IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.: **12/787,283**	Examiner: **LAU, Jonathan S**
Applicant: **HELENEK, Mary Jane**	Group Art Unit: **1623**
Filed: **May 25, 2010**	Confirmation No.: **4251**
Title: **30015730-0053**	Customer No.: **26263**
Docket No.: **Methods and Compositions for Administration of Iron**	

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

I, Richard P. Lawrence, declare and state as follows:

1. I am Director of Research and Development for Luitpold Pharmaceuticals, Inc.

2. I have a B.S. Degree/Fairleigh Dickinson University, with a focus in Chemistry.

I am a named inventor in the following US patents:

7,754,702	Methods and Compositions for Adminsitration of Iron
7,169,359	Bioequivalence test for iron-containing formulations
6,911,342	Bioequivalence test for iron-containing formulations
5,624,668	Iron Dextran Formulations

I have authored the peer-reviewed manuscript:

Lawrence, "Development and Comparison of Iron Dextran Products," *PDA Journal of Pharmaceutical Science & Technology*, Vol. 52, No. 5, September-October 1998, pp. 190-197.

The following provides a brief overview of my experience:

Training:

BS: Chemistry/Mathematics, Fairleigh Dickinson University, Madison, New Jersey, June 1979

Positions:

Luitpold Pharmaceuticals, Inc. (Shirley, New York)

04/03 – Present	Director, Research & Development
09/02 – 04/03	Director, Quality Assurance
05/02 – 09/02	Director, Quality Control
03/83 – 05/02	Manager, Product Development

Gibco Invenex (Milburn, New Jersey)

10/79 – 03/83	Research Chemist

3. I am a named inventor of the subject matter claimed in present U.S. Patent Application 12/787,283 (the "'283 application"), entitled "Methods and Compositions for Administration of Iron", filed on May 25, 2010.

4. Based on my experience, an iron polyisomaltose is a type of iron carbohydrate complex that includes isomaltose units in the carbohydrate component. An isomaltose is a disaccharide similar to maltose, but with a α-(1-6)-linkage between two glucose units instead of an α-(1-4)-linkage. One example of an iron polyisomaltose complex is an iron isomaltoside (e.g., Monofer®), where the carbohydrate component is a pure linear chemical structure of repeating α1-6 linked glucose units. In contrast, a dextran is a branched glucan with straight chains having α1-6 glycosidic linkages and

branches beginning from α1-3 linkages. Physiochemical properties of the iron isomaltoside Monofer® are described in Jahn et al. 2011 Eur J Pharma and Biopharma 78, 480-49 (Jahn et al.).

5. Jahn et al. evidences that the iron isomaltoside Monofer® (i.e., one example of an iron polyisomaltose) avoids dextran-induced anaphylactic reactions (see page 487, col. 2, ¶1; page 489, col. 2, ¶2) and reduces immunogenicity compared to dextran (see page 489, col. 1, ¶4; page 489, col. 2, ¶6). Jahn et al. evidences that even in the 1960s it was known that isomaltose oligomers prevent or block anaphylaxis and that later research in the 1970s and 1980s showed that isomaltose oligomers acted as haptens against circulating anti-dextran antibodies (page 489, col. 1, ln. 53-58, ¶5). Per Jahn et al. and consistent with the understanding in the art at the time of filing, a hapten can bind an antibody without inducing anaphylaxis or an immune response (see page 489, col. 2, ¶1). According to Jahn et al., the ability to administer high doses (e.g., up to 1,600 mg elemental iron) of the the iron isomaltoside Monofer® (i.e., one example of an iron polyisomaltose) arises from reduced immunogenic potential and absence of dextran-induced anaphalytic reactions (see page 481, col. 1, ¶3; page 487, col. 2, ¶1; page 489, col. 2, ¶3, ¶6).

7. Claim 1 of the '283 application recites, inter alia, "wherein the iron carbohydrate complex has a substantially non-immunogenic carbohydrate component". It is my opinion that Jahn et al. provides evidence that the iron isomaltoside Monofer® (i.e., one example of an iron polyisomaltose) is substantially non-immunogenic.

8. Claim 3 of the '283 application recites "wherein the iron carbohydrate complex has substantially no cross reactivity with anti-dextran antibodies". Based on my experience, cross-reactivity at the time of filing was understood as a reaction between an antibody and an antigen (that differs from an immunogen) resulting in an immune response. In other words, mere binding of an antibody and an antigen was not understood as "cross-reactivity" in the absence of an immune response. It is my opinion that Jahn et al. provides evidence that the iron isomaltoside Monofer® (i.e., one example of an iron polyisomaltose) has substantially no cross reactivity with anti-dextran

antibodies, i.e., Monofer® does not effect a substantial immune response and there is substantially no dextran-induced anaphalytic reactions.

9. I hereby declare that the statements made of my own knowledge are true and that all statements made on information made on belief are believed to be true. I acknowledge that willful false statements and alike are punishable by fine or imprisonment or both (18 U.S.C. § 1001) and may jeopardize the validity of the application or any patent issuing thereon.

Date: December 5, 2012

Richard P. Lawrence