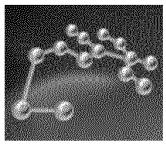

By Electronic Submission Only

European Patent Office
Erhardtstrasse 27
D-80469 Munich
Germany

14 December 2012

Our Ref: LUI-P873EP

Dear Sirs

Re: European Patent Application Number 07716309.5
in the name of Luitpold Pharmaceuticals, Inc.

Thank you for your communication under Article 94(3) EPC dated 4 June 2012. The Applicant has now considered the Examiner's objections and we therefore submit amended claims. Our comments on the objections are set out below.

Claim amendments

Claim 1 has been amended to include the limitation that the single dosage unit is adapted for administration to a patient in 15 minutes or less. Basis for this claim can be found in previous claim 6 and also in the specification as filed at page 8, line 34. The claim has also been amended to remove the feature that the iron carbohydrate complex has substantially no cross reactivity with anti-dextran antibodies. We submit that no subject matter has been added by the deletion of this feature since the specification as filed in the passage bridging pages 11 and 12 makes it clear that this is an optional (though preferred) feature by the use of the wording:

> "Preferably iron carbohydrate complexes for use in the methods described herein are those which have one or more of the following characteristics: . . . no cross reactivity with anti-dextran antibodies".

Thus, we submit that amended claim 1 does not contain added subject matter contrary to Article 123(2) EPC.

The feature that the iron carbohydrate complex has substantially no cross reactivity with anti-dextran antibodies has now been made the subject of new claim 19.

Claim 2 has been amended in a similar way to claim 1.

Claims 3 to 5 are unamended.

Claim 6 has been restricted to the case where the single dosage unit is administered in about ten minutes or less.

Claims 7 to 16 are unamended.

Claim 17 is new and specifies that the single unit dose of iron carbohydrate complex is formulated for administration as an intravenous bolus injection without dilution. Basis for this claim can be found in the specification at page 8, lines 9-10 of the application as filed.

Claim 18 is also new and specifies that the single unit dose of iron carbohydrate complex is formulated for administration once per week. Basis for this claim can be found at page 9, line19-20 of the application as filed.

Claim 19 is new and, as set out above relates to the feature that the iron carbohydrate complex has substantially no cross reactivity with anti-dextran antibodies.

We submit that no subject matter has been added and that the amended claims comply with Article 123(2) EPC.

Novelty

In Section 1 of the communication, the Examiner asserts that several claims lack novelty over **D3**. In particular, the Examiner refers to the passage on page 8, lines 26-28 of D3. However, claims 1 and 2 have now been amended and are limited to a dosage form which is adapted for administration to a patient in 15 minutes or less.

In contrast to amended claims 1 and 2 of the present application, D3 specifies that the dose can be administered over the course of 1 hour (D3, page 8, lines 27-28). Thus, the present invention is novel over D3 because the single dosage unit to which it relates is adapted for administration to a patient in a time of 15 minutes or less.

Inventive Step

In Section 2 of the communication, the Examiner asserts that all claims are obvious over **D2** when combined with **D3**. With respect, however, we submit that the amended claims submitted herewith are inventive over the prior art.

The Examiner has defined the problem to be solved by the present invention as the provision of a means for iron delivery in fewer sessions. However, we submit that following the amendment of the claims, the problem to be solved should now be the provision of a means for iron delivery in fewer sessions and in a reduced time.

The Examiner has designated D2 as the most relevant prior art document and has commented that D2 discloses the administration of 100 mg iron (III) hydroxide polymaltose to anaemic patients. However, it should be noted that this 100 mg of iron (III) hydroxide polymaltose was infused over a period of 10 minutes (page 854). This corresponds to an infusion rate of 10 mg iron (III) hydroxide polymaltose per minute and means that if the dose of iron (III) hydroxide polymaltose in D2 were to be raised to 1000mg as taught in D3, the time taken for the infusion would be 100 minutes; and if raised to 0.6 g as in present claim 1, the time taken for infusion would be 1 hour.

D3 teaches that the dose of 500 to 1000 mg of an iron carboxymaltose can be administered over a period of 1 hour (D3, page 8, lines 27-28).

Therefore neither D2 nor D3 teaches or suggests a single dosage unit of an iron carbohydrate complex which is adapted for administration over a period of 15 minutes or less as specified in amended claims 1 and 2 of the present application.

Surprisingly, however, the present inventors have found that, in spite of the teaching of the prior art, it is possible to administer high doses of iron over a relatively short period of time without causing adverse side effects in the patient. Example 5 describes studies A to J in which VIT-45 was administered to patients. In studies A, B, C, D, I and J a 500-1000mg dose of VIT-45 was administered over 15 minutes. The results showed that the high dose administered over a short period of time did not lead to adverse side effects.

The reduced administration time has considerable advantages as it is less unpleasant for the patient and less time consuming for the medical staff supervising the treatment. In view of this we submit that the amended claims are inventive over D2 when combined with D3.

We note that in paragraph 2.3 the Examiner comments that the technical problem does not appear to be solved over the whole range claimed. In response to this objection, we submit a copy of Jahn *et al*, *European Journal of Pharmaceutics and Biopharmaceutics*, **78** (2011), 480-491. This document describes a study of the physicochemical properties of iron isomaltoside and other iron carbohydrate complexes.

An iron isomaltoside (e.g., Monofer®) is an iron carbohydrate complex where the carbohydrate component is a pure linear chemical structure of repeating α-(1-6)-linked glucose units; i.e. repeating isomaltose units. Thus, an iron isomaltoside is an example of an iron polyisomaltose complex.

Table 4 on page 490 of Jahn *et al* compares several iron carbohydrate complexes, some of which fall within the scope of amended claim 1 and some of which do not.

Thus, Cosmofer® and Venofer® are respectively iron dextran and an iron sucrose complexes and are therefore not encompassed by claim 1. Ferrlecit® is an iron gluconate complex, Ferinject® is an iron carboxymaltose complex and both of these fall within the scope of claim 1. Monofer ® is an iron isomaltoside, which as discussed above is an iron polyisomaltose complex and so falls within the scope of claim 1.

Feraheme® (ferumoxytol) is described by Jahn *et al* as an iron carboxymethyl dextran. As discussed on page 16, lines 2-10 of the present application, ferumoxytol (i.e. polyglucose sorbitol carboxymethyl ether-coated non-stoichiometric magnetite) is a preferred complex for use in the present invention. It falls within the scope of claim 1 as it is an iron sorbitol complex.

Table 4 of Jahn *et al* shows that large doses (1000 mg) of Ferinject® and Monofer ® can be administered over less than 1 hour without adverse side effects (page 490, Table 4 and column 1). The document concludes that Monofer ® can be administered as a rapid high dose infusion in doses over 1000mg (page 490, conclusion). Table 4 of Jahn *et al* also shows that a 510 mg dose of Feraheme® can also be administered over less than 1 hour. Although this dose is slightly lower than

the 0.6g dosage specified in claim 1, we submit that it is still evidence that larger doses of Feraheme® can be rapidly administered to a patient without adverse side effects.

In contrast, neither Cosmofer® nor Venofer® can be administered over less than 1 hour. These complexes both fall outside the scope of claim 1. No results were obtained for the iron gluconate complex Ferrlecit®.

It is clear from Jahn *et al* that other iron carbohydrate complexes encompassed by the claims can be administered in a similar way to the iron carboxymaltose complex VIT-45 which is used in the examples and that they therefore have similar advantages. In view of this, we submit that the inventive step has been demonstrated over the scope of the claims.

Further to paragraphs 3.3 and 3.4 of the communication, we request that the amendment of the description should be deferred until an acceptable set of claims has been agreed with the Examiner.

We submit that the claims are now in an allowable form but if the Examiner has further objections, we request that we be notified either in writing or by telephone. In the event that the Examiner intends to refuse the application, we request oral proceedings.

Yours faithfully

/ANDREW TEUTEN/

Andrew Teuten
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Authorised Representative

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