Patents Act 1977 **Opinion Number** **07/24**

OPINION UNDER SECTION 74A

Patent	EP 2782559 B1
Proprietor(s)	LO. LI. Pharma SRL
Exclusive Licensee	
Requester	Dr A Hersi
Observer(s)	
Date Opinion issued	28 June 2024

The request

1. The Comptroller has received a request from Dr A Hersi of Polybiotics (the requester) to issue an opinion covering both the validity of EP 2782559 B1 (the patent) and whether or not that patent is infringed by one of Polybiotics products (the product).

2. The patent has a filing date of 21 November 2012 and a claim to an earlier priority date of 22 November 2011. It was originally published as PCT application WO 2013/076121 before entering the European regional phase. The patent was granted on 6 June 2018 and it remains in force. The proprietor is LO. LI. Pharma SRL.

3. No observations were received.

The patent

4. The patent describes a medicinal composition comprising both myo-inositol and chiro-inositol. The patent specifies that it is a treatment for polycystic ovary syndrome (PCOS).

5. Claims 1 and 7 of the patent read:

> *1. A pharmaceutical composition containing myo-inositol and D-chiro-inositol in a weight ratio between 10:1 to 100:1.*
>
> *7. A pharmaceutical composition according to claims 1-6 for use in a method of treating polycystic ovary syndrome (PCOS).*

6. On the face of it, the claimed priority date is valid for at least these claims, with the priority application appearing to contain equivalent claims (1 and 6 – in Italian).

Preliminary matters

7. The patent was the subject of post-grant opposition proceedings at the EPO (European Patent Office). Although the party that initiated the opposition proceedings subsequently withdrew from the procedure, the opposition division nevertheless issued a decision finding that the patent was valid.

8. Section 74A(3) states that the comptroller shall not issue an opinion "in such circumstances as may be prescribed" or "if for any reason he considers it inappropriate" to do so. Rule 94 of the Patent Rules provides for refusal of opinion requests as follows:

> *94 (1) The comptroller shall not issue an opinion if –*
>
> *(a) The request appears to him to be frivolous or vexatious, or*
>
> *(b) The question upon which the opinion is sought appears to him to have been sufficiently considered in any relevant proceedings.*
>
> *(2)* …

9. *Relevant proceedings* are defined in Rule 92 as "proceedings (whether pending or concluded) before the comptroller, the court or the European Patent Office". Consequently, Opposition proceedings before the EPO are understood to be *relevant proceedings*. As decisions coming out of the EPO are binding on the parties involved whilst opinions are not, Rules 92 and 94 serve to prevent the Opinions service offering an opinion on matters already settled. The opinion service is not intended to offer a second opinion or to require a proprietor to deal again with matters which have already been dealt with to the satisfaction of the examiner.

10. In the case of the validity aspect of this opinion request, the question to be determined is considered to be the same as that considered by the EPO opposition division.

11. Although new documents have been referred to in the request, they are not considered to represent new evidence. In particular, they are mainly concerned with showing that myo-inositol and chiro-inositol are known to be used individually, but such evidence appears to have been considered by the opposition division. I do not consider that the new documents go as far as showing that this formed part of the skilled person's common general knowledge.

12. Certain of the other new documents are published too late for any consideration to be given to them. Whilst the requester would like me to infer from them the state of knowledge at the filing date, that is not a step I can take based on these documents.

13. The evidence provided in the request is summarised below:

Annexe 1 *"Myo-inositol in patients with polycystic ovary syndrome: A novel method for ovulation induction";* Papaleo E., Unfer V., Baillargeon J-P, De Santis L., Fusi F., Brigante C., Marelli G., Cino I., Redaelli A. & Ferrari, A.
Gynecological Endocrinology, 23(12): 700–703; December 2007.

Annexe 2 *"Myo-inositol administration positively affects hyperinsulinemia and hormonal parameters in overweight patients with polycystic ovary syndrome";* Genazzani A.D., Lanzoni C.; Ricchieri F. & Jasonni V.M."
Gynecological Endocrinology, 24(3): 139–144; March 2008.

Annexe 3 *"Ovulatory And Metabolic Effects Of D-Chiro-Inositol In The Polycystic Ovary Syndrome";* Nestler J. E., Jakubowicz D. J., Reamer P., Gunn R. D., Allan G.
The New England Journal of Medicine, pp 1314-1320; April 29, 1999.

Annexe 4 *"D-Chiro-Inositol (INS-1) Enhances Ovulatory Rate In Hyperandrogenemic, Oligomenorrheic Women With The Polycystic Ovary Syndrome";* Nestler J. E., Gunn R., Bates S., Gregory J., Jacobson W., Rogol A. D.
Fertility & Sterility, Vol. 76, No. 3, Suppl. 1; September 2001.

Annexe 5 *"Effects Of D-Chiro-Inositol In Lean Women With The Polycystic Ovary Syndrome";* Iuorno M. J., Jakubowicz D. J., Baillargeon J. P., Dillon P., Gunn R. D., Allan G., Nestler J. E.
Endocrine Practice, Vol. 8 No. 6; November/December 2002

Annexe 6 JP 2006/213684 A1 (HOKKO CHEM IND CO) 17 August 2006.

Annexe 7 Notice of Reasons for Refusal of JP 2006/213684 A1.

Annexe 8 *"Altered D-Chiro-Inositol Urinary Clearance in Women With Polycystic Ovary Syndrome*"; Baillargeon J.-P., Diamanti-Kandarakis E., Ostlund Jr R. E., Apridonidze T., Iuorno M. J., Nestler J. E.
Diabetes Care, Volume 29, Number 2; February 2006.

Annexe 9 WO 2013/076121 (LO.LI Pharm SRL.) 30 May 2013. [The original PCT Application from which this patent derives.]

Annexe 10 *"The Combined therapy with myo-inositol and D-Chiro-inositol reduces the risk of metabolic disease in PCOS overweight patients compared to myo-inositol supplementation alone";* Nordio M., Proietti E.
European Review for Medical and Pharmacological Sciences, 16(5): 575-581; May 2012.

Annexe 11 "*Myo-inositol in a new pharmaceutical form: a step forward to a broader clinical use*"; Carlomagno G., De Grazia S., Unfer V. & Manna F.
Expert Opinion Drug Delivery, 9(3): 267-271; March 2012.

14. Annexe 6 was the main document considered by the EPO in the opposition proceedings. It is a Japanese patent application. It also appears to form the main basis of the requester's invalidity argument.

15. Annexe 6 describes a medicinal composition for improving insulin resistance (i.e. treating diabetes) comprising myo-inositol and d-chiro-inositol. In particular, it describes such a composition where the ratio of myo-inositol to d-chiro-inositol lies in the range 1:3 to 9:1. The EPO opposition decision found that the range of myo-inositol to d-chiro-inositol of 10:1 to 100:1 required by the patent was novel and inventive over the disclosure made by this document.

16. That EPO decision was based on additional evidence which showed the connection between insulin resistance and PCOS, and the use of, individually, D-chiro-inositol and myo-inositol to treat PCOS or insulin resistance. This request does not appear to provide any additional relevant evidence which would change the decision reached by the EPO opposition division.

17. Annexe 7 is the reasoned refusal of the application of Annexe 6 by the Japanese patent office. It is not clear how the arguments regarding the refusal of that application contribute to the requester's argument, as the range of ratios in Annexe 6 are different to those of the patent.

18. As will be apparent from their titles, Annexes 1 and 2 refer only to the use of myo-inositol, while Annexes 3, 4, 5 and 8 refer only to d-chiro-inositol. Additionally, Annexes 3 and 8 were specifically considered in the opposition proceedings (as D8 and D9 respectively) and so do not advance a new argument not previously considered by the EPO.

19. Annexes 10 and 11 were both published in 2012 after the priority date of the invention. As such they were published too late to be considered. Annexe 10 appears to be the only document besides Annexe 6 to disclose the use of both myo-inositol and d-chiro-inositol.

20. The requester makes particular reference to Annexe 8 which has a table from which the requester alleges a normal blood plasma ratio of myo-inositol to d-chiro-inositol of between 70:1 and 176:1 can be calculated. That range includes ratios falling within the scope of claim 1 and I do not doubt the requester's calculation. The requester further claims that it would be obvious to use such a physiological ratio as a supplement. I do not agree with this suggestion. In particular, Annexe 8 is specifically directed to normalising that ratio by providing only d-chiro-inositol to patients with PCOS whose blood plasma ratio of myo-inositol to d-chiro-inositol is outside the normal range, i.e. deficient in d-chiro-inositol. The findings of this paper appear to specifically teach against using a physiological ratio.

21. In view of the above, no specific argument has been provided to persuade me that there is any error in the decision made by the EPO Opposition Division, nor is there any relevant new evidence which would persuade me to revisit it. I will not therefore provide an opinion on the question of the validity of the patent.

22. As the request was not confined to the question of validity, I do not need to refuse the request. I can issue an opinion directed to whether or not the patent is infringed

by the product.

Infringement

23. Section 60 of the Act governs what constitutes infringement of a patent:

(1) Subject to the provisions of this section, a person infringes a patent for an invention if, but only if, while the patent is in force he does any of the following things in the United Kingdom in relation to the invention without the consent of the proprietor of the patent, that is to say-

> *(a) Where the invention is a product, he makes, disposes of, offers to dispose of, uses or imports the product or keeps it whether for disposal or otherwise;…*
>
> *(b) …*
>
> *(c) …*

(2) Subject to the following provisions of this section, a person (other than the proprietor of the patent) also infringes a patent for an invention if, while the patent is in force and without the consent of the proprietor, he supplies or offers to supply in the United Kingdom a person other than a licensee or other person entitled to work the invention with any of the means, relating to an essential element of the invention, for putting the invention into effect when he knows, or it is obvious to a reasonable person in the circumstances, that those means are suitable for putting, and are intended to put, the invention into effect in the United Kingdom.

24. In the Supreme Court in *Actavis v Eli Lilly*[1], Lord Neuberger stated that the problem of infringement is best approached by addressing two issues, each of which is to be considered through the eyes of the notional addressee of the patent in suit, i.e. the person skilled in the relevant art. Those issues are:

> (i) does the variant infringe any of the claims as a matter of normal interpretation; and, if not,
>
> (ii) does the variant nonetheless infringe because it varies from the invention in a way or ways which is or are immaterial?

25. If the answer is “yes”, there is infringement; otherwise, there is not.

Claim construction

26. Before I can determine whether there would be infringement of the claims of the patent I must first construe them. This means interpreting them in light of the description and drawings as instructed by Section 125(1). In doing so I must interpret the claims in context through the eyes of the person skilled in the art. Ultimately, the

[1] *Actavis UK Limited and Others v Eli Lilly and Company* [2017] UKSC 48

question is what the person skilled in the art would have understood the patentee to be using the language of the claims to mean. This approach has been confirmed in the decisions of the High Court in *Mylan v Yeda*[2] and the Court of Appeal in *Actavis v ICOS*[3].

27. The most pertinent of the claims granted in the patent is claim 1, given that this claim has the broadest scope. Claim 1 of the patent, set out in paragraph 5 of this opinion, defines 'a pharmaceutical composition containing myo-inositol and D-chiro-inositol in a weight ratio between 10:1 to 100:1'. Such a claim is straightforward to construe and I construe it as defining a composition suitable for use as a pharmaceutical wherein the composition comprises both myo-inositol and D-chiro-inositol in a ratio, by weight, of 10:1 to 100:1. The key point is that, in line with IPO guidance at paragraph 31 of "Examining patent applications relating to chemical inventions"[4], a claim to 'a pharmaceutical composition comprising X' is construed as a composition comprising X that is *suitable for* such use and, consequently, such a claim may be infringed by a composition that is not intended for such a use.

28. Such a construction is entirely consistent with the authority of the High Court as given in *Brundle v Perry*[5] where Hacon J noted that the 'suitable for' construction is entirely conventional. I also note the judgment of Parker J within *Adhesive Dry Mounting Co Ltd v Trapp and Co*[6] in which he (see especially line 48 of page 352 to line 8 of page 353) commented that a claim defining an article for use in a process should be construed as a claim to the article itself. Following that judgment, a claim to a pharmaceutical composition must be construed as a claim defining the composition itself and the claim is not to be construed as being limited to specific pharmaceutical use.

29. As a final point on the construction of claim 1 of the patent, language of the type 'composition containing' is construed as 'composition including', i.e. other integers/active components may also be present. The EPO Technical Board of Appeal took such a line in T589/89.[7]

Does the product infringe as a matter of normal interpretation?

30. The product, Inositol Infusion Plus, comprises both myo-inositol and D-chiro-inositol in a ratio close to 40:1. This appears to be common ground between the patent proprietor (see correspondence 1) and the requester (see opinion request). From marketing information available for the product,[8] the product comprises 2439 mg myo-inositol and 61 mg D-chiro inositol and this near 40:1 ratio between the two components is undoubtedly a weight ratio. As such the composition of Inositol Infusion Plus lies within the parameter of claim 1.

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[2] *Generics UK Ltd (t/a Mylan) v Yeda Research and Dev. Co. Ltd & Anor* [2017] EWHC 2629 (Pat)
[3] *Actavis Group & Ors v ICOS Corp & Eli Lilly & Co.* [2017] EWCA Civ 1671
[4] Examining patent applications relating to chemical inventions, accessible at https://www.gov.uk/government/publications/examining-patent-applications-relating-to-chemical-inventions/examining-patent-applications-relating-to-chemical-inventions-may-2017
[5] *Brundle v Perry* [2014] EWHC 475 [42]
[6] Adhesive Dry Mounting Co Ltd v Trapp and Co 27 RPC 341
[7] T 589/89 NATIONAL RESEARCH/Polyurethane compositions [1994] (EPOR 17), see 3.1
[8] https://polybiotics.co.uk/products/inositol-infusion

31. The requestor's main arguments with respect to infringement are that the product is intended for use as a food supplement, not as a pharmaceutical composition as is required by the claims, and that the product comprises further ingredients (such as zinc, chromium and vitamin D to provide nutritional support) not specifically named in claim 1. As discussed at paragraph 29 of this opinion, claim 1 of the patent comprises the word 'containing' and, consequently, if the other features of the claim are met, the product cannot be saved from infringing purely by comprising further active components, e.g. zinc, vitamin D or chromium. Turning to the point raised by the requester that the product is intended for use as a food supplement, as opposed to a pharmaceutical, the product will not avoid infringement purely based upon intention if the product is suitable for use as a pharmaceutical. Given the product comprises at least two components that are pharmaceutically active (myo-inositol and D-chiro-inositol) and that the product is also safe for human consumption, the product itself will be suitable for use as a pharmaceutical. I also note that the product is marketed[8] as being able to reduce insulin resistance and to improve fertility. Given the role of insulin resistance in diabetes, a clinical condition, and the relevance of improving fertility and promoting menstruation as a means of alleviating symptoms[9] of a disorder, the product is clearly suitable for, and sold with the intention of being used for, treatment, i.e. the product is a pharmaceutical composition.

32. Consequently, the product does infringe the patent. It is a matter of agreed fact that the product contains myo-inositol and D-chiro-inositol in a weight ratio of 40:1 and, given my construction of the patent, neither the provision of further active components, nor the lack of any explicit reference to use of the product as a pharmaceutical, alters my conclusion that the product infringes the patent.

Opinion

33. In my opinion, the product infringes at least claim 1 of the patent as a matter of normal interpretation.

Robert Goodwill
Examiner

NOTE

This opinion is not based on the outcome of fully litigated proceedings. Rather, it is based on whatever material the persons requesting the opinion and filing observations have chosen to put before the Office.

[9] As stated at 2.7 of T24/91 (Cornea) the term 'therapy' covers any treatment designed to alleviate, remove or lessen symptoms of a disorder or malfunction of the human body.