

2012 WL 8667473 (D.N.J.) (Expert Report and Affidavit)
United States District Court, D. New Jersey.

INSITE VISION INCORPORATED, Inspire Pharmaceuticals, Inc. Pfizer Inc., Plaintiffs,
v.
SANDOZ INC., Sandoz GmbH, Sandoz Industrial Products S.A., Defendants.

No. 11-cv-03080-MLC-LHG.
April 12, 2012.

Declaration of Uday B. Kompella, Ph.D. in Support of Plaintiffs' Proposed Claim Constructions

Case Type: Intellectual Property >> Patent

Jurisdiction: D.N.J.

Name of Expert: Uday D. Kompella, Ph.D.

Area of Expertise: Health Care-Physicians & Health Professionals >>Pharmacist/Pharmacologist

Representing: Plaintiff

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I, Uday B. Kompella, declare as follows:

I. EXPERIENCE AND QUALIFICATIONS

1. I received my Ph.D. in 1994 from the University of Southern California, Los Angeles in the area of pharmaceutical sciences. I am currently a professor of pharmaceutics, ophthalmology, and bioengineering at University of Colorado Denver.
2. I have extensive experience in ophthalmic pharmaceutical formulation development, including ocular drug delivery.
3. My research includes the study of ocular drug delivery and the development of ophthalmic dosage forms, including sustained release formulations. I have directed the research of many graduate students, postdoctoral fellows, and technicians in the study of ocular drug delivery. I have co-edited three books on drug product development, one of which was specific to ophthalmic drugs. I have also been published in more than 130 scientific papers and presented over 150 abstracts at scientific meetings, and in many instances my publications and abstracts address ophthalmic drug formulations. I have also extensively lectured on drug delivery, including drug delivery to the eye.
4. I am Editor-in-Chief of Expert Opinion on Drug Delivery. I was an editor of Clinical Research and Regulatory Affairs from 2004 to 2008. I have been an editor of Pharmaceutical Research since 2004. I also currently serve on the editorial board of the following publications: International Journal of Pharmaceutical Sciences and Nanotechnology; Drug Delivery Technology; Journal of Ocular Pharmacology and Therapeutics; and Journal of Ocular Biology, Diseases and Informatics.
5. I have received many honors and awards, specifically in ophthalmology, in recent years, such as the 2012 ARVO/AFER/Pfizer/Carl Camras Translational Research Award in Ophthalmology; Keynote lecturer at Thadikonda Pharmaceutical Sciences Symposium, LV Prasad Eye Institute (LVPEI) in 2011; FARVO Designation, Silver Fellow, Association for Research in Vision and Ophthalmology in 2010; Keynote lecture, ASIA-ARVO, Association for Research in Vision and Ophthalmology in 2009; and an innovation award in recognition of successful commercialization of functionalized particles to treat eye disorders from the University of Nebraska Medical Center in 2008.
6. I am a member of the American Association of Pharmaceutical Scientists and the Association for Research in Vision and Ophthalmology and have held several elected offices in both professional associations. From 2009 to 2012, I was a Physiology and Pharmacology section Representative on the Annual Meeting Program Committee for the Association for Research in Vision and Ophthalmology. From 2003 to 2004, I was the Chair of the Regulatory Sciences Section of the American Association of Pharmaceutical Scientists. From 2001 to 2003, I was the Chair of the Ocular Drug Delivery and Disposition Focus Group of the American Association of Pharmaceutical Scientists.
7. I have served on the scientific advisory boards at Appian Laboratories and PCAsso Diagnostics since 2008. I have served on the scientific advisory board at The Glaucoma Foundation since 2009. I have also served on the Combination Products Advisory Committee at Vistakon (A Johnson & Johnson Co.) since 2009. From 2008-2010, I served on the scientific advisory board at Visionary Therapeutics Corporation.
8. My curriculum vitae, including a list of my publications, is attached as Exhibit A. I am being compensated for my work at my customary rate of \$650 per hour, in addition to being reimbursed for expenses. My compensation is not dependent upon the opinions rendered or the outcome of this litigation.

II. MATERIALS REVIEWED

9. I have been informed by Plaintiffs' counsel that the Plaintiffs InSite Vision Inc., Inspire Pharmaceuticals, Inc., and Pfizer Inc. (collectively "Plaintiffs") have sued Sandoz Inc., Sandoz GmbH, and Sandoz Industrial Products S.A. (collectively "Sandoz") for infringement of U.S. Patent Nos. 6,861,411 ("the '411 patent"), 6,159,458 ("the '458 patent"), 6,239,113 ("the '113 patent"), 6,569,443 ("the '443 patent"), and 7,056,893 ("the '893 patent") (collectively "the patents-in-suit").

10. In connection with this suit, I have been asked by Plaintiffs' counsel to comment on the meaning of the following terms from the patents-in-suit, which were identified by the parties for claim construction. These claims and phrases are as follows: "administered once daily," "one or two doses per day," "ophthalmic composition," and "ophthalmic medicament."

11. In connection with my declaration, I have reviewed the '411 patent, the '443 patent, the '893 patent, and the '458 patent, the Joint Claim Construction and Prehearing Statement, submitted to the court on February 27, 2012 ("Joint Statement"), and the references in Exhibit B of this declaration.

12. The opinions set forth below are based on the education, knowledge, and experience that I have acquired over the past 20 years in practicing, teaching, and consulting in the field of pharmaceutical sciences and ophthalmology, as well as information available to me as of the date of this declaration.

III. THE PERSON OF ORDINARY SKILL IN THE ART

13. I understand that the terms and phrases in patent claims must be interpreted as they would have been understood by a person having ordinary skill in the art ("POSA") to which the invention related at the time of the invention.

14. A person of ordinary skill with respect to the '411 patent, the '443 patent, the '893 patent, and the '458 patent is a person having a PharmD or bachelor's degree in pharmacy, pharmaceutical sciences, or related disciplines. This person would also have about three years of formulation experience.

15. This declaration sets forth my opinions as to how a person of ordinary skill in the art would have understood the above-identified terms and phrases. This declaration also provides my opinions on Sandoz's proposed construction as reflected in the Joint Statement. I reserve the right to rebut any expert opinion or argument offered by Sandoz in support of its proposed claim constructions. I also reserve the right to modify or expand my opinions based on information not currently available to me.

IV. ANALYSIS OF CLAIM TERMS RELATING TO DOSING REGIMENS

16. Due to the nature of bacterial infections, a physician needs dosing flexibility of the antibiotic in order to provide the patient with effective therapeutic drug concentrations. Antibiotics are routinely administered in a regimen that requires more doses on one day than on subsequent days. For example, ophthalmic antibiotics are commonly administered more frequently on day one than subsequent days.

17. Examples of topical ophthalmic antibiotics that were known to be dosed at a higher initial frequency followed by lower frequency include tobramycin, ofloxacin, and ciprofloxacin.

A. "administered once daily"

18. I have been asked to examine the term "administered once daily" in claim 3 of the '411 patent.

19. Claim 3, which depends from claim 1, claims a method of treatment "comprising" a composition that is "administered once daily." In the context of the claims and knowledge in the art, a person of ordinary skill in the art would understand that the "administered once daily" claim term means that the dosing regimen includes, but is not limited to once daily dosing.

20. In the art, dosing regimens are not limited to fixed dosing regimens for the entire duration of treatment. Taking into consideration how antibiotics are administered, *see supra* ¶¶ 16-17, a person of ordinary skill in the art would understand that

the dosing of antibiotics could include days on which the antibiotic is administered once and days on which the antibiotic is administered more than once.

21. It is my understanding that Sandoz's construction of "administered once daily" is "administered only once per day for the entire duration of treatment." However, the claim language does not include limiting words of "for the entire duration of treatment."

22. The specification of the '411 patent states, "In a preferred embodiment, the concentration of azithromycin in the vehicle is such that a single dose (approx. 5 mg per eye) of said composition administered once daily for five days remedies the infection." '411 patent, col. 1, 11. 58-62. A person of ordinary skill in the art would understand this description to be one type of dosing regimen that is preferred, but not the exclusive dosing regimen that could be used.

B. "one or two doses per day"

23. I have been asked to examine the term "one or two doses per day" in claim 40 of the '893 patent.

24. Claim 40 claims, "The method of treating a patient of claim 23, wherein said administering is one or two doses of said composition per day for at least six days." A person of ordinary skill in the art would understand "one or two doses per day" to mean "one or two doses per day."

25. A person of ordinary skill in the art, who would be knowledgeable about how antibiotics are administered and formulated, *see supra* ¶¶ 16-17, would understand that this claim term means that on some days of the treatment regimen, one dose is administered and on other days, two doses are administered. There are examples of antibiotics that are initially administered with more doses than on subsequent days.

26. It is my understanding that Sandoz's construction of "one or two doses per day" is "either one dose per day for the entire duration of treatment or two doses per day for the entire duration of treatment." However, the language of the claims does not limit the regimens of the invention to just those two possibilities.

27. Additionally, nowhere in the specification is the dosing regimen of the invention limited to once a day for the entire period of treatment or twice a day for the entire period of treatment.

V. ANALYSIS OF OPHTHALMIC CLAIM TERMS

A. "ophthalmic composition"

28. I have been asked to examine the term "ophthalmic composition" in claim 1 of the '458 patent, claims 16 and 44 of the '443 patent, and claim 2 of the '893 patent.

29. A person of ordinary skill in the art would understand that an "ophthalmic composition" in the context of the '458, '443, and '893 patents is a composition that is instilled in the eye, as contrasted with, for example, an oral composition, which is for oral ingestion.

30. The chapter on Ophthalmic Formulations in the 18th Edition of Remington's Pharmaceutical Sciences (a reference commonly used by drug formulators) states that "[o]phthalmic preparations are sterile products essentially free from foreign particles, suitably compounded and packaged for instillation into the eye." Remington's Pharmaceutical Sciences, 1581, 1581-1595 (18th Ed. 1990) (Exhibit C).

31. The '458 patent specification states that the invention of this patent is “easily administered in liquid drop form to the eye” by “topically applying” the formulations to the eye. '458 patent, col. 2, 11. 1-16.

32. Throughout the specification of the '443 patent, the composition that is the subject of the invention is described as being instilled into the eye. *See, e.g.*, '443 patent, col. 5, 11. 49-54; col. 2, 11. 37-40; col. 4, 11. 14-29. The '443 patent also cites the '458 patent, which consistently defines “ophthalmic composition.” *See supra* ¶ 31.

33. The '893 patent also describes “ophthalmic composition” as compositions that are instilled in the eye. *See e.g.*, '893 patent, col. 3, 11. 6-20.

34. I understand that Sandoz's interpretation of “ophthalmic composition” is “composition of or relating to the eye.” It is my understanding that Sandoz relies on the Webster's II New Riverside University Dictionary definition of “ophthalmic.” (Exhibit D). A person of ordinary skill in the art would look to the context of the specifications to understand that “ophthalmic composition” means “a composition instilled into the eye.”

B. “ophthalmic medicament”

35. I have been asked to examine the term “ophthalmic medicament” in claim 1 of the '458 patent.

36. For similar reasons that a person of ordinary skill in the art would understand that an “ophthalmic composition”, in the context of the '458 patent, requires “instillation in the eye,” a person of ordinary skill in the art would understand that “ophthalmic medicament,” described in the '458 patent, is intended for “instillation in the eye.” *See supra* ¶¶ 28-34.

37. In fact, the objects of the '458 patent invention are described as “a novel ophthalmic composition that has a low viscosity and is easily administered in liquid drop form to the eye,” and “a novel method for treating diseases by topically applying to eyes a novel ophthalmic composition that exhibits sustained release of a medicament.” '458 patent, col. 2, 1-3; 12-15.

38. “Medicament” is defined in the specification of the '458 patent as “any substance or drug that is useful in treating or ameliorating a disease or medical condition,” which is consistent with what a person of ordinary skill in the art would understand this term to mean. *See* '458 patent, col. 3, 11. 3-5.

39. Consequently, a person of ordinary skill in the art would understand “ophthalmic medicament,” as it appears in claim 1 of the '458 patent, to mean “any substance or drug that is useful in treating a disease or medical condition that is instilled into the eye.”

40. A person of ordinary skill in the art would find that this definition is consistent with the specification of the '458 patent, which states, “A medicament means any substance or drug that is useful in treating or ameliorating a disease or medical condition. The disease or medical condition can be in the eye or its surrounding tissue, but is not limited thereto; i.e. treating a condition remote from the eye *via topical administration on the eye.*” *See* '458 patent, col. 3, 11. 3-8 (emphasis added).

41. It is my understanding that Sandoz's proposed meaning for “ophthalmic medicament” is “any substance or drug that is useful in treating a disease or medical condition, which can be in the eye or its surrounding tissue or can be remote from the eye.” Sandoz's interpretation ignores the rest of the sentence in the '458 patent which makes clear that an “ophthalmic medicament” would be instilled in the eye (“via topical administration on the eye”). *See supra* ¶ 40.