

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

**PADAGIS ISRAEL PHARMACEUTICALS LIMITED;
PADAGIS US LLC; AND PADAGIS, LLC**
Petitioners,

v.

BAUSCH HEALTH US, LLC
Patent Owner.

IPR2023-01114
Patent No. 11,311,482

**DECLARATION OF DR. ROBERT SCHWARTZ
IN SUPPORT OF PETITION FOR *INTER PARTES* REVIEW OF
U.S. PATENT NO. 11,311,482**

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1003	Declaration of Dr. Robert Schwartz
1004	Curriculum Vitae of Dr. Robert Schwartz
1005	Declaration of Dr. Narasimha Murthy
1006	Curriculum Vitae of Dr. Narasimha Murthy
1007	International Patent Publication WO 2016/205001 (“ WO ’001 ”)
1008	Topical Tazarotene in Acne Vulgaris: Treatment Approaches, CUTIS 2004;74 (suppl 4): 16-21 (“ Anderson ”)
1009	Kircik, L., Tretinoin Microsphere Gel Pump 0.04% Versus Tazarotene Cream 0.05% in the Treatment of Mild-to-Moderate Facial Acne Vulgaris, J. of Drugs in Dermatology, 2009;8(7): 650-654 (“ Kircik ”)
1010	Chim, C., Acne Vulgaris, ACSAP 2016 Book 2, pp. 7 – 22 (“ Chim ”)
1011	Shalita et al., Tazarotene Gel is Safe and Effective in the Treatment of Acne Vulgaris, CUTIS, 1999;63(6): 349-354 (“ Shalita ”)
1012	U.S. Patent Pub. No. US 2012/0129824 (“ ’824 publication ”)
1013	Prescribing Information for Tazorac® Cream (December 2013) (“ Tazorac® Label ”)
1014	ClinicalTrials.gov, “A Phase 2 Dosing Ranging, Evaluator-Blinded Study to Evaluate the Safety of Topical IDP-118” (“ IDP-118 Study ”)

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1015	IQVIA Sales Data For 0.05% Tazarotene For The Indication Of Acne Vulgaris, February 2017-January 2018 (“ IQVIA ”)
1016	Declaration of James Booydegraaf
1017	Prescribing Information for FABIOR® Foam (May 2012) (“ Fabior® Label ”)
1018	Eichenfield et al., Evidence-Based Recommendations for the Diagnosis and Treatment of Pediatric Acne, Pediatrics 2013;131(Suppl. 3): S163 – S186 (“ Eichenfield ”)
1019	Zaenglein et al., Guidelines of care for the management of acne vulgaris, J. Am. Acad. Dermatol. 2016;74(5): 945-973 (“ Zaenglein ”)
1020	Gregoriou et al., Use of tazarotene foam for the treatment of acne vulgaris, Clinical, Cosmetic and Investigational Dermatology 2014;7 165–170 (“ Gregoriou ”)
1021	Kober, M-M. et al., Acneiform Eruptions in Dermatology: A Differential Diagnosis, 19-25 (2014) (“ Kober ”)
1022	Dosik et al., Cumulative Irritation Potential of Adapalene 0.1% Cream and Gel Compared With Tazarotene Cream 0.05% and 0.1%, CUTIS 2005;75 289-293 (“ Dosik ”)
1023	Patel et al., Novel microemulsion-based gel formulation of tazarotene for therapy of acne, Pharm. Dev. Technol, 2016;21(8): 921-932 (“ Patel ”)
1024	U.S. Pat. Appl. Pub. No. US 2012/0328670 (“ ’670 publication ”)
1025	Kircik, L., Importance of Vehicles in Acne Therapy, J. of Drugs in Dermatology, 201;10(6): s18-s23 (“ Kircik 2011 ”)
1026	Bausch Health Companies, Inc. Duobrii® Citizen Petition (May 28, 2021)

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1027	Arazlo Webpage, <i>available at</i> https://www.arazlo.com/hcp
1028	Arazlo Vehicle Webpage, <i>available at</i> https://www.arazlo.com/hcp/vehicle
1029	Prosecution History of U.S. Pat. App. No. 16/179,576
1030	'482 patent and '576 application claim comparison chart
1031	Singh et al., Dosage Forms: Non-Parenteral in Encyclopedia of Pharmaceutical Technology, 2002 (“ Singh ”)
1032	U.S. Patent Pub. No. 2012/0328670 (“ Donello ”)
1033	<i>Bausch Health Ireland Ltd. v. Padagis Israel Pharms. Ltd.</i> , Case No. 2:20-cv-05426, Testimony of Dr. Radhakrishnan Pillai (Oct. 4, 2022) (“ Pillai Trial Testimony ”)
1034	Prescribing Information for DIFFERIN® Lotion (April 2013) (“ Differin® Label ”)
1035	Tegeli et al., Pemulen as a Versatile Emulsifier, International Journal of Drug Formulation & Research, 2011;2(1): 52-63 (“ Tegeli ”)
1036	Federal Court Management Statistics, U.S. District Courts (March 31, 2023)
1037	NDA 20600 Tazorac 0.05% and 0.01% Medical Review Part 3 (May 17, 1996) <i>available at</i> https://www.accessdata.fda.gov/drugsatfda_docs/nda/97/20600_TAZORAC%200.05%25%20AND%200.1%25_MEDR_P3.PDF
1038	National Medical and Treatment Audit Diagnosis Allocation Fact Sheet, <i>available at</i> https://www.iqvia.com/-/media/iqvia/pdfs/us/fact-sheet/national-medical-and-treatment-audit-diagnosis-allocation.pdf (“ NMTA Fact Sheet ”)

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1039	Eastman et al., Assessing Attributes of Topical Vehicles for the Treatment of Acne, Atopic Dermatitis, and Plaque Psoriasis, CUTIS 2014; 94: 46-53. (“ Eastman ”)
1040	Russell, J., Topical Therapy for Acne, Am Fam Physician 2000; 61(2):357-365. (“ Russell ”)
1041	Draelos, Z., Therapeutic Moisturizers, Dermatologic Aspects of Cosmetics 2000;18(4): 597-607. (“ Draelos ”)
1042	Rawlings, A.V. & Lombard, K. J., A review on the extensive skin benefits of mineral oil, International Journal of Cosmetic Science, 2012;34: 511-518. (“ Rawlings ”)
1043	Lubrizol, Pharmaceutical Bulletin No. 8, Emulsification Properties, October 29, 2008. (“ Bulletin ”)
1044	Ismail et al., Subchronic and Chronic Toxicity of Tazarotene Gel Following Topical Administration in Hanford Miniswine, 16 Int’l. J. Tox. 571 (1997). (“ Ismail ”)
1045	Gennaro, A. (1990). Remington’s Pharmaceutical Sciences (18th ed., pp. 257-309). Mack Publishing Company. (“ Remington’s ”)
1046	Fiume et al., Int. J. Toxicol. 2012 Jul-Aug (“ Fiume ”)
1047	Prosecution History of U.S. Pat. App. No. 17/366,871
1048	WO 2012/087443

I, Dr. Robert Schwartz, do hereby declare:

I. INTRODUCTION

A. Engagement

1. I have been retained on behalf of Padagis Israel Pharmaceuticals Ltd., Padagis US LLC, and Padagis LLC (collectively, “Padagis” or “Petitioner”) to provide my opinions regarding the patentability of claims 1-11 of U.S. Patent No. 11,311,482 (“the ’482 patent”). For the reasons discussed herein, I have concluded that claims 1-11 of the ’482 patent are unpatentable because the prior art references render them obvious.

2. I understand that this Declaration supports Padagis’s Petition for the above-captioned *inter partes* review (“IPR”) of the ’482 patent. I have reviewed the Petition and agree with the unpatentability arguments contained therein.

3. I reserve the right to supplement, change, clarify, or modify my opinions should additional information and/or documentation become available to me. I also reserve the right to submit a rebuttal declaration in response to any expert declaration(s) submitted on behalf of the owner of the ’482 patent, Bausch Health US, LLC (“Bausch” or “Patent Owner”).

4. I am being compensated at my customary hourly rate for my work in this matter, and I am being reimbursed at cost for my expenses. My compensation in no way depends upon the substance of my opinions or the outcome of this

proceeding. I have no financial interest in any of the parties to this proceeding.

B. Experience and Qualifications

5. My experience and qualifications are summarized in my *curriculum vitae*, a copy of which is included as Exhibit 1004.

6. I am a board-certified dermatologist, and I have been treating patients, including patients suffering from acne vulgaris, for more than 40 years. I am a Professor and Head of Dermatology at Rutgers New Jersey Medical School, a position that I have held since 1983.

7. I graduated from the University of California, Berkeley with a Bachelor of Arts in Political Science in 1969. I then obtained a Master of Public Health from the University of California Berkely School of Public Health in 1970. I obtained my M.D. from New York Medical College in 1974. After obtaining my M.D., I performed a one-year internship at St. Mary's Hospital in San Francisco, where I was the First Year House Officer. I then performed a two-year residency from 1975-1977 in dermatology at the University of Cincinnati College of Medicine. In 1977, I continued my residency in dermatology at the Roswell Park Memorial Institute, State University of New York at Buffalo, where I was the Chief Resident. I completed my residency at the Roswell Park Memorial Institute in 1978. From 1989 to 1990, I performed a fellowship in dermatopathology at Rutgers New Jersey Medical School.

8. I have published more than 690 peer-reviewed articles in the area of dermatology, many of which involve the treatment of acne. I have also authored six books in the field of dermatology, including a book titled Acne, which was published in 2013. I have also authored more than 340 book chapters in the field of dermatology, several of which involve the treatment of acne.

9. In addition to my written publications, I have given many lectures and seminars on issues in the field of dermatology, including acne, both within the United States and internationally. I have also served on the Editorial Boards for more than 40 academic and medical journals related to Dermatology, including the Journal of Acne and Related Disorders.

C. Topics of Opinions

10. I offer opinions in this Declaration on the following general topics:

- The subject matter described and claimed in the '482 patent;
- The level of ordinary skill in the art pertaining to the '482 patent;
- The teachings of the prior art; and
- Whether claims 1-11 of the '482 patent would have been obvious to a person of ordinary skill in the art at the time of the alleged invention, in view of the prior art.

11. I also provide background information on medical products and the treatment of skin disorders, including the topical treatment of acne vulgaris with

retinoids, such as tazarotene.

D. Materials Considered

12. In preparing this Declaration, I have considered the materials referenced in this Declaration and those identified in the attached list of exhibits.

13. I also have relied on my education, training, and experience, and my knowledge of pertinent literature in the field of the '482 patent.

II. APPLICABLE LEGAL STANDARDS

A. Claim Construction

14. In determining whether a patent claim is unpatentable in view of the prior art, the Patent Office construes the claim by giving the claim its ordinary and customary (i.e., plain and ordinary) meaning ascribed to it by a person of ordinary skill in the art (“POSITA”) at the time of the invention, consistent with the specification and prosecution history. For the purposes of my analysis and opinions, and to the extent necessary, I have construed each claim term in accordance with its ordinary and customary meaning under the required standard.

B. Anticipation

15. I have been instructed that a claim is “anticipated” if a prior art reference describes, either expressly or inherently, each limitation of the claim. I understand that this description must be recognizable to a POSITA at the time of the alleged invention.

16. I understand that an element is “inherent in,” and therefore taught by, the prior art, if it necessarily flows from the explicit disclosure of the prior art. The fact that a certain result or characteristic may be present in the prior art is not sufficient to establish inherency. However, if the result or characteristic is necessarily present based upon the explicit disclosure in the prior art, it is inherent in the prior art and is therefore disclosed.

C. Obviousness

17. I have been instructed that a claim is “obvious” if the claimed subject matter as a whole would have been obvious to a POSITA at the time of the alleged invention. An obviousness analysis takes into account the scope and content of the prior art, the differences between the claimed subject matter and the prior art, and the level of ordinary skill in the art at the time of the invention.

18. In determining the scope and content of the prior art, I understand that a reference is considered analogous (i.e., appropriate) prior art if it falls within the field of the inventor’s endeavor. In addition, a reference is analogous prior art if it is reasonably pertinent to the particular problem with which the inventor was involved. A reference is reasonably pertinent if it logically would have commended itself to an inventor’s attention in considering the problem. If a reference relates to the same problem as the claimed invention, that supports use of the reference as prior art in an obviousness analysis.

19. The prior art references applied in this Declaration are analogous art that is usable in an obviousness combination. The references are from the same field as the '482 patent, e.g., topical formulations containing lipophilic active ingredients (e.g. retinoids and corticosteroids) as the active ingredient. The references are also pertinent to the problem the inventor was focused on, e.g., treating skin diseases, such as acne vulgaris.

20. To assess the differences between the prior art and the claimed subject matter, I have been instructed that the law requires the claimed invention to be considered as a whole. This “as a whole” assessment requires showing that one of ordinary skill in the art at the time of invention, confronted by the same problems as the inventor and with no knowledge of the claimed invention, would have selected the elements from the prior art and combined them in the claimed manner.

21. I am also informed that the law recognizes several rationales for combining references or modifying a reference to show obviousness of claimed subject matter. Some of these rationales include:

- combining prior art elements according to known methods to yield predictable results;
- simple substitution of one known element for another to obtain predictable results;

- a predictable use of prior art elements according to their established functions;
- applying a known technique to a known method or product ready for improvement to yield predictable results;
- choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; and
- some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

22. A prior art reference may also suggest a limitation of the claims. In that case, even if the prior art reference does not explicitly or inherently disclose the limitation, the motivation to modify the prior art reference to include the limitation may exist within the prior art reference itself. Thus, the limitation would have been obvious over that prior art reference alone. This is the case if a person of ordinary skill in the art would have had a simple design choice or a finite number of identified, predictable solutions, for example, and if the modification furthers the goals of the prior art reference.

23. I have also been informed that the obviousness analysis must be performed from the perspective of a POSITA at the time of the alleged invention. This is to avoid using impermissible hindsight in the analysis. The claims of the

patent must not be used to provide a road map for obviousness; instead, the claims would have been obvious if a person of ordinary skill in the art would have been motivated to combine the teachings of the prior art to arrive at the claimed invention and had a reasonable expectation of success in doing so.

24. An obviousness analysis also must consider whether there are additional factors that would indicate that the invention would not have been obvious. These factors include whether there was: (i) a long-felt need in the industry; (ii) any unexpected results; (iii) skepticism of the invention; (iv) a teaching away from the invention; (v) commercial success; (vi) praise by others for the invention; and (vii) copying by others. I am not aware of any evidence that would suggest that claims 1-11 of the '482 patent would have been non-obvious, as further explained in §§ IV. – XI. below.

D. Person of Ordinary Skill in the Art

25. It is my understanding that when interpreting the claims of the '482 patent, I must do so based on the perspective of a POSITA at the relevant priority date. I have been instructed to assume for the purposes of my opinions that the relevant priority date of the '482 patent is May 12, 2017.

26. I am informed that the POSITA is a hypothetical person who is presumed to have known all of the relevant art at the time of the invention. This is a person of ordinary creativity, not an automaton.

27. I am informed that in determining the level of ordinary skill in the art, several factors are considered. Those factors may include: (i) the type of problems encountered in the art; (ii) prior art solutions to those problems; (iii) the rapidity with which innovations are made; (iv) the sophistication of the technology; and (v) the educational level of active workers in the field. A POSITA must have the capability of understanding the scientific principles applicable to the pertinent art.

28. Based on my review of the specification and claims of the '482 patent, it is my opinion that a person of ordinary skill in the art would have been a dermatologist with several years of experience in treating skin disorders, such as acne and psoriasis, with topical medications and/or a formulation scientist having a PhD or equivalent experience relating to the development of topical compositions useful for the treatment of skin disorders. One of skill in the art may have worked as part of a multi-disciplinary team of scientists and medical professionals, including both a dermatologist and a formulation scientist, and, therefore, would have drawn from the knowledge and skills of the team as a whole to solve a given problem.

29. I would have met this definition of a person of ordinary skill in the art in May 2017. At that time, I had over 40 years of clinical experience as a practicing dermatologist treating patients with acne with topical medications.

III. BACKGROUND OF USING TAZAROTENE TO TREAT ACNE

VULGARIS

A. Tazarotene was a Well-Known Drug for Treating Acne Prior to May 2017

30. Acne vulgaris is one of the most common skin disorders in children and adolescents, and it can frequently affect adults as well. *See* Ex. 1010 (Chim) at 7. Acne can present in a range of severities, from mild to severe, and can manifest as inflammatory lesions on the patient's skin and/or as noninflammatory comedones, either open or closed. *Id.* at 9. Acne has a multifactorial pathology that originates from excess sebum production, skin keratinization changes, *Propionibacterium acnes*, and inflammatory processes. *Id.* at 7. Acne is primarily a result of overproduction of oils in the sebaceous follicles of the skin, but alterations in follicular development, including hyperkeratinization, also contribute to acne development. *Id.*

31. Topical retinoids, including tazarotene, were well known in the art for treating acne prior to May 2017. Topical retinoids help prevent and reduce comedones by altering cell differentiation of the skin and also have anti-inflammatory properties to aid in treating inflammatory lesions. *Id.* at 13; *see also* Ex. 1018 (Eichenfield) at 168. This is consistent with my understanding of prescribing practices of dermatologists prior to May 2017.

32. Retinoids belong to a class of compounds that are derived from vitamin A. Ex. 1010 (Chim) at 13; Ex. 1018 (Eichenfield) at 168. There were three topical retinoids used for treating acne prior to May 2017: tretinoin, adapalene, and tazarotene. *See* Ex. 1010 (Chim) at 13; *see also* Ex. 1018 (Eichenfield) at 168. Prior to May 2017, clinical studies had suggested that tazarotene was superior to both tretinoin and adapalene for the treatment of acne. Ex. 1010 (Chim) at 13. Additionally, unlike the two other known retinoids, tazarotene was approved for the treatment of psoriasis in addition to acne. *See, e.g.*, Ex. 1013 (Tazorac® Label) at Indications and Usage.

33. Prior to May 2017, tazarotene was commercially available in multiple dosage forms (i.e., vehicles) and at two different concentrations – 0.05% and 0.1%. *See* Ex. 1013 (Tazorac® Label) at Indications and Usage; Ex. 1017 (Fabior® Label); Ex. 1010 (Chim) at 13, Table 1-3. Tazarotene was initially approved for topical use in the United States in 1997 and had been approved by the FDA for the treatment of acne in both cream and foam dosage forms at the 0.1% concentration since at least 2013. *See* Ex. 1013 (Tazorac® Label); Ex. 1017 (Fabior® Label).

34. Although the 0.05% concentration of tazarotene was not approved for the indication of acne in the United States, compositions with 0.05% tazarotene were commonly prescribed “off-label” for treating acne prior to May 2017. *See, e.g.*, Ex. 1008 (Anderson) at 17-21 (several authors disclosing their use of topical 0.05%

tazarotene to treat acne”); *see also* Ex. 1010 (Chim) at Table 1-3 (listing tazarotene cream and gel 0.05% as an “Available Prescription Option[] to Treat Acne Vulgaris.”) Off-label use of pharmaceutical compositions is common in dermatology, and 0.05% tazarotene compositions provided a particularly attractive option for off-label treatment of acne prior to May 2017 because of the well-known irritation issues associated with the 0.1% concentration and because the 0.05% concentration was shown to be efficacious for acne in multiple publications prior to 2017. *See* Ex. 1009 (Kircik) at 651-652, Figs. 1-2; Ex. 1011 (Shalita) at 351, Figs. 1-2. It is my opinion that as Dr. Zane explains in the Anderson reference, dermatologists would have found 0.05% tazarotene compositions “fit[] well in to the retinoid ladder in moderate to severe inflammatory acne or comedonal acne.” Ex. 1008 (Anderson) at 20. My opinion is also supported by data collected by Petitioner on the prescriptions of 0.05% tazarotene compositions for the year of 2017. *See* Ex. 1015 (IQVIA); *see also* Ex. 1016 (Booydegraff Decl.). This data shows that at least between February 2017 and May 2017, millions of dollars and thousands of units of compositions comprising tazarotene at 0.05% were prescribed and sold for the treatment of acne vulgaris. *See* Ex. 1015 (IQVIA). This data is not surprising and is consistent with what a POSITA would have expected given the common practice of off-label prescriptions in dermatology.

B. Local Skin Irritation was a Well-Known Problem with Topical Retinoid Treatments

35. Although they were commonly used to treat acne prior to May 2017, topical retinoids, including tazarotene, were also known to cause local skin irritation, which could be severe in some cases. Ex. 1010 (Chim) at 13; *see also* Ex. 1018 (Eichenfield) at 169; Ex. 1013 (Tazorac® Label) at Sections 5.2, 14, 16.1. The tendency of tazarotene to cause irritation was known generally to be dose-dependent. Ex. 1013 (Tazorac® Label) at Sections 5.2, 14, 16.1; Ex. 1018 (Eichenfield) at 169.

36. Because skin irritation can affect patient adherence to a treatment regimen, which necessarily impacts the efficacy of the treatment, prior to May 2017 POSITAs were actively investigating ways to reduce the irritation caused by topical tazarotene therapy without sacrificing its efficacy. *See* Ex. 1010 (Chim) at 13 (disclosing that topical retinoids “are limited by their adverse effects, which may result in nonadherence or discontinuation”); Ex. 1025 (Kircik 2011) at s18. There were multiple known approaches for addressing this issue.

37. One known way to address the irritation issue was to reduce the dose (i.e., concentration) of the tazarotene applied to the skin. *See, e.g.*, Ex. 1022 (Dosik) at 290-293; Ex. 1013 (Tazorac Label®) at Sections 5.2, 14, 16.1; Ex. 1018 (Eichenfield) at 169; Ex. 1011 (Shalita) at 354; Ex. 1010 (Chim) at 13. This was expressly taught in a clinical study comparing the irritation profiles of 0.1%

tazarotene with 0.05%, the results of which were published in Dosik, a 2005 article. Ex. 1022 (Dosik) at 289. Dosik reported that the 0.1% tazarotene cream was significantly more irritating than the 0.05% cream, which is consistent with what a POSITA would have expected at the time given their clinical experience. *Id.* at 293. The FDA labeling for Tazorac® Cream, the commercial tazarotene product, also reflected this understanding. The Tazorac® Label instructed that patients who cannot tolerate treatment with 0.1% tazarotene cream be switched to 0.05% tazarotene cream because it produced less irritation in clinical studies. Ex. 1013 (Tazorac® Label) at Sections 5.2, 14, 16.1. Again, a POSITA would have found this instruction to be consistent with their clinical experience in using tazarotene treatments. Additional prior art medical journals similarly suggested that treatment for acne with topical retinoids be initiated with the “lowest strength” available to minimize irritation. Ex. 1018 (Eichenfield) at 169; *see also* Ex. 1011 (Shalita) at 354.

38. The approach of lowering the concentration of retinoid products over time was not limited to tazarotene. This pattern is also reflected with the retinoid tretinoin. Tretinoin was originally commercialized at a concentration of 0.1%. *See* Ex. 1010 (Chim) at Table 1-3. Thereafter, lower concentration formulations were eventually developed and commercialized, including 0.05%, 0.025%, and even 0.01% creams and 0.04% and 0.08% gels. *See id.*

39. Another recognized solution for addressing the irritation caused by topical tazarotene treatment was to have patients apply a moisturizer along with the tazarotene product. *See* Ex. 1010 (Chim) at 13; Ex. 1018 (Eichenfield) at 169; Ex. 1017 (Fabior® Label) at Dosage and Administration; Ex. 1013 (Tazorac® Label) at Patient Counseling Information. Given this knowledge, it is my opinion that dermatologists would have been highly interested in vehicle formulations for topical tazarotene compositions that included moisturizing ingredients within the vehicle, which may reduce or eliminate the need for application of a separate moisturizing agent. Such a vehicle would help to simplify the treatment regimen, which would help improve patient adherence to the treatment.

40. A third approach for addressing the irritation caused by topical tazarotene was to formulate the tazarotene in vehicle formulations that could increase the penetration of tazarotene into the skin, allowing for greater efficacy with a lower concentration of tazarotene. *See* Ex. 1010 (Chim) at 13. Prior to May 2017, dermatologists and clinicians would have understood the vehicle of a topical composition can have a significant effect on the efficacy and adverse events observed with the composition. Thus, clinicians would have known that altering the vehicle of a composition could allow the concentration of the active to be reduced without causing a proportional reduction in efficacy, and clinicians would have sought the expertise of a formulator to help develop such a vehicle. Indeed, as I

discuss in detail below, the '824 publication disclosed vehicles for topical compositions to achieve this exact purpose – reducing the concentration of the active ingredient without reducing the efficacy of the composition. *Infra* §§ IX – XI.

C. Prior Art 0.045% Tazarotene Lotions

41. In addition to the commercial 0.05% tazarotene compositions that were commonly used to treat acne, the prior art also disclosed lotion compositions with a similar, but slightly lower, concentration of tazarotene – 0.045%. Both WO '001 and IDP-118 Study disclosed such lotions.

42. WO '001 is a published patent application directed toward topical compositions and methods for treating psoriasis with tazarotene and halobetasol propionate. *See* Ex. 1007 (WO '001) at [002]. One of the compositions disclosed in WO '001 is a lotion that contains 0.045% tazarotene as the only active ingredient. *Id.* at Table 4. WO '001 discloses that this lotion was used in a clinical study to treat psoriasis. *See id.* at [0062]. However, as I explained above, topical tazarotene was approved and used for treating both psoriasis and acne. *Supra* ¶ 32. Thus, an ordinarily skilled clinician in May 2017 would look to references dealing with using topical tazarotene to treat either, and they would have recognized WO '001's 0.045% tazarotene lotion as a highly attractive candidate for treating acne, particularly because that lotion contained a similar concentration of tazarotene as the commercially available 0.05% compositions, which were commonly used to treat

acne and were known to cause less irritation than the 0.1% commercial compositions. *Supra* ¶ 34.

43. The prior art IDP-118 Study also discloses a 0.045% tazarotene lotion that was used for treating psoriasis. *See* Ex. 1014 (IDP-118 Study) at Arms and Interventions. The IDP-118 Study is a study record from ClinicalTrials.gov on a phase II clinical trial comparing treatment of psoriasis with a lotion comprising a combination of 0.01% halobetasol propionate and 0.045% tazarotene against treatment with two monotherapy lotions, one comprising 0.01% halobetasol propionate and the other comprising 0.045% tazarotene. *Id.* As I explained above for WO '001, ordinarily skilled clinicians interested in treating acne would have looked to clinical studies using topical tazarotene to treat either acne or psoriasis, and they would have recognized the 0.045% tazarotene lotion as a particularly attractive option for treating acne because of its similarity to the 0.05% compositions used in the prior art. *Supra* ¶ 41-43.

IV. THE '482 PATENT

A. Summary of the '482 Patent

44. The '482 patent describes topical compositions of the retinoid tazarotene in an oil-in-water emulsion vehicle that forms a lotion for treating skin diseases, such as acne and psoriasis. Ex. 1001 ('482 patent) at Abstract, 2:42-44. The tazarotene is included at a concentration less than 0.05 wt %. *Id.* at 2:48-53.

The '482 patent provides example formulations encompassed by the alleged inventions in Tables 1-2:

TABLE 1

Compositions of the Present Invention for Treating Skin Diseases			
Ingredient	Concentration (wt %)		
	Range 1	Range 2	Range 3
Tazarotene or Tazarotenic Acid Compound	0.01-0.049	0.02-0.045	0.03-0.045
Emollient, Solvent, and/or Thickener	0.5-40	1-25	2-20
Emulsifier	0.25-10	0.5-7	1-5
Humectant	0-15	2-12	3-10
Polymeric Thickener	0.05-2	0.1-1.5	0.3-1
Pharmaceutical Aids	q.s.	q.s.	q.s.
Purified water	q.s. to 100	q.s. to 100	q.s. to 100

TABLE 2

Some Emulsion Compositions of the Present Invention for Treating Acne					
Ingredient	Function	Concentration (wt %)			
		Range 1	Range 2	Range 3	Composition A
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Id. at Tables 1-2.

45. The '482 patent also discloses three clinical studies in acne patients conducted with Composition A (Table 2). In the first study, patients were treated with either Composition A, a placebo lotion, commercially available 0.1% tazarotene cream (Tazorac® 0.1% cream), or a placebo cream once daily for twelve weeks. *Id.* at 7:25-59. Efficacy was measured by the improvement in the Evaluator's Global Severity Score (EGSS), and the numbers of inflammatory and non-inflammatory lesions were also assessed. *Id.* at 7:60-8:5. The efficacy results of the first study are disclosed in Tables 3-7:

TABLE 3

Baseline Characteristics - Inflammatory Lesions and Non-inflammatory lesions			
	Combined Placebo N = 69	Composition A N = 69	Tazorac ® 0.1% Cream N = 72
Inflammatory Lesions			
Mean (SD)	27.2 (5.49)	28.3 (6.0)	27.3 (5.95)
Median	26.0	27.0	26.0
Non-inflammatory Lesions			
Mean (SD)	36.6 (13.17)	37.6 (14.70)	36.6 (13.31)
Median	34.0	34.0	34.0

TABLE 4

EGSS (Clear or Almost Clear) by Visit (ITT)			
	Combined Placebo N = 69	Composition A N = 69	Tazorac ® 0.1% Cream N = 72
Week 2	0%	0%	0%
Week 4	0%	1.4%	1.4%
Week 8	4.3%	7.2%	5.6%
Week 12	10.1%	18.8%	16.7%

TABLE 5

Inflammatory Lesions by Visit Absolute Change from Baseline			
	Combined Placebo N = 69	Composition A N = 69	Tazorac ® 0.1% Cream N = 72
Week 2	-4.7	-2.9	-2.4
Week 4	-7.2	-5.8	-7.8
Week 8	-10.9	-13.2	-12.0
Week 12	-14.0	-18.1	-16.8

TABLE 6

Treatment % Success (ITT) at 12 Weeks			
	Combined Placebo N = 69	Composition A N = 69	Tazorac ® 0.1% Cream N = 72
EGSS - Clear or Almost Clear Inflammatory Lesions	10.1%	18.8%	16.7%
Absolute Change	-14.0	-18.1	-16.8
% Change	-51.41%	-63.75%	-59.99%
Non-inflammatory Lesions			
Absolute Change	-13.1	-21.6	-20.3
% Change	-35.18%	-56.86%	-54.09%

TABLE 7

Treatment % Success (PP)			
	Combined Placebo N = 57	Composition A N = 54	Tazorac ® 0.1% Cream N = 56
EGSS -	12.3%	20.4%	16.1%
Clear or Almost Clear			
Inflammatory Lesions	-14.2	-18.3	-18.2
Non-inflammatory Lesions	-11.8	-20.8	-21.9

Id. at Tables 3-7. Tolerability was also assessed based on burning, stinging, or itching reported by the subjects, and cutaneous safety was assessed by scaling, erythema, hypo-pigmentation and hyper-pigmentations as evaluated by the investigator. *Id.* at 9:34-36. The tolerability results are disclosed in Figures 4A-C:

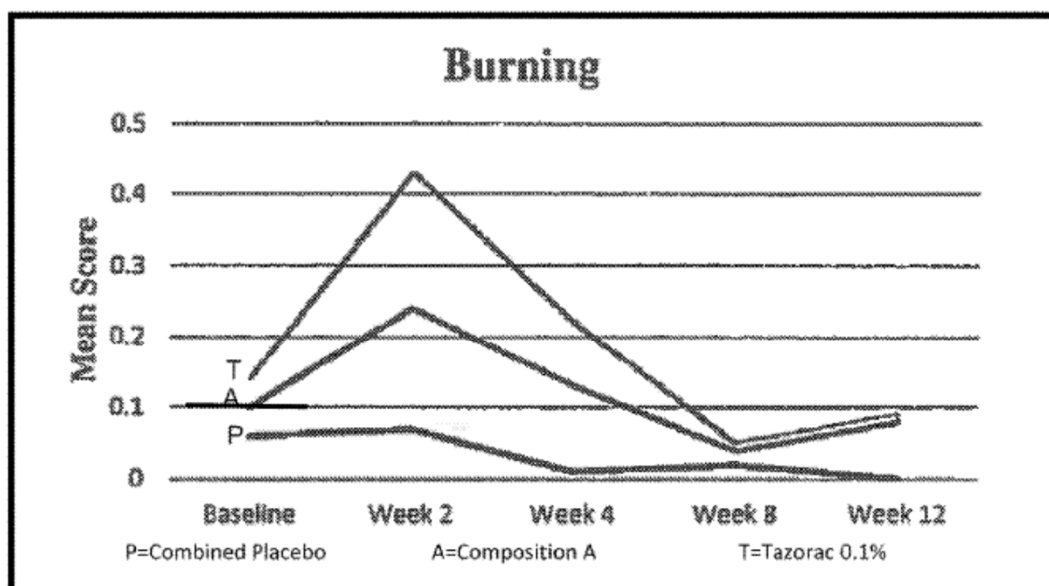


FIG. 4A

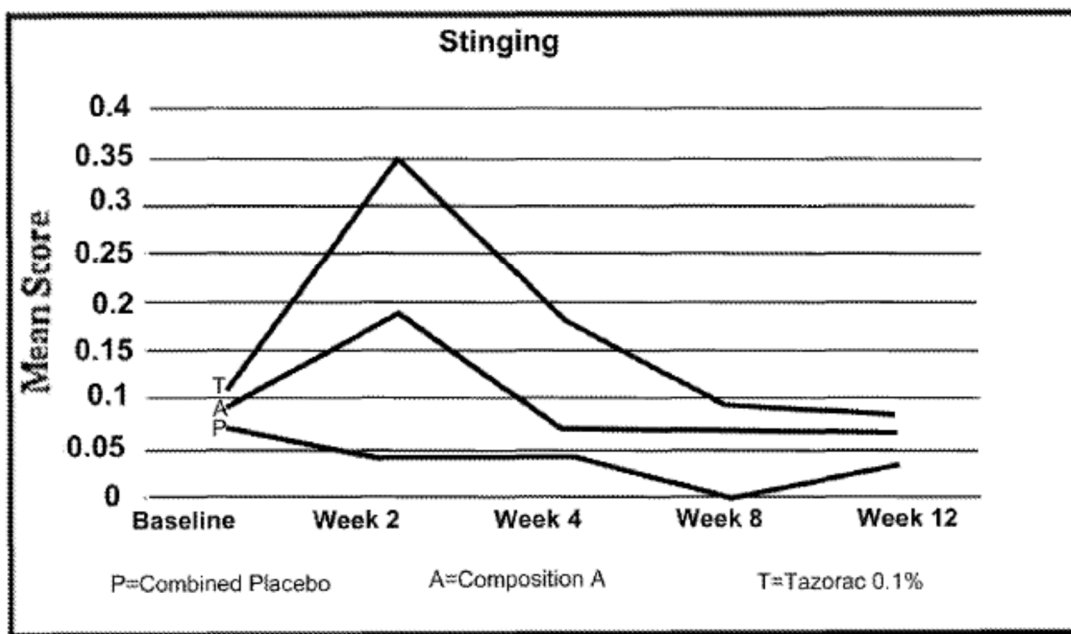


FIG. 4B

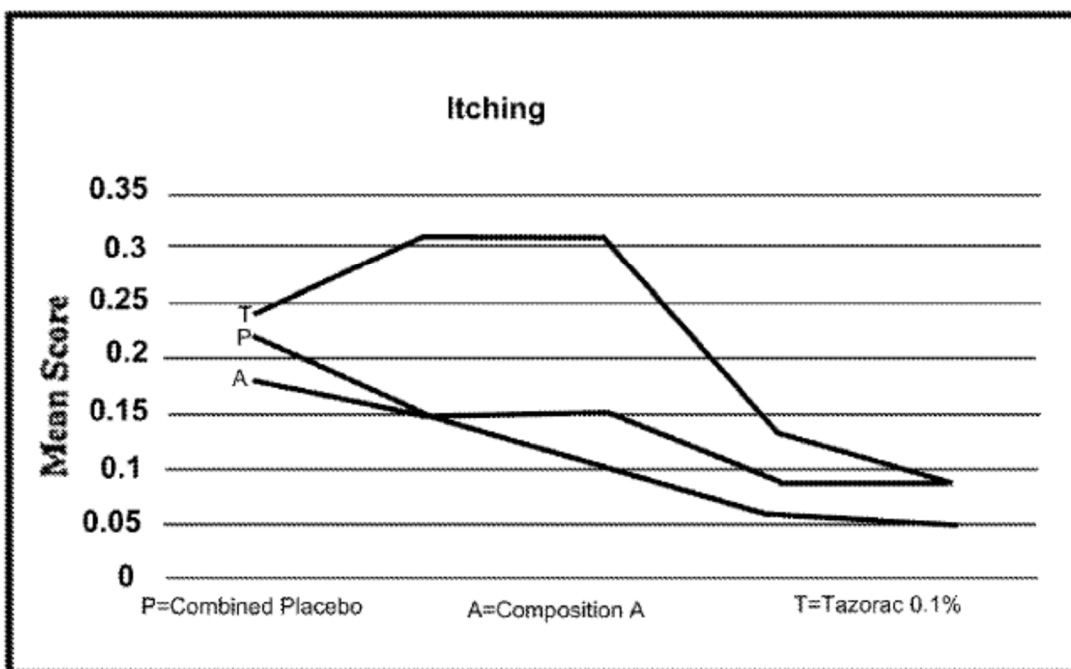


FIG. 4C

Id. at Figs. 4A-C.

46. I note that the '482 patent does not provide any statistical analysis for the results of the first clinical study indicating whether the results were statistically significant. This is surprising, given that the '482 patent does provide such an analysis for the larger clinical studies I discuss below. In my opinion, POSITAs would expect such an analysis to be provided with this type of clinical data and would rely on that analysis when assessing clinical data because a lack of statistical significance would undermine the confidence one may have that the reported results were merely the result of random chance. Such an analysis would be particularly important when drawing any conclusions from the data on the relative efficacies of Composition A versus Tazorac® 0.1% cream.

47. The '482 patent also discloses two larger, phase-3 clinical studies in acne patients where patients applied either Composition A (Table 2) or placebo lotion once daily for twelve weeks. (*Id.* at 10:29-57.) Efficacy, cutaneous safety, and tolerability were measured via the same means as the first study, and the results are disclosed in Tables 10-13:

TABLE 10

EGSS (Clear or Almost Clear) at Week 12 (ITT)				
	Study 301		Study 302	
	Composition A Lotion N = 402	Placebo Lotion N = 411	Composition A Lotion N = 397	Placebo Lotion N = 404
Week 12	25.5% (p < 0.001)	13.0%	29.6% (p < 0.001)	17.3

TABLE 11

Inflammatory and Non-Inflammatory Lesions Absolute Changes from Baseline at Week 12				
	Study 301		Study 302	
	Composition A Lotion N = 402	Placebo Lotion N = 411	Composition A Lotion N = 397	Placebo Lotion N = 404
Inflammatory Lesions	-15.6 (p < 0.001)	-12.4	-16.7 (p < 0.001)	-13.4
Non-inflammatory Lesions	-21.0 (p < 0.001)	-16.4	-24.6 (p < 0.001)	-16.6

TABLE 12

Treatment Success (Per-Protocol Basis)				
	Study 301		Study 302	
	Composition	Placebo	Composition	Placebo
	A Lotion	Lotion	A Lotion	Lotion
	N = 402	N = 411	N = 397	N = 404
EGSS -	26.8%	14.4%	30.6%	18.3%
Clear or Almost Clear				
Inflammatory Lesions	-15.8	-12.4	-16.4	-13.4
Non-inflammatory	-21.3	-16.3	-24.1	-15.4
Lesions				

TABLE 13

Cutaneous Safety and Tolerability				
	Study 301		Study 302	
	Composition A Lotion N = 387	Placebo Lotion N = 392	Composition A Lotion N = 392	Placebo Lotion N = 399
<u>Scaling</u>				
Moderate	4	2	6	1
Severe	0	0	1	0
<u>Erythema</u>				
Moderate	7	8	13	6
Severe	0	0	1	0
<u>Hypopigmentation</u>				
Moderate	1	1	0	0
Severe	0	0	0	0
<u>Hyperpigmentation</u>				
Moderate	7	9	8	17
Severe	1	2	0	1
<u>Itching</u>				
Moderate	4	2	4	4
Severe	0	0	0	0
<u>Burning</u>				
Moderate	2	0	5	0
Severe	0	0	2	0
<u>Stinging</u>				
Moderate	1	1	3	0
Severe	0	0	1	0

Id., 10:64-12:32, Tables 10-13. As I mentioned above, Tables 10 and 11 provide results of a statistical analysis of the comparison of Composition A against placebo, which is not provided for the first study. *See id.* at Tables 10-11.

B. The Challenged Claims

48. The challenged claims are claims 1-11 of the '482 patent. Claims 1 and 11 are independent claims.

49. Claim 1 is illustrative (but not representative) of some of the limitations in the challenged claims. Claim 1 states:

1. A method of treating acne vulgaris, the method comprising topically applying a pharmaceutical composition once per day to an affected area of a body of a subject suffering from acne vulgaris, wherein:
the composition comprises tazarotene at a concentration of about 0.045 percent by weight of the composition as a sole active pharmaceutical ingredient
the composition is an oil-in-water emulsion lotion comprising an oil phase and an aqueous phase;
the oil phase comprises a dicarboxylic acid ester and a mineral oil at a total concentration of 10-12 percent by weight of the composition;
the aqueous phase comprises water and a carbomer homopolymer, wherein the concentration of the carbomer homopolymer is 0.5-0.7 percent by weight of the composition; and
the composition further comprises a polymeric emulsifier at a concentration of 0.3-0.5 percent by weight of the composition.

C. Prosecution History

50. I have reviewed the '482 patent's prosecution history. The Patent Examiner issued two non-final office actions and two final office actions.

51. In the first non-final office action, the Examiner rejected the pending claims over the FDA labeling for Fabior® lotion, both alone and in combination with two additional prior art references, Singh (Ex. 1031) and Fiume (Ex. 1046). *See* Ex. 1002 ('482 patent prosecution history excerpt) at 296-306.

52. In the first final office action, the Examiner rejected the pending claims over WO '001 (Ex. 1007) and Donello (Ex. 1032). *See* Ex. 1002 ('482 patent prosecution history excerpt) at 210-221.

53. In the second non-final office action, the Examiner again rejected the pending claims over WO '001 and Donello. *Id.* at 179-191.

54. In the second final office action, the Examiner maintained the rejection of the pending claims over WO '001 and Donello. *Id.* at 134-152.

55. The Patent Office issued a Certificate of Correction for the '482 patent on March 14, 2023 that replaced the term “carbomer polymer type B” in claims 9-11 with the term “carbomer copolymer type B.” *Id.* at 1. My opinions herein are provided for the claims of the '482 patent as corrected in the March 14, 2023 Certificate of Correction.

V. PROSECUTION OF PATENT OWNER'S RELATED APPLICATIONS

A. The '576 Application

56. I have also reviewed the prosecution history of U.S. Pat. App. No. 16/179,576 (“'576 application”), which I understand from counsel claims priority to the same patent application as the '482 patent. The specification of the '576 application and the '482 patent are substantively identical, and the claims are also very similar, as illustrated in the chart comparing pending independent claim 1 of the '576 application with claim 1 of the '482 patent below:

Claim 1 of the '482 Patent	Claim 1 of the '576 Application (as of December 8, 2022 Amendment)
<p>1. A method of treating acne vulgaris, the method comprising topically applying a pharmaceutical composition once per day to an affected area of a body of a subject suffering from acne vulgaris, wherein:</p> <p>the composition comprises tazarotene at a concentration of about 0.045 percent by weight of the composition as a sole active pharmaceutical ingredient</p> <p>the composition is an oil-in-water emulsion lotion comprising an oil phase and an aqueous phase;</p> <p>the oil phase comprises a dicarboxylic acid ester and a mineral oil at a total concentration of 10-12 percent by weight of the composition;</p> <p>the aqueous phase comprises water and a carbomer homopolymer, wherein the concentration of the carbomer homopolymer is 0.5-0.7 percent by weight of the composition; and</p> <p>the composition further comprises a polymeric emulsifier at a concentration of 0.3-0.5 percent by weight of the composition.</p>	<p>1. (Previously presented) A topical pharmaceutical composition for treating acne, comprising:</p> <p>a sole active pharmaceutical ingredient consisting of tazarotene at a concentration of 0.045 percent by weight of the composition;</p> <p>wherein said composition is an oil-in-water emulsion lotion comprising an oil phase and an aqueous phase,</p> <p>wherein the oil phase comprises a dicarboxylic acid ester and a mineral oil,</p> <p>wherein the aqueous phase comprises water and a carbomer homopolymer,</p> <p>wherein the composition further comprises a polymeric emulsifier, and</p> <p>wherein the tazarotene is in solution in the oil phase.</p>

Ex. 1001 ('482 patent) at claim 1; Ex. 1029, ('576 application prosecution history) at 25-36.

57. I understand that the Patent Examiner has finally rejected all pending claims of the '576 application as obvious over the combination of the '824 publication and the Tazorac® Label. Ex. 1029 ('576 application prosecution history) at 1-20. In that rejection, the Examiner noted that Applicant's argument that POSITAs would not expect to achieve effective delivery of tazarotene from a composition formulated for delivery of halobetasol propionate had "been fully considered but has not been found persuasive [because] the formulation for delivery as applicants assert is the very same formulation as instant claimed. Therefore, it would have been obvious to substitute tazarotene in the same lotion formulation." *Id.* at 4.

58. Regarding the claimed concentration of tazarotene in the '576 application – 0.045% – the Examiner found that "[t]he amounts of active agents to be used, the pharmaceutical forms, e.g., tablets, etc; mode of administration, flavors, surfactant are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations and modes of administration." *Id.* at 11. The Examiner further concluded that "it is obvious to vary and/or optimize the amount of tazarotene provided in the composition, according to the guidance provided by Tazorac, to provide a composition having the desired properties such as the desired (ratios, concentrations, percentages, etc.)." *Id.* at 12.

59. I understand that the Examiner also rejected the Applicants' arguments regarding unexpected results because the Applicants failed to compare the claimed 0.045% tazarotene composition to the 0.05% tazarotene composition disclosed in the Tazorac® Label. *Id.* at 5-6.

B. The '871 Application

60. I have also reviewed the prosecution history of U.S. Application No. 17/366,871 (the "'871 application"), which shares a substantively identical specification as the prior art WO '001 reference. *Compare* Ex. 1047 ('871 application prosecution history) at 367-412 *with* Ex. 1007 (WO '001). Like, WO '001, the '871 application discloses halobetasol propionate and tazarotene compositions for treating psoriasis. *See* Ex. 1047 ('871 application prosecution history) at 367-412. However, independent claim 1 of the '871 application recites a pharmaceutical composition that is similar to the finally rejected claims of the '576 application. *Compare id.* at 61 *with* Ex. 1029 ('576 application prosecution history) at 35-36.

61. I understand that like the '576 application, the Patent Examiner had rejected the pending claims of the '871 application as obvious over the combination of the '824 publication¹ and the Tazorac® Label. Ex. 1047 ('871 application

¹ The Examiner asserted Dow (WO 2012/087443) during prosecution of the '871 application, which I understand from counsel to be the PCT publication of the '824 publication. *See* Ex. 1048 (WO 2012/087443).

prosecution history) at 155-163. Also like the '576 application, I understand that in response, the Applicants argued that the claims would not have been obvious due to unexpected results based on the clinical trial data relating to the treatment of acne that is disclosed in the '576 application. *Id.* at 60-75. Unlike the Patent Examiner for the '576 application, however, the Examiner for the '871 application allowed the claims over the prior art following Applicant's unexpected results arguments. *Id.* at 8-15.

62. Thus, it appears that different Patent Examiners have reached different, inconsistent conclusions on the same evidence and arguments for the '576 and '871 applications.

VI. SUMMARY OF IPR GROUNDS

63. I have identified the following grounds of unpatentability in this Declaration:

Ground	Claims Challenged	AIA 35 U.S.C. §	References
1	1-11	103	WO '001 + Anderson
2	1-11	103	WO '001 + Kircik
3	1-11	103	WO '001 + Chim
4	1-11	103	WO '001 + Anderson + Shalita

Ground	Claims Challenged	AIA 35 U.S.C. §	References
5	1-11	103	'824 Publication + Tazorac® Label
6	1-11	103	'824 Publication + Tazorac® Label + Anderson
7	1-11	103	'824 Publication + Anderson + IDP-118
8	1-11	103	'824 Publication + Kircik + IDP-118
9	1-11	103	'824 Publication + Chim + IDP-118

**VII. GROUNDS 1-3: CLAIMS 1-11 WOULD HAVE BEEN OBVIOUS
OVER WO '001 AND ANDERSON, KIRCIK, OR CHIM**

64. As I discussed previously, POSITAs in May 2017 would have been motivated to develop new topical tazarotene formulations with less irritating side effects. *Supra* § III. As I also explained, POSITAs would have known that one way to reduce the irritation caused by tazarotene compositions was to reduce the concentration of tazarotene in the formulation. *Id.* POSITAs would have recognized WO '001 as providing a topical composition with a lower concentration of tazarotene than prior commercial formulations that would be useful in treating acne and would result in less irritation for patients. WO '001 disclosed topical pharmaceutical compositions comprising a combination of a corticosteroid and a

retinoid. *See* Ex. 1007 (WO '001) at [0002]. WO '001 discloses a lotion formulation that includes 0.045% tazarotene as the sole active ingredient, which is a slightly lower concentration than the commercial 0.05% Tazorac® compositions. *Id.* at Table 4. That lotion is ***identical*** to the composition disclosed and claimed in the '482 patent.

65. Although WO '001 is focused on treating psoriasis, it is my opinion that a POSITA would have been motivated to use the 0.045% tazarotene lotion disclosed by WO '001 to treat acne and would have reasonably expected success in doing so. As I explained previously, tazarotene was the only topical retinoid approved to treat both psoriasis and acne, so POSITAs would have looked to references dealing with both diseases when working with tazarotene. *Supra* ¶¶ 32, 42. Moreover, the 0.045% tazarotene in the WO '001 lotion is nearly the same concentration as topical tazarotene compositions that had been effectively and routinely used to treat acne for years prior to May 2017, as evidenced by Anderson, Kircik, and Chim.

66. Accordingly, based on my review of the prior art, it is my opinion that claims 1-11 of the '482 patent would have been obvious over WO '001 in combination with Anderson, Kircik, or Chim. My opinions are further confirmed by the expert declaration of Dr. Murthy, an expert in the field of topical drug formulation, as I explain below.

A. Claim 1

67. In my opinion, claim 1 of the '482 patent would have been obvious over WO '001 in combination with Anderson, Kircik, or Chim.

1. Preamble

68. The preamble of Claim 1 recites “[a] method of treating acne vulgaris, the method comprising topically applying a pharmaceutical composition once per day to an affected area of a body of a subject suffering from acne vulgaris.”

69. Anderson, Kircik, and Chim each disclose this limitation.

a. Anderson

70. Anderson is a review article on the treatment of acne with topical tazarotene and teaches that “topical tazarotene is efficacious and well tolerated in a variety of patients with acne.” Ex. 1008 (Anderson) at 16. The authors of the article were all practicing dermatologists. *Id.* at 16. In the article, the authors described their clinical use of topical tazarotene as an acne treatment for a broad-spectrum of patients. *Id.* at 16-21. Anderson discloses that Dr. Valerie Callender “initiates treatment with tazarotene 0.05% cream applied every night” and then “after 2 or 3 weeks, she switches patients to a stronger concentration.” *Id.* at 17. Anderson discloses that Dr. Lee Zane “thinks that topical tazarotene can be a useful part of the treatment regimen and that tazarotene 0.05% cream fits well into the retinoid ladder in moderate to severe inflammatory acne or comedonal acne, with every-other-night

dosing (advancing to nightly, as tolerated).” *Id.* at 20. Anderson discloses that Dr. Emil Tanghetti “starts treatment with lower-strength tazarotene cream or gel and increases (or decreases) the strength according to tolerability.” *Id.* According to Dr. Tanghetti, “[p]atients with sensitive skin show increased tolerability with tazarotene 0.05% cream.” *Id.* Thus, as reflected by Anderson, treating acne by topically applying a tazarotene composition once per day to an affected area of a body was a common part of dermatologic practice prior to May 2017.

b. Kircik

71. Kircik is a medical journal article in the Journal of Drugs in Dermatology that disclosed the results of a clinical study comparing tretinoin microsphere gel 0.04% deliver by pump (“TMP PUMP”) to tazarotene cream 0.05% in the treatment of mild-to-moderate facial acne. Ex. 1009 (Kircik) at 650-51. Subjects in the study topically applied either TMP PUMP or tazarotene cream 0.05% once daily for 12-weeks. *Id.* at 651. Kircik disclosed that tazarotene 0.05% cream produced a 36.86, 64.54, and 70.06% reduction in total inflammatory lesions at weeks 4, 8, and 12 respectively and a 37.26, 58.94, and 75.50% reduction in total non-inflammatory lesions at weeks 4, 8, and 12, all of which were statistically significant. *Id.* at 651-52, Figs. 1-2. Thus, Kircik teaches topically treating acne by applying a tazarotene composition once per day to an affected area of a body.

c. **Chim**

72. Chim is a chapter from the 2016 Ambulatory Care Self-Assessment Program (ACSAP) book on dermatologic care that provides a review of acne vulgaris and various known treatments for that condition. Chim teaches that “[s]ubstantial evidence supports the use of [topical retinoids] across all stages of acne severity.” Ex. 1010 [Chim] at 7. Chim disclosed that the three available topical retinoids for treating acne—tazarotene, tretinoin, and adapalene—were available in various formulations, which Chim lists in Table 1-3.

Table 1-3. Available Prescription Options to Treat Acne Vulgaris				
Drugs	Available Formulations (Concentrations)	Dose	Common Adverse Effects	Place in Therapy
Topical Retinoids				
Adapalene	Cream (0.1%) Gel (0.1%, 0.3%) Lotion (0.1%)	Once daily (cream, gel: daily in the evening)	Dryness, erythema, photosensitivity, pruritus, scaling, stinging	Any stage
Tazarotene	Cream (0.05%, 0.1%) Foam (0.1%) Gel (0.05%, 0.1%)	Once daily in the evening		
Tretinoin	Cream (0.025%, 0.05%, 0.1%) Gel (0.01%, 0.025%) Micronized gel (0.04%, 0.08%, 0.1%)	Once daily in the evening		

Id. at 7, Table 1-3 (excerpt). Chim teaches that “[d]osing of [topical retinoids] should start at the lowest concentration a few times a week and be titrated to nightly, as tolerated.” *Id.* at 13. This is consistent with my experience and clinical practice. Chim lists 0.05% tazarotene compositions as “Available Prescription Options to Treat Acne Vulgaris.” *Id.* at Table 1-3. Thus, like Anderson and Kircik, Chim

teaches treating acne by topically applying a tazarotene composition once per day to an affected area of a body.

2. Composition of Tazarotene at 0.045% as Sole Active Ingredient

73. Claim 1 next recites “wherein the composition comprises tazarotene at a concentration of about 0.045 percent by weight of the composition as a sole active pharmaceutical ingredient.” WO ’001 in view of the teachings of Anderson, Kircik, or Chim teaches this limitation.

74. WO ’001 discloses a topical pharmaceutical composition wherein the sole active ingredient is tazarotene at a concentration of 0.045%.

WO '001

Ingredient	Function	Concentration (wt%)			
		IDP-118 (Present Invention)	Placebo (Vehicle)	Halobeta- sol propio- nate only	Tazaro- tene only
Halobetasol propionate, micronized	Active Ingredient	0.01	0	0.01	0
Tazarotene	Active Ingredient	0.045	0	0	0.045
Diethyl sebacate	Emollient & Solvent	2.97	2.97	2.97	2.97
Light mineral oil	Emollient & Solvent	8.03	8.03	8.03	8.03
Sorbitan monooleate	Surfactant/ Emulsifying Agent	0.1	0.1	0.1	0.1
Sorbitol solution, 70%	Humectant	10.7	10.7	10.7	10.7
Methyl paraben	Antimicrobial Preservative	0.17	0.17	0.17	0.17
Propyl paraben	Antimicrobial Preservative	0.03	0.03	0.03	0.03
Edetate disodium dihydrate	Chelating Agent	0.05	0.05	0.05	0.05
Carbomer copolymer type B (Pemulen TM TR-1)	Emulsifying Agent	0.4	0.4	0.4	0.4
Carbomer homopolymer type A (Carbomer 981)	Thickener	0.6	0.6	0.6	0.6
Sodium hydroxide	pH-adjusting agent	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Solvent	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Ex. 1007 [WO '001], Table 3; Table 4. Although WO '001 is focused on treating psoriasis, it is my opinion that a POSITA would have been motivated to use the 0.045% tazarotene lotion disclosed by WO '001 to treat acne and would have reasonably expected success in doing so. As I explained previously, tazarotene was the only topical retinoid approved to treat both psoriasis and acne, so POSITAs would have looked to references dealing with both diseases when working with

tazarotene. *Supra* ¶¶ 32, 42. Moreover, the 0.045% tazarotene in the WO '001 lotion is nearly the same concentration as topical tazarotene compositions that had been effectively and routinely used to treat acne for years prior to May 2017, as evidenced by Anderson, Kircik, and Chim, which I discuss in further detail below.

a. Anderson

75. Anderson disclosed the clinical use of 0.05% tazarotene compositions to treat acne by practicing dermatologists. Ex. 1008 (Anderson) at 17-21. Anderson disclosed that Dr. Valerie Callender “initiates treatment with tazarotene 0.05% cream applied every night” and then “after 2 or 3 weeks, she switches patients to a stronger concentration.” *Id.* at 17. Anderson disclosed that according to Dr. Emil Tanghetti, “[p]atients with sensitive skin show increased tolerability with tazarotene 0.05% cream.” *Id.* at 18. Anderson disclosed that, according to Dr. Lee Zane, “topical tazarotene can be a useful part of the treatment regimen and that tazarotene 0.05% cream fits well into the retinoid ladder in moderate to severe inflammatory acne or comedonal acne.” *Id.* at 20. Anderson further discloses that according to Dr. Zane, “in those patients with very oily skin and widespread comedones that required repeated extraction procedures, topical tazarotene 0.05% or 0.1% cream—or gel if tolerated—can be particularly useful for minimizing comedonal burden.” *Id.* at 21.

76. Anderson’s teachings on the clinical use of 0.05% tazarotene

compositions to acne are consistent with my understanding of clinical practice prior to May 2017. Off-label use of pharmaceutical compositions is common in dermatology, and 0.05% tazarotene compositions provided a particularly attractive option for off-label treatment of acne prior to May 2017 because of the well-known irritation issues associated with the 0.1% concentration. This is reflected by data collected by Petitioner on the prescriptions of 0.05% tazarotene compositions for the year of 2017, which shows that at least between February 2017 and May 2017, millions of dollars and thousands of units of compositions comprising tazarotene at 0.05% were prescribed and sold for the treatment of acne vulgaris. *See* Ex. 1015 (IQVIA); *see also* Ex. 1016 (Booydegraff Decl.). It is my opinion that a POSITA in May 2017 would have been aware of the common off-label use of 0.05% tazarotene compositions to treat acne. Indeed, as demonstrated by Anderson, it is very likely that a POSITA would have personally prescribed 0.05% tazarotene compositions for the treatment of acne.

77. Persons of ordinary skill in the art would have been motivated by Anderson's teachings, as well as their knowledge and experience in off-label use of 0.05% tazarotene compositions to treat acne, to use the 0.045% tazarotene composition disclosed by WO '001 with a reasonable expectation of success. In my opinion, persons of ordinary skill in the art would not have expected the difference in concentration between 0.045% tazarotene and 0.05% tazarotene to have a

significant effect on the efficacy of the composition.

78. Persons of skill in the art would have been motivated to combine the teachings of WO '001, which focused on treating psoriasis with tazarotene compositions, and Anderson, which focused on treating acne with tazarotene, because they would have known that tazarotene was the only topical retinoid used and approved by the FDA for treating both indications. *Supra* ¶ 32. Additionally, persons of ordinary skill would have known that local skin irritation was a common side effect when treating either psoriasis or acne with topical tazarotene, and therefore, they would have been motivated to look to formulations used for treating either disease to address the irritation issue while maintaining efficacy. Persons of ordinary skill would have recognized that WO '001 provides one such formulation, given its lower concentration of tazarotene relative to existing commercial compositions, which were known to cause irritation. Additionally, I understand from the expert declaration of Dr. Murthy that the formulation in WO '001 contains several ingredients that were known to have moisturizing properties. *See* Ex. 1005 (Murthy Decl.) ¶ 37. Given that applying moisturizers was another known means of combating the irritation caused by tazarotene, the moisturizing properties of WO '001's formulation would have provided POSITAs with even further motivation to use that composition to treat acne. *See supra* ¶ 39.

b. Kircik

79. Kircik disclosed a clinical study comparing tretinoin microsphere gel 0.04% delivered by pump to tazarotene cream 0.05% in the treatment of mild-to-moderate facial acne. Ex. 1009 (Kircik) at 650-651. Kircik disclosed that tazarotene 0.05% cream produced a 36.86, 64.54, and 70.06% reduction in total inflammatory lesions at weeks 4, 8, and 12 respectively and a 37.26, 58.94, and 75.50% reduction in total non-inflammatory lesions at weeks 4, 8, and 12, all of which were statistically significant. *Id.* at 651-52, Figs. 1-2. Based on these results, persons of ordinary skill in the art would have reasonably expected that compositions with tazarotene at 0.05% or a similar concentration, including 0.045%, would have been efficacious in treating acne. As I explained in the preceding section, Kircik's teachings regarding the efficacy of 0.05% tazarotene compositions would have been consistent with the person of ordinary skill in the art's clinical experience prior to May 2017 and the common practice of off-label prescriptions of 0.05% tazarotene to treat acne during that time. *Supra* § VII.A.1.b.

80. Kircik's teachings of the efficacy of a 0.05% tazarotene composition in the topical treatment of acne would have motivated persons of ordinary skill in the art to use the 0.045% tazarotene composition disclosed by WO '001 with a reasonable expectation of success for the same reasons I explained above with respect to Anderson. *Supra* § VII.A.1.a. Persons of ordinary skill would have been

motivated to combine the teachings of WO '001, which focused on treating psoriasis with tazarotene compositions, and Kircik, which focused on treating acne with tazarotene, for the same reasons explained in the previous section regarding WO '001 and Anderson. *Supra* § VII.A.1.b.

c. Chim

81. Chim disclosed that “[s]ubstantial evidence supports the use of [topical retinoids] across all stages of acne severity.” Ex. 1010 (Chim) at 7. Chim teaches that “[d]osing of [topical retinoids] should start at the lowest concentration a few times a week and be titrated to nightly, as tolerated.” *Id.* at 13. This is consistent with my understanding of clinical practice prior to May 2017, as I noted above. Persons of ordinary skill in the art would have known that 0.05% tazarotene was the “lowest concentration” commercially available prior to May 2017. This is confirmed by Table 1-3 in Chim, which is titled “Available Prescription Options to Treat Acne Vulgaris” and lists tazarotene cream 0.05% and gel 0.05% as available prescription options to treat acne.

Table 1-3. Available Prescription Options to Treat Acne Vulgaris				
Drugs	Available Formulations (Concentrations)	Dose	Common Adverse Effects	Place in Therapy
Topical Retinoids				
Adapalene	Cream (0.1%) Gel (0.1%, 0.3%) Lotion (0.1%)	Once daily (cream, gel: daily in the evening)	Dryness, erythema, photosensitivity, pruritus, scaling, stinging	Any stage
Tazarotene	Cream (0.05%, 0.1%) Foam (0.1%) Gel (0.05%, 0.1%)	Once daily in the evening		
Tretinoin	Cream (0.025%, 0.05%, 0.1%) Gel (0.01%, 0.025%) Micronized gel (0.04%, 0.08%, 0.1%)	Once daily in the evening		

Id. at Table 1-3. Chim disclosed that limited evidence had suggested that tazarotene was more effective than tretinoin and adapalene, which would have motivated persons of ordinary skill in the art to use and develop new tazarotene compositions for treating acne. *Id.* at 13. Chim also teaches that topical retinoids “are limited by their adverse effects, which may result in nonadherence or discontinuation” and teaches that irritation can be managed through application of moisturizers or by “dosing or choice of vehicle.” *Id.* This teaching would have motivated persons of ordinary skill in the art to develop new tazarotene compositions with less irritating side effects.

82. Chim’s teaching that dosing of topical retinoids, like tazarotene, should start at the lowest concentration due to tolerability concerns would have motivated persons of ordinary skill in the art to use a lower-concentration tazarotene composition, such as the 0.045% tazarotene composition in WO ’001, to treat acne. *Id.* Chim’s teachings of the efficacy and irritation benefits of a 0.05% tazarotene

composition in the topical treatment of acne would have further motivated persons of ordinary skill in the art to use the 0.045% tazarotene composition disclosed by WO '001 with a reasonable expectation of success for the same reasons explained above with respect to Kircik and Anderson. *Supra* §§ VII.A.2.a.-b. Persons of ordinary skill would have been motivated to combine the teachings of WO '001, which focused on treating psoriasis with tazarotene compositions, and Chim, which focused on treating acne with tazarotene, for the same reasons explained previously regarding WO '001 and Anderson and WO '001 and Kircik. *Id.*

3. Oil-in-Water Emulsion Lotion

83. Claim 1 next recites “wherein the composition is an oil-in-water emulsion lotion comprising an oil phase and an aqueous phase.” WO '001 discloses this limitation.

84. I am not an expert in the field of drug formulation; however, the tazarotene-only composition disclosed in WO '001 has the exact same ingredients as Composition A disclosed in the '482 patent:

TABLE 2					
Some Emulsion Compositions of the Present Invention for Treating Acne					
Ingredient	Function	Concentration (wt %)			Composition A
		Range 1	Range 2	Range 3	
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Note:

⁽¹⁾These ingredients are broadly classified as Pharmaceutical Aids.

Table 4					
Compositions for Clinical Studies					
Ingredient	Function	Concentration (wt%)			
		IDP-118 (Present Invention)	Placebo (Vehicle)	Halobetasol propionate only	Tazarotene only
Halobetasol propionate, micronized	Active Ingredient	0.01	0	0.01	0
Tazarotene	Active Ingredient	0.045	0	0	0.045
Diethyl sebacate	Emollient & Solvent	2.97	2.97	2.97	2.97
Light mineral oil	Emollient & Solvent	8.03	8.03	8.03	8.03
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.1	0.1	0.1	0.1
Sorbitol solution, 70%	Humectant	10.7	10.7	10.7	10.7
Methyl paraben	Antimicrobial Preservative	0.17	0.17	0.17	0.17
Propyl paraben	Antimicrobial Preservative	0.03	0.03	0.03	0.03
Edetate disodium dihydrate	Chelating Agent	0.05	0.05	0.05	0.05
Carbomer copolymer type B (Pemulen™ TR-1)	Emulsifying Agent	0.4	0.4	0.4	0.4
Carbomer homopolymer type A (Carbomer 981)	Thickener	0.6	0.6	0.6	0.6
Sodium hydroxide	pH-adjusting agent	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Solvent	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1007 (WO '001) at Table 4.

WO '001 also expressly discloses that the tazarotene-only composition in Table 4 is an oil-in-water emulsion lotion having an aqueous phase and an oil phase.

WO '001

[0055] A lotion having a composition as shown in the last column of Table 2 was prepared as follows.

[0056] A separate aqueous phase was made. In a manufacturing vessel equipped with a mixing implement (such as a propeller) and temperature control, purified water and disodium edetate dihydrate were combined and the mixture was agitated until a clear solution is achieved. Sorbitol, methylparaben, and propylparaben were then added to the mixture. The mixture was continuously mixed and was heated to approximately 75 °C. The mixture was agitated until a solution was obtained. The mixture was then removed from the heat source and allowed to cool to below 40 °C with continued mixing. With continuous mixing, Carbopol® 981 was added to the mixture and dispersed. Mixing continued until Carbopol® 981 was fully dispersed and hydrated.

[0057] A separate oil phase was made. In a vessel equipped with a mixing implement such as a propeller, diethyl sebacate, halobetasol propionate, and tazarotene were combined. The mixture was agitated until a solution was achieved. With continuous mixing, light mineral oil and sorbitan monooleate were added. Mixing is continued until a solution is obtained.

See Ex. 1007 (WO '001) at Table 4 at [0054]-[0060] (describing preparation of oil-in-water emulsion lotion involving preparation of an aqueous phase and an oil phase).

85. My opinions regarding WO '001 are further confirmed by the expert

declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that WO '001 disclosed a topical tazarotene composition comprising an oil-in-water emulsion comprising an oil phase and an aqueous phase. Ex. 1005 (Murthy Decl.) at ¶¶ 90-91. I agree with Dr. Murthy's analysis of WO '001.

4. Oil Phase

86. Claim 1 next recites "wherein the oil phase comprises a dicarboxylic acid ester and a mineral oil at a total concentration of 10-12 percent by weight of the composition." WO '001 discloses this limitation.

87. The tazarotene-only composition disclosed in WO '001 has the exact same ingredients as Composition A disclosed in the '482 patent:

'482 patent

TABLE 2					
Some Emulsion Compositions of the Present Invention for Treating Acne					
Ingredient	Function	Concentration (wt %)			Composition A
		Range 1	Range 2	Range 3	
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Note:
⁽¹⁾These ingredients are broadly classified as Pharmaceutical Aids.

WO '001

Table 4					
Compositions for Clinical Studies					
Ingredient	Function	Concentration (wt%)			
		IDP-118 (Present Invention)	Placebo (Vehicle)	Halobetasol propionate only	Tazarotene only
Halobetasol propionate, micronized	Active Ingredient	0.01	0	0.01	0
Tazarotene	Active Ingredient	0.045	0	0	0.045
Diethyl sebacate	Emollient & Solvent	2.97	2.97	2.97	2.97
Light mineral oil	Emollient & Solvent	8.03	8.03	8.03	8.03
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.1	0.1	0.1	0.1
Sorbitol solution, 70%	Humectant	10.7	10.7	10.7	10.7
Methyl paraben	Antimicrobial Preservative	0.17	0.17	0.17	0.17
Propyl paraben	Antimicrobial Preservative	0.03	0.03	0.03	0.03
Edetate disodium dihydrate	Chelating Agent	0.05	0.05	0.05	0.05
Carbomer copolymer type B (Pemulen™ TR-1)	Emulsifying Agent	0.4	0.4	0.4	0.4
Carbomer homopolymer type A (Carbomer 981)	Thickener	0.6	0.6	0.6	0.6
Sodium hydroxide	pH-adjusting agent	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Solvent	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1007 (WO '001) at Table 4. WO '001 also expressly discloses that the oil phase of the tazarotene-only composition in Table 4 comprises 2.97% diethyl sebacate, which the '482 patent identifies as a dicarboxylic acid ester, and 8.03% light mineral oil.

WO '001

[0057] A separate oil phase was made. In a vessel equipped with a mixing implement such as a propeller, diethyl sebacate, halobetasol propionate, and tazarotene were combined. The mixture was agitated until a solution was achieved. With continuous mixing, light mineral oil and sorbitan monooleate were added. Mixing is continued until a solution is obtained.

See Ex. 1007 (WO '001) at [0057], Table 4 (describing preparation of the oil phase by adding diethyl sebacate and light mineral oil).

88. My opinions regarding WO '001 are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that WO '001 disclosed a topical tazarotene composition comprising an oil-in-water emulsion wherein the oil phase comprises 2.97% diethyl sebacate, which the '482 patent identifies as a dicarboxylic acid ester, and 8.03% light mineral oil. Ex. 1005 (Murthy Decl.) at ¶¶ 92-93. I agree with Dr. Murthy's analysis of WO '001.

5. Aqueous Phase

89. Claim 1 next recites “wherein the aqueous phase comprises water and a carbomer homopolymer, wherein the concentration of the carbomer homopolymer is 0.5-0.7 percent by weight of the composition.” WO ’001 discloses this limitation.

90. The tazarotene-only composition disclosed in WO ’001 has the exact same ingredients as Composition A disclosed in the ’482 patent:

'482 patent						WO ’001					
TABLE 2						Table 4					
Some Emulsion Compositions of the Present Invention for Treating Acne						Compositions for Clinical Studies					
Ingredient	Function	Concentration (wt %)				Ingredient	Function	Concentration (wt%)			
		Range 1	Range 2	Range 3	Composition A			IDP-118 (Present Invention)	Placebo (Vehicle)	Halobetasol propionate only	Tazarotene only
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	Halobetasol propionate, micronized	Active Ingredient	0.01	0	0.01	0
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	Tazarotene	Active Ingredient	0.045	0	0	0.045
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	Diethyl sebacate	Emollient & Solvent	2.97	2.97	2.97	2.97
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	Light mineral oil	Emollient & Solvent	8.03	8.03	8.03	8.03
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	Sorbitan monooleate	Surfactant/Emulsifying Agent	0.1	0.1	0.1	0.1
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	Sorbitol solution, 70%	Humectant	10.7	10.7	10.7	10.7
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	Methyl paraben	Antimicrobial Preservative	0.17	0.17	0.17	0.17
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	Propyl paraben	Antimicrobial Preservative	0.03	0.03	0.03	0.03
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	Edetate disodium dihydrate	Chelating Agent	0.05	0.05	0.05	0.05
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	Carbomer copolymer type B (Pemulen™ TR-1)	Emulsifying Agent	0.4	0.4	0.4	0.4
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	Carbomer homopolymer type A (Carbomer 981)	Thickener	0.6	0.6	0.6	0.6
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	Sodium hydroxide	pH-adjusting agent	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Note: ⁽¹⁾ These ingredients are broadly classified as Pharmaceutical Aids.						Purified water	Solvent	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Compare Ex. 1001 (’482 patent) at Table 2 with Ex. 1007 (WO ’001) at Table 4.

WO ’001 also expressly discloses that the aqueous phase of the oil-in-water emulsion lotions in Table 4 comprised water and Carbopol 981, which Table 4 identifies as carbomer homopolymer type A, at 0.6%.

WO '001

[0056] A separate aqueous phase was made. In a manufacturing vessel equipped with a mixing implement (such as a propeller) and temperature control, purified water and disodium edetate dihydrate were combined and the mixture was agitated until a clear solution is achieved. Sorbitol, methylparaben, and propylparaben were then added to the mixture. The mixture was continuously mixed and was heated to approximately 75 °C. The mixture was agitated until a solution was obtained. The mixture was then removed from the heat source and allowed to cool to below 40 °C with continued mixing. With continuous mixing, Carbopol® 981 was added to the mixture and dispersed. Mixing continued until Carbopol® 981 was fully dispersed and hydrated.

See Ex. 1007 (WO '001) at [0056], Table 4 (describing preparation of aqueous phase by adding Carbopol 981 to mixture including purified water).

91. My opinions regarding WO '001 are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that WO '001 disclosed a topical tazarotene composition containing water, q.s. to 100 weight % and 0.6 weight % carbomer homopolymer type A. Ex. 1005 (Murthy Decl.) at ¶¶ 94-95. I agree with Dr. Murthy's analysis of WO '001.

6. Polymeric Emulsifier

92. Lastly, Claim 1 recites "wherein the composition further comprises a polymeric emulsifier at a concentration of 0.3-0.5 percent by weight of the

composition.” WO ’001 discloses this limitation.

93. The tazarotene-only composition disclosed in WO ’001 has the exact same ingredients as Composition A disclosed in the ’482 patent:

'482 patent						WO ’001					
TABLE 2						Table 4					
Some Emulsion Compositions of the Present Invention for Treating Acne						Compositions for Clinical Studies					
Ingredient	Function	Concentration (wt %)				Ingredient	Function	Concentration (wt%)			
		Range 1	Range 2	Range 3	Composition A			IDP-118 (Present Invention)	Placebo (Vehicle)	Halobetasol propionate only	Tazarotene only
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	Halobetasol propionate, micronized	Active Ingredient	0.01	0	0.01	0
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	Tazarotene	Active Ingredient	0.045	0	0	0.045
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	Diethyl sebacate	Emollient & Solvent	2.97	2.97	2.97	2.97
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	Light mineral oil	Emollient & Solvent	8.03	8.03	8.03	8.03
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	Sorbitan monooleate	Surfactant/Emulsifying Agent	0.1	0.1	0.1	0.1
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	Sorbitol solution, 70%	Humectant	10.7	10.7	10.7	10.7
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	Methyl paraben	Antimicrobial Preservative	0.17	0.17	0.17	0.17
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	Propyl paraben	Antimicrobial Preservative	0.03	0.03	0.03	0.03
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	Edetate disodium dihydrate	Chelating Agent	0.05	0.05	0.05	0.05
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	Carbomer copolymer type B (Pemulen™ TR-1)	Emulsifying Agent	0.4	0.4	0.4	0.4
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	Carbomer homopolymer type A (Carbomer 981)	Thickener	0.6	0.6	0.6	0.6
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	Sodium hydroxide	pH-adjusting agent	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Note: ⁽¹⁾ These ingredients are broadly classified as Pharmaceutical Aids.						Purified water	Solvent	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Compare Ex. 1001 (’482 patent) at Table 2 with Ex. 1007 (WO ’001) at Table 4.

WO ’001 also expressly discloses that the tazarotene-only composition in Table 4 includes 0.4% Pemulen TR-1 (carbomer copolymer type B), which the ’482 patent identifies as a polymeric emulsifier.

WO '001

[0059] With high speed mixing, the oil phase containing the active ingredients (halobetasol propionate and tazarotene) was added to the aqueous phase. Pemulen™ TR-1 was slowly added into the mixture. Mixing was continued until a homogeneous emulsion was obtained. Mixing speed was decreased and mixing continued for an additional time of 10 minutes to 1 hour. With continuous mixing, an appropriate amount of the sodium hydroxide solution was added incrementally to obtain a pH of 5.5 ± 0.5 . Mixing continued further until a homogeneous lotion was obtained, such as for 30 minutes to 3 hours.

See Ex. 1007 (WO '001) at [0059], Table 4 (describing addition of Pemulen TR-1 to oil-in-water emulsion composition); *see also* Ex. 1001 ('482 patent) at 4:10-14 (“[P]olymeric emulsifiers such as those known under the trade name Pemulen™ (The Lubrizol Corporation, Wickliffe, Ohio) may be used.”).

94. My opinions regarding WO '001 are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that WO '001 disclosed a topical tazarotene composition comprising Pemulen TR-1 (carbomer copolymer type B), which is a polymeric emulsifier. Ex. 1005 (Murthy Decl.) at ¶¶ 96-98. I agree with Dr. Murthy's analysis of WO '001.

B. Claim 2

95. Claim 2 recites “[t]he method of claim 1, wherein the dicarboxylic acid ester in the oil phase is diethyl sebacate.”

96. WO '001 discloses this limitation for the reasons I explained in claim 1. *Supra* § VII.A.2.

C. Claim 3

97. Claim 3 recites “[t]he method of claim 1, wherein the oil phase comprises diethyl sebacate and light mineral oil.”

98. WO '001 discloses the limitations of claim 3 for the reasons I explained in claim 1. *Supra* § VII.A.2.

D. Claims 4-6

99. Claims 4-6 recite the method of claim 1, wherein the application is carried out for at least eight weeks (claim 4), at least twelve weeks (claim 5), or twelve weeks (claim 6). These claims would have been obvious over WO '001 in combination with Anderson, Kircik, or Chim.

100. WO '001 disclosed a composition comprising 0.045% tazarotene as the sole active ingredient, which was used to treat psoriasis for a period of 8 weeks. *See* Ex. 1007 (WO '001) at Table 4 [0084]. As I explained in claim 1, persons of ordinary skill in the art would have been motivated to use the 0.045% tazarotene composition from WO '001 to treat acne and would have had a reasonable expectation of success in doing so. *Supra* § VII.A. Persons of ordinary skill in the art would have found it obvious to use WO '001's 0.045% tazarotene lotion to treat acne for the lengths of time recited in claims 4-6 in view of Anderson, Kircik, or

Chim and their clinical experience.

101. Persons of ordinary skill in the art would have understood that the treatment of acne vulgaris requires a flexible approach that takes into account factors that may vary between individual patients, including the severity of the patient's disease and the patient's response to the prescribed treatment. This same flexibility applies to the length of treatment as well. Because there is no cure for acne, persons of ordinary skill in the art would have understood that there is not a set boundary on the duration of treatment with topical retinoids. Instead, the length of treatment would depend on the patient's response to the treatment and their ability to tolerate it. As reflected by Anderson, Kircik, and Chim, discussed below, a treatment period of 12-weeks was commonly used in the prior art for clinical studies. However, persons of ordinary skill in the art would have understood that topical retinoids would commonly be used for even longer periods due to the chronic nature of acne, or for shorter periods if the patient experienced difficulty tolerating the treatment.

1. Anderson

102. As I explained above, Anderson disclosed that several practicing dermatologists used 0.05% tazarotene compositions to treat acne as of 2004. *Supra* § VII.A.2.a. Anderson's teachings are consistent with my own clinical practice and experience. As I also explained above, Anderson would have motivated persons of ordinary skill in the art to use WO '001's 0.045% tazarotene lotion to treat acne and

would have given them a reasonable expectation of success in doing so. In my opinion, persons of ordinary skill in the art would have been motivated to have patients carry out that treatment for a period of at least 12-weeks or longer depending on the patient's response to the treatment. A 12-week period of treatment was common in clinical trials with topical retinoid therapies, including tazarotene, prior to May 2017, and a 12-week or longer treatment period was common in clinical practice. *See, e.g.*, Ex. 1013 (Tazorac® Label) at Clinical Studies (disclosing 12-week treatment of acne with topical tazarotene); Ex. 1017 (Fabior Label) at Clinical Studies (disclosing 12-week treatment of acne with topical tazarotene); Ex. 1034 (Differin® Label) at Clinical Studies (disclosing 12-week treatment of acne with topical adapalene). A 12-week treatment period would meet the at least 8-weeks, at least 12-weeks, and 12-weeks limitations of claims 4-6.

2. Kircik

103. Kircik disclosed treatment of acne vulgaris with once daily application of tazarotene 0.05% cream for 12-weeks. Ex. 1009 (Kircik) at 651. Kircik disclosed that tazarotene 0.05% cream produced a 36.86, 64.54, and 70.06% reduction in total inflammatory lesions at weeks 4, 8, and 12 respectively and a 37.26, 58.94, and 75.50% reduction in total non-inflammatory lesions at weeks 4, 8, and 12, all of which were statistically significant. *Id.* at 651-52, Figs. 1-2.

104. In my opinion, these results would have motivated POSITAs to use the

0.045% tazarotene composition in WO '001 to treat acne for a period of up to twelve weeks or longer, particularly because Kircik's 0.05% composition demonstrated the highest efficacy at week 12. *Id.* at 651-52, Figs. 1-2. Moreover, as I explained in the preceding section, a 12-week treatment period was common in clinical studies with topical retinoid therapies, including tazarotene, prior to May 2017, and a 12-week or longer treatment period was common in clinical practice. *Supra* ¶ 100. The 12-week treatment period disclosed in Kircik encompasses the 8 week, at least twelve week, and 12-week treatment period recited in claims 4-6.

3. Chim

105. Chim teaches that “[b]est results [with treating acne with topical retinoids] may be expected in about 3 months.” Ex. 1010 [Chim] at 13. This teaching is consistent with my clinical experience and understanding of clinical practice prior to May 2017, and it reflects the common understanding of clinical use with topical retinoids, which was that retinoids could be used to treat acne over a wide range of time periods, depending on individual patient factors. Thus, Chim reinforces that persons of ordinary skill in the art would have found it obvious to use the WO '001's 0.045% tazarotene lotion for at least 12-weeks (i.e., about 3 months) or longer, which encompasses the 8-week, at least 12-week, and 12-week treatment period recited in claims 4-6.

E. Claim 7

106. Claim 7 recites “wherein the tazarotene is in solution in the oil phase of the oil-in-water emulsion lotion.” WO ’001 discloses this limitation.

107. The tazarotene-only composition disclosed in WO ’001 has the exact same ingredients as Composition A disclosed in the ’482 patent:

'482 patent						WO ’001					
TABLE 2						Table 4					
Some Emulsion Compositions of the Present Invention for Treating Acne						Compositions for Clinical Studies					
Ingredient	Function	Concentration (wt %)				Ingredient	Function	Concentration (wt%)			
		Range 1	Range 2	Range 3	Composition A			IDP-118 (Present Invention)	Placebo (Vehicle)	Halobetasol propionate only	Tazarotene only
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	Halobetasol propionate, micronized	Active Ingredient	0.01	0	0.01	0
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	Tazarotene	Active Ingredient	0.045	0	0	0.045
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	Diethyl sebacate	Emollient & Solvent	2.97	2.97	2.97	2.97
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	Light mineral oil	Emollient & Solvent	8.03	8.03	8.03	8.03
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	Sorbitan monooleate	Surfactant/Emulsifying Agent	0.1	0.1	0.1	0.1
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	Sorbitol solution, 70%	Humectant	10.7	10.7	10.7	10.7
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	Methyl paraben	Antimicrobial Preservative	0.17	0.17	0.17	0.17
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	Propyl paraben	Antimicrobial Preservative	0.03	0.03	0.03	0.03
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	Edetate disodium dihydrate	Chelating Agent	0.05	0.05	0.05	0.05
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	Carbomer copolymer type B (Pemulen™ TR-1)	Emulsifying Agent	0.4	0.4	0.4	0.4
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	Carbomer homopolymer type A (Carbomer 981)	Thickener	0.6	0.6	0.6	0.6
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	Sodium hydroxide	pH-adjusting agent	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Note: ⁽¹⁾ These ingredients are broadly classified as Pharmaceutical Aids.						Purified water	Solvent	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Compare Ex. 1001 (’482 patent) at Table 2 with Ex. 1007 (WO ’001) at Table 4.

WO ’001 also expressly discloses that during preparation of the oil-in-water emulsion lotions, the tazarotene is added to the oil phase and “[t]he mixture was agitated until a solution was achieved,” which a clinician would understand to mean that the tazarotene was in solution in the oil phase.

WO '001

[0057] A separate oil phase was made. In a vessel equipped with a mixing implement such as a propeller, diethyl sebacate, halobetasol propionate, and tazarotene were combined. The mixture was agitated until a solution was achieved. With continuous mixing, light mineral oil and sorbitan monooleate were added. Mixing is continued until a solution is obtained.

See Ex. 1007 (WO '001) at [0057], Table 4.

108. My opinions regarding WO '001 are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that WO '001 disclosed that the tazarotene was in solution in the oil phase of the oil-in-water emulsions. Ex. 1005 (Murthy Decl.) at ¶¶ 111-113. I agree with Dr. Murthy's analysis of WO '001.

F. Claim 8

109. Claim 8 recites "wherein the composition has a pH of about 4 to about 6." WO '001 discloses this limitation.

110. The tazarotene-only composition disclosed in WO '001 has the exact same ingredients as Composition A disclosed in the '482 patent:

TABLE 2					
Some Emulsion Compositions of the Present Invention for Treating Acne					
Ingredient	Function	Concentration (wt %)			Composition A
		Range 1	Range 2	Range 3	
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Note:

⁽¹⁾These ingredients are broadly classified as Pharmaceutical Aids.

Table 4					
Compositions for Clinical Studies					
Ingredient	Function	Concentration (wt%)			
		IDP-118 (Present Invention)	Placebo (Vehicle)	Halobetasol propionate only	Tazarotene only
Halobetasol propionate, micronized	Active Ingredient	0.01	0	0.01	0
Tazarotene	Active Ingredient	0.045	0	0	0.045
Diethyl sebacate	Emollient & Solvent	2.97	2.97	2.97	2.97
Light mineral oil	Emollient & Solvent	8.03	8.03	8.03	8.03
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.1	0.1	0.1	0.1
Sorbitol solution, 70%	Humectant	10.7	10.7	10.7	10.7
Methyl paraben	Antimicrobial Preservative	0.17	0.17	0.17	0.17
Propyl paraben	Antimicrobial Preservative	0.03	0.03	0.03	0.03
Edetate disodium dihydrate	Chelating Agent	0.05	0.05	0.05	0.05
Carbomer copolymer type B (Pemulen™ TR-1)	Emulsifying Agent	0.4	0.4	0.4	0.4
Carbomer homopolymer type A (Carbomer 981)	Thickener	0.6	0.6	0.6	0.6
Sodium hydroxide	pH-adjusting agent	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Solvent	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1007 (WO '001) at Table 4.

WO '001 also expressly discloses that during preparation of the oil-in-water emulsion lotions, “[w]ith continuous mixing, an appropriate amount of the sodium hydroxide solution was added incrementally to obtain a pH of 5.5 ± 0.5.”

WO '001

[0059] With high speed mixing, the oil phase containing the active ingredients (halobetasol propionate and tazarotene) was added to the aqueous phase. Pemulen™ TR-1 was slowly added into the mixture. Mixing was continued until a homogeneous emulsion was obtained. Mixing speed was decreased and mixing continued for an additional time of 10 minutes to 1 hour. With continuous mixing, an appropriate amount of the sodium hydroxide solution was added incrementally to obtain a pH of 5.5 ± 0.5. Mixing continued further until a homogeneous lotion was obtained, such as for 30 minutes to 3 hours.

See Ex. 1007 (WO '001) at [0059], Table 4.

111. My opinions regarding WO '001 are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that WO '001 disclosed that the tazarotene only composition has a pH of about 4 to about 6. Ex. 1007 (Murthy Decl.) at ¶¶ 113-115. I agree with Dr. Murthy's analysis of WO '001.

G. Claims 9-10

112. Claim 9 recites "[t]he method of claim 1, wherein the composition consists essentially of: 0.045 weight % tazarotene; diethyl sebacate; light mineral oil; sorbitan monooleate; sorbitol solution, 70%; methylparaben; propylparaben; edetate disodium dihydrate; carbomer polymer type B; carbomer homopolymer type A; sodium hydroxide; purified water." Claim 10 recites "[t]he method of claim 1, wherein the composition consists essentially of: 0.045 weight % tazarotene; 2.5-3.5 weight % diethyl sebacate; 7.5-8.5 weight% light mineral oil; 0.05-0.2 weight % sorbitan monooleate; 10-11 weight% sorbitol solution, 70%; 0.1-0.2 weight % methylparaben; 0.02-0.04 weight % propylparaben; 0.03-0.06 weight % edetate disodium dihydrate; 0.3-0.5 weight % carbomer polymer type B; 0.5-0.7 weight% carbomer homopolymer type A; sodium hydroxide, q.s. to pH 5.5±0.5; and purified water, q.s. to 100 weight%." WO '001 discloses both the claim 9 limitations and the

claim 10 limitations.

113. The tazarotene-only composition disclosed in WO '001 has the exact same ingredients as Composition A disclosed in the '482 patent:

'482 patent						WO '001					
TABLE 2						Table 4					
Some Emulsion Compositions of the Present Invention for Treating Acne						Compositions for Clinical Studies					
Ingredient	Function	Concentration (wt %)				Ingredient	Function	Concentration (wt%)			
		Range 1	Range 2	Range 3	Composition A			IDP-118 (Present Invention)	Placebo (Vehicle)	Halobetasol propionate only	Tazarotene only
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	Halobetasol propionate, micronized	Active Ingredient	0.01	0	0.01	0
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	Tazarotene	Active Ingredient	0.045	0	0	0.045
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	Diethyl sebacate	Emollient & Solvent	2.97	2.97	2.97	2.97
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	Light mineral oil	Emollient & Solvent	8.03	8.03	8.03	8.03
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	Sorbitan monooleate	Surfactant/Emulsifying Agent	0.1	0.1	0.1	0.1
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	Sorbitol solution, 70%	Humectant	10.7	10.7	10.7	10.7
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	Methyl paraben	Antimicrobial Preservative	0.17	0.17	0.17	0.17
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	Propyl paraben	Antimicrobial Preservative	0.03	0.03	0.03	0.03
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	Edetate disodium dihydrate	Chelating Agent	0.05	0.05	0.05	0.05
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	Carbomer copolymer type B (Pemulen™ TR-1)	Emulsifying Agent	0.4	0.4	0.4	0.4
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	Carbomer homopolymer type A (Carbomer 981)	Thickener	0.6	0.6	0.6	0.6
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	Sodium hydroxide	pH-adjusting agent	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Note: ⁽¹⁾ These ingredients are broadly classified as Pharmaceutical Aids.						Purified water	Solvent	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1007 (WO '001) at Table 4. Based on my review of Table 4, the tazarotene-only composition in WO '001 contains all of the ingredients recited in claims 9 and 10 within the recited concentration ranges. See Ex. 1007 (WO '001) at Table 4.

114. My opinions regarding WO '001 are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that WO '001 disclosed that the tazarotene only composition in Table 4 disclosed all of the ingredients recited in claims 9 and 10 within the claimed concentration ranges.

Ex. 1005 (Murthy Decl.) at ¶¶ 117-119. I agree with Dr. Murthy's analysis of WO '001.

H. Claim 11

115. Claim 11 is an independent claim that recites “[a] method of treating acne vulgaris, the method comprising topically applying a pharmaceutical composition to an affected area of a body of a subject suffering from acne vulgaris; wherein the composition consists essentially of: 0.045 weight % tazarotene; 2.97 weight % diethyl sebacate; 8.03 weight % light mineral oil; 0.1 weight% sorbitan monooleate; 10.7 weight% sorbitol solution, 70%; 0.17 weight % methylparaben; 0.03 weight % propylparaben; 0.05 weight % edetate disodium dihydrate; 0.4 weight % carbomer polymer type B; 0.6 weight % carbomer homopolymer type A; sodium hydroxide, q.s. to pH 5.5±0.5; and purified water, q.s. to 100 weight%.”

116. In my opinion, the preamble of claim 11 would have been obvious in view of WO '001 in combination with Anderson, Kircik, or Chim as previously explained for claim 1. *Supra* § VII.A.

117. Regarding the remaining limitations of claim 11, the tazarotene-only composition disclosed in WO '001 has the exact same ingredients as Composition A disclosed in the '482 patent:

TABLE 2					
Some Emulsion Compositions of the Present Invention for Treating Acne					
Ingredient	Function	Concentration (wt %)			Composition A
		Range 1	Range 2	Range 3	
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Note:

⁽¹⁾These ingredients are broadly classified as Pharmaceutical Aids.

Table 4					
Compositions for Clinical Studies					
Ingredient	Function	Concentration (wt%)			
		IDP-118 (Present Invention)	Placebo (Vehicle)	Halobetasol propionate only	Tazarotene only
Halobetasol propionate, micronized	Active Ingredient	0.01	0	0.01	0
Tazarotene	Active Ingredient	0.045	0	0	0.045
Diethyl sebacate	Emollient & Solvent	2.97	2.97	2.97	2.97
Light mineral oil	Emollient & Solvent	8.03	8.03	8.03	8.03
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.1	0.1	0.1	0.1
Sorbitol solution, 70%	Humectant	10.7	10.7	10.7	10.7
Methyl paraben	Antimicrobial Preservative	0.17	0.17	0.17	0.17
Propyl paraben	Antimicrobial Preservative	0.03	0.03	0.03	0.03
Edetate disodium dihydrate	Chelating Agent	0.05	0.05	0.05	0.05
Carbomer copolymer type B (Pemulen™ TR-1)	Emulsifying Agent	0.4	0.4	0.4	0.4
Carbomer homopolymer type A (Carbomer 981)	Thickener	0.6	0.6	0.6	0.6
Sodium hydroxide	pH-adjusting agent	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Solvent	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1007 (WO '001) at Table 4.

Based on my review of Table 4, the tazarotene-only composition in WO '001 contains all of the ingredients recited in claim 11 at the recited concentrations. See Ex. 1007 (WO '001) at Table 4.

118. My opinions regarding WO '001 are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that WO '001 disclosed that the tazarotene only composition in Table 4 disclosed all of the ingredients recited in claim 11 at the claimed concentrations. Ex. 1005 (Murthy Decl.) at ¶¶ 120-123. I agree with Dr. Murthy's analysis of WO '001.

**VIII. GROUND 4: CLAIMS 1-11 WOULD HAVE BEEN OBVIOUS OVER
WO '001 AND ANDERSON IN COMBINATION WITH SHALITA**

119. As explained in Grounds 1-3, WO '001 and Anderson render claims 1-11 of the '482 patent obvious. *Supra* § VII.

120. Shalita would have provided POSITAs with even further motivation to use the 0.045% tazarotene lotion from WO '001 to treat acne.

121. Shalita disclosed a 12-week multicenter, double-blind, vehicle-controlled study of tazarotene 0.1% and 0.05% gel in the treatment of acne. Ex. 1011 (Shalita) at 350. Shalita disclosed that treatment with 0.05% tazarotene gel was significantly more effective than treatment with vehicle gel in terms of both reduction in lesion count and treatment success rate. *Id.* at 351, Figs. 1-2. Shalita also disclosed that irritation caused by topical tazarotene treatment “[is] consistent with the known effects of topical retinoids” and “can be managed in ways similar to other retinoids: reducing treatment to every other day until skin ‘hardens’ to the retinoid; reducing the strength of the treatment, from 0.1% gel to 0.05% gel until the skin adjusts; or a combination of the two.” *Id.* at 354.

122. In my opinion, Shalita’s teachings of the efficacy and irritation-reducing benefits of a 0.05% tazarotene composition in the topical treatment of acne would have further motivated persons of ordinary skill in the art to use the 0.045% tazarotene composition disclosed by WO '001 with a reasonable expectation of

success. This is particularly so given Anderson's teachings regarding the clinical use of 0.05% tazarotene to treat acne (*supra* § VII.A.2.a.) and the person of ordinary skill's awareness that topical compositions comprising 0.05% tazarotene were commonly prescribed by physicians prior to May 2017. *See supra* § III. Given this common practice and the efficacy results disclosed in Shalita, persons of ordinary skill in the art would have reasonably expected a topical composition with a similar concentration of tazarotene, such as the 0.045% tazarotene composition in WO '001, to be efficacious in treating acne. Persons of ordinary skill in the art would have expected that the difference in concentration between the 0.05% and 0.045% tazarotene compositions is minor and would have expected that difference to have little, if any, impact on the efficacy of the treatment.

123. Shalita would have also given persons of ordinary skill in the art a reasonable expectation that the 0.045% tazarotene composition in WO '001 would cause less irritation than higher concentrations of tazarotene, for example 0.1%, providing further motivation to use that composition to treat acne. *See* Ex. 1011 (Shalita) at 354. Persons of ordinary skill in the art would have been motivated to combine the teachings of WO '001, which focused on treating psoriasis with tazarotene compositions, with Anderson and Shalita, which focused on treating acne with tazarotene, for the reasons explained in Grounds 1-3 for WO '001 and Anderson. *Supra* § VII. Accordingly, it is my opinion that claims 1-11 of the '482

patent would have been obvious over WO '001 in combination with Anderson and Shalita.

A. Claims 4-6

124. Claims 4-6 recite the method of claim 1, wherein the application is carried out for at least eight weeks (claim 4), at least twelve weeks (claim 5), or twelve weeks (claim 6).

125. Shalita would have provided persons of ordinary skill in the art further motivation to use the 0.045% tazarotene formulation from WO '001 to treat acne for the length of time recited in claims 4-6 of the '482 patent. Shalita discloses treatment of acne vulgaris with once daily application of tazarotene 0.05% gel for 12-weeks. Ex. 1011 (Shalita) at 350. Shalita teaches that treatment with 0.05% tazarotene gel was statistically significantly more effective than vehicle at decreasing noninflammatory and total lesion count at week 12 and provided a statistically significantly higher success rate than vehicle at week 8. *Id.* at 351, Figs. 1-2. These teachings would have further motivated persons of ordinary skill in the art to use the 0.045% tazarotene composition in WO '001 to treat acne for a period of up to twelve weeks or longer. Moreover, as I explained in Grounds 1-3, a 12-week treatment period was common with clinical trials of topical retinoid therapies, including tazarotene, prior to May 2017, and a 12-week or longer treatment period was common in clinical practice. *Supra* ¶ 100. The 12-week treatment period disclosed

in Shalita encompasses the 8-week, at least twelve week, and 12-week treatment period recited in claims 4-6.

**IX. GROUND 5: CLAIMS 1-11 WOULD HAVE BEEN OBVIOUS OVER
THE '824 PUBLICATION AND THE TAZORAC® LABEL**

126. As I discussed previously, persons of ordinary skill in the art in May 2017 would have been motivated to develop new topical tazarotene formulations with less irritating side effects. *Supra* § III. As I also explained, persons of skill in the art would have known that the irritation caused by tazarotene composition could be reduced by lowering the concentration of tazarotene in the formulation (e.g., from 0.1% to 0.05%) and using non-irritating, moisturizing formulations. *Id.* Persons of ordinary skill in the art would have recognized the '824 publication as providing a vehicle that allowed for lower concentrations of the active ingredient to maintain similar efficacy as compositions with much higher concentrations.

127. The '824 publication disclosed oil-in-water lotion emulsion vehicles for formulating corticosteroid compositions that were able to maintain potency even when the concentration of the corticosteroid was significantly reduced, by as much as five times. *See* Ex. 1012 ('824 publication) at [0035]. The '824 publication achieved this through use of lotion vehicles containing a “liquid oil component” comprising a dicarboxylic acid ester that dissolves the active ingredient, enabling enhanced delivery of the active ingredient into the skin, rather than through the skin

into systemic circulation. *Id.* at [0016]. One such vehicle disclosed by the '824 publication is **identical** to the vehicle of the tazarotene composition disclosed and claimed in the '482 patent.

'482 patent						'824 publication		
TABLE 2						TABLE 4		
Some Emulsion Compositions of the Present Invention for Treating Acne						% w/w		
Ingredient	Function	Concentration (wt %)				Ingredients	Formula 4A	Formula 4B
		Range 1	Range 2	Range 3	Composition A			
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	Halobetasol Propionate	0.01	0.025
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	Diethyl Sebacate	2.97	2.90
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	Light Mineral Oil	8.03	2.90
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	Sorbitan Monooleate	0.10	0.10
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	Sorbitol Solution, 70%	10.7	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	Disodium Edetate, Dihydrate	0.05	0.05
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	Pemulen TR-1	0.40	0.40
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	Carbopol 981	0.60	0.60
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	Methylparaben	0.17	0.17
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	Propylparaben	0.03	0.03
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	Sodium Hydroxide, q. s.	pH 4.0-6.0	pH 4.0-6.0
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	Purified Water, q.s. ad	100	100

Note:
⁽¹⁾These ingredients are broadly classified as Pharmaceutical Aids.

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1012 ('824 publication) at Table 4.

128. I have read the declaration submitted by Dr. Murthy, and I understand from Dr. Murthy's declaration that he has opined that a person skilled in the art of formulation would have been motivated to formulate 0.045% tazarotene in the oil-in-water emulsion vehicles with the specific components disclosed in the '824 publication. Ex. 1005 (Murthy Decl.) at ¶¶ 131-133, 141-145. Dr. Murthy's opinions are consistent with my own opinions regarding the '824 publication, which I offer from the perspective of an ordinarily skilled clinician.

129. The Tazorac[®] Label disclosed Tazorac[®] Cream in amounts of 0.05% and 0.1%, which are applied once daily. See Ex. 1013 (Tazorac[®] Label) at

Indications and Usage. Tazorac® Label disclosed that the most common adverse reactions associated with treatment are pruritus, erythema, and burning. *See id.* at Adverse Reactions. The 0.1% Tazorac® Cream produced a greater degree of local irritation than the 0.05% Tazorac® Cream. *Id.* at Adverse Reactions. The Tazorac® Label instructs that patients may use moisturizers as frequently as desired during application of Tazorac®. *Id.* at Patient Counseling Information.

130. Accordingly, based on my review of the prior art, it is my opinion that claims 1-11 of the '482 patent would have been obvious over the '824 publication in combination with the Tazorac® Label. My opinions are further confirmed by the expert declaration of Dr. Murthy, an expert in the field of topical drug formulation, as I explain below.

A. Claim 1

131. In my opinion, claim 1 of the '482 patent would have been obvious over the '824 publication in combination with the Tazorac® Label.

1. Preamble

132. The preamble of Claim 1 recites “[a] method of treating acne vulgaris, the method comprising topically applying a pharmaceutical composition once per day to an affected area of a body of a subject suffering from acne vulgaris.”

133. The Tazorac® label discloses a method of treating acne vulgaris by applying the pharmaceutical composition once per day to an affected area of a body

of a subject suffering from acne vulgaris. Ex. 1013 (Tazorac® Label) at Indications and Usage.

2. Composition of Tazarotene at 0.045% as Sole Active Ingredient

134. Claim 1 next recites “wherein the composition comprises tazarotene at a concentration of about 0.045 percent by weight of the composition as a sole active pharmaceutical ingredient.”

135. The Tazorac® label disclosed topical tazarotene compositions with two different concentrations of tazarotene: 0.1% and 0.05%. Ex. 1013 (Tazorac® Label) at Indications and Usage.

136. Persons of ordinary skill in the art would have been motivated to select a tazarotene concentration of about 0.045% in view of the Tazorac® Label’s teaching that the “0.1% was associated with a greater degree of local irritation than the 0.05% cream.” *Id.* at Adverse Reactions. As I explained previously, skin irritation was a well-known side effect with tazarotene treatment, and persons of ordinary skill in the art would have known that it could negatively impact patient compliance with the treatment regimen, and thereby reduce the efficacy of the treatment. Persons of ordinary skill in the art would have therefore been motivated to minimize local skin irritation to improve patient compliance and would have recognized lowering the concentration of tazarotene in the formulation to about 0.05% as one means for doing so in view of the Tazorac Label® and their general

knowledge regarding tazarotene treatments. *See* Ex. 1022 (Dosik) at 293; Ex. 1010 (Chim) at 13.

137. Persons of ordinary skill in the art would have reasonably expected that a composition with 0.045% tazarotene would have been effective in treating acne. As I explained above, off-label use of 0.05% tazarotene compositions to treat acne was common prior to May 2017, and a person of ordinary skill in the art would have been aware of that practice. *Supra* § III.A. In my opinion, persons of ordinary skill in the art would not have expected the difference in concentration between 0.045% tazarotene and 0.05% tazarotene to have had a significant effect on the efficacy of the composition.

138. Persons of ordinary skill in the art would have particularly expected success in treating acne with a 0.045% tazarotene composition that is formulated in the vehicles disclosed by the '824 publication. As I explained above, the '824 publication teaches that its lotion vehicle improves the penetration of the active ingredient into the patient's skin, which allows for the compositions to have the same or better efficacy even when the concentration of the active ingredient is greatly reduced. Ex. 1012 ('824 publication), [0035], [0037]-[0040], Tables 1 & 3. These teachings would have motivated a person of ordinary skill in the art to use the vehicles of the '824 publication to formulate a tazarotene composition with a lower concentration of about 0.05% tazarotene to reduce irritating side effects while

maintaining efficacy.

139. My opinions regarding the '824 publication are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that an ordinarily skilled formulator would have been motivated to formulate 0.045% tazarotene in the vehicles disclosed by the '824 publication, particularly Formula 4A in Table 4. Ex. 1005 (Murthy Decl.) at ¶¶ 131-133, 141-145. Dr. Murthy's opinions therefore reinforce my view that an ordinary skilled clinician would have been motivated to use the vehicles disclosed in the '824 publication to formulate a lower-concentration (about 0.05%) tazarotene composition for treating acne.

3. Oil-in-Water Emulsion Lotion

140. Claim 1 next recites "wherein the composition is an oil-in-water emulsion lotion comprising an oil phase and an aqueous phase." The '824 publication discloses this limitation.

141. Formula 4A disclosed in the '824 publication has the exact same ingredients as Composition A disclosed in the '482 patent with the exception of tazarotene:

'482 patent

TABLE 2					
Some Emulsion Compositions of the Present Invention for Treating Acne					
Ingredient	Function	Concentration (wt %)			
		Range 1	Range 2	Range 3	Composition A
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100

Note:

⁽¹⁾These ingredients are broadly classified as Pharmaceutical Aids.

'824 publication

TABLE 4		
Ingredients	% w/w	
	Formula 4A	Formula 4B
Halobetasol Propionate	0.01	0.025
Diethyl Sebacate	2.97	2.90
Light Mineral Oil	8.03	2.90
Sorbitan Monooleate	0.10	0.10
Sorbitol Solution, 70%	10.7	10.7
Disodium Edetate, Dihydrate	0.05	0.05
Pemulen TR-1	0.40	0.40
Carbopol 981	0.60	0.60
Methylparaben	0.17	0.17
Propylparaben	0.03	0.03
Sodium Hydroxide, q. s.	pH 4.0-6.0	pH 4.0-6.0
Purified Water, q.s. ad	100	100

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1012 ('824 publication) at Table 4. The '824 publication also expressly discloses that the oil phase of the formulations in Table 4 are oil-in-water emulsion lotion having an aqueous phase and an oil phase.

Lotion Formulations

[0041] Lotion formulations 4a and 4b of the present invention contain the ingredients shown in Table 4. These formulations may be made as follows.

[0042] A separate aqueous phase is made. In a manufacturing vessel, purified water and disodium edetate dihydrate are combined and the mixture is agitated until a clear solution is achieved. Sorbitol, methylparaben, and propylparaben are then added to the mixture. The mixture is continuously mixed and is heated to approximately 75° C. The mixture is agitated until a solution is obtained. The mixture is then removed from the heat source and allowed to cool to below 40° C. with continued mixing. With continuous propeller agitation Carbopol 981 and Pemulen TR-1 are added to the mixture and dispersed. The propeller mixing is continued until the polymers are fully dispersed and hydrated.

[0043] A separate oil phase is made. In a vessel diethyl sebacate and halobetasol propionate are combined. The mixture is agitated until a solution is achieved. With continuous propeller mixing, light mineral oil and sorbitan monooleate are added. Mixing is continued until a solution is obtained.

[0044] In a separate vessel, a 1N solution of sodium hydroxide is prepared.

[0045] With high speed rotor-stator mixing, the oil phase containing the drug (halobetasol propionate) is, added to the aqueous phase. Mixing is continued until a homogeneous emulsion is obtained. Propeller mixing is then used in place of the high speed rotor-stator mixing. With continuous mixing an appropriate amount of the sodium hydroxide solution is added incrementally to obtain a pH of 5.5±0.5. Propeller mixing is continued until a homogeneous lotion is obtained.

See Ex. 1012 ('824 publication) at [0041]-[0045], Table 4 (describing preparation of oil-in-water emulsion lotion involving preparation of an aqueous phase and an oil phase).

142. My opinions regarding the '824 publication are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that the '824 publication disclosed vehicles comprising an oil-in-water emulsion comprising an oil phase and an aqueous phase. Ex. 1005 (Murthy Decl.) at ¶¶ 146-147. Dr. Murthy further opines that an ordinarily skilled formulator would have been particularly motivated to use Formula 4A in the '824 publication as a vehicle for a 0.045% tazarotene composition because it includes several ingredients that were known to be moisturizing on the skin and does not include propylene glycol, which was known to induce irritation. *Id.* at ¶ 144. I agree with Dr. Murthy's analysis of the '824 publication.

4. Oil Phase

143. Claim 1 next recites "wherein the oil phase comprises a dicarboxylic acid ester and a mineral oil at a total concentration of 10-12 percent by weight of the composition." The '824 publication discloses this limitation.

144. Formula 4A disclosed in the '824 publication has the exact same ingredients as Composition A disclosed in the '482 patent with the exception of

tazarotene:

'482 patent						'824 publication		
TABLE 2						TABLE 4		
Some Emulsion Compositions of the Present Invention for Treating Acne						% w/w		
Ingredient	Function	Concentration (wt %)				Ingredients	Formula 4A	Formula 4B
		Range 1	Range 2	Range 3	Composition A			
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	Halobetasol Propionate	0.01	0.025
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	Diethyl Sebacate	2.97	2.90
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	Light Mineral Oil	8.03	2.90
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	Sorbitan Monooleate	0.10	0.10
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	Sorbitol Solution, 70%	10.7	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	Disodium Edetate, Dihydrate	0.05	0.05
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	Pemulen TR-1	0.40	0.40
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	Carbopol 981	0.60	0.60
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	Methylparaben	0.17	0.17
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	Propylparaben	0.03	0.03
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	Sodium Hydroxide, q. s.	pH 4.0-6.0	pH 4.0-6.0
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	Purified Water, q.s. ad	100	100

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1012 ('824 publication) at Table 4. The '824 publication also expressly discloses that the oil phase of the formulations in Table 4 comprises 2.97% diethyl sebacate, which the '482 patent identifies as a dicarboxylic acid ester, and 8.03% light mineral oil.

'824 publication

[0043] A separate oil phase is made. In a vessel diethyl sebacate and halobetasol propionate are combined. The mixture is agitated until a solution is achieved. With continuous propeller mixing, light mineral oil and sorbitan monooleate are added. Mixing is continued until a solution is obtained.

See Ex. 1012 ('824 publication) at [0043], Table 4 (describing preparation of the oil phase by adding diethyl sebacate and light mineral oil).

145. My opinions regarding the '824 publication are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug

formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that the '824 publication disclosed vehicles comprising an oil-in-water emulsion wherein the oil phase comprises 2.97% diethyl sebacate, which the '482 patent identifies as a dicarboxylic acid ester, and 8.03% light mineral oil. Ex. 1005 (Murthy Decl.) at ¶¶ 148-149. Dr. Murthy further opines that an ordinarily skilled formulator would have been particularly motivated to use Formula 4A in the '824 publication as a vehicle for a 0.045% tazarotene composition because it includes several ingredients that were known to be moisturizing on the skin and does not include propylene glycol, which was known to induce irritation. *Id.* at ¶ 144. I agree with Dr. Murthy's analysis of the '824 publication.

5. Aqueous Phase

146. Claim 1 next recites "wherein the aqueous phase comprises water and a carbomer homopolymer, wherein the concentration of the carbomer homopolymer is 0.5-0.7 percent by weight of the composition." The '824 publication discloses this limitation.

147. Formula 4A disclosed in the '824 publication has the exact same ingredients as Composition A disclosed in the '482 patent with the exception of tazarotene:

'482 patent					'824 publication		
TABLE 2					TABLE 4		
Some Emulsion Compositions of the Present Invention for Treating Acne					% w/w		
Ingredient	Function	Concentration (wt %)				Formula 4A	Formula 4B
		Range 1	Range 2	Range 3	Composition A		
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	0.01	0.025
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	2.97	2.90
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	8.03	2.90
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	0.10	0.10
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	10.7	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	0.05	0.05
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	0.40	0.40
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	0.60	0.60
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	0.17	0.17
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	0.03	0.03
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	pH 4.0-6.0	pH 4.0-6.0
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	100	100

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1012 ('824 publication) at Table 4. The '824 publication also expressly discloses that the aqueous phase of the oil-in-water emulsion lotions in Table 4 comprised water and Carbopol 981, which Table 4 identifies as carbomer homopolymer type A, at 0.6%.

'824 publication

[0042] A separate aqueous phase is made. In a manufacturing vessel, purified water and disodium edetate dihydrate are combined and the mixture is agitated until a clear solution is achieved. Sorbitol, methylparaben, and propylparaben are then added to the mixture. The mixture is continuously mixed and is heated to approximately 75° C. The mixture is agitated until a solution is obtained. The mixture is then removed from the heat source and allowed to cool to below 40° C. with continued mixing. With continuous propeller agitation Carbopol 981 and Pemulen TR-1 are added to the mixture and dispersed. The propeller mixing is continued until the polymers are fully dispersed and hydrated.

See Ex. 1012 ('824 publication) at [0042], Table 4 (describing preparation of aqueous phase by adding Carbopol 981 to mixture including purified water).

148. My opinions regarding the '824 publication are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that the '824 publication disclosed vehicles comprising an oil-in-water emulsion wherein the aqueous phase contains water, q.s. to 100 weight % and 0.6 weight % carbomer homopolymer type A. Ex. 1005 (Murthy Decl.) at ¶¶ 150-151. Dr. Murthy further opines that an ordinarily skilled formulator would have been particularly motivated to use Formula 4A in the '824 publication as a vehicle for a 0.045% tazarotene composition because it includes several ingredients that were known to be moisturizing on the skin and does not include propylene glycol, which was known to induce irritation. *Id.* at ¶ 144. I agree with Dr. Murthy's analysis of the '824 publication.

6. Polymeric Emulsifier

149. Lastly, Claim 1 recites "wherein the composition further comprises a polymeric emulsifier at a concentration of 0.3-0.5 percent by weight of the composition." The '824 publication discloses this limitation.

150. Formula 4A disclosed in the '824 publication has the exact same ingredients as Composition A disclosed in the '482 patent with the exception of tazarotene:

'482 patent					'824 publication		
TABLE 2					TABLE 4		
Some Emulsion Compositions of the Present Invention for Treating Acne					% w/w		
Ingredient	Function	Concentration (wt %)				Formula 4A	Formula 4B
		Range 1	Range 2	Range 3	Composition A		
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	0.01	0.025
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	2.97	2.90
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	8.03	2.90
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	0.10	0.10
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	10.7	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	0.03	0.03
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	pH 4.0-6.0	pH 4.0-6.0
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	100	100
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4		
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6		
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5		
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100		

Note:
⁽¹⁾These ingredients are broadly classified as Pharmaceutical Aids.

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1012 ('824 publication) at Table 4. The '824 publication also expressly discloses that the tazarotene-only composition in Table 4 includes 0.4% Pemulen TR-1 (carbomer copolymer type B), which the '482 patent identifies as a polymeric emulsifier.

'824 publication

[0042] A separate aqueous phase is made. In a manufacturing vessel, purified water and disodium edetate dihydrate are combined and the mixture is agitated until a clear solution is achieved. Sorbitol, methylparaben, and propylparaben are then added to the mixture. The mixture is continuously mixed and is heated to approximately 75° C. The mixture is agitated until a solution is obtained. The mixture is then removed from the heat source and allowed to cool to below 40° C. with continued mixing. With continuous propeller agitation Carbopol 981 and Pemulen TR-1 are added to the mixture and dispersed. The propeller mixing is continued until the polymers are fully dispersed and hydrated.

See Ex. 1012 ('824 publication) at [0042], Table 4 (describing addition of Pemulen TR-1 to oil-in-water emulsion composition); see also Ex. 1001 ('482 patent) at 4:10-

14 (“[P]olymeric emulsifiers such as those known under the trade name Pemulen™ (The Lubrizol Corporation, Wickliffe, Ohio) may be used.”).

151. My opinions regarding the ’824 publication are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy’s declaration, and I understand that Dr. Murthy opines that the ’824 publication disclosed vehicles comprising Pemulen TR-1 (carbomer copolymer type B), which is a polymeric emulsifier. Ex. 1005 (Murthy Decl.) at ¶¶ 152-154. Dr. Murthy further opines that an ordinarily skilled formulator would have been particularly motivated to use Formula 4A in the ’824 publication as a vehicle for a 0.045% tazarotene composition because it includes several ingredients that were known to be moisturizing on the skin and does not include propylene glycol, which was known to induce irritation. *Id.* at ¶ 144. I agree with Dr. Murthy’s analysis of the ’824 publication.

B. Claim 2

152. Claim 2 recites “[t]he method of claim 1, wherein the dicarboxylic acid ester in the oil phase is diethyl sebacate.” The ’824 publication discloses this limitation for the reasons explained in claim 1. *Supra* § IX.A.2.

C. Claim 3

153. Claim 3 recites “[t]he method of claim 1, wherein the oil phase comprises diethyl sebacate and light mineral oil.” The ’824 publication discloses this

limitation for the reasons explained in Claim 1. *Supra* § IX.A.2.

D. Claims 4-6

154. Claims 4-6 recite the method of claim 1, wherein the application is carried out for at least eight weeks (claim 4), at least twelve weeks (claim 5), or twelve weeks (claim 6). The '824 publication in combination with the Tazorac® Label renders claims 4-6 obvious.

155. In multiple clinical trials disclosed in the Tazorac® Label, treatment of acne with topical tazarotene was carried out for 12-weeks. Ex. 1013 (Tazorac® Label) at 14, Clinical Studies. Persons of ordinary skill in the art would have therefore found it obvious to use the 0.045% tazarotene lotion resulting from the combination of the '824 publication and the Tazorac® Label for 12-weeks. Moreover, As I explained in Grounds 1-3, persons of ordinary skill in the art would have understood that the treatment of acne vulgaris requires a flexible approach that accounts for individual patient characteristics and response to treatment, and persons of ordinary skill in the art would have known that topical retinoids, including tazarotene, would commonly be used for periods exceeding 12-weeks due to the chronic nature of acne. *Supra* ¶ 100. Because 12-weeks encompasses “at least 8 weeks” as well as “at least 12-weeks,” the Tazorac® Label in combination with the '824 publication renders claims 4-6 obvious.

E. Claim 7

156. Claim 7 recites “wherein the tazarotene is in solution in the oil phase of the oil-in-water emulsion lotion.” I have read Dr. Murthy’s declaration, and I understand that Dr. Murthy opines that an ordinarily skilled formulator would have expected that tazarotene would have been soluble in the oil-phase of the vehicles disclosed in the ’824 publication, including Formula 4A because like halobetasol propionate, tazarotene was known to be a lipophilic molecule. Ex. 1005 (Murthy Decl.) at ¶¶ 160-163. Based on Dr. Murthy’s opinion regarding the expectations of an ordinarily skilled formulator, it is my opinion that claim 7 would have been obvious over the ’824 publication in combination with the Tazorac® Label.

F. Claim 8

157. Claim 8 recites “wherein the composition has a pH of about 4 to about 6.” The ’824 publication discloses the limitations of claim 8.

158. Formula 4A disclosed in the ’824 publication has the exact same ingredients as Composition A disclosed in the ’482 patent with the exception of tazarotene:

'482 patent					'824 publication		
TABLE 2					TABLE 4		
Some Emulsion Compositions of the Present Invention for Treating Acne					% w/w		
Ingredient	Function	Concentration (wt %)				Formula 4A	Formula 4B
		Range 1	Range 2	Range 3	Composition A		
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	0.01	0.025
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	2.97	2.90
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	8.03	2.90
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	0.10	0.10
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	10.7	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	0.05	0.05
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	0.40	0.40
Edetate disodium	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	0.60	0.60
dihydrate						0.17	0.17
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	0.03	0.03
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	pH 4.0-6.0	pH 4.0-6.0
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	100	100
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100		

Note:
⁽¹⁾These ingredients are broadly classified as Pharmaceutical Aids.

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1012 ('824 publication) at Table 4.

'824 publication

[0045] With high speed rotor-stator mixing, the oil phase containing the drug (halobetasol propionate) is, added to the aqueous phase. Mixing is continued until a homogeneous emulsion is obtained. Propeller mixing is then used in place of the high speed rotor-stator mixing. With continuous mixing an appropriate amount of the sodium hydroxide solution is added incrementally to obtain a pH of 5.5±0.5. Propeller mixing is continued until a homogeneous lotion is obtained.

The '824 publication also expressly discloses that during preparation of the formulations in Table 4, "[w]ith continuous mixing an appropriate amount of the sodium hydroxide solution is added incrementally to obtain a pH of 5.5-0.5." See Ex. 1012 ('824 publication) at [0045].

159. My opinions regarding the '824 publication are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug

formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that the '824 publication disclosed vehicles having a pH of about 4 to about 6. Ex. 1005 (Murthy Decl.) at ¶¶ 164-166. Dr. Murthy further opines that an ordinarily skilled formulator would have been particularly motivated to use Formula 4A in the '824 publication as a vehicle for a 0.045% tazarotene composition because it includes several ingredients that were known to be moisturizing on the skin and does not include propylene glycol, which was known to induce irritation. *Id.* at ¶ 144. I agree with Dr. Murthy's analysis of the '824 publication.

G. Claims 9-10

160. Claim 9 recites "[t]he method of claim 1, wherein the composition consists essentially of: 0.045 weight % tazarotene; diethyl sebacate; light mineral oil; sorbitan monooleate; sorbitol solution, 70%; methylparaben; propylparaben; edetate disodium dihydrate; carbomer polymer type B; carbomer homopolymer type A; sodium hydroxide; purified water." Claim 10 recites "[t]he method of claim 1, wherein the composition consists essentially of: 0.045 weight % tazarotene; 2.5-3.5 weight % diethyl sebacate; 7.5-8.5 weight% light mineral oil; 0.05-0.2 weight % sorbitan monooleate; 10-11 weight% sorbitol solution, 70%; 0.1-0.2 weight % methylparaben; 0.02-0.04 weight % propylparaben; 0.03-0.06 weight % edetate disodium dihydrate; 0.3-0.5 weight % carbomer polymer type B; 0.5-0.7 weight% carbomer homopolymer type A; sodium hydroxide, q.s. to pH 5.5±0.5; and purified

water, q.s. to 100 weight%.”

161. Formula 4A disclosed in the '824 publication has the exact same ingredients as Composition A disclosed in the '482 patent with the exception of tazarotene:

'482 patent						'824 publication		
TABLE 2						TABLE 4		
Some Emulsion Compositions of the Present Invention for Treating Acne						% w/w		
Ingredient	Function	Concentration (wt %)				Ingredients	Formula 4A	Formula 4B
		Range 1	Range 2	Range 3	Composition A			
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	Halobetasol Propionate	0.01	0.025
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	Diethyl Sebacate	2.97	2.90
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	Light Mineral Oil	8.03	2.90
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	Sorbitan Monooleate	0.10	0.10
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	Sorbitol Solution, 70%	10.7	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	Disodium Edetate, Dihydrate	0.05	0.05
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	Pemulen TR-1	0.40	0.40
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	Carbopol 981	0.60	0.60
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	Methylparaben	0.17	0.17
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	Propylparaben	0.03	0.03
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	Sodium Hydroxide, q. s.	pH 4.0-6.0	pH 4.0-6.0
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	Purified Water, q.s. ad	100	100

Note:

⁽¹⁾These ingredients are broadly classified as Pharmaceutical Aids.

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1012 ('824 publication) at Table 4. Based on my review of Table 4, Formula 4A contains all of the ingredients recited in claims 9 and 10 within the recited concentration ranges except for tazarotene. Ex. 1012 ('824 publication) at Table 4. It is my opinion that persons of ordinary skill in the art would have been motivated to use Formula 4A to formulate a composition comprising 0.045% tazarotene as the active ingredient for the reasons I explained for claim 1.

162. My opinions regarding the '824 publication are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy

opines that Formula 4A of the '824 publication disclosed all of the ingredients recited in claims 9 and 10 within the claimed concentration ranges except for tazarotene. Ex. 1005 (Murthy Decl.) at ¶¶ 167-169. Dr. Murthy further opines that an ordinarily skilled formulator would have been particularly motivated to use Formula 4A in the '824 publication as a vehicle for a 0.045% tazarotene composition because it includes several ingredients that were known to be moisturizing on the skin and does not include propylene glycol, which was known to induce irritation. *Id.* at ¶ 144. I agree with Dr. Murthy's analysis of the '824 publication.

H. Claim 11

163. Claim 11 is an independent claim that recites “[a] method of treating acne vulgaris, the method comprising topically applying a pharmaceutical composition to an affected area of a body of a subject suffering from acne vulgaris; wherein the composition consists essentially of: 0.045 weight % tazarotene; 2.97 weight % diethyl sebacate; 8.03 weight % light mineral oil; 0.1 weight% sorbitan monooleate; 10.7 weight% sorbitol solution, 70%; 0.17 weight % methylparaben; 0.03 weight % propylparaben; 0.05 weight % edetate disodium dihydrate; 0.4 weight % carbomer polymer type B; 0.6 weight % carbomer homopolymer type A; sodium hydroxide, q.s. to pH 5.5±0.5; and purified water, q.s. to 100 weight%.”

164. The preamble of claim 11 relates to the clinical treatment of acne vulgaris with a topical composition. To the extent the preamble of claim 11 is

limiting, a person of ordinary skill in the art would have been motivated to treat acne with once daily application of a composition comprising 0.045% tazarotene with a reasonable expectation of success for the reasons discussed previously. *Supra* § III.

165. Formula 4A disclosed in the '824 publication has the exact same ingredients as Composition A disclosed in the '482 patent with the exception of tazarotene:

'482 patent					'824 publication		
TABLE 2					TABLE 4		
Some Emulsion Compositions of the Present Invention for Treating Acne					% w/w		
Ingredient	Function	Concentration (wt %)				Formula 4A	Formula 4B
		Range 1	Range 2	Range 3	Composition A		
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045		
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	0.01	0.025
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	2.97	2.90
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	8.03	2.90
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	0.10	0.10
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	10.7	10.7
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	0.05	0.05
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	0.40	0.40
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	0.60	0.60
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	0.17	0.17
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	0.03	0.03
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	pH 4.0-6.0	pH 4.0-6.0
Note: ⁽¹⁾ These ingredients are broadly classified as Pharmaceutical Aids.						100	100

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1012 ('824 publication) at Table 4. Based on my review of Table 4, Formula 4A contains all of the ingredients recited in claim 11 at the recited concentrations except for tazarotene. Ex. 1012 ('824 publication) at Table 4. It is my opinion that persons of ordinary skill in the art would have been motivated to use Formula 4A to formulate a composition comprising 0.045% tazarotene as the active ingredient for the reasons I explained for claim 1.

166. My opinions regarding the '824 publication are further confirmed by

the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand that Dr. Murthy opines that Formula 4A of the '824 publication disclosed all of the ingredients recited in claim 11 at the claimed concentrations except for tazarotene. Ex. 1005 (Murthy Decl.) at ¶¶ 170-174. Dr. Murthy further opines that an ordinarily skilled formulator would have been particularly motivated to use Formula 4A in the '824 publication as a vehicle for a 0.045% tazarotene composition because it includes several ingredients that were known to be moisturizing on the skin and does not include propylene glycol, which was known to induce irritation. *Id.* at ¶ 144. I agree with Dr. Murthy's analysis of the '824 publication.

**X. GROUND 6: CLAIMS 1-11 WOULD HAVE BEEN OBVIOUS OVER
THE '824 PUBLICATION AND THE TAZORAC® LABEL IN VIEW OF
ANDERSON**

167. As I explained in Ground 5, it is my opinion that the '824 publication and the Tazorac® Label render claims 1-11 of the '482 patent obvious. *Supra* § IX. In my opinion, Anderson would have provided POSITAs with even further motivation to use the 0.045% tazarotene lotion resulting from the combination of the '824 publication and the Tazorac® Label to treat acne.

168. As explained previously, Anderson disclosed the clinical use of 0.05% tazarotene compositions to treat acne by practicing dermatologists, who described

0.05% tazarotene compositions as “a useful part of the treatment regimen . . . [that] fits well into the retinoid ladder in moderate to severe inflammatory acne or comedonal acne.” *Supra* §§ VII.A.1.a, VII.A.2.a. Anderson’s teachings for 0.05% tazarotene, and the person of ordinary skill in the art’s knowledge of the use and prescription of 0.05% tazarotene for treating acne, would have provided persons of ordinary skill with further motivation and expectation of success in using a composition with a similar concentration of tazarotene – 0.045% – to treat the same disease.

169. Accordingly, it is my opinion that claims 1-11 of the ’482 patent would have been obvious over the ’824 Publication and the Tazorac® Label in view of Anderson.

XI. GROUNDS 7-9: CLAIMS 1-11 WOULD HAVE BEEN OBVIOUS OVER
THE ’824 PUBLICATION AND THE IDP-118 STUDY IN VIEW OF
KIRCIK, CHIM, OR ANDERSON

170. As explained in Ground 5, the ’824 publication discloses all of the components of the formulation claimed in the ’482 patent except for the 0.045% tazarotene and the treatment of acne vulgaris. *See supra* § IX. As I also explained in Ground 5 and elsewhere, persons of ordinary skill in the art would have been motivated to develop and use an effective, lower-concentration tazarotene composition (e.g., about 0.05%) for treating acne to reduce the irritating side effects

known in the prior art. *Id.* The IDP-118 Study disclosed a phase two clinical trial for psoriasis involving four treatment arms: (1) a combination lotion containing 0.045% tazarotene and 0.01% halobetasol propionate (the active ingredient disclosed in the '824 publication); (2) a 0.045% tazarotene monotherapy lotion; (3) a 0.01% halobetasol propionate monotherapy lotion; and (4) a placebo lotion. Ex. 1014 (IDP-118 Study) at Arms and Interventions. Given the motivation for lower-concentration tazarotene compositions for treating acne, persons of ordinary skill in the art would have been highly interested in exploring the 0.045% tazarotene monotherapy lotion in the IDP-118 Study as a treatment for acne. Persons of ordinary skill would have then looked for a vehicle for the 0.045% tazarotene monotherapy lotion in the IDP-118 Study. That investigation would have led them to the '824 publication, one of the only references disclosing formulations for a 0.01% halobetasol propionate lotion, one of the other treatment arms in the IDP-118 Study.

171. As I explained in Grounds 1-3, Anderson, Kircik, and Chim all disclose that topical compositions containing nearly the same concentration of tazarotene as that in the IDP-118 Study (0.05%) were effectively used to treat acne prior to May 2017. Accordingly, it is my opinion that claims 1-11 of the '482 patent would have been obvious over the '824 Publication and the IDP-118 Study in further combination with Anderson, Kircik, or Chim as further explained below. My

opinions are further confirmed by the expert declaration of Dr. Murthy, an expert in the field of topical drug formulation, as I explain below.

A. Claim 1

172. In my opinion, the '824 publication and the IDP-118 Study in view of Anderson, Kircik, or Chim renders claim 1 obvious.

1. Preamble

173. The preamble of Claim 1 recites “[a] method of treating acne vulgaris, the method comprising topically applying a pharmaceutical composition once per day to an affected area of a body of a subject suffering from acne vulgaris.” To the extent the preamble is limiting, Anderson, Kircik, and Chim disclose that limitation as explained in Grounds 1-3. *Supra* § VII.A.1.

2. Composition of tazarotene at 0.045% as sole active ingredient

174. Claim 1 next recites “wherein the composition comprises tazarotene at a concentration of about 0.045 percent by weight of the composition as a sole active pharmaceutical ingredient.” The IDP-118 Study discloses a lotion with 0.045% tazarotene as the sole active ingredient, and as I explain in detail below, persons of ordinary skill in the art would have been motivated to use such a lotion to treat acne and would have reasonably expected success doing so.

175. The IDP-118 Study disclosed a phase two clinical trial for psoriasis involving four treatment arms: (1) a combination lotion containing 0.045%

tazarotene and 0.01% halobetasol propionate; (2) a 0.045% tazarotene monotherapy lotion; (3) a 0.01% halobetasol propionate monotherapy lotion; and (4) a placebo lotion. Ex. 1014 (IDP-118 Study) at Arms and Interventions. Persons of ordinary skill in the art would have been motivated to use the 0.045% tazarotene lotion disclosed in the IDP-118 Study to treat acne through once daily topical application in view of the teachings of Anderson, Kircik, or Chim for the same reasons I explained in Grounds 1-3. *Supra* § VII.A.2.

3. Oil-in-Water Emulsion Lotion

176. Claim 1 next recites “wherein the composition is an oil-in-water emulsion lotion comprising an oil phase and an aqueous phase.”

177. The ’824 publication discloses this limitation for the reasons I explained in Ground 5. *Supra* § IX.A.3.

178. The IDP-118 Study would have provided a person of ordinary skill in the art with further motivation to use the vehicles disclosed in the ’824 publication to formulate the 0.045% tazarotene lotion. The IDP-118 Study disclosed a phase two clinical trial for psoriasis involving four treatment arms: (1) a combination lotion containing 0.045% tazarotene and 0.01% halobetasol propionate (the active ingredient disclosed in the ’824 publication); (2) a 0.045% tazarotene monotherapy lotion; (3) a 0.01% halobetasol propionate monotherapy lotion; and (4) a placebo lotion. Ex. 1014 (IDP-118 Study) at Arms and Interventions. Persons of ordinary

skill in the art who were developing tazarotene therapies for acne would have looked to references and clinical studies on the treatment of psoriasis with tazarotene because tazarotene was the only topical retinoid used and approved for treating both conditions. *Supra* ¶ 32. Moreover, clinicians would have known that topical tazarotene was associated with skin irritation when used to treat either disease. *See, e.g.,* Ex. 1013 (Tazorac® Label) at Adverse Reactions, Sections 5.2, 14, 16.1. Accordingly, clinicians investigating formulations that may reduce the irritation caused by tazarotene would have been particularly motivated to look to references dealing with either psoriasis or acne because they would have expected that means for reducing irritation for one disease would likely be applicable for treating the other disease as well.

179. A person of ordinary skill in the art would have understood that in a clinical trial such as the IDP-118 Study, all four treatment arms would have been formulated in the same vehicle to ensure that comparisons among the arms could be attributed to differences in the active ingredients. Given this knowledge, the person of ordinary skill in the art would have been motivated to investigate vehicles for both 0.01% halobetasol compositions as well as 0.045% tazarotene compositions, and that investigation would have led them to the '824 publication, which disclosed vehicles for a 0.01% halobetasol lotion. Thus, the IDP-118 Study's disclosure of a 0.01% halobetasol lotion formulated in the same vehicle as a 0.045% tazarotene

lotion would have reinforced the person of ordinary skill in the art's motivation and reasonable expectation of success for using the '824 publication's vehicles, including Formula 4A, for a 0.045% tazarotene composition.

180. The IDP-118 Study would have particularly drawn a person of ordinary skill in the art to the two examples in the '824 publication that include 0.01% halobetasol propionate – Formulation C in Table 1 and Formula 4A in Table 4. *See* Ex. 1012 ('824 publication) at Tables 1 & 4. As I have explained above, Formula 4A disclosed in the '824 publication has the exact same ingredients as Composition A disclosed in the '482 patent with the exception of tazarotene:

'482 patent						'824 publication		
TABLE 2						TABLE 4		
Some Emulsion Compositions of the Present Invention for Treating Acne						% w/w		
Ingredient	Function	Concentration (wt %)				Ingredients	Formula 4A	Formula 4B
		Range 1	Range 2	Range 3	Composition A			
Tazarotene	Retinoid	0.02-0.049	0.03-0.049	0.04-0.049	0.045	Halobetasol Propionate	0.01	0.025
Diethyl sebacate	Liquid Oil & Solvent	1-5	2-4	2.5-3.5	2.97	Diethyl Sebacate	2.97	2.90
Light mineral oil	Liquid Oil & Co-Solvent	5-15	5-10	7.5-8.5	8.03	Light Mineral Oil	8.03	2.90
Sorbitan monooleate	Surfactant/Emulsifying Agent	0.01-1	0.02-0.5	0.05-0.2	0.1	Sorbitan Monooleate	0.10	0.10
Sorbitol solution, 70%	Humectant	5-15	7-12	10-11	10.7	Sorbitol Solution, 70%	10.7	10.7
Methyl paraben	Antimicrobial Preservative ⁽¹⁾	0.05-0.3	0.1-0.3	0.1-0.2	0.17	Disodium Edetate, Dihydrate	0.05	0.05
Propyl paraben	Antimicrobial Preservative ⁽¹⁾	0.01-0.1	0.01-0.05	0.02-0.04	0.03	Pemulen TR-1	0.40	0.40
Edetate disodium dihydrate	Chelating Agent ⁽¹⁾	0.02-0.1	0.02-0.7	0.03-0.06	0.05	Carbopol 981	0.60	0.60
Carbomer copolymer type B (e.g., Pemulen™ TR-1)	Emulsifying Agent	0.1-1	0.2-0.7	0.3-0.5	0.4	Methylparaben	0.17	0.17
Carbomer homopolymer type A (e.g., Carbomer 981)	Thickener	0.2-1.5	0.3-1	0.5-0.7	0.6	Propylparaben	0.03	0.03
Sodium hydroxide, 10% Solution	pH-adjusting Agent ⁽¹⁾	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	q.s. to pH of 5.5 ± 0.5	Sodium Hydroxide, q. s.	pH 4.0-6.0	pH 4.0-6.0
Purified water	Carrier	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	Purified Water, q.s. ad	100	100

Note:
⁽¹⁾These ingredients are broadly classified as Pharmaceutical Aids.

Compare Ex. 1001 ('482 patent) at Table 2 with Ex. 1012 ('824 publication) at Table 4.

181. My opinions regarding the IDP-118 Study and the '824 publication are further confirmed by the expert declaration submitted by Dr. Murthy, an expert in the field of drug formulation. I have read Dr. Murthy's declaration, and I understand

that Dr. Murthy opines that the IDP-118 Study would have motivated an ordinarily skilled formulator to use Formula 4A of the '824 publication as a vehicle for the 0.045% tazarotene lotion disclosed in the IDP-118 Study. Ex. 1005 (Murthy Decl.) at ¶¶ 185-190. I agree with Dr. Murthy's analysis of the IDP-118 Study and the '824 publication.

4. Oil Phase

182. Claim 1 next recites “wherein the oil phase comprises a dicarboxylic acid ester and a mineral oil at a total concentration of 10-12 percent by weight of the composition.”

183. The '824 publication discloses this limitation for the reasons referenced explained in Ground 5. *Supra* § IX.A.4. Persons of ordinary skill in the art would have been motivated to use the vehicles in the '824 publication, particularly Formula 4A, in view of the '824 publication and the IDP-118 Study for the reasons I explained previously. *Supra* §§ XI.A.1.-3.

5. Aqueous Phase

184. Claim 1 next recites “wherein the aqueous phase comprises water and a carbomer homopolymer, wherein the concentration of the carbomer homopolymer is 0.5-0.7 percent by weight of the composition.”

185. The '824 publication discloses this limitation for the reasons I explained in Ground 5. *Supra* § IX.A.5. Persons of ordinary skill in the art would

have been motivated to use the vehicles in the '824 publication, particularly Formula 4A, in view of the '824 publication and the IDP-118 Study for the reasons I explained previously. *Supra* §§ XI.A.1.-3.

6. Polymeric Emulsifier

186. Lastly, Claim 1 recites “wherein the composition further comprises a polymeric emulsifier at a concentration of 0.3-0.5 percent by weight of the composition.”

187. The '824 publication discloses this limitation for the reasons I explained in Ground 5. *Supra* § IX.A.6. Persons of ordinary skill in the art would have been motivated to use the vehicles in the '824 publication, particularly Formula 4A, in view of the '824 publication and the IDP-118 Study for the reasons I explained previously. *Supra* §§ XI.A.1.-3.

B. Claim 2

188. Claim 2 recites “[t]he method of claim 1, wherein the dicarboxylic acid ester in the oil phase is diethyl sebacate.” The '824 publication discloses the limitations of claim 2 for the reasons explained and referenced in Ground 5. *Supra* § IX.A.4. Persons of ordinary skill in the art would have been motivated to use the vehicles in the '824 publication, particularly Formula 4A, to formulate a 0.045% tazarotene lotion in view the '824 publication and the IDP-118 Study for the reasons I explained previously. *Supra* §§ XI.A.1.-3.

C. Claim 3

189. Claim 3 recites “[t]he method of claim 1, wherein the oil phase comprises diethyl sebacate and light mineral oil.” The ’824 publication discloses the limitations of claim 3 for the reasons explained and referenced in Ground 5. *Supra* § IX.A.4. Persons of ordinary skill in the art would have been motivated to use the vehicles in the ’824 publication, particularly Formula 4A, to formulate a 0.045% tazarotene lotion in view the ’824 publication and the IDP-118 Study for the reasons I explained previously. *Supra* §§ XI.A.1-3.

D. Claims 4-6

190. Claims 4-6 recite the method of claim 1, wherein the application is carried out for at least eight weeks (claim 4), at least twelve weeks (claim 5), or twelve weeks (claim 6). Persons of ordinary skill in the art would have been motivated to use the 0.045% tazarotene lotion disclosed in the IDP-118 Study to treat acne for the reasons I explained for claim 1. *Supra* §§ XI.A.1.-3. Persons of ordinary skill in the art would have been motivated to carry out that treatment for at least 12-weeks or longer in view of Anderson, Kircik, or Chim for the reasons I explained in Grounds 1-3. *Supra* § VII.A.D. Therefore, the ’824 publication and the IDP-118 study in combination with Anderson, Kircik, or Chim renders claims 4-6 obvious.

E. Claim 7

191. Claim 7 recites “wherein the tazarotene is in solution in the oil phase of the oil-in-water emulsion lotion.”

192. The ’824 publication discloses this limitation or renders it obvious for the reasons explained and referenced in Ground 5. *Supra* §§ IX.A.3, IX.E. Persons of ordinary skill in the art would have been motivated to use the vehicles in the ’824 publication, particularly Formula 4A, to formulate a 0.045% tazarotene lotion in view the ’824 publication and the IDP-118 Study for the reasons I explained previously. *Supra* §§ XI.A.1-3.

F. Claim 8

193. Claim 8 recites “wherein the composition has a pH of about 4 to about 6.” The ’824 publication discloses the limitations of claim 8 for the reasons explained and referenced in Ground 5. *Supra* § IX.F. Persons of ordinary skill in the art would have been motivated to use the vehicles in the ’824 publication, particularly Formula 4A, to formulate a 0.045% tazarotene lotion in view the ’824 publication and the IDP-118 Study for the reasons I explained previously. *Supra* §§ XI.A.1.-3.

G. Claims 9-10

194. Claim 9 recites “[t]he method of claim 1, wherein the composition consists essentially of: 0.045 weight % tazarotene; diethyl sebacate; light mineral

oil; sorbitan monooleate; sorbitol solution, 70%; methylparaben; propylparaben; edetate disodium dihydrate; carbomer polymer type B; carbomer homopolymer type A; sodium hydroxide; purified water.” Claim 10 recites “[t]he method of claim 1, wherein the composition consists essentially of: 0.045 weight % tazarotene; 2.5-3.5 weight % diethyl sebacate; 7.5-8.5 weight% light mineral oil; 0.05-0.2 weight % sorbitan monooleate; 10-11 weight% sorbitol solution, 70%; 0.1-0.2 weight % methylparaben; 0.02-0.04 weight % propylparaben; 0.03-0.06 weight % edetate disodium dihydrate; 0.3-0.5 weight % carbomer polymer type B; 0.5-0.7 weight% carbomer homopolymer type A; sodium hydroxide, q.s. to pH 5.5±0.5; and purified water, q.s. to 100 weight%.”

195. The '824 publication disclosed each of the limitations recited in claims 9 and 10 except for 0.045% tazarotene for the reasons explained and referenced in Ground 5. *Supra* § IX.G.

196. A person with ordinary skill in the art would have been motivated to treat acne with the 0.045% tazarotene lotion disclosed by the IDP-118 Study for the reasons I discussed in claim 1. *Supra* § XI.A. Persons of ordinary skill in the art would have been motivated to use the vehicles in the '824 publication, particularly Formula 4A, to formulate a 0.045% tazarotene lotion in view the '824 publication and the IDP-118 Study for the reasons I explained previously. *Supra* §§ XI.A.1.-3.

197. Accordingly, claims 9-10 of the '482 patent would have been obvious

over the '824 Publication and the IDP-118 Study in further combination with Anderson, Kircik, or Chim.

H. Claim 11

198. Claim 11 is an independent claim that recites “[a] method of treating acne vulgaris, the method comprising topically applying a pharmaceutical composition to an affected area of a body of a subject suffering from acne vulgaris; wherein the composition consists essentially of: 0.045 weight % tazarotene; 2.97 weight % diethyl sebacate; 8.03 weight % light mineral oil; 0.1 weight% sorbitan monooleate; 10.7 weight% sorbitol solution, 70%; 0.17 weight % methylparaben; 0.03 weight % propylparaben; 0.05 weight % edetate disodium dihydrate; 0.4 weight % carbomer polymer type B; 0.6 weight % carbomer homopolymer type A; sodium hydroxide, q.s. to pH 5.5±0.5; and purified water, q.s. to 100 weight%.”

199. The preamble of claim 11 relates to the clinical treatment of acne vulgaris with a topical composition. To the extent the preamble of claim 11 is limiting, a person of ordinary skill in the art would have been motivated to treat acne with once daily application of with the 0.045% tazarotene lotion disclosed by the IDP-118 Study with a reasonable expectation of success for the reasons I explained in claim 1. *Supra* § XI.A.1.

200. The '824 publication disclosed each of the remaining limitations of claim 11 except for 0.045% tazarotene for the reasons I explained in Ground 5.

Supra § IX. Persons of ordinary skill in the art would have been motivated to use the vehicles in the '824 publication, particularly Formula 4A, to formulate a 0.045% tazarotene lotion in view the '824 publication and the IDP-118 Study for the reasons I explained previously. *Supra* §§ XI.A.1.-3.

201. Accordingly, claim 11 of the '482 patent would have been obvious over the '824 Publication and the IDP-118 Study in further combination with Anderson, Kircik, or Chim.

XII. SECONDARY CONSIDERATIONS

202. I am aware that the Applicants argued during prosecution that the results of the clinical trials disclosed in the '482 patent demonstrated unexpected results that are indicative of non-obviousness because the Composition A allegedly provided similar efficacy and less irritation than the commercial 0.1% Tazorac® product. *See* Ex. 1002 ('482 patent prosecution history) at 81-84, 167-170, 205-206. In my opinion, an ordinarily skilled dermatologist in May 2017 would not have found the results relied upon by Applicants to be unexpected. As I explained above, it was well known in the prior art that reducing the concentration of tazarotene in a topical formulation would lead to a decrease in observed irritation. *See supra* § III. Thus, it would have been entirely expected for a composition comprising 0.045% tazarotene (Composition A) to produce less irritation than a composition comprising 0.1% tazarotene (Tazorac® 0.1%).

203. Additionally, as I explained previously, it was common practice prior to May 2017 to treat acne with topical compositions comprising 0.05% tazarotene, a concentration very similar to the 0.045% concentration in the '482 patent. *Supra* § III.C. Despite this, the clinical study the Applicants relied upon did not compare the 0.045% tazarotene composition to 0.05% Tazorac® or any other 0.05% tazarotene formulation, which would have been an appropriate control arm to include in the study. Moreover, as I explained previously, the clinical study Applicants relied upon included small sample sizes, and there is no statistical analysis of the results provided in the '482 patent indicating whether the results were statistically significant. Such an analysis would be particularly important when drawing any conclusions from the data on the relative efficacies of Composition A versus Tazorac® 0.1% cream, and the absence of such an analysis greatly undermines any conclusions that a person of ordinary skill in the art would draw from the study. § IV.A. Given these serious shortcomings with the study Applicants relied upon, it is my opinion that a person of ordinary skill in the art would not have found the results surprising or unexpected in May 2017.

204. Further, given that the formulations claimed in the '482 patent are not new, and were invented and publicly disclosed before May 2017, I am not aware of any long-felt need in the industry, skepticism of the invention, or teaching away from the invention. I am also not aware of any praise for the alleged inventions or copying

of the alleged inventions by other companies. If Patent Owner identifies any alleged evidence of secondary considerations in the future, I reserve the right to respond to that information.

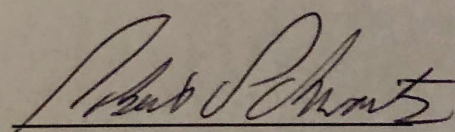
XIII. CONCLUSION

205. For the foregoing reasons, it is my opinion that the treatment limitations of claims 1-11 of the '482 patent are rendered obvious by the prior art discussed above in view of the knowledge of one of ordinary skill in the art at the time of the alleged invention.

206. I reserve the right to supplement my opinions in the future to address or respond to any arguments that Patent Owner may raise, as well as new information, including, but not limited to, any claim constructions advanced by Patent Owner or adopted by the Board in the Institution Decision, and respond to any alleged secondary considerations as they become available to me.

207. I declare that the foregoing is true and correct, and further that the foregoing statements were made with the knowledge that willful, 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.

Dated: June 21, 2023


Dr. Robert Schwartz