Federal Court  Cour fédérale

Date: 20161209

Docket: T-200-15

Citation: 2016 FC 1362

Ottawa, Ontario, December 9, 2016

PRESENT: The Honourable Mr. Justice Manson

BETWEEN:

MEDA AB, MEDA PHARMACEUTICALS LTD. AND VALEANT CANADA LP/VALEANT CANADA S.E.C.

Applicants

and

THE MINISTER OF HEALTH AND PHARMASCIENCE INC.

Respondents

and

OREXO AB

Respondent/Patentee

PUBLIC JUDGMENT AND REASONS

Table of Contents

I. Background

A. The Underlying Application

[1] Meda AB, Meda Pharmaceuticals, and Valeant Canada LP ("Valeant") (together, the "Applicants") are "first persons" as defined in the *Patented Medicines (Notice of Compliance) Regulations,* SOR/93-133, subsections 2(1) and 4(1) (*PM(NOC) Regulations*).

[2] The Applicants filed New Drug Submissions with the Minister of Health (the "Minister") for 10 and 5 mg zolpidem tartrate sublingual orally disintegrating tablets (the "SUBLINOX® Tablets") for which Notices of Compliance ("NOC") for Submissions (Submissions 140675 and 153453) were issued on July 19, 2011 and February 15, 2012, respectively.

[3] On January 16, 2014, the Applicants (Meda AB and Meda Pharmaceuticals), licensees of the Canadian Patent No. 2,629,988 (the "'988 Patent"), requested the listing of the '988 Patent on the Patent Register in respect of the above submissions and the SUBLINOX® Tablets. The Minister found the '988 Patent eligible for listing in respect of these submissions and added it to the Patent Register on January 28, 2014. On January 8, 2015, the Patent Register was updated to reflect Valeant, a sublicensee under the '988 Patent, as the current holder of the NOCs and Drug Identification Numbers for the SUBLINOX® Tablets.

[4] Orexo AB owns the '988 Patent (issued in Canada January 7, 2014, based on a Patent Cooperation Treaty ("PCT") application dated September 24, 1999) and is party to the prohibition application under subsection 6(4) of the *PM(NOC) Regulations*.

[5] On May 30, 2014, the respondent, Pharmascience Inc. (“Pharmascience”), filed an Abbreviated New Drug Submission (“ANDS”) seeking a NOC for 5 and 10 mg zolpidem tartrate sublingual orally disintegrating tablets (“PMS-Zolpidem”) and compared its proposed tablets to the SUBLINOX® Tablets.

B. The Notice of Allegation (“NOA”)

[6] On December 23, 2014, Pharmascience served the Applicants with a letter, purporting to be a NOA pursuant to subsections 5(1)(b)(iii) and 5(1)(b)(iv) of the *PM(NOC) Regulations* in respect to the ‘988 Patent and the medicinal ingredient zolpidem in Pharmascience’s PMS-Zolpidem compared to the Applicants’ SUBLINOX® Tablets.

[7] The NOA is 87 pages and lists over 200 documents in its attached Schedule B. It raises numerous arguments on the issues of patent and claim construction, non-infringement and validity of the ‘988 Patent (including a “Gillette Defence”, anticipation, obviousness, insufficiency, inutility, overbreadth, ambiguity and improper patent listing).

[8] At the hearing, Pharmascience abandoned the invalidity allegations of insufficiency, ambiguity and improper patent listing.

[9] The Applicants commenced this prohibition application on February 12, 2015, seeking an order that the Minister be prohibited from issuing a NOC to Pharmascience for PMS-Zolpidem until the ‘988 Patent expires on September 24, 2019.

[10] On September 11, 2015, the Applicants served their evidence on Pharmascience consisting of three affidavits:

a) Dr. Patrick J. Sinko;
b) Dr. Loyd V. Allen Jr.;
c) Ms. Sonica Soares (law clerk at Lenczner Slaght Royce Smith Griffin LLP).

[11] On December 11, 2015, Pharmascience served its responding affidavits:

a) Dr. Reza Fassihi ;
b) Dr. John David Smart (served December 14, 2015);
c) Dr. Rajesh N. Davé;
d) Dr. Yuriy Ososkov.

[12] Reply affidavits of the Applicants were served in March, 2016:

a) Reply affidavit of Dr. Allen;
b) Reply affidavit of Dr. Sinko.

[13] Sur-Reply affidavits of Pharmascience were served in March, 2016:

a) Sur-Reply affidavit of Dr. Fassihi;
b) Sur-Reply affidavit of Dr. Smart.

[14] Cross-examinations of Drs. Allen, Sinko, Fassihi, Smart and Davé on their affidavits were conducted in March and April, 2016.

[15] The Applicants seek not only the order prohibiting the Minister from issuing a NOC to Pharmascience for its proposed PMS-Zolpidem tablets until expiry of the ‘988 Patent, but as well as an order striking the affidavits of Dr. Fassihi and Dr. Davé, on the basis that Pharmascience’s counsel obstructed the cross-examinations of these affiants to the extent that the conduct was abusive and frustrated the process such that their evidence should be rejected.

[16] Further, the Applicants claim that only approximately half of the over 200 references listed in Schedule B are discussed in the NOA, many without pinpoints, and the other half are not referenced in relation to any propositions raised in the NOA.

[17] Therefore, the Applicants challenge Pharmascience's evidence as listed in Schedule "A" to this decision on the basis that the evidence in Schedule "A" exceeds the NOA.

II. Issues

[18] The issues are:

A. Preliminary Issues:
    i. Should the affidavits of Dr. Fassihi and Dr. Davé be struck?
    ii. Is Pharmascience's evidence in Schedule A beyond the facts alleged in the NOA and therefore, improper?
B. Validity
    i. Is the Pharmascience allegation of anticipation justified?
    ii. Is the Pharmascience allegation of obviousness justified?
    iii. Is the Pharmascience allegation of inutility justified?
    iv. Is the Pharmascience allegation of overbreadth justified?
C. Infringement
    i. Is the Pharmascience allegation of non-infringement justified, and/or does the Gillette Defence apply?

A. Summary of Decision

A. The affidavits of Dr. Fassihi and Dr. Davé are not struck.
   The evidence in Schedule A is not improper.
B. Pharmascience's allegation of:
    i. anticipation is not justified;
    ii. obviousness is not justified;
    iii. inutility is not justified;
    iv. overbreadth of claim 1 is justified; otherwise, the allegation is not justified.
C. Pharmascience's allegation of non-infringement is justified.

B. Preliminary Issues

(1) The Affidavits of Drs. Fassihi and Davé

[19] The Applicants argued that both Dr. Fassihi and Dr. Davé were shielded against meaningful cross-examination by abusive conduct by Pharmascience's counsel. They cite *Federal Courts Rules*, SOR/98-106, Rule 97(c), which states that "[w]here a person fails to…answer a proper question…the Court may strike all or part of the person's evidence, including an affidavit made by the person". Moreover, the Applicants rely on the Court's inherent jurisdiction to redress abuses of its process.

[20] I agree with Pharmascience that the alleged "abusive conduct" in the cross-examination of Dr. Fassihi in fact consisted of assisting counsel for the Applicants who confused Schedule A with Schedule B to the NOA; ensuring that the witness understood the question; advising that the NOA document numbers had been inserted to assist with cross-examinations; assisting counsel in the pronunciation of benzodiazepines; and raising an objection when the question related to what the inventors were doing. As to the complaint that counsel suggested answers, the examples in the Applicants' factum consist of asking for clarification of a question; objecting when the question was misleading the witness; objecting to questions based on erroneous facts; advising as to the NOA document number; advising the witness to look at the document which was the subject of questioning; and objecting to questions on the ultimate issue of infringement.

[21] As to the three refusals which are the focus of the allegation of abusive conduct in the Applicants' factum, counsel for the Applicants admit on the transcript that it was not necessary

to enter the Remington text as an exhibit since the question was already answered by Dr. Fassihi. Further, Dr. Fassihi did answer questions on Ativan.

[22] With respect to the cross-examination of Dr. Fassihi, there were five objections in a transcript of 165 pages. With respect to the cross-examination of Dr. Davé, there were three objections in a transcript of 165 pages. The Applicants chose not to bring a motion to compel answers to the questions that were the subject of the eight objections. Nor did the Applicants bring a motion to strike the evidence of Dr. Fassihi and Dr. Davé, but instead have relied upon their evidence in their factum.

[23] Therefore, while these interruptions and objections by counsel for Pharmascience were not always necessary or useful, they were not abusive.

(2) Alleged "ambush evidence" of Pharmascience

[24] The Applicants pointed out that the NOA filed by Pharmascience lists some 200 documents—which comprise more than 10,000 pages, not including text books—in Schedule B to the NOA, and that of these documents, only approximately 95 were described within the text of the NOA.

[25] Pharmascience's experts relied on approximately one third of the documents listed in Schedule B, and 31 of these citations refer to documents that were not discussed in the text of the NOA (the "Table 1 Documents") (listed in Schedule A, Table 1 to the Applicants' factum). Further, the Applicants pointed to three instances where the Pharmascience's experts allegedly

cited documents for propositions that were different from the propositions set out in the NOA (the "Impugned Propositions") (listed in Schedule A, Table 2 to the Applicants' factum).

[26] The Applicants contended that both the Table 1 Documents and the Impugned Propositions are improper evidence that should be struck from the record. They argued that including this evidence would be allowing Pharmascience to stray from its NOA, causing the Applicants irreparable prejudice. Additionally, they claimed that, because many of the documents in Schedule B were not fully discussed, the NOA did not give them proper notice of the case to be met, and that Pharmascience had split its case.

[27] The Applicants stated that, at the motion to strike hearing in February 2016 (the "Motion to Strike"), they reserved the right to challenge Pharmascience's evidence to the full extent that it exceeded the NOA. They argued that the Table 1 Documents and the Impugned Propositions were "ambush evidence", which expanded the legal and factual basis detailed in the NOA, and which should be found to be inadmissible.

[28] Pharmascience contended that the Table 1 Documents could not be "ambush evidence" because they were all listed in the NOA, and they all related to facts covered in the NOA. Further, they asserted that the Impugned Propositions did not actually introduce new facts into the application before this Court, because the propositions all related to facts discussed in the NOA.

[29] As stated in the Amended Confidential Reasons and Order, dated March 8, 2016, issued as a result of the Motion to Strike, striking evidence is an extraordinary remedy, to be exercised rarely; and where an applicant will not be prejudiced in a manner that cannot be compensated for by costs, evidence is best left for the hearing judge based on the full record (*Meda v Pharmascience*, 2016 FC 219, citing *Proctor & Gamble Pharmaceuticals Canada Inc v Canada (Minister of Health),* 2009 FC 113 [*Proctor & Gamble*] and *Janssen-Ortho Inc v Apotex Inc,* 2010 FC 81).

[30] However, both the Federal Court and the Federal Court of Appeal have consistently held that the NOA must raise all legal and factual arguments, which the party crafting the NOA will rely on, and that subsequently introducing new arguments and facts is improper, no matter how draconian this may seem (*Bayer Inc v Cobalt Pharmaceuticals Co,* 2013 FC 1061 at para 37 [*Cobalt*], aff'd in 2015 FCA 116; *Aventis Pharma Inc v Mayne Pharma (Canada Inc),* 2005 FCA 50 at para 25 [*Aventis*]; *AB Hassle v Canada (Minister of Health and Welfare),* [2000] FCJ No 855 (FCA) at paras 19, 21, 23 [*AB Hassle*]).

[31] Factual and legal arguments must be raised in the NOA in a manner that is sufficient to meet the requirement of section 5(3)(b)(ii) of the *PM(NOC)Regulations*: "A second person who makes an allegation under paragraph (1)(b) or (2)(b) shall include in the notice of allegation … a detailed statement of the legal and factual basis for the allegation". The intent of this section is that the entire factual basis be set forth in the statement, rather than revealed piecemeal when some need happens to arise in the proceeding (*AB Hassle*, above, at para 23)

[32] The NOA must contain a detailed statement of the legal and factual basis for every allegation raised because of the unusual scheme established by the *PM(NOC) Regulations*, where the allegations are framed by the second person, but the application for prohibition is brought by the patent holder, who frames their arguments to deal with the allegations made in the NOA (*Aventis*, above, at para 20). Enough information needs to be included to allow the patent holder to make an informed decision as to whether to respond to the NOA by commencing an application for a prohibition order (*AB Hassle v Apotex Inc*, 2006 FCA 51 at para 4).

[33] Proceedings under the *PM(NOC) Regulations* are designed to be expeditious. The patent holder only has 45 days to assess its course of action in response to the NOA (subsection 6(1)), and the question of whether the Minister is free to issue the requested NOC, should be resolved within 24 months of the patent holder filing their NOA. Therefore, sufficiency of information must be assessed with the NOC scheme's time constraints in mind (*Cobalt*, above, at para 32).

[34] However, there is a key distinction between the facts in a document and the document itself. A document cannot be assimilated to a factual basis; therefore, it is not that a second person is precluded from relying on any document not cited in the NOA, but rather that the second person may not rely on facts not cited in the NOA (*Eli Lilly Canada Inc v Mylan Pharmaceuticals ULC*, 2015 FC 178 at para 137; *Proctor & Gamble*, above, at para 12).

[35] Finally, the lack of an affidavit, describing how the patent holder had not been able to decide whether to challenge an NOA because of the lack of specificity in the NOA, has been found to be a relevant factor in determining whether the patent holder has been prejudiced by

new issues that were not raised in the NOA (*Alcon Canada Inc v Apotex Inc*, 2014 FC 791 at paras 80 and 82). The Federal Court of Appeal has confirmed that a lack of an affidavit on the part of the patent holder can be considered "to be telling" in a determination of the sufficiency of the NOA (*Alcon*, above, at para 81).

(a) *The Table 1 Documents*

[36] There was no argument that the Table 1 Documents were introduced in the NOA. The real question was whether the experts cited those documents in a manner that introduced facts not raised in the NOA. A related question was whether facts in those documents, but not stated in the body of the NOA, were raised in the NOA in a manner that was sufficient to meet the requirement of subsection 5(3)(b)(ii) of the *PM(NOC) Regulations*.

[37] If merely attaching the document was all that was required for sufficient citation of a factual basis in an NOA, it would place an undue burden on a patent holder, who would have to assess all of the possible facts for which a Schedule B-type document could be evidence. This goes against the objective of the scheme set out in the *PM(NOC) Regulations*.

[38] It is not appropriate for a document that is merely attached to the NOA, and not discussed in any way, to stand for all of the facts that could be teased out of that document. Attachment in a list or table is not sufficient to meet the requirement of section 5(3)(b)(ii) of the *PM(NOC) Regulations*. However, as stated above the prohibition against raising new facts does not mean that experts cannot rely upon documents not discussed in the NOA to support facts clearly in the NOA.

[39] The Pharmascience experts, particularly Dr. Fassihi, gave very generic, high-level descriptions of the contents of each document. For example, regarding Schedule B, Document #35 ("NOA #35"), Dr. Fassihi stated (paras 150 to 151 of his affidavit):

> This is a paper on order mixtures from 1983 discusses [*sic*] terminology for power mixing including ordered mixture, random mixture, degree of homogeneity and interactive powder.
>
> In this article, the authors discuss the nomenclature for ordered mixture suggesting that "interactive" instead of ordered more closely reflects the interaction mechanism, i.e., the cohesive aspects between find drug particles and the carrier.

[40] Pharmascience, in their Response to Schedule A to the Applicants' factum (the "RSA"), stated that these facts proffered by Dr. Fassihi related to the following facts in the NOA: (1) ordered mixtures were known; (2) ordered mixing is different from random mixing; and (3) there is a difference between obtaining homogeneity through [redacted] versus an ordered mixture. His statement is clearly related to the fact that ordered mixtures were known, and while it is unclear from his synopsis whether NOA #35 also stands for the facts that ordered mixing is different from random mixing, and/or that different amounts homogeneity is obtained via [redacted] versus an ordered mixture, he was not adding new facts.

[41] I am not convinced that any of the expert statements relating to the Table 1 Documents stand for new facts. Accordingly, I did not think that it was appropriate for these statements to be struck. In the few instances where any statement by one of the Pharmascience experts did raise a fact that was broader than what is in the NOA, it was given no weight in the decision, as it would have been inappropriate for Pharmascience to use the Table 1 Documents for facts beyond the factual statements made explicitly in the body of NOA.

(b) *The Impugned Propositions*

[42] The key issue with regards to the Impugned Propositions was whether by discussing the underlying documents (listed as NOA #17, 54, and 128) in the body NOA, Pharmascience had sufficiently raised all of the facts within each document, and whether those facts could be used to support any/or all of the legal arguments made in the NOA.

[43] In the NOA, most of the Schedule B documents are discussed under the heading "Relevant Common General Knowledge of the Person Skilled in the Art". This is a broad category, which suggests that all of the documents could support any of the validity attacks raised. In *Eli Lilly Inc v Apotex Inc*, 2007 FC 455 at paragraph 109, Justice Johanne Gauthier writes:

> It is obviously important for a first person to know exactly on what basis the validity of the patent is challenged for this will have a major impact on the type of evidence it will be required to put forward. The analysis and evidential concerns that arise in response to allegations of invalidity based on anticipation or obviousness are very different from those that would arise in response to a challenge of validity based on insufficiency or lack of utility.

[44] However, the heading "Relevant Common General Knowledge of the Person Skilled in the Art" is located between two headings that have to do with the obviousness analysis: "Obviousness" and "The Test for Obviousness". Therefore, it was reasonable to infer that the facts contained within these documents, except if the document was explicitly referenced in another section of the NOA, were all directed to an allegation of obviousness. To the extent that one of Pharmascience's experts cited a proposition that was different from what was stated in the

NOA, but which was used in an obviousness analysis, it was allowed. The way that the documents were disclosed in the body of the NOA was sufficient notice to the Applicants that any of the facts in each document, including the Impugned Propositions, would be put forward in an obviousness analysis.

[45] Under the headings “Anticipation”, “Insufficiency of the Description”, and “Lack of Utility and Lack of Sound Prediction”, Pharmascience has referenced specific documents, out of the Schedule B documents, in support of their arguments. It was appropriate to consider the whole of those specific documents, in the analysis under which each is listed. However, if Pharmascience used any one of documents NOA #17, 54, and 128 outside of a section where the document is explicitly listed, for a fact not explicitly stated in that section of the NOA (e.g., the document is listed in the section “Anticipation”, but not in the section “Lack of Utility”, and Pharmascience references it for a fact not explicitly stated in “Lack of Utility”), I gave that evidence no weight, because the NOA did not give sufficient notice that this was a fact that would be relied upon for that particular analysis. Therefore, it was not appropriate to strike the Impugned Propositions.

(c) *Prejudice and Abuse of Process*

[46] There was no evidence that the Applicants were prejudiced because the NOA lacked particulars. Specifically, it was “telling” that they did not raise more vigorous objections to the Schedule B evidence during the Motion to Strike, nor had they filed any evidence suggesting that they would not have brought the application or that they had difficulty deciding whether to bring the application. However, it is clear that a NOA of this sort—that is one where there is a very

long list of prior art references attached but not discussed in the body of the NOA—could lead to real prejudice in other cases. Given the scheme of the *PM(NOC) Regulations*, it is important that the NOA contain sufficient information to enable a patent holder to make an informed decision quickly. An overwhelming amount of information that has to be processed in a short time period can be just at stymying as an absence of information.

[47] Having carefully reviewed the NOA, I am not satisfied there was an abuse of process.

(3) Conclusion of the Preliminary Issues

[48] The cross-examinations of Drs. Fassihi and Smart had interruptions and objections by counsel for Pharmascience which were not always necessary or useful, and which created a less than ideal situation. However, these interruptions did not rise to the level of shielding Pharmascience's experts from meaningful cross-examination, and I find that they were not abusive.

[49] Regarding the Table 1 Documents, I find that these documents do relate facts that are laid out in the NOA. Further, the experts' statements regarding these documents largely repeat facts that are raised in the NOA, as laid out Pharmascience's RSA. To the extent that the experts' statements go beyond the facts that are explicitly raised in the NOA, as highlighted in the RSA by Pharmascience, I give those specific facts no weight.

[50] Finally, although the Pharmascience experts did raise slightly different propositions in their expert affidavits than were raised in the NOA, these Impugned Propositions appear to be

directed to same analysis in both the NOA and the expert affidavits. Because the underlying documents were raised in detail in the NOA, I find that the Applicants were given enough information for all of the facts in the documents to be considered sufficiently raised to meet the requirement of subsection 5(3)(b)(ii) of the *PM(NOC) Regulations*.

III. Burden of Proof

[51] The burden of proof for infringement of a patent lies with the party alleging infringement (*Monsanto Canada Inc v Schmeiser,* 2004 SCC 34 at para 29; *Eli Lilly v Apotex,* 2009 FC 991 at para 211, aff'd 2010 FCA 240 [*Eli Lilly*]; *Merck & Co Inc v Apotex,* 2010 FC 1265 at para 135, aff'd 2011 FCA 363).

[52] The presumption of validity in subsection 43(2) of the *Patent Act,* RSC, 1985, c P-4, is weak and once Pharmascience adduced evidence that has an "air of reality" to rebut that presumption, the legal burden shifted to the Applicants to establish on a balance of probabilities that all the allegations of invalidity asserted are not justified (*Abbott Laboratories v Canada (Minister of Health),* 2007 FCA 153 at paras 9 to 10; *Hoffman-La Roche Ltd v Apotex Inc*, 2013 FC 718 at paras 58 to 61).

IV. Applicants' Expert Witnesses

A. Dr. Loyd Allen, Jr.

[53] Dr. Loyd V. Allen, Jr. obtained a B.Sc. and M.S. in Pharmacy from the University of Oklahoma College of Pharmacy in 1966 and 1970, respectively. He completed a residency in

hospital pharmacy at the US Public Health Service Hospital in Boston, MA in 1967; and he received a Ph.D. in Pharmaceutics from the University of Texas at Austin in 1972.

[54] Dr. Allen is currently the CEO of the Midwest Institute of Research and Technology, and a Professor Emeritus of the University of Oklahoma College of Pharmacy. He is a named inventor on 13 US patents in the field of drug formulations, and is widely published (i.e., over 200 experimental publications; 25 books, chapters and monographs; and over 500 professional publications, including two text books). He is also the founder and current Editor-in-Chief of the International Journal of Pharmaceutical Compounding, and has held or currently holds many distinguished fellowships and/or committee positions.

[55] Dr. Allen is an expert in the areas of pharmaceutical formulation and pharmaceutical compounding.

B. Dr. Patrick J. Sinko

[56] Dr. Patrick J. Sinko received a B.Sc. in Pharmacy from the College of Pharmacy, Rutgers University, New Brunswick, New Jersey in 1982; and a Ph.D. in Pharmaceutics from the College of Pharmacy, the University of Michigan, in 1988.

[57] He is currently the Associate Vice President for Research at Rutgers University, and a Distinguished Professor of Pharmaceutics in the Ernest Mario School of Pharmacy. He is also appointed to the Parke-Davis Endowed Chair in Pharmaceutics and Drug Delivery, which is a

distinguished professorship. He teaches biopharmaceutics, pharmaceutics, physical pharmacy, and drug delivery systems.

[58] He was the editor and principal author of the Fifth (2005) and Sixth (2010) Editions of Martin's Physical Pharmacy and Pharmaceutical Sciences. He has published 159 articles in scientific journals; and 282 books, reviews, and contributed chapters. He has served as a reviewer for numerous scientific journals, and has held or holds many distinguished fellowships and/or committee positions.

[59] Dr. Sinko is an expert in the areas of pharmaceutical science and formulation.

V. Pharmascience's Expert Witnesses

A. Dr. Yuriy Ososkov

[60] Dr. Yuriy Ososkov received a combined Bachelor's and Master's degree in Engineering from the Moscow Institute of Steel and Alloys in 1991; and a Ph.D. in Materials Engineering from the Warsaw University of Technology in 1997. He holds the designation of Professional Engineer, certified by the Professional Engineers of Ontario.

[61] From 2006 to 2015, Dr. Ososkov was employed by Exova Canada Inc., where he was the Manager, until February 2014, and then the Senior Materials Scientist, Physical Characterization in the Health Sciences Division. As the Senior Materials Scientist, he acted as the technical lead

in implementing materials services, such as X-Ray Diffraction, Scanning Electron Microscopy ("SEM"), and Energy-dispersive X-ray Spectroscopy.

[62] [redacted]

B. Dr. Reza Fassihi

[63] Dr. Reza Fassihi received a B.Sc. in Pharmacy from Punjab University, in India, in 1974; and a Ph.D. in Pharmaceutics from Brighton University, in England, in 1978.

[64] He is currently a Professor of Biopharmaceutics and Industrial Pharmacy at Temple University, School of Pharmacy in Philadelphia, and the Co-Chair of the Philadelphia Pharmaceutical Forum. He is a named author on more than 130 publications in peer-reviewed journals, and a named inventor on 9 US patents. He is also a Fellow of the American Association of Pharmaceutical Sciences, and a member of the American Association of Colleges of Pharmacy.

[65] Dr. Fassihi is an expert in the area of pharmaceutical formulation, and has experience in biopharmaceutics and pharmacokinetics.

C. Dr. John D. Smart

[66] Dr. John D. Smart received a B.Sc. in Pharmacy from Brighton Polytechnic (now University of Brighton) in 1979; and a Ph.D. in Pharmacy from the Welsh School of Pharmacy (now the University of Wales, College of Cardiff) in 1983.

[67] He is currently a Professor of Pharmaceutical Sciences and Academic Director of Pharmacy at the School of Pharmacy and Biomolecular Sciences at the University of Brighton. He is the co-author of 65 peer-reviewed research articles, and a named author/co-author of six book chapters. He is a founding member of the Pharmacy Schools Council, and is a member of the Royal Society of Chemistry, the Royal Pharmaceutical Society, and the Royal Society's Expert Advisory Panel.

[68] He is an expert in the area of pharmaceutical formulation and in particular the area of bioadhesive agents.

D. Dr. Rajesh Davé

[69] Dr. Rajesh Davé received a B.Tech. in Mechanical Engineering from the Indian Institute of Technology, Bombay, in 1978; a M.S. in Mechanical Engineering from Utah State University in 1981; and a Ph.D. in Mechanical Engineering from Utah State University in 1983.

[70] He is currently a Distinguished Professor of Chemical, Biological, and Pharmaceutical Engineering at the New Jersey Institute of Technology. He is the founding director of the

Research and Development Excellence Center, New Jersey Center for Engineered Particulates, and a New Jersey Institute of Technology Site-Leader, Thrust Leader and Test-bed Leader of the National Science Foundation Engineering Research Center on Structured Organic Particular Systems. He is a Senior Member of the American Institute of Chemical Engineers, and a Member of the American Association of Pharmaceutical Sciences. He is a named author on over 100 peer-reviewed papers.

[71] Dr. Davé is an expert in engineered formulations, including micronization and other methods for formulating poorly soluble drugs.

VI. The ‘988 Patent

[72] The ‘988 Patent has an International Filing Date of September 24, 1999; was published on March 30, 2000; and will expire on September 24, 2019. Orexo AB owns the ‘988 Patent, and consented to listing it on the Patent Register against the innovative drug, SUBLINOX, which is marketed by the Applicants.

[73] The ‘988 Patent relates to novel rapid-onset sublingual pharmaceutical compositions for treating the acute disorder insomnia, involving ordered mixtures—of microparticles of the active pharmaceutical ingredient (“API”) and water-soluble carrier particles—and bio/mucoadhesives, a method for making such compositions, and their use in the manufacture of a medicament.

[74] The ‘988 Patent has one independent claim, and 21 dependent claims. Independent claim 1 states:

> Claim 1:
>
> A pharmaceutical composition for the treatment of insomnia by sublingual administration, comprising an ordered mixture of microparticles of at least one pharmaceutically active agent selected from diazepam, oxazepam, zopiclone, zolpidem, propiomazin, valeriana, leomepromazin or a sleep inducing peptide, which agent is adhered to the surfaces of carrier particles, said particles being larger than said microparticles and being water-soluble, and a bioadhesion and/or mucoadhesion promoting agent.

[75] The ‘988 Patent abstract describes the invention as follows:

> A pharmaceutical composition for the treatment of an acute disorder is described. The composition comprises an essentially water-free, ordered mixture of at least one pharmaceutically active agent in the form of microparticles which are adhered to the surfaces of carrier particles which are substantially larger than the particles of the active agent or agents, and are essentially water-soluble, in combination with the bioadhesion and/or mucoadhesion promoting agent. The invention also relates to a method for preparing the composition and to the use of the composition for the treatment of acute disorders.

[76] Accordingly, the essential elements of claim 1 are:

i. a pharmaceutical composition for the treatment of insomnia by sublingual administration;
ii. comprising an ordered mixture of microparticles;
iii. of at least one API selected from diazepam, oxazepam, zopiclone, zolpidem, propiomozin, valeriana, leomepromazin or a sleep inducing peptide;
iv. which is adhered to the surfaces of carrier particles;
v. said particles being larger than the API microparticles and being water-soluble; and
vi. a bioadhesion and/or mucoadhesion promoting agent.

[77] The parties agreed that each of these elements was known in the prior art, but the Applicants argued that the combination of these elements is novel, unobvious and useful.

[78] Particularly, the Applicants said that sublingual administration and use of an ordered mixture of API adhered to the surfaces of carrier particles, in combination with a bioadhesion and/or mucoadhesion promoting agent, was both novel and unobvious. Not surprisingly, Pharmascience took a contrary view.

A. The Person Skilled in the Art (POSITA)

[79] The experts generally agreed that a POSITA for the '988 Patent would be (1) an individual with a Ph.D. in Pharmaceutical Sciences, or an equivalent field, and one to two years of experience in the development of oral pharmaceutical formulations; or (2) an individual with an advanced degree in a field other than Pharmaceutical Sciences (i.e., a Ph.D. in chemical engineering, physical chemistry, or similar) and three to five years of experience in development of oral pharmaceutical formulations.

B. Common general knowledge

[80] The Applicants' experts disagreed that the list of statements found at paragraph 108 of the NOA represented an accurate picture of what would comprise a POSITA's common general knowledge at the relevant time.

[81] Dr. Sinko explained that, while NOA paragraph 108 points (a) to (m) are general concepts that would have been known to a POSITA at the relevant time, it would not have been part of the common general knowledge that these concepts would apply to the issues addressed by the '988 Patent. Additionally, he stated that paragraph 108 points (n) to (cc) would not have

been interconnected in the common general knowledge at the relevant time, and criticized the list as being collected via hindsight.

[82] Dr. Allen addressed all of the articles and patents listed in the NOA as forming a part of the common general knowledge, individually, and commented that this was a disjointed list, without an obvious relationship between the different articles cited.

[83] Drs. Allen and Sinko agreed that the general information in Lieberman et al., *Pharmaceutical Dosage Forms, Second Edition, 1989* (the "Lieberman Text") would have been part of the common general knowledge at the relevant time. However, they were of the opinion that there would have been no reason for a POSITA to combine the 16 specific references listed in the NOA. Further, they pointed out that the Lieberman Text contains a lot of material that is either completely irrelevant to the '988 Patent, or teaches away from the '988 Patent. Dr. Sinko stated that what is evident from the Lieberman Text is that sublingual administration was rare, and there was little known about sublingual administration at the relevant time.

[84] Dr. Fassihi, Dr. Smart, and Dr. Davé approached their assessments of what would comprise the common general knowledge differently than Drs. Allen and Sinko, basing their answers upon the questions posed to them by counsel for Pharmascience rather than the information presented in the NOA.

[85] Dr. Fassihi stated that by 1998 orally disintegrating tablets were known, and that Ativan (lorazepam) was a sublingual, orally disintegrating tablet on the market at that time and, because

Ativan was on the market, it would have been part of the common general knowledge that orally disintegrating tablets would have to dissolve quickly (less than three minutes). He believed that standard excipients, at the time, would have included water soluble fillers and powerful disintegrates, and that known bio/mucoadhesive excipients included hydrophilic polymers such as hydroxypropyl cellulose, carboxymethyl cellulose, carbomers and trangacanth gum or gelatin. Additionally, he asserted that a POSITA would have been familiar with ordered mixtures and how to make them.

[86] Dr. Smart claimed that sublingual tablets for nitroglycerin were known decades before the relevant date. He stated that the transmucosal formulations that were known had mannitol, with "super disintegrants" such as Ac-Di-Sol, and were made by normal tableting procedures using wet granulation, dry granulation, or direct compression. A POSITA would have known about nitroglycerin sublingual and buccal, slow release tablets; and Ativan (lorazepam) fast dissolving sublingual tablets. He also believed that a POSITA would be aware of how to make an ordered mixture.

[87] Dr. Davé opined that the process for making an ordered mixture, and the benefits of ordered mixtures would have been part of the common general knowledge at the relevant time.

[88] Based upon consideration of the expert evidence, what does form part of the prior art and common general knowledge is as follows.

(1) Acute disorders and insomnia

[89] A POSITA would have known about acute disorders. An acute disorder is a disorder that is treated through emergency medical, general medical and surgical treatment rather than through long-term care for chronic conditions. Acute disorders can include pain and insomnia. Insomnia is the inability to sleep, in the absence of external impediments (e.g., noise, bright light, etc.) during the period when sleep should normally occur. There are two broad classes of treatment for insomnia: psychologic and pharmacologic.

[90] At the relevant time, there were multiple drug products listed for insomnia, including Diazepam (Valium); Lorazepam (Ativan); Zolpidem (Ambien); and Phenobarbital (Luminal). Dosage forms for insomnia included tablets and capsules, elixirs and syrups, suppositories, and transdermal gels and/or creams.

(2) Dosage form development

[91] Drug substances, at the relevant time and continuing to the present, are generally given as part of a formulation, which is a combination of the API and one or more excipients, which are non-medicinal and which serve varied pharmaceutical functions (e.g., solubilize, thicken, dilute, emulsify, stabilize, preserve, etc.). Excipients are added to produce efficacious and appealing dosage forms.

[92] If the medication is intended for systemic use and oral administration is appropriate, tablets or capsules are usually prepared because they are easy to handle and convenient for

patients to self-administer. The vast majority of the tablets on the market, at the relevant time, were taken orally, to be swallowed whole, for the active drug to be absorbed in the gastrointestinal tract. Other methods of administering tablets included sublingually, buccally, rectally, or intravaginally.

(3) Rapidly disintegrating or dissolving tablets

[93] A POSITA would have known that disintegration is an important factor affecting drug release, absorption into the system, and subsequent pharmacological effects. Rapidly disintegrating or dissolving tablets ("RDTs") are characterized by the ability to disintegrate or dissolve in the mouth within one to two minutes. RDTs, used to create dosage forms for patients who have difficulty swallowing tablets, were part of the common general knowledge.

(4) Sublingual Tablets

[94] Oromucosal delivery, a drug delivery route that promotes rapid absorption and high bioavailability with subsequent rapid onset of pharmacological effect would have been known at the relevant time. Oromucosal delivery utilizes either the buccal (cheek) or sublingual (under the tongue) mucosa as the absorption site. The advantage of this delivery method is that the drug enters the systemic circulation directly, bypassing the gastrointestinal tract and the first pass effect in the liver. This allows efficacious delivery of drugs that are destroyed by the gastric juice and/or are poorly absorbed from the gastrointestinal tract.

[95] By 1998, the sublingual mucosa had been used for fast absorption of drugs, such as nitroglycerin, for decades. A POSITA would have known that one of the problems associated with sublingual tablet formulations is that there is a risk that the patient will swallow part of the dose before all of the active substance has been released and absorbed locally. They would also have known that there are specific formulation aspects that must be taken into consideration, such as dose homogeneity, rapid disintegration, and bioadhesive properties. In the 1998 to 1999 time period, only a handful of sublingual tablet products were on the market.

(5) Ordered Mixtures

[96] A POSITA would have known that creating an ordered mixture is one method of achieving a high degree of homogeneity in a formulation. One type of ordered mixing occurs when small particles of one component in the mixture become lodged in the surface irregularities or adhere to the surface of a larger carrier component. Ordered mixing can be obtained by (1) mechanical means, (2) adhesion, and (3) coating.

[97] In practice, coarse carrier molecules are mixed with a fine drug component for a relatively long time so that the drug particles adhere to the surface of the carrier molecules through adhesional forces (i.e., electrostatic or surface tensional forces). This dispersion of the fine drug component over the carrier molecules creates a mixture where the drug is evenly distributed amongst the carrier molecules, and there are few instances of agglomerates of the drug.

(6) [redacted]

[98] [redacted]

[99] [redacted]

C. Claim Construction

(1) Relevant Date

[100] The relevant date for construing the claims of the '988 Patent is the date of publication of the patent application: March 30, 2000.

[101] While there was some disagreement by the experts on the essential elements of the claims in the '988 Patent, I understand and construe the claims' essential features to be as summarized in Drs. Allen and Sinko's affidavits, at paragraphs 75 to 76 and 44 to 47, respectively:

Claim	Depends from	Essential Elements
1	N/A	(i) A pharmaceutical composition (ii) for the treatment of insomnia (iii) by sublingual administration (iv) comprising an ordered mixture of (v) microparticles of an active agent (vi) selected from *inter alia* zolpidem (vii) adhered to the surface of carrier particles (viii) which are larger than the active agent microparticles and are water soluble and (ix) a bio/mucoadhesion promoting agent.
2	1	The bio/mucoadhesion agent is adhered to the surface of the carrier particles.
3	1-2	The active agent is Zolpidem.
4	1-3	The active agent microparticles have a weight based mean diameter < 10 µm.
5	1-4	The carrier particles have a mean sieve diameter of less than 750 µm.

6	5	The carrier particles have a mean sieve diameter between 100 and 600 µm.
7	1-6	The carrier particles are brittle and will fragmentize easily when compressed.
8	1-7	The bio/mucoadhesion promoting agent is selected from the group consisting of acrylic polymers, cellulose derivatives, natural polymers having bio/mucoadhesive properties, and mixtures thereof.
9	8	The bio/mucoadhesion promoting agent is selected from the group consisting of cellulose derivatives and comprising *inter alia* croscarmellose.
10	1-9	The composition also contains a pharmaceutically acceptable surfactant in a finely dispersed form and intimately mixed with the active agent(s).
11	10	The surfactant is present in 0.5 to 5 weight percent of the composition.
12	10	The surfactant is present in 0.5 to 3 weight percent of the composition.
13	10-12	The surfactant is selected from *inter alia* sodium lauryl sulfate.
14	1-13	The carrier particles are water-soluble, pharmaceutically acceptable carbohydrates and/or inorganic salt.
15	14	The carrier particles contain at least one of *inter alia* mannitol.
16	1-15	The carrier particles also contain at least one disintegrating agent.
17	16	The disintegrating agent is selected from cross-linked polyvinylpyrrolidone, carboxymethyl starch, natural starch, microcrystalline cellulose, cellulose gum and their mixtures.
18	16-17	The disintegrating agent is present from 1 to 10 weight percent.
19	1-18	No additional essential elements.
20	19	No additional essential elements.
21	20	No additional essential elements.
22	1-21	The use of the compositions in any one of the previous claims for the manufacture of a medicament for the treatment of insomnia.

(2) Claim terms that need construction

(a) *Bio/mucoadhesive promoting agent*

[102] Dr. Fassihi stated that it was not clear from the patent how a "mucoadhesive promoting" agent is different from a mucoadhesive agent. He commented that a POSITA would understand that a mucoadhesive agent is one that adheres to the mucosa and maintains integrity for a long period of time (e.g., 15 minutes to 10 hours). In his opinion, a mucoadhesive promoting agent does not make sense in a tablet that is designed to disintegrate and dissolve rapidly, because said tablet would not have time to adhere to the mucosa before disintegrating.

[103] The Applicants argued that the Pharmascience experts misunderstood the function of the bio/mucoadhesive promoting agent. Drs. Fassihi and Smart asserted that the bio/mucoadhesive promoting agent's purpose was to promote the adhesion of the tablet to the sublingual mucosa. The Applicants contended that the bio/mucoadhesive promoting agent is simply an excipient that creates a local environment that allows the particles comprising the formulation to adhere after release to achieve rapid absorption.

[104] Further, Drs. Allen, Sinko and Smart stated that [redacted] can be both a disintegrant and a bio/mucoadhesive, as disclosed and claimed in the '988 Patent. In contrast, Dr. Fassihi opined that [redacted] cannot be a bio/mucoadhesive promoting agent or a bioadhesive agent, since it is a disintegrant.

[105] The Applicants relied on the NOA, paragraph 108(v), [redacted] and argued that any concession made in an NOA is binding on Pharmascience: *Teva Canada Innovation v Apotex Inc*, 2014 FC 1070 at paragraph 66; *Merck & Co v Pharmascience Inc*, 2010 FC 510 at paragraphs 95 to 96.

[106] I agree with the Applicants that the bio/mucoadhesive promoting agent is not an excipient that engenders the adherence of the tablet to the sublingual mucosa. Construing the term purposively, I find that a bio/mucoadhesive promoting agent is an excipient that creates a local effect that promotes the adherence and absorption of drug particles to the mucosa.

[107] Having considered the parties' evidence and references to bio/mucoadhesives, I agree [redacted]. The manner of use in a process is an important factor on the nature of the effect [redacted], discussed in more detail below.

(b) *Ordered mixtures*

[108] The summary of the '988 invention states that the "sublingual composition comprises an ordered mixture of one or more bioadhesive and/or mucoadhesive carrier substances coated with the pharmaceutically active agent or agents in a fine particulate form" (page 4, lines 21 to 23).

[109] Claim 1 states that the invention comprises a pharmaceutical composition comprising an ordered mixture of microparticles of at least one API which is adhered to the surfaces of carrier particles, and a bioadhesion and/or mucoadhesion promoting agent. To formulate the composition, the specification teaches that one should use the technology for formulating rapidly

dissolving, ordered-mixture compositions disclosed in European patent EPO 324725 (the "'725 Patent"). In these compositions, the drug, in a finely dispersed state, covers the surface of substantially larger carrier particles (page 4, lines 25 to 29).

[110] The experts disagreed as to whether the term ordered mixture encompassed the product resulting from the Pharmascience process [redacted]. The Pharmascience experts asserted that, [redacted]. Additionally, they stated that [redacted] would prevent the bio/mucoadhesion promoting agent from forming an ordered mixture with the API and carrier particles, [redacted]. The Applicants' experts argued that the Pharmascience product would be sufficiently ordered to be considered an ordered mixture [redacted].

[111] As discussed above, ordered mixtures are more homogenous than random mixtures because the dispersion of the small API particle over the carrier reduces aggregation of the small API particle in the mixture. In an ideal ordered mixture, API and carrier particles form ordered units where the standard deviation of the amount of API between any given samples of the mixture nears zero, as long as the sample size is greater than an ordered unit. In practice, ordered mixtures achieve a lesser degree of homogeneity.

[112] Unfortunately, nowhere in the specification is there any indication of what degree of order is necessary to constitute a pharmaceutical composition "comprising an ordered mixture". Further, the experts disagreed on what degree of homogeneity is necessary for there to be an ordered mixture of microparticles of API, carrier particles, and bio/mucoadhesion promoting agents.

[113] Drs. Allen and Sinko argued that a sufficiently ordered mixture will be formed [redacted]. Drs. Fassihi, Smart and Davé disagreed, stating that one could not get a uniform distribution of API, carrier particles, and bio/mucoadhesion promoting particles [redacted] because the [redacted] results in a mixture which will not be homogenous enough to be considered an ordered mixture. In particular, the Pharmascience experts contended that [redacted].

[114] Additionally, counsel for Pharmascience urged the Court to find that statements made during prosecution of a corresponding foreign (European) patent application should be taken as an admission against interest on construing the term ordered mixture. Specifically, statements suggesting [redacted].

[115] The Supreme Court of Canada has made it quite clear that such statements, made either during prosecution of Canadian patent applications or during prosecution of corresponding foreign patent applications, are neither relevant nor admissible with respect to construing terms used in issued Canadian patents (*Free World Trust v Électro Santé Inc*, 2000 SCC 66 [*Free World Trust*]). They are equally irrelevant as part of the common general knowledge to be considered.

[116] This is particularly true in dealing with the prosecution histories of foreign patent applications, where different cannons of patent construction, different laws and different jurisprudence has evolved, differentiating doctrines applied elsewhere from Canadian patent law. If a party or parties believe that a different course should be taken on this front in Canada, such

that doctrines like the United States doctrine of file wrapper estoppel should be applied in this country, the Court is not the appropriate forum to effect that change—legislative amendments would be required.

[117] Having considered the documents and expert evidence relied upon by the parties and giving the term "ordered mixtures", a purposive construction, I find that such a mixture will necessarily be essentially free from water and that the API will be substantially uniformly distributed over the surfaces of the carrier particles; in other words, the degree of order must be substantial throughout the composition and the API must be substantially disaggregated.

VII. Prior Art

[118] In addition to the articles that Pharmascience alleged form part of the common general knowledge in the body of the NOA, at Schedule B, Pharmascience lists 209 pieces of prior art.

[119] Neither of the Applicants' experts discussed this list in a detailed way in their reports.

[120] Dr. Allen stated that he briefly reviewed all of these documents, except for the "file wrappers", which he felt were outside his area of expertise, and only noted one paper of interest: Shojaei, A.H., "Buccal Mucosa As a Route for Systemic Drug Delivery: A Review", (1998) J Pharm Pharmaceut Sci 1(1): 15-30 [Shojaei, 1998]. He summarized this review article as a discussion of the buccal cavity as a preferred route of administration of drugs for systemic delivery. It highlights some of the advantages of buccal administration, compares sublingual

administration with buccal administration, and concludes that the buccal mucosa is superior to the sublingual mucosa for drug delivery.

[121] Dr. Sinko remarked that there are three articles worth addressing from the Schedule B to the NOA: Harris, D. et al., "Drug Delivery via the Mucous Membranes of the Oral Cavity," (1992) J Pharm Sci 81:1-10; Shojaei, 1998; and G. Hunt, P. Kearney and I.W. Kellaway, *Drug Delivery system: Fundamentals and Techniques, Chapter 11 Mucoadhesive Polymers in Drug Delivery Systems*, (Chichester: Elis Horwood, 1987) at 180. All three articles teach away from the use of the sublingual mucosa as the absorption site for drug delivery.

[122] Counsel for Pharmascience provided Drs. Fassihi, Smart, and Davé with the set of patents and publications set out in Schedule B and asked each to choose documents that they thought were pertinent to the '988 Patent, and taught the invention disclosed in the '988 Patent. Counsel for Pharmascience also asked them whether or not a POSITA would have been able to locate the patents and publications provided through a reasonably diligent search.

[123] All three Pharmascience experts stated that a POSITA would have been able to obtain the documents provided by searching the usual places (i.e., Merck Index, Chemical Abstracts, text books, scientific journals, international patent agencies, and university libraries). Dr. Fassihi picked 26 different pieces of prior art that are pertinent to and teach some aspect of the '988 Patent. Dr. Smart identified 55 publications and patents that are pertinent to and teach some aspect of the '988 Patent. Finally, Dr. Davé selected 16 publications that could teach a POSITA about making ordered mixtures.

VIII. Anticipation of the ‘988 Patent by the ‘725 Patent

[124] Anticipation is found where performance of the prior art necessarily infringes the patent under review. Both disclosure and enablement are required for a prior art reference to anticipate a claim (*Apotex Inc v Sanofi-Synthelabo*, 2008 SCC 61, at paras 25 to 27 [*Sanofi*]):

a. The prior patent must disclose subject matter that would infringe the patent under review if performed, such that the POSITA, reading the prior patent, with no trial and error, would understand whether it discloses the invention claimed; and
b. Would the POSITA be able to work the invention disclosed by the prior patent, without undue burden but which may involve a reasonable amount of trial and error.

[125] What constitutes a reasonable amount of trial and error is set out at paragraph 37 of *Sanofi*, above:

> … When considering whether there is undue burden, the nature of the invention must be taken into account. For example, if the invention takes place in a field of technology in which trials and experiments are generally carried out, the threshold for undue burden will tend to be higher than in circumstances in which less effort is normal … But experiments or trials and errors are not to be prolonged even in fields of technology in which trials and experiments are generally carried out. No time limits on exercises of energy can be laid down; however, prolonged or arduous trial and error would not be considered routine.

[126] The ‘725 Patent was filed on January 1, 1989 at the European Patent Office, with a Swedish priority date of January 13, 1988, and published on July 19, 1989. It is the only document relied upon by Pharmascienceto support the validity attack based on anticipation.

[127] The ‘725 Patent discloses an invention that relates generally to the field of drug formulation, and more specifically, but not exclusively, to ordered solid mixtures of particulate

pharmaceutical carrier substances and smaller particles of at least one pharmaceutically active substance that can be produced by means of a dry mixing process, in which the smaller particles adhere or bind to the surfaces of the larger carrier particles. The invention also relates to pharmaceutical preparations produced from the ordered mixtures and to a method for producing such preparations.

[128] The carrier substance disclosed in the ‘725 Patent may be any substance which is acceptable pharmaceutically, highly soluble in water, and has a size from 50 to 1000 microns and preferably 100 to 500 microns. It can be formed into particles that embody or incorporate a disintegrant. According to the patent, the disintegrant can be embodied in the carrier particles in various ways, for example, the carrier and the disintegrant can be granulated together in a liquid which will not dissolve the disintegrant. Further, the ordered mixture should be 25% carrier by weight, and up to 10% disintegrant by weight.

[129] Examples of different kinds of active substances which are useable according to the ‘725 Patent include benzodiazepines, ergotamine tartarate, isosorbide dinitrate, and griseofulvin. These substances have a size of at most 25 microns, and are preferably no larger than 10 microns.

[130] Pharmascience argued that the ‘725 Patent discloses:

a. formulations with an ordered mixture comprising smaller active ingredients (not greater than 10 microns) adhered to larger soluble carrier particles (100 to 400 microns);
b. rapid dissolution (less than two minutes) that is consistent with an orally disintegrating tablet;
c. formulations providing rapid release and absorption;

d. oral formulations, including examples of APIs that are given sublingually, such as isosorbide dinitrate for angina;
e. an example of a formulation that contains an ordered mixture with the API oxazepam (which is covered in claim 1 of the ‘988 Patent); and
f. an example of a formulation that also contains Ac-Di-Sol—which, according to the ‘988 Patent, is a bio/mucoadhesive compound.

[131] Moreover, Pharmascience asserted that a skilled person could make a sublingual tablet following the teachings of the ‘725 Patent by simply scaling down the tablet size of the examples to make it acceptable for sublingual delivery. The excipient percentages are similar in the ‘725 Patent and in the ‘988 Patent, and within the generally recommended amounts for those excipients.

[132] The Applicants argued that the ‘725 Patent neither discloses nor enables claim 1 or any of the dependant claims. Their position was that neither sublingual administration nor bio/mucoadhesion, both essential elements of claim 1, are taught or enabled:

a. although the formulations taught by the ‘725 Patent include Ac-Di-Sol, the ‘725 Patent does not disclose or enable bio/mucoadhesive formulations—Ac-Di-Sol is only disclosed as a disintegrant;
b. there is no disclosure of the use of Ac-Di-Sol as a sublingual bio/mucoadhesion promoting agent; in fact, there is no disclosure of sublingual administration;
c. while the class of drugs “benzodiazepines” is mentioned in the ‘725 Patent, and lorazepam, which is from that class, was sublingually administered in 1998, the Pharmascience experts agreed or conceded on cross-examination that the choice of lorazepam was a hindsight approach and sublingual lorazepam was a specifically-indicated special drug.

[133] Finally, the Applicants pointed out that Dr. Davé did not think that the ‘725 Patent was worth considering when selecting prior art from Schedule B that taught the ‘988 Patent.

[134] Having considered the expert evidence and reviewed and construed the ‘725 Patent, the sole reference relied upon for anticipation, I agree with the Applicants that the ‘725 Patent neither discloses nor enables a POSITA to make, at the relevant date, a sublingually administrated formulation comprising an ordered mixture with of Ac-Di-Sol as a bio/mucoadhesive, or any other bio/mucoadhesive, and therefore neither claim 1 nor any of the dependant claims of the ‘988 Patent are anticipated by the ‘725 Patent.

[135] The use of the dry mixing process to achieve ordered mixtures, essentially free from water, including use of Ac-Di-Sol as a pharmaceutical disintegrant, or “explosive”, is counter-intuitive to the use of Ac-Di-Sol as a bio/adhesive, which is an essential element of the ‘988 Patent claims.

[136] However, in construing the ‘725 Patent in this light, the Applicants face the problem of non-infringement by the Pharmascience product, discussed below.

IX. Obviousness

[137] Obviousness is determined using a four-part analysis: (i) identify the skilled person and the common general knowledge; (ii) identify or construe the inventive concept of the claim at issue; (iii) identify the differences between the state of the art and the inventive concept; and (iv) determine whether, without any knowledge of the alleged invention as claimed, those differences would have been obvious to the skilled person or whether they required any degree of invention (*Sanofi*, at para 67).

[138] Obviousness is a difficult test to meet. It must be shown that the skilled person would have come directly and without difficulty to the invention, and it is important to keep in mind that hindsight analysis is 20-20 (*Uponor AB v Heatlink Group*, 2016 FC 320 at paras 227 to 228 [*Uponor*]; *Sanofi-Aventis Canada Inc v Apotex Inc*, 2009 FC 676 at para 267, aff'd 2011 FCA 300; *Zero Spill Systems (Int'l) Inc v 614248 Alberta Ltd. (cob. Lea-Der Coatings*), 2015 FCA 115 at paras 81 to 83, 84 to 94; *Bridgeview Mfg v 931409 Alberta Ltd*, 2010 FCA 188 at para 51 [*Bridgeview*]).

[139] Simplicity does not negate invention (*Janssen-Ortho Inc v Novopharm*, 2006 FC 1234 at para 113 [*Janssen*], aff'd 2007 FCA 217 [*Janssen FCA*]). From the moment it is established that a technician skilled in the art would not himself have been able to conceive what was conceived it matters not whether it was easy or hard afterwards (*Diversified Products Corp v Tye-Sil Corp* (1991), 35 CPR (3d) 350 at 370 (FCA); *Merck & Co Inc v Apotex Inc*, 2005 FC 755).

[140] The parties generally agreed and I have found that the inventive concept of claim 1 of the '988 Patent is a three-part combination of (i) an ordered mixture of API microparticles and water-soluble carrier particles (ii) incorporated with a bio/mucoadhesive for (iii) sublingual administration. The NOA recognizes a similar inventive concept:

> The apparent "inventive concept" is a combination of an ordered mixture of micronized particles of active including oxazepam and zolpidem on water soluble carrier particles and a bio/mucoadhesive agent for use in a sublingual tablet formulation.

[141] The Applicants submitted that combining the three aspects of the inventive concept—(i) an ordered mixture and (ii) a bio/mucoadhesive promoting agent in (iii) a sublingual dosage form—was counterintuitive.

[142] Moreover, the Applicants argued the fact that Pharmascience's experts required so much prior art to cobble together an obviousness attack speaks only to the ingenuity of the claimed invention. In addition, all but a handful of these documents were provided by counsel. They referred the Court to the decision in *Uponor*, above, which states at paragraph 203 that "[e]xperts are expected to conduct their own prior art searches, and not simply rely on documents provided by counsel." The Applicants' position was that without hindsight, the skilled person in 1998 would not have compiled the prior art list replied upon for obviousness in the NOA.

[143] Finally, the Applicants argued that the NOA and Pharmascience's affiants mentioned only a handful of sublingual drugs from even fewer drug classes, and that prevailing attitudes, in 1998, taught away from the inventive concept of the '988 Patent. The majority of those drugs mentioned also had conventional routes of administration. Dr. Sinko, who practiced for years as a pharmacist, testified that nitroglycerin was one of the few sublingual drugs he had ever dispensed. For his part, Dr. Smart was not aware of any commercially available modern-day drugs that used ordered mixing technology. Therefore, the use of ordered mixing to create formulations for sublingual administration was not known in 1998.

[144] Pharmascience's position was that the inventive concept of the '988 Patent, was known:

i. sublingual formulations with an ordered mixture of a smaller active ingredient on larger soluble carrier particles were known to provide rapid release and there had existed drugs using this formulation method for many years—for example, nitroglycerin tablets;
ii. ordered mixtures were known, and were known to dissolve rapidly and to provide rapid release (the '725 Patent);
iii. ordered mixtures made with water soluble carriers were known (the '725 Patent); and
iv. bio/mucoadhesive materials were known to provide bio/mucoadhesion and could be added to try to limit swallowing.

[145] As such, Pharmascience contended that there was no difference in the inventive concept from the prior art. Further, scaling down the product of the '725 Patent would be routine for the POSITA, enabling him or her to come to the solution taught by the '988 invention.

[146] During cross-examination, Drs. Allen and Sinko admitted that the inventors of the '988 Patent did not invent zolpidem or its use in treating insomnia, ordered mixtures, microparticles of drug adhered to the surface of carrier particles, bioadhesive materials or sublingual formulations.

[147] Moreover, it was admitted by the Applicants' experts that if a POSITA was asked to make a sublingual tablet that would adhere to the mucosa, he or she would have been able to do it at the relevant time. Finally, there was no question that there is nothing inventive in using common excipients in standard amounts for their know uses.

[148] Counsel for Pharmascience argued that the specific combination for the formulation claimed would have been a matter of routine experimentation and that it would have been self-evident that the formulation would work, given the limited number of choices to make the

invention work at the relevant time—even the examples in the ‘988 Patent evidence routine testing.

[149] The real question for the Court is whether the claimed ‘988 formulation, by using a bio/mucoadhesive with other constituent particles, for sublingual administration, though not specifically disclosed in a single document, would have been obvious, in light of the ‘725 Patent, the common general knowledge and other articles relating to use of bio/mucoadhesives.

[150] It is important to remember that obviousness means that while the claimed invention may not have been presumably known, it is nonetheless unpatentable because it is something a POSITA would have been expected to come up with (*Janssen,* above)). Additionally, two of the eight factors of the obviousness analysis considered in the Federal Court of Appeal’s affirmation of the decision in *Janssen* should be kept in mind (*Janssen FCA*, at para 25):

i. the climate in the relevant field at the time of the alleged invention; and
ii. the motivation at the time to solve a recognized problem.

[151] The Applicants relied on Pharmascience’s own expert’s evidence, that of Dr. Smart, who on cross-examination admitted that, in his 2004 review article “Recent Developments in the Use of Bioadhesive Systemps for Delivery of Drugs to the Oral Cavity”, the ‘988 invention was “an unusual approach” and “very different from all the formulations that [he’d] read. So [he] thought it was worth reporting…this was not like everything else [he] was looking at”.

[152] The Applicants highlighted the fact that many documents in the prior art, produced by Pharmascience, taught away from using sublingual administration. Further, the use of

bio/mucoadhesion was directed primarily towards slow release formulations where the entire dosage form would adhere to the mucosa and slowly disintegrate. Therefore, it is evident that the question of whether one could make a rapidly dissolving, sublingual dosage form with a bio/mucoadhesive was not being asked in the field; and the common general knowledge would likely have biased a POSITA away from the invention.

[153] Accordingly, the combination of an ordered mixture, a bio/mucoadhesive promoting agent, in a sublingual dosage form, was counterintuitive.

[154] Given all the evidence presented, I find on a balance of probabilities that the pharmaceutical composition in claim 1 is not obvious and this allegation is not justified. The hindsight analysis of claim 1 the ‘988 formulation encouraged by Pharmascience is not persuasive.

X. Claims Overbroad

[155] A claim is overbroad if it claims more than the invention made or disclosed (*Farbwerke Hoechst Aktiengesellschaft Vormals Meister Lucius & Bruning v Canada (Commissioner of Patents)*, 1965 CarswellNat 34 at para 34 (Exct); *Leithiser v Pengo Hydra-Pull of Canada, Ltd*, [1974] 2 FC 954 at paras 21, 23 to 27 (FCA); *Pfizer Canada Inc v Pharmascience Inc*., 2013 FC 120 at paras 84, 85, 91 to 93).

[156] When determining the extent of the exclusive property and privileged claimed, the entire specification is to be used (*Consolboard Inc v MacMillan Bloedel (Sask) Ltd*, [1981] 1 SCR 504

at 520). Additionally, the claims are to be read in a purposive way, enquiring as to what the inventors had in mind (*Biovail Pharmaceuticals v Canada (Ministry of National Health and Welfare)*, 2005 FC 9 at paras 57 to 59).

[157] The Applicants stated that the POSITA, having read the '988 Patent specification, would read the claims with a mind willing to understand, such that even though claim 1 and the dependent claims do not include the limitations that the '988 formulations:

a. have a bio/mucoadhesive agent positioned on the surface of carrier particles (missing from claim 1), and
b. be essentially free from water,

nevertheless, the claims should not be construed as being overly broad.

[158] However, it is admitted that it is important for the formulations to be free from water so that the composition will have its full bio/mucoadhesive properties and maximum potential for swelling, and that "in order for the pharmaceutical composition to function properly when a bio/mucoadhesion promoting agent is added thereto, this agent must be positioned at the surfaces of the carrier particles". Both of these limitations are discussed the '988 Patent's disclosure.

[159] At page 10, lines 22 to 25, the '988 Patent teaches:

> The ordered mixtures prepared in accordance with the present invention can be incorporated into various kinds of pharmaceutical preparations intended for sub lingual administration. Irrespective of the form given to the preparation, it is important that the preparation is essentially free from water, since its bio/mucoadhesion promoting character results from its practically instantaneous hydration when brought into contact with water or saliva.

[160] Moreover, at page 8 lines 9 to 12, the ‘988 Patent provides:

> In order for the pharmaceutical composition of the invention to function properly when a bio/mucoadhesion promoting agent is added thereto, this agent must be positioned at the surface of the carrier particles … In a preferred embodiment of the invention, a fine particulate quality of the bio/mucoadhesion promoting agent is mixed together with the coarse carrier for a sufficient time to produce an ordered mixture, where the finer particles exist as discrete primary particles adhered to the surfaces of the carrier particles.

[161] Thus, the real question for the Court is whether the claims, by omitting either limitation—“essentially free from water”, or that the “bio/mucoadhesive agent must be positioned at the surface of the carrier products”—renders the claim(s) overly broad and invalid.

[162] The Applicants assert that the claims are not overbroad: the two alleged missing limitations are specific directors in the ‘988 Patent itself and the POSITA would have knowledge of these features when reading each of the claims with a mind willing to understand.

[163] Pharmascience argued that, because there is no explicit limitation on water in any of the claims, the claims would cover formulations with water and excipients containing water, contrary to the specification. They relied upon the admission of Dr. Sinko that the composition of claim 1 of the ‘988 Patent must be essentially free from water and noted that:

i. the patent disclosure states this feature is important;
ii. all the examples are made without the use of water; and
iii. no example provides tablets made [redacted].

[164] The Applicants contended that there are indicators in the patent specification that would enable a POSITA, with a mind willing to understand, to discern that water should be excluded from the process of making the ‘988 formulation.

[165] With regards to the omission of the location of the bio/mucoadhesion promoting agent, given that claim 1 does not contain this limitation, Pharmascience argued that claim 1 is too broad.

[166] However, claims 2 to 22 do contain this limitation, and therefore all these claims, when dependent in claim 2 and any subsequent claim, would not be subject to this attack—only claim 1 and claims dependent on claim 1 alone would be possibly invalid on this basis.

[167] The Applicants argued that, similar to a purposive reading of the claims which would encompass the exclusion of water, a purposive reading would also enable a POSITA to understand that the bio/mucoadhesive excipient must be on the outside of the particle.

[168] I agree that a POSITA, reading claim 1 in light of the specification as a whole, with a mind willing to understand, would know that the formulation would have to be essentially free from water to work. However, because the limitation of the bio/mucoadhesion agent being adhered to the surface of the carrier particles is provided in claims 2 and following, the presumption against redundancy precludes this limitation from being implied into claim 1 (see *Patent Rules*, SOR/96-423, s 87; *Bridgeview* at paras 27; *Eli Lilly* at paras 90, 122). Since this

limitation is an essential feature of the invention and necessary for the invention to work, claim 1 is broader than the invention made or disclosed.

XI. Utility

[169] It is settled law that utility must be assessed on a claim by claim basis: *Astrazeneca Canada Inc v Apotex Inc*, 2015 FC 158 at para 4 [*Astrazeneca 2015*].

[170] The material question is whether the utility of the invention was either demonstrated or soundly predicted based on the information and expertise available by the filing date (*Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77 at para 56; *Teva Canada Ltd v Pfizer Canada Inc*, 2012 SCC 60 at para 39 [*Teva*]). That is, could a POSITA make the invention work through the application of "some basic knowledge or routine testing"? (*Astrazeneca 2015*, above, at para 281).

[171] Additionally, the inventor will only be held to a promise where the patent explicitly and unambiguously promises a specific result (*Sanofi-Aventis v Apotex Inc*, 2013 FCA 186 at paras 48 to 49; *Astrazeneca 2015* at para 4).

[172] Following construction, the question is whether the utility was either demonstrated or soundly predicted by the Canadian filing date, September 24, 1999 (*Teva* at para 39).

[173] Pharmascience argued that, given that bio/mucoadhesion is part of the '988 invention, it is part of the utility and given that the only example in the patent that should demonstrates bio/mucoadhesion (i.e., Example 4), ostensibly fails to do so, the patent is invalid for inutility.

[174] Pharmascience claimed that Example 4 does not demonstrate mucoadhesion/bioadhesion of the claimed formulations, in that it:

a. does not follow the methodology of the journal article it refers to—that is, in the Sala paper, the number of particles were counted to determine how many had adhered;
b. does not use oral cavity conditions and uses the wrong tissue—intestinal rather than oral mucosal tissue (a criticism made by the Applicants' experts when considering the prior art);
c. does not run a control test with identical tablets with and without a bio/mucoadhesive material—instead, the "comparator" tablet has a different formulation from the example tablet;
d. prevents the skilled person from determining whether there is a real difference among the tablets because the exact numbers are not provided—e.g., > 95% fentanyl removed (test not done with zolpidem) and there is no statistical analysis or standard deviation provided;
e. does not exclude alternate explanations for the numbers provided—e.g., the drug and excipients could be binding to each other, or the gel layer of bio/mucoadhesive could be restricting water flow to the active (even if it is not sticking to the tissue sample).

[175] Additionally, to establish utility, Dr. Smart wanted scientific proof: proof that the formulations were better than existing formulations, including comparative date, and statistical analysis (i.e., the kind of data required for regulatory approval but beyond that required to show utility in patents).

[176] The Applicants argued that while bio/mucoadhesion is discussed as part of the means by which the promise of rapid release, absorption, and ultimately rapid relief from the acute disorder of insomnia occurs no particular strength or duration of bio/mucoadhesion is required, nor is any

absolute prevention of swallowing. All that is required is sufficient bio/mucoadhesion to achieve the promised rapid release and absorption.

[177] I agree with the Applicants that the promise is demonstrated and soundly predicted.

[178] The skilled person would understand the promise to be demonstrated by the information presented in Examples 3 and 4. Example 3 presents information about rapid uptake, demonstrating that the invention will result in peak blood concentration of the API within five minutes. Example 4 presents information about the propensity of the formulations to adhere and maintain the API at the absorption site, as compared to a conventional tablet. The formulations taught, in Example 4, had greater than 45% higher retention on the tissue than the control formulation.

[179] Moreover, on cross-examination, Dr. Fassihi agreed that Example 4 showed at least 46% less drug removal. Dr. Smart conceded that many test systems could have been used, and that while separation force experiments are suitable for assessing polymers and would have been preferable to him, that a degree of artificiality is inherent in all such testing. The Sala paper, on which Example 4 is based, describes a method for testing formulations and explains that “already published methods are more suited to evaluate the polymeric material”. Therefore, it is evident that there are multiple methods for assessing bio/mucoadhesion.

[180] Further, I agree with the Applicants that if utility is not actually demonstrated, Examples 3 and 4, taken with the common general knowledge, soundly predict the required utility of the ‘988 invention.

[181] Finally, Drs. Smart and Fassihi said that the claims lack utility because the list of bio/mucoadhesive ingredients in the description includes microcrystalline cellulose, which is not bio/mucoadhesive. The Applicants argued that the claims refer to “bio/mucoadhesive promoting agents” and are limited to compounds that, in fact, promote bio/mucoadhesion. While including microcrystalline cellulose is an error in the description, the POSITA would on a purposive construction and with a mind willing to understand, given the common general knowledge at the relevant time, know to disregard this one ingredient.

[182] Therefore, I find that the inutility attack is not justified.

XII. Infringement

[183] As stated above, the onus is on the Applicants to prove infringement of the ‘988 Patent.

[184] It is settled law that “a patent owner has a remedy against an alleged infringer who does not take the letter of the invention but nevertheless appropriates its substance” (*Free World Trust*, above, at para 28). However, it is equally settled that the Court must be careful not to construe the claims of a patent so broadly such that it confers onto the patentee the benefit of inventions not in fact made. In *Free World Trust*, at paragraph 30, Mr. Justice Binnie enumerated

six propositions that must be considered ensure that a fair and predictable result is achieved while construing claims to determine whether there is infringement:

1. The *Patent Act* promotes adherence to the language of the claims.
2. Adherence to the language of the claims in turn promotes both fairness and predictability.
3. The claim language must, however, be read in an informed and purposive way.
4. The language of the claims thus construed defines the monopoly. There is no recourse to such vague notions as the "spirit of the invention" to expand it further.
5. The claim language will, on a purposive construction, show that some elements of the claimed invention are essential while others are non-essential. The identification of elements as essential or non-essential is made:
    a. on the basis of the common knowledge of the worker skilled in the art to which the patent relates;
    b. as of the date the patent is published;
    c. having regard to whether or not it was obvious to the skilled reader at the time the patent was published that a variant of a particular element would *not* make a difference to the way in which the invention works; or
    d. according to the intent of the inventor, expressed or inferred from the claims, that a particular element is essential irrespective of its practical effect;
    e. without, however, resort to extrinsic evidence of the inventor's intention.
6. There is no infringement if an essential element is different or omitted. There may still be infringement, however, if non-essential elements are substituted or omitted.

[185] The interpretive task of the Court, therefore, is to purposively construe the claims of a patent to define the scope of the patent holder's monopoly, and then determine whether the allegedly infringing product falls within the scope of those claims (*Mobil Oil Corp v Hercules Canada Inc* (1995), 63 CPR (3d) 473 at 489; *Free World Trust* at paras 48 to 49).

[186] The Applicants argued that claims 1 to 10 and 13 to 22 of the '988 Patent are infringed by the Pharmascience product. It was their position that the PMS-Zolpidem product is:

a. a pharmaceutical composition for treating insomnia by sublingual administration;
b. containing API zolpidem [redacted];
c. [redacted];
d. [redacted];
    a. [redacted];
    b. [redacted].

[187] It was Pharmascience's position that the PMS-Zolpidem formulation has neither an ordered mixture nor a bio/mucoadhesive component, and therefore does not infringe the '988 Patent.

[188] The Applicants admitted that the Pharmascience PMS-Zolpidem formulation is made by [redacted] which is distinct from the common methods of making an ordered mixture.

[189] During the hearing, I questioned the parties on the degree of ordered mixture that would be necessary to meet the limitation of the claims in issue. The expert evidence was inconclusive and vague, at best, on the point.

[190] [Redacted] lacked sufficient specificity, controls and reference data to be probative or reliable.

[191] The inability of the Applicants' experts to reasonably construe "ordered mixture" was also not helpful.

[192] However, the evidence does support the view that [redacted] let alone a mixture with any substantial ordered mixture. That is, there was no convincing evidence adduced showing that [redacted] any degree of ordered mixture.

[193] I agree with Pharmascience that there is no article or patent relied upon in the NOA or in the expert affidavits of the Applicants that shows an ordered mixture resulting [redacted].

[194] Moreover, as I alluded to above with respect to my finding on no anticipation in view of the '725 Patent, I also find that the PMS-Zolpidem formulation [redacted]. There is no evidence that [redacted] in the PMS-Zolpidem formulation does anything other than what the Handbook of Pharmaceutical Excipients and journal articles relied on by the experts say it does—[redacted].

[195] Therefore, Pharmascience's allegation of non-infringement is justified.

XIII. The Gillette Defence

[196] Given my finding of no justification for the Applicants' allegation of infringement, I need not consider the alleged Gillette defence.

XIV. Conclusion

[197] In conclusion, the affidavits of Drs. Fassihi and Davé are not struck, and the evidence in Schedule A is not improper. Pharmascience's allegations of anticipation, obviousness, and inutility are not justified. The allegation of overbreadth is justified only for claim 1, and otherwise the allegation is not justified. Pharmascience's allegation of non-infringement is justified.

[198] Therefore, the application is dismissed.

XV. Costs

[199] Costs will follow the event, and are to be assessed at the middle of Column IV of Tariff B. Pharmascience is also entitled to be paid its reasonable disbursements, and applicable taxes. If the parties are unable to agree on costs, the parties may make submissions to the Court within two weeks of the date of this judgment.

JUDGMENT

THIS COURT's JUDGMENT that

1. This application in respect of Canadian Patent 2,629,988 is dismissed;
2. The affidavits of Drs. Fassihi and Davé are not struck;
3. The Schedule A evidence is not improper;
4. Pharmascience's allegations of anticipation, obviousness, and inutility are not justified;
5. Pharmascience's allegation that claim 1 is overbroad is justified;
6. Pharmascience's allegation that claims 2 to 22 are overbroad is not justified;
7. Pharmascience's allegation of non-infringement is justified;
8. Pharmascience shall have their costs of the application, assessed at the middle of Column IV of Tariff B. If the parties cannot agree on a costs disposition, concise written cost submissions, not exceeding 5 pages in length, shall be submitted no later than 14 days of the date of this Judgment.
9. The protective order of Madam Prothonotary Martha Milczynski, dated March 31, 2015, is continued. If the Minister of Health issues an NOC to Pharmascience for PMS-Zolpidem, Pharmascience shall advise the Court within 48 hours of the issuance of the NOC to facilitate amendment to the Public Judgment and Reasons by removing redactions dealing with the contents of PMS-Zolpidem.

"Michael D. Manson"

Judge

Schedule "A" – Ambush Evidence

Table 1: Evidence Concerning Documents Not Described in the NOA

Ambush Document	Fassihi Affidavit	Davé Affidavit	Smart Affidavit
Hersey, 1974 (NOA #6)	134-36	44-45	108
Ampolsuk, 1974 (NOA #7)	-	46	-
Ishida, 1981 (NOA #27)	181	-	117
Ishida, 1982 (NOA #32)	181	-	117
US 163 (NOA#28)	186-87	-	-
US 314 (NOA #29)	169-71, 203	-	-
US 198 (NOA #37)	169-71, 203	-	-
Egermann, 1983 (NOA#35)	150-51	-	-
EP 944 (NOA #38)	95(b)	-	-
Smart, 1984 (NOA #43)	184-85	-	120
US 365 (NOA #71)	190-93	-	63, 127
US 386 (NOA #74)	-	-	128-29
US 616 (NOA #75)	-	-	130
Sala, 1989 (NOA #82)	74 (sentences 6-11)	-	-
US 142 (NOA # 87)	-	-	133
US 093 (NOA #91)	-	-	135-37
US 092 (NOA #92)	-	-	135-37
CA 277 (NOA #94)	-	-	135-37
CA 471 (NOA #101)	-	-	141
US 910 (NOA #103)	-	-	143-45
Lehr, 1992 (NOA #105)	-	-	143-45
Westerberg, 1993 (NOA #121)	-	69-75	-
Bolhuis, 1997 (NOA #156)	-	69-75	-
US 498 (NOA #135)	-	-	149-50
US 086 (NOA #136)	-	-	149-50
Mort, 1995 (NOA #140)	-	-	152
US 861 (NOA #150)	-	-	155
WO 067 (NOA #159)	-	-	159
AU 373 (NOA #176)	-	-	163-65
WO 213 (NOA #180)	-	-	163-65
US 541 (NOA #181)	-	-	163-65

Table 2: Impugned Propositions

NOA Description	Davé Affidavit	Smart Affidavit
Bryan, 1979 (NOA #17) 134. This publication describes the preparation of ordered mixtures from the drug sodium salicylate in micronized form and starch-lactose granules as carrier material having a particle size fraction of 400-700 This publication describes the preparation of ordered mixtures from the drug sodium salicylate in micronized form and starch-lactose granules as carrier material having a particle size fraction of 400-700 μm. 135. This article is another example of a disclosure of ordered mixtures of micronized drug applied to a soluble carrier of less than 750 microns.	51. This article investigated the effect of drug concentration on ordered mixing. The authors found that 1% sodium salicylate produced a satisfactory mix but that mixing profiles for 5% and 10% sodium salicylate revealed large coefficients of variation. The 5% and 10% amounts exceeded the saturation concentration . At the 10% mixture, the excess sodium salicylate was present as aggregates. 52. The authors conclude that the selection of drug concentration is an important consideration in achieving homogeneity in ordered mixing of drugs and direct compression vehicles of particular particle size distributions.	112. From this article, the POSITA would learn that demixing can occur in random powder mixes, but less so in ordered mixes. In the case of ordered mixtures, however if too much of the fine powder is added to saturate the surface binding sites of the carrier, this effect may be lost.
EP 243 (NOA #54) 293. This patent application is directed to an analgesic composition in parenteral or sublingual dosage form comprising an active dose of buprenorphinc and an amount of naloxone (p. 5). 294. Compositions in the form of sublingual tablets are described to contain soluble excipients or mixtures thereof, granulating and disintegrating agents such as starch. Binding agents such as povidone or hydroxypropyl-methyl cellulose and lubricating agents such as magnesium stearate (p. 8). 295. The sublingual tablets of Example 4 of the patent application are described as having been produced by screening all material (active, mannitol, maize starch and povidone) with the exception of the magnesium stearate through a 750 μm sieve and blending together followed by aqueous granulation. The resulting granules are described to be forced through a 750 μm sieve and blended with magnesium		124. This patent application would teach the POSITA that rapid blood levels could be achieved for appropriate drugs via the sublingual route using a rapidly dissolving formulation with water soluble excipients…

stearate (pre-sieved through a 500 µm sieve) and compressed intotablets (p. 10). 296. This patent application discloses a sublingual tablet composition which contains the bioadhesivc agent HPMC and a water soluble cxcipient namely mannitol.		
Miyazaki, 1994 (NOA #128) 473. This publication describes an investigation of the use of sodium alginate and chitosan as bioadhesive excipients for preparation of oral mucosal adhesive dosage forms. The authors note that one of the properties of alginate is its ability to cause significant bioadhesion with the mucosal membrane. Tablets containing the drug ketoprofen and varying ratios of sodium alginate and chitosan (4:1, 1:1 and 1:4) were prepared by compressing the dry powder mixture. The bioadhesive properties of the tablets were examined in-vitro by measuring the force of adhesion to rat peritoneal membrane and it was found that the bioadhesive properties increased with increasing sodium alginate content, demonstrating the strong bioadhesive properties of alginate. The effect of the sodium alginate content on the rate of drug release from tablets was determined by measuring dissolution according to the Japanese Pharmacopoeia (XII) dissolution test. 474. The dissolution data reported demonstrates that the rate increased with increasing sodium alginate content. The authors concluded that "the hydrophilic polymer sodium alginate, present throughout the tablet, rapidly hydrates, swells, and dissolves, allowing the drug to be rapidly released." 475. The in-vivo properties of the tablets were investigated by inserting a tablet into the sublingual site of rabbits and measuring plasma		148 …Chitosan is polyglucosamine with a positive charge and alginate has a negative charge so the two will interact and form complexes with each other, which will reduce their bioadhesive properties…

concentrations of ketoprofen. The dosage form was reported to have adhered tightly to the mucosa and swelled gradually to a gellike state. The plasma concentration profiles showed rapid absorption and a greater AUC with increasing sodium alginate content of tablets. 476. This article discloses the use of the bio/mucoadhesion agent sodium alginate which both adheres to the mucosa and results in swelling and dissolution allowing for rapid release.		

FEDERAL COURT

SOLICITORS OF RECORD

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