means the substance claimed in the patent.

The Full Court’s interpretation is inconsistent with the legislative purpose of the extension of term regime: to compensate pharmaceutical companies for regulatory delays until obtaining marketing approval for a product (that is covered by a patent).

The Full Court’s interpretation has a number of absurd or illogical consequences which demonstrate the difficulties with its interpretation.

1 Lundbeck could have obtained an extension of term based on CIPRAMIL even if it had never marketed the substance claimed in the patent, i.e. LEXAPRO. Again, this is clearly inconsistent with the legislative purpose of the extension of term regime.

2 The starting date for calculating an extension of term of a patent can be the date of marketing approval for a substance that is not the subject of the claims of the patent (i.e. is not protected by the patent). This is counter-intuitive and contrary to the parliamentary intention to compensate a patentee for patent term lost as a result of delays in obtaining marketing approval from the Therapeutics Goods Administration (TGA).

1.3 The position in other jurisdictions

As noted in the Issues Paper, the Full Court’s decision is inconsistent with the law in major jurisdictions. This is significant because when enacting the extension of term provisions it was Parliament’s intention to bring Australia into line with major jurisdictions, namely with the UK and USA. Lundbeck has been granted extensions of its patent for escitalopram based on regulatory approval for LEXAPRO in the UK, USA, Germany and many other jurisdictions.

1.4 Patent Office practice and the view of the patent attorney profession

In addition, the Full Court’s interpretation was inconsistent with patent office practice and the prevailing understanding of patent attorneys as to the operation of the extension of term provisions. The Examiner’s Manual, at 3.23.1 still provides:

*Essentially, to obtain an extension of the term of a patent:*

- the patent must contain at least one claim covering a pharmaceutical substance per se; and
- that pharmaceutical substance must be included in the ARTG…

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As discussed, the Full Court found that regulatory approval for a substance that did not fall within the scope of the claims of the patent could nevertheless form the basis of an extension of term application (i.e. not that pharmaceutical substance as claimed).

On 4 December 2012, the Administrative Appeal Tribunal (AAT) handed down a decision, affirming IP Australia’s decision to grant Lundbeck an extension of time of 10 years to file a new extension of term application which accords with the interpretation of the Full Court. In its reasons, the AAT accepts the evidence of prominent patent attorneys, Mr Michael Caine and Ms Shahnaz Irani, that the Full Court’s interpretation did not accord with views held by patent attorneys practising in the area of patent term extensions.

1.5 Consequences of the Full Court’s decision for Lundbeck Australia

As a result of the Full Court’s decision, the extension of term of the escitalopram patent was removed and the patent expired on 14 June 2009. Had the extension of term been upheld the escitalopram patent would have expired in 2014. Within two days, Australian pharmaceutical companies had launched generic escitalopram products. This had severe and detrimental consequences for Lundbeck Australia, which had to radically downsize its operations and activities leading to a substantial loss of expertise and market presence. In 2008, the Australian subsidiary had 72 Full Time Equivalent employees (FTEs) and planned to increase its sales force to gain a better “share of voice”. Following the Full Court’s decision, the Australian subsidiary had to scale down the organization leaving it with only 52 FTEs (a 28% reduction).

The period following the Full Court’s decision was a time of turbulence, distress and frustration for Lundbeck Australia both during and following the huge reorganization and there was a significant loss of human talent and a devastating loss of market presence. Key employee talents were lost and others chose to leave the company due to the lack of opportunities and a poor future outlook. In general, the morale in the organization was very low with the corporate Employee Satisfaction Surveys obtaining only very low scores in Lundbeck Australia.

Due to smaller budgets following the Full Court’s decision, Lundbeck Australia:

• reduced its presence in the medical community and cancelled educational activities; and

• was not able to fund research initiatives proposed by Advisory Board members (e.g. Investigators Initiated Trials (IITs)).

1.6 Recommendation

Section 70(3) should be amended to clarify that the registration on which an extension of term is based should be a product, the use of which would infringe a claim of the patent. Lundbeck further recommends that s70(3) be amended to address the difficulty that has arisen as a result of the Federal Court’s decision in Merck & Co Inc v Arrow

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3 Aspen Pharma & Ors v Commissioner of Patents and Lundbeck [2012] AATA 851. Reference was made, in the Issues Paper, to the then imminent AAT decision.
4 Paragraphs 84 – 91.
In that case Justice Wilcox held that the word “contain” in s 70(3) encompassed substances that were not the primary pharmaceutical substance in the goods. Lundbeck believes that the Merck decision is also contrary to the legislative purpose of the extension of term regime and that s70(3) should be amended so that it is clear that the product must “contain” the substance claimed in the patent as an active ingredient.

Submissions on selected questions in the Issues Paper

Question 1: Is the breadth of pharmaceutical patents eligible for an extension of term appropriate?

If the objectives of the current regime are to adjust the patent term to compensate the patent owner for unreasonable curtailment of the effective patent term as a result of the marketing approval process and to foster innovation and investment in healthcare, patents covering new therapeutic indications (as well as patents for new compounds) should be subject to patent term extension. Therapeutic indications are classified as either “first medical use” or “second medical use”. A “first medical use” is the first indication for which a compound has been granted regulatory approval. A “second medical use” refers to any additional indication for which the compound has received approval. Currently, Australia does not permit patent term extensions for patents covering a medical use. In contrast, the US, Europe and other jurisdictions grant patent term extensions for patents covering the first medical use of a compound. In addition, the US grants patent term extensions for patents covering the second medical use of a compound.

Let us assume the following factual scenario –

Patent 1 is issued for Indication A based on clinical studies conducted by Company X. A patent term extension (PTE) has been granted for Patent 1 and the patent term for Patent 1 has been extended by 3 years and 9 months (average PTE in Australia as stated on page 13 of Issues Paper). Company X then files Patent Application 2 covering Indication B and begins clinical studies in order to obtain regulatory approval for Indication B.

There are several outcomes which could result from this fact scenario. The first outcome is that the IP Australia denies Patent Application 2, alleging that Indication B is not patentable. Accordingly, a PTE will never be granted for Indication B because a patent covering Indication B will not be granted. One would predict that this fact scenario will become more prevalent when the Intellectual Property Laws Amendment (Raising the Bar) Act 2011 comes into force and the standards of patentability are raised.

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A second outcome is that Patent 2 covering Indication B is granted but the PTE is denied because none of the effective patent term was lost due to regulatory delay. This scenario assumes that the approval of Indication B is so straightforward given the prior approval of Indication A that minimal time and effort was expended by Company X. Under this fact scenario Company X does not need to have the patent term of Patent 2 extended to compensate for the time lost due to regulatory delay.

The third outcome is that Patent 2 covering Indication B is granted and it is later determined that Company X lost three years off the patent term of Patent 2 due to regulatory delay. Under this scenario, the patent term of Patent 2 is extended by three years to compensate Company X for the loss of patent term due to regulatory delay.

It would seem that most companies – both generic and innovative – would not disagree that the outcome of the third scenario above is equitable and advances the stated purpose of the PTE provisions. Similarly, if a patent covering a first medical use (first indication) is novel and inventive then it should equally be capable of being extended. It appears, from the Issues Paper, that the hesitancy to extend PTEs to patents for medical uses lies in the fear that this could lead to abuse of patents and to unreasonable costs by delaying the introduction of generic medicines. The safeguards exemplified in outcomes 1 and 2 above, namely, a robust patent system and the requirement that any extension must correspond directly to the loss of patent term due to regulatory delay, adequately address the concerns identified in the Issues Paper. Accordingly, Lundbeck believes that the scope of patents for which PTEs are available under the Australian Patents Act should be expanded to include patents covering new therapeutic indications.

While Lundbeck believe that first medical use patents should be capable of extension, it recognises that it is particularly important that extensions are available for patents covering new uses for known compounds. There is a considerable effort underway to investigate whether known compounds have additional uses. The theory behind this effort is that these compounds – by virtue of their age and the fact that they have been utilized by millions of people worldwide – have proven to be safe and non-toxic. Accordingly, developing additional uses for these compounds removes the safety and uncertainty that surrounds new chemical compounds. Assuming that such new uses are determined to be patentable but that it takes time to obtain regulatory approval, it is equitable that the entities that identify new therapeutic uses for these compounds should be granted a PTE to compensate for regulatory delay.

Question 2: Is the length of the extension of term provided for appropriate?

As stated on page 5 of the Issues Paper, Australia, Japan and European countries provide a maximum effective patent life of 15 years. Lundbeck believes that a maximum effective patent life of 15 years is appropriate. However, it should be noted that in order to achieve an effective patent life of 15 years, the term of a patent may need to be extended for more than 5 years. We believe that instead of focusing on the duration of the patent term and capping the permitted length of extension at 5 years, the focus should be to achieve an effective patent term of 15 years even if that model results in an
actual patent term extension of 6 to 8 years. The Australian government may wish to consider the US model in this regard since the US model only compensates for regulatory delay that is attributable to the government agency responsible for assessing the application and providing regulatory approval. This is an equitable model because it encourages companies to proceed efficiently through the regulatory process but does not punish them for delays which are outside of their control.

Question 9: Is the law on data exclusivity appropriate?

The same “first regulatory approval date” issue in s70(3) of the Patents Act 1990 identified in the section of this submission entitled “The escitalopram case”, arises in relation to the data exclusivity provisions under the Therapeutics Goods Act 1989. Under the Federal Court’s interpretation of s25A of the Therapeutic Goods Act (the “TG Act”), Lundbeck was not entitled to any data exclusivity for the clinical data it had submitted in support of its application for marketing authorisation for LEXAPRO because of the earlier registration of CIPRAMIL.6 This was even though entirely new clinical data had been generated and lodged in respect of LEXAPRO. Lundbeck submits that the relevant product for the calculation of the term of data exclusivity should be the product in respect of which the data has been lodged.

A further problem with the present law on data exclusivity is that, as borne out in the escitalopram case, when a company is attempting to enforce data exclusivity, it bears an immense burden to prove that the relevant information is “protected information” within the meaning of the TG Act. This is because the information is not dealt with as a package of information – rather each example of relevant information must be independently proved not to have become available to the public. The discussion at paragraphs [545] – [633] of the decision of Justice Lindgren in the escitalopram case7 illustrates the difficulties involved in proving this negative proposition.

The escitalopram case demonstrates that the present data exclusivity provisions are unworkable and require revision to provide effective data exclusivity and a workable framework for enforcement.

Question 10: Are the laws on patent certificates appropriate?

The current laws regarding patent certificates cause uncertainty for all parties. Neither generic companies nor innovator companies fare well under the present scheme. Lundbeck believes that the “linchpin” for a scheme that benefits all parties is notice. Accordingly, Lundbeck supports amending the current law to require generic companies to inform innovator companies of their intention to apply for registration of a generic therapeutic good on the ARTG at the same time the generic companies lodge their application. The Issues Paper discusses the financial burdens associated with researching patent dockets and determining the validity of such patents but the Issues

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7 [2008] FCA 559.
Paper ignores the additional costs and adverse consequences for pharmaceutical companies and their employees when neither of the parties can accurately predict the date of generic entry. An early notice period would allow both parties to adjust their personnel issues accordingly. For example, if an innovator knew when generic entry was likely, the innovator could scale down its hiring efforts and/or assign current staff to other products in advance of such date. Similarly the generic company could confidently invest in bringing the generic version to market since they would be assured that sales would occur.