

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Applicant: | Ashley, Robert | Examiner: | Susan Tran |
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| For: | Methods of Treating Acne | | |

Commissioner for Patents
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Declaration under 37 C.F.R. §1.132

Sir:

1. I, Vasant Manna, am a Senior Medical Advisor / Project Leader at Galderma R&D Inc., the assignee of the instant application. I am a medical doctor with a specialty in dermatology. My curriculum vitae is attached.
2. I am familiar with the prosecution history of the instant application. I have reviewed the following references cited in the application: US 6,365,623 (“*Perricone*”) and US 6,455,583 (“*Pflugfelder*”).
3. Meibomian glands are sebaceous glands that are located on the rim of the eyelids. These glands are responsible for the supply to the eye of sebum, an oily substance that, *inter alia*, prevents evaporation of the eye's tear film.
4. Meibomian glands do not appear anywhere in the body except on the rim of the eyelids, and have no function outside of the eye. Meibomian glands are anatomically and functionally organs of the eye.

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| Dr. Reddy's Laboratories, Ltd., et al. v. Galderma Laboratories, Inc. IPR2015- |
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5. Meibomian gland disease (MGD) involves dysfunction of the meibomian gland. Such dysfunction can lead to inflammation of the meibomian glands (meibomianitis) and excess oil in the tear film

6. Meibomian gland disease frequently presents with at least one of the following symptoms: dry eye; burning, itching and stickiness of the eye; foreign body sensation in the eye; eye watering; photophobia; and intermittent blurred vision. All these symptoms are unique to the eye.

7. Since MGD is a disease of the eye, a patient presenting with the symptoms of MGD should be referred to a physician specializing in ocular disorders, such as an ophthalmologist.

8. *Pflugfelder* discloses the use of tetracyclines to treat MGD. Since MGD is an ailment that solely affects the eye, a skilled artisan would understand *Pflugfelder* as disclosing the use of tetracyclines to treat the eye.

9. Patients sometimes present with both symptoms of rosacea and symptoms of MGD. However, MGD is a condition which is distinct from rosacea. MGD is not rosacea.

10. In the paragraph bridging columns 3 and 4 of *Pflugfelder*, it is stated that the activity of gelatinase B "... is markedly increased in the tear fluid of patients with meibomian gland disease associated with rosacea," and that the "... activity of gelatinase B appears to be inversely correlated with tear clearance." From this description of tear composition and clearance, a skilled artisan would understand that, in this case, MGD happened to appear with ocular rosacea.

11. At col. 4, lines 17-21, *Pflugfelder* discusses treating MGD "associated with rosacea" by topical administration of a tetracycline analogue in an ointment or in solution (e.g., "eye drops"). From this description, a skilled artisan would recognize that *Pflugfelder* discloses a topical treatment of the eye for ocular symptoms.

12. At col. 8, beginning at line 55, of *Pflugfelder*, the treatment of eleven patients with MGD associated with rosacea is described. The treatment included "... topical administration to the ocular surface or the eyelids" of oxytetracycline. A skilled artisan would understand that treatment of MGD by topical administration "to the ocular surface or the eyelids" means treating the eye.

13. A skilled artisan would clearly understand, therefore, that the rosacea with which *Pflugfelder* reports MGD is somehow "associated" is ocular rosacea. There is no suggestion in *Pflugfelder* of treating the skin.

14. Facial rosacea is a disease of the skin. A patient presenting with the symptoms of facial rosacea, such as, for example, the papules and pustules of rosacea, should be referred to a dermatologist.

15. A skilled artisan reading *Perricone* would understand that *Perricone* discloses treating acne with an antibiotic amount of tetracycline. That the amount of tetracycline must be antibiotic is readily apparent for several reasons.

16. First, at col. 8, lines 27-32, of *Perricone*, the following is stated: "Lipoic acid may be added to an antibiotic preparation, or applied before, during, or after antibiotic treatment..." Thus, *Perricone* is clearly prescribing an antibiotic treatment.

17. Second, *Perricone* groups tetracycline together with clindamycin and erythromycin. Clindamycin and erythromycin do not have anti-inflammatory properties. The property that these three compounds have in common is that they are all antibiotic. Thus, it is apparent that such antibiotic property is what *Perricone* teaches is required for his treatment.

18. Third, at the time *Perricone* was filed, i.e., December 1999, as well as the priority date of the instant application, i.e., September 26, 2001, acne was thought to be caused by bacteria, *P. acnes*. Thus, a skilled artisan would have understood from *Perricone* that an antibiotic preparation was required for the treatment of acne.

19. At a certain threshold dose and above, tetracycline exhibits antibiotic properties. Depending on various factors, including the severity of an ailment, a physician may prescribe tetracycline at a dose that is well above the antibiotic threshold dose, at a minimum antibiotic dose, or at a dose somewhere in between such doses. As the dosage is increased, adverse effects increase. Nonetheless, above the threshold dose, treatment with tetracycline will be an antibiotic treatment.

20. Although a skilled artisan may have believed that a sub-antibiotic dose of tetracycline may lead to fewer side effects, the skilled artisan would have no reason to believe that such sub-antibiotic dose would be effective in the method of *Perricone*.

21. Before the present invention, a dermatologist would not have prescribed a 40 mg dose of doxycycline to treat acne or to treat rosacea.

22. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. Further that these statements were made with the knowledge that willfully false statements and the like so made are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code, and that such willfully false statements may jeopardize the validity of the application of any patent issued thereon.

Respectfully submitted,



Vasant Manna

Dated: 22nd Feb 2013