

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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LUPIN LTD., and LUPIN PHARMACEUTICALS INC.,

Petitioners,

v.

SENJU PHARMACEUTICAL CO., LTD.,

Patent Owner.

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IPR2015-01097 (Patent 8,754,131)

IPR2015-01099 (Patent 8,669,290)

IPR2015-01100 (Patent 8,927,606)

IPR2015-01105 (Patent 8,871,813)

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**PETITIONERS' OPPOSITION TO PATENT OWNER'S MOTION FOR  
OBSERVATION REGARDING CROSS-EXAMINATION OF  
REPLY WITNESSES DR. M. JAYNE LAWRENCE, Ph.D.  
AND IVAN T. HOFMANN, CPA/CFF, CLP<sup>1</sup>**

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<sup>1</sup> A word-for-word identical paper has been filed in each proceeding identified in the heading. IPR2016-00089 has been joined with IPR2015-01097; IPR2016-00091 has been joined with IPR2015-01100; and IPR2016-00090 has been joined with IPR2015-01105. Each of these joined proceedings includes Petitioners InnoPharma Licensing, Inc., InnoPharma Licensing LLC, InnoPharma Inc., Mylan Pharmaceuticals Inc., and Mylan Inc. (collectively, "InnoPharma") in addition to the parties identified above.

Pursuant to the Scheduling Order (Paper No. 10 at 4), Petitioners file their Opposition to Patent Owner's Motion for Observation Regarding Cross-Examination of Dr. M. Jayne Lawrence and Mr. Ivan T. Hofmann.

Patent Owner's Motion for Observation mischaracterizes the testimony of Dr. Lawrence and Mr. Hofmann, and further includes several arguments to the merits, which is an improper use of the Motion for Observation as a vehicle to make arguments in sur-reply. Regardless, those arguments to the merits, which ultimately fail to contradict any of Petitioner's positions in this proceeding, further show why Patent Owner's Motion to Exclude Under 37 C.F.R. § 42.64(C) (Paper No. 46) is without merit. Accordingly, the Board should expunge or give no weight to Patent Owner's purported observations.

**Response to Observation #1:** Patent Owner's observation is not relevant and mischaracterizes Dr. Lawrence's Reply Declaration and testimony. Dr. Lawrence offered statements and conclusions in her Reply Declaration (EX1094) that are well within her qualifications, which include: a PhD in Pharmacy, EX1005, ¶ 3; prior expert qualification in the field of formulation and drug delivery, EX1094, ¶¶ 4-5; acting Head of the Pharmaceutical Biophysics Group of the Institute of Pharmaceutical Science at Kings College, and previously the Chief Scientist at the Royal Pharmaceutical Society, EX1005, ¶¶ 7-8; professor at Kings College of multiple courses related to physical chemistry of micelles, physical

chemistry of emulsions and biopharmaceutics and bio-pharmacy, EX1054 at 7; and publications in the field of physical and colloid chemistry. *Id.* at 8.

Dr. Lawrence is also more than qualified under Patent Owner's own definition of a POSA by Patent Owner's "chemistry" expert, Dr. Davies: someone with at least a Bachelor's degree in a field of science which includes "pharmaceutical sciences or a related discipline with about three to five years of work experience in this area, or a comparable level of education and training." EX2105, ¶ 41. Dr. Lawrence is similarly more than qualified under the definition given by Patent Owner's formulation expert, Dr. Williams. *See* EX2082 at 45.

**Response to Observation #2:** Patent Owner mischaracterizes Dr. Lawrence's testimony. The testimony cited by Patent Owners is in response to "preliminary questions" vaguely directed to general differences between metals and metal cations, and therefore is not related directly to the teachings in the Merck Index and Remington. *See* EX2342, 179:4-180:1. Patent Owner omits the testimony that is directly related to the patents-at-issue, which is consistent with Dr. Lawrence's opinion that tyloxapol has antioxidant properties. *Id.* at 180:4-10. Patent Owner also omits Dr. Lawrence's testimony that "a person of skill in the art would expect an antioxidant to interact with [partially reduced oxygen species], with these partially reduced species." EX2342, 228:7-9. This testimony is relevant to whether an antioxidant such as tyloxapol would be oxidized by an

oxidizing agent (i.e., oxygen), much like the statements in the Merck Index and Remington that tyloxapol is “oxidized by metals.” EX1096, 1751; EX1051, 1415.

Furthermore, Patent Owner’s allegation is not a proper distinction of the general teaching in the Merck Index and Remington, which provide a more generalized teaching that tyloxapol has antioxidant properties. EX1096, 1751; EX1051, 1415; EX1114, 114:6-16; EX1094, ¶¶31, n.5. If tyloxapol were not an antioxidant, and instead were an oxidizing agent (which it is not), then it would not be oxidized by oxidizing agents. Whether or not the sodium in bromfenac sodium is in cation form or not has no relevance to Dr. Lawrence’s analysis.

**Response to Observation #3:** Patent Owner’s observation is misleading, not relevant, and mischaracterizes Dr. Lawrence’s testimony. First, Patent Owner cites to vague questions seeking legal conclusions whether a prior art is relevant in view of the preamble of the claims. EX2342, 180:2-5; 180:21-181:8. Second, Patent Owner omits testimony that the specifications of the ’290, ’131, ’813 and ’606 patents discuss nasal drops. *Id.* at 181: 10-15. This testimony is relevant to whether nasal formulations would have been relevant to a POSA. Dr. Lawrence also testified that references directed to lung and nasal formulations show that tyloxapol is a good antioxidant. *Id.* at 192: 16-21; 203:2-15. Third, while Patent Owner’s observation implies it, Patent Owner tellingly never questioned Dr. Lawrence if nasal and pulmonary formulations are relevant to ophthalmic

formulations.

Patent Owner's own expert's testimony also contradicts Patent' Owner's improper legal conclusion, stating that inhalation and nasal formulations have the same characteristics as ophthalmic formulations. EX1099, 20:13-21. As noted, Patent Owner omits that the '290, '131, '606 and '813 patents, as well as Ogawa similarly involve nasal formulations. EX1001, 4:10-13, 11:48-51; EX1002, 4 :8-11, 11 :48-54, EX1003, 43:56-59, 11:11-17;EX1004, 4:60-62, 10:64-11:10, Example 10.

**Response to Observation #4:** Patent Owner mischaracterizes Dr. Lawrence's testimony and is not relevant. Testimony regarding the general stability of the examples of Ogawa is unrelated to whether a POSA would be motivated to replace polysorbate 80. Also, the cited portions of Dr. Lawrence's testimony relate to what the Ogawa reference discloses—specifically whether the Ogawa reference identifies the formulations of Examples 6, 7, and 8 as not forming red insoluble matters and describes them as “stable, excellent for a long period of time”—not what Dr. Lawrence's own opinions on the matter are. *See* EX2342, 62:22-64:2. Patent Owner instead omits Dr. Lawrence's testimony about her own opinions. When asked if the formulation of Example 6 of Ogawa did not exhibit significantly greater stability than the formulations of examples 7 or 8, Dr. Lawrence testified, “I would look at those formulations, and to me, example 6 gave

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