IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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MERIAL, INC.,

Petitioner,

v.

FIDOPHARM, INC.,

Patent Owner.

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CASE IPR: Unassigned

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**PETITION FOR INTER PARTES REVIEW OF**

**U.S. PATENT NO. 8,829,038**

**Claims 1–21**

**UNDER 35 U.S.C. §§ 311–319 and 37 C.F.R. §§ 42.1–.80, 42.100–.123**

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## Table of Authorities

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**CASES**

**STATUTES, RULES & OTHER AUTHORITIES**

## Exhibit List

| Exhibit Number | Exhibit Name |
|---|---|
| 1001 | [NOT USED] |
| 1002 | U.S. Patent No. 8,829,038 ("'038 patent") |
| 1003 | U.S. Patent No. 8,580,837 ("'837 patent") |
| 1004 | File Wrapper of U.S. Patent Application No. 13/852,513 ("'513 application") |
| 1005 | File Wrapper of U.S. Patent Application No. 12/727,003 ("'003 application") |
| 1006 | Declaration of David Petrick, VMD ("Petrick Declaration") |
| 1007 | U.S. Patent No. 6,395,765 ("Etchegaray") |
| 1008 | International Patent Publication No. WO 2009/027506 ("Freehauf") |
| 1009 | Chinese Patent Publication No. CN101129357 ("Pan") |
| 1010 | Otranto, *et al*., "Efficacy of a combination of imidacloprid 10%/permethrin 50% versus fipronil 10%/(S)-methoprene 12%, against ticks in naturally infected dogs," *Veterinary Parasitology*, 130: 293-304 (2005) ("Otranto") |
| 1011 | Declaration of Mr. Randy Sheppard ("Sheppard Declaration") |
| 1012 | European Patent No. EP1066854 ("Bruce") |
| 1013 | Declaration of Jeffery N. Clark, DVM, Ph.D. ("Clark Declaration") |
| 1014 | *Curriculum Vitae* of Jeffery N. Clark, DVM, Ph.D. |
| 1015 | Declaration of Leonore C.Witchey-Lakshmanan, Ph.D. ("Witchey Declaration") |

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| 1016 | *Curriculum Vitae* of Leonore C.Witchey-Lakshmanan, Ph.D |
| 1017 | Declaration of Saijun Gong ("Gong Declaration") |
| 1018 | [NOT USED] |
| 1019 | [NOT USED] |
| 1020 | Material and Safety Data Sheet for FRONTLINE® TOP SPOT, (Printing Date, 10/23/2001) ("2001 FRONTLINE® TOP SPOT MSDS") |
| 1021 | U.S. Patent No. 5,612,047 |
| 1022 | Mackley, *et al.*, "Contact dermatitis from Frontline Top Spot," *Dermatitis*, 16(3)149–50 (2005) ("Mackley") |
| 1023 | International Patent Publication No. WO 2008/067991 |
| 1024 | "Physical Constants of Organic Compounds," in CRC HANDBOOK OF CHEMISTRY AND PHYSICS, Internet Version 2005, David R. Lide, ed., <http://www.hbcpnetbase.com>, CRC Press, Boca Raton, FL (2005) (3-168, 3-169, 3-222, 3-223, 3-232, and 3-233) |
| 1025 | [NOT USED] |
| 1026 | [NOT USED] |
| 1027 | U.S. Patent No. 6,426,333 ("Huet") |
| 1028 | Dudley, *Whole Dog J.*, 2002: 18–22 (2002), page 19 ("Dudley") |
| 1029 | U.S. Patent No. 6,096,329 ("Jeannin") |
| 1030 | Certified English Translation of Chinese Patent Publication No. CN101129357 ("Pan") |
| 1031 | U.S. Patent No. 7,481,273 |
| 1032 | Declaration of Morris M. Jackson Under 37 C.F.R. § 1.68 ("Jackson Declaration") |

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|---|---|
| 1033 | Young, *et al*., "Efficacy of fipronil/(S)-methoprene combination spot-on for dogs against shed eggs, emerging and existing adult cat fleas (*Ctenocephalides felis*, Bouché)," *Veterinary Parasitology*, 125: 397–407 (2004) ("Young") |
| 1034 | JILL E. MADDISON, *ET AL.*, SMALL ANIMAL CLINICAL PHARMACOLOGY (2002) (""Maddison) |
| 1035 | Material and Safety Data Sheet for FRONTLINE® PLUS FOR DOGS (Printing Date, 10/23/2001) ("2001 FRONTLINE® PLUS MSDS") |
| 1036 | AU Patent No. 2007341647 |
| 1037 | [NOT USED] |
| 1038 | U.S. Patent Application Publication No.: US 2009/0312387 A1 |

## Mandatory Notices

**Real Party-In-Interest (37 C.F.R. § 42.8 (b)(1))**: The real party-in-interest is Merial, Inc.

**Related Matters (**37 C.F.R. § **42.8(b)(2)):** Petitioner certifies that U.S. Patent No. 8,829,038 is not a subject of any other proceedings.

**Lead and Back-Up Counsel (37 C.F.R. § 42.8(b)(3**)): Lead counsel is J. Patrick Elsevier, Ph.D. (Reg. No. 44,668). Backup counsels are Dr. Judy Jarecki-Black (Reg. No. 44,170), Philip Sheng (Reg. No. 67,527), Matthew W. Johnson (Reg. No. 59,108), Wanli Tang, Ph.D. (Reg. No. 70,737), and Mark Russell (Reg. No. 37,514), and the backup agent is Dr. John Ezcurra (Reg. No. 61,004).

**Service Information (37 C.F.R. § 42.8(b)(4))**: Service of any documents in this matter should be made as follows:

| | |
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## I. Statement of the Precise Relief Requested and the Grounds for Standing (37 C.F.R. § 42.22(a) and 42.104(a))

Merial, Inc. ("Merial" or "Petitioner") hereby requests *inter partes* review and cancellation claims 1–21 of U.S. Patent No. 8,829,038 (the "'038 patent", Exh. 1002) based on one or more grounds under pre-AIA 35 U.S.C. § 102 or § 103 identified herein. Petitioner submits that there is a reasonable likelihood that it will prevail on at least one of the challenged claims because, as shown below, each element of every challenged claim is anticipated and/or rendered obvious by the prior art.

Petitioner certifies that '038 patent is available for *inter partes* review and that Petitioner is not barred or estopped from requesting *inter partes* review challenging the patent claims on the grounds identified herein.

## II. Summary of Relevant Information Concerning the '038 Patent

The '038 patent (Exh. 1002) issued from U.S. Patent Application No. 13/852,513 (the "'513 application", Exh. 1004), filed on March 28, 2013, which is a continuation of Application No. 12/727,003 (the "'003 application", Exh. 1005), filed on March 18, 2010, and issued as U.S. Patent No. 8,580,837 ("the '837 patent", Exh. 1003) on November 12, 2013. The '003 application claims priority to provisional Application No. 61/161,361, filed on March 18, 2009.

The ’038 patent is directed to formulations comprising the well-known parasiticide fipronil for controlling ectoparasites, such as fleas and ticks, in domestic animals. Claim 1, the only independent claim, recites:

> A parasiticidal formulation comprising:
> from about 8 to about 12% by weight Fipronil, or a veterinary acceptable derivative thereof;
> less than about 5% by weight of the formulation of ethanol; and
> at least one organic solvent which is not ethanol.

Thus, claim 1 has three limitations: a formulation containing (1) from about 8 to about 12% w/w fipronil or a veterinary acceptable derivative thereof; (2) less than about 5% w/w ethanol; and (3) at least one non-ethanol organic solvent.

Parasiticidal formulations comprising fipronil as an active ingredient in various non-ethanol organic solvents, with or without various amounts of ethanol included as a co-solvent, were well known in the art before March 18, 2009, the earliest possible effective filing date of the ’038 patent. Indeed, during the prosecution of the ’038 patent, the only alleged point of novelty for any of the claims was element (2), the “less than about 5% by weight of the formulation of ethanol” limitation. According to the Examiner’s Reason for Allowance, “the composition is unexpectedly effective in controlling parasites with *a decreased amount of ethanol*,” and “[t]here is neither motivation, nor reason given by the prior art to [decrease the amount of ethanol] to arrive at the instant composition,

nor a reasonable expectation of success in doing so." (Exh. 1004, p. 13 (emphasis added).) As demonstrated below, the Examiner was mistaken. Not only are the claims of the '038 patent anticipated by the prior art, it was well known in the art that the amount of ethanol in efficacious fipronil-containing parasiticidal formulations can vary greatly, from, for example, as low as 0% to at least as high as 32%.

## III. Summary of the Reasons Why Relief Should Be Granted

Little deference should be given to the Examiner's decision to allow the '038 patent. First, much of the prior art—including International Patent Publication No. WO 2009/027506 ("Freehauf"; Exh. 1008) and Chinese Patent Publication No. CN 101129357 ("Pan"; Exh. 1009; certified English translation is Exh. 1030), as well as the combinations of references relied on herein—was not before the Examiner during prosecution. Second, there was no substantive analysis during prosecution comparing the claimed formulations to the prior art. Apart from a provisional double-patenting rejection (Exh. 1004, p. 67–71 and p. 13), no substantive rejections were issued.

A thorough comparison of the claims of the '038 patent with the prior art would have revealed that the claims are unpatentable. First, there was no dispute during prosecution that the first and third limitations of claim 1—*i.e.*, formulations having fipronil from between about 8–12% w/w and at least one non-ethanol

solvent—were well known in the prior art. Fipronil was known as an effective active ingredient for controlling parasites in domestic animals long before the earliest possible effective filing date of the '038 patent, and many prior art paraciticidal formulations had both fipronil at between about 8–12% w/w and at least one organic solvent that was not ethanol, such as those disclosed in Freehauf, U.S. Patent No. 6,395,765 ("Etchegaray"), and Pan. (Exh. 1007–1009, 1030).

The prior art also anticipates the second limitation of claim 1 of the '038 patent—"less than about 5% by weight of the formulation of ethanol." Freehauf teaches such a fipronil formulation having a non-ethanol organic solvent and 0% ethanol. Etchegaray discloses (i) a specific fipronil formulation having a non-ethanol organic solvent and 5.77% w/w ethanol as a co-solvent, and (ii) fipronil formulations having a non-ethanol organic solvent and as low as 3.8% w/w ethanol as the co-solvent (which Etchegaray teaches can also be replaced by, *e.g.*, isopropanol, resulting in formulations with 0% ethanol). (Exh. 1015, ¶ 47–58; Exh. 1017, ¶ 26 and App. D.) Furthermore, Pan discloses such a fipronil containing antiparasitic formulation having a non-ethanol organic solvent and 3.74% w/w ethanol. (Exh. 1015, ¶ 69–74; Exh. 1017, ¶ 46 and App. H.) Accordingly, each of these references disclose all of the limitations of, and therefore, anticipate claim 1 of the '038 patent.

Freehauf also meets the additional limitations of claims 3–5 and 7–17; Etchegaray also meets the additional limitations of claims 2–3 and 7–19; and Pan also meets the additional limitations of claims 2–3, 9 and 18–19. Accordingly, Petitioner respectfully submits that claims 1–5 and 7–19 of the '038 patent are anticipated by the prior art and are therefore unpatentable.

If Etchegaray is not determined to anticipate claim 1, then Etchegaray and certain other references, such as the 2001 FRONTLINE® TOP SPOT MSDS (Exh. 1020), that describe the formulation of a commercial embodiment of Etchegaray having 7.7% w/w ethanol as the co-solvent (Exh. 1020), certainly would have rendered claim 1 obvious to a person of ordinary skill in the art at the earliest possible effective filing date of the '038 patent ("POSA"). As explained by Dr. Leonore C. Witchey-Lakshmanan ("Dr. Witchey") (Exh. 1015), any asserted variation in the ethanol co-solvent level from those prior art formulations (*e.g.* 5.77% w/w or 7.7% w/w) to the claimed formulation (less than about 5% w/w) would at most constitute a predictable variation of a known element of the formulation. (*Id.*, ¶ 119 and 130.) Furthermore, a POSA would not have expected such slight variations in the amount of ethanol to impair the efficacy of the formulation since the prior art showed that similar variations in ethanol amounts had no discernible impact on efficacy. (*Id.*)

A POSA would have been motivated to reduce the ethanol content in the prior art formulations to, for example, reduce any flammable risk or any dryness or irritation of the pet's skin. (*Id.*, ¶ 119–126.) As ethanol was known to be flammable and a drying agent, a POSA would have expected its reduction to increase the flash point of the formulation and/or reduce the dryness of the pet's skin at the spot of application. (*Id*.)

During prosecution of the '003 application, the patentee contended that the claimed formulations contained lower ethanol than the prior art, yet were "unexpectedly" effective. (Exh. 1005, p. 99–101.) As explained by Dr. Jeffery N. Clark ("Dr. Clark") and Dr. Witchey, the evidence relied on by the patentee, however, does not establish any properties of the claimed formulations that would have been "unexpected" to a POSA, and therefore cannot overcome the obviousness of the claims. (Exh. 1015, ¶ 132–36; and Exh. 1013, ¶ 23–61.)

Etchegaray also teaches each of the additional limitations set forth in dependent claims 2–3 and 7–21, rendering these claims obvious to a POSA.

Finally, dependent claims 4–6—which further include limitations related to an insect growth regulator ("IGR")—are also invalid for being obvious, because it was known in the prior art to add an IGR, such as methoprene, at a concentration that falls within the claimed range to fipronil-containing parasiticidal formulations to achieve improved efficacy. (Exh. 1015, ¶ 142–53.)

In view of the foregoing, there is at least a reasonable likelihood that Petitioner will prevail on the asserted grounds to establish that each of the claims of the ’038 patent are invalid. The *inter partes* review of the ’038 patent is warranted in order to give the PTO an opportunity to consider the patentability of the ’038 patent claims in view of the prior art discussed herein.

## IV. A Person of Ordinary Skill in the Art

A POSA with respect to the subject matter of the ’038 patent would be a formulation scientist having at least a college degree in chemistry, chemical engineering, pharmacy, pharmaceutical sciences or an equivalent field and several years of experience formulating parasiticidal compositions. (Exh. 1015, ¶ 33.) A POSA with respect to the subject matter of the ’038 patent would also have several years of experience evaluating the efficacy and aesthetic and other characteristics of parasiticidal compositions through whole organism and animal studies, or would have access to a skilled team of colleagues, such as veterinarians and parasitologists, with such experience. (*Id*.)

## V. Claim Construction

### A. Parasiticidal formulation

Petitioner submits that the broadest reasonable interpretation of the term “parasiticidal formulation” in view of the specification of the ’038 patent is a formulation that is capable of killing one or more types of parasites, including

ectoparasites such as fleas, ticks, and flies. (Exh. 1015, ¶ 34 and Exh. 1002, col. 1, ll. 27–30.)

### B. Less than about 5% by weight of the formulation of ethanol

Petitioner also submits that the broadest reasonable construction of the phrase "less than about 5% by weight of the formulation of ethanol" encompasses formulations having from 0 to 5.9% by w/w ethanol. This construction is guided by the ordinary meanings of the terms "about" and "less than," and the teachings in the specification. (Exh. 1015, ¶ 35–39.)

First, with regard to the lower end of this range, a POSA would understand that "*less than* about 5% by weight of the formulation of ethanol" would encompass a formulation having 0% ethanol. (*Id.*, ¶ 36); *see, e.g.*, *Google, Inc. v. Traffic Info.*, *LLC*, No. CV09-642-HU, 2011 WL 4828894, at *6 (D. Or. May 04, 2011) (construing term "less than all available traffic information" to mean "between zero and one hundred percent of the traffic information"); *Application of Mochel*, 470 F.2d 638, 640 (C.C.P.A. 1972) (holding that the phrase "up to" includes zero as the lower limit); *Ex parte Dobson*, *et al*., 165 U.S.P.Q 29, 30 (Pat.& Tr. Office Bd. App. 1970) (holding claim limitation "'up to about 50% by weight of dimethyl sulfoxide' [is] readable upon compositions totally lacking DMSO, i.e. 0-50% of the latter"); *Ex parte Perrin, et al*., 133 USPQ 207, 208–09 (Pat.& Tr. Office Bd. App. 1957) (holding "[s]ince [the claim limitation 'up to 20%

by weight'] does not exclude 0%, it is clear that the above constituent is optional"); *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1560–61 (Fed. Cir. 1996) (holding that "one composition containing essentially no cerium" meets the claim limitation of "less than 0.5 weight %" of cerium).

Second, a POSA would understand from the claim's use of the term "about" that the upper limit of the claimed range must be greater than exactly 5%, and would encompass at least up to 5.9% w/w ethanol. (Exh. 1015, ¶ 37–38.) As the Federal Circuit has explained, the use of the word "about" clearly signifies the patentee's intent to claim something beyond the exact specified numerical limitation. *See Cohesive Technologies, Inc. v. Waters Corp*., 543 F.3d 1351, 1368 (Fed. Cir. 2008) ("[B]y including the word 'about,' the patentee plainly intended the limitation 'greater than about 30 μm' to encompass columns with particles with average diameters that are less than 30 μm, but are still greater than 'about' 30 μm."); *Ortho–McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd*., 476 F.3d 1321, 1326 (Fed. Cir. 2007) ("[t]he use of the word 'about,' avoids a strict numerical boundary to the specified parameter."); *In re Harris*, 409 F.3d 1339, 1343 (Fed. Cir. 2005) ("[U]se of the term 'about' shows that the applicants did not intend to limit the claimed ranges to their exact end-points.").

Just how far beyond the specified numerical limitation the term "about" extends should depend on "the criticality of the [numerical limitation] to the

invention." *Ortho–McNeil Pharm.,* 476 F.3d at 1327; *see also Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 1217 (Fed. Cir. 1995) ("[T]he meaning [of the term 'about'] depends on the technological facts of the particular case" and "[i]t is appropriate to consider the effects of varying that parameter, for the inventor's intended meaning is relevant.") For example, in *Cohesive Technologies,* the limitation of "greater than about 30 μm" for the particle size was construed to include at least "greater than 25.434 μm" because the specification provides that the function of the lower-end limit on particle size relates to the ability of the column to attain turbulence, and the purpose can be achieved when the particle size is 30 μm ± 15.22% (namely, between 25.434 μm and 34.566 μm). *Cohesive Technologies, Inc.*, 543 F.3d at 1368–70.

Also, when, as here, the claim limitation is expressed as a number with no decimal places, *i.e.*, as one significant digit, it suggests that "the claim limitation is not especially precise, and that strict adherence to a numerical boundary is not critical to practicing the invention." *P&G v. Team Techs., Inc.*, No. 1:12-cv-552, 2014 U.S. Dist. LEXIS 119598, at 36 (S.D. Ohio July 3, 2014).

The teachings in the '038 patent indicates that the term "about 5% by weight of the formulation of ethanol" should be construed to encompass at least up to 5.9% w/w ethanol. Nothing in the specification suggests that a variation of the amount of ethanol, an optional cosolvent, within 1% would affect the formulation in any

significant manner. (Exh. 1015, ¶ 38.) In fact, the specification explains that the patentee's technological aim of ensuring that the formulations "have a flashpoint of greater than 36°C. (97°F.)" can be achieved by keeping the $C_1$–$C_6$ alcohol cosolvent (*e.g.* ethanol) at 8% w/w or lower. (Exh. 1015, ¶ 38–39; Exh. 1002, Abstract, col. 2, ll. 3–4, 39–43.) Accordingly, a POSA would understand that formulations having from 0–5.9% w/w ethanol would achieve the patent's intended purpose, while also accommodating the intended variation in the claim scope introduced by patentee's use of the word "about." (Exh. 1015, ¶ 39.) Of course, the broadest reasonable construction of this term could even be greater than 5.9%, but for purposes of this Petition it is sufficient to recognize that the term "about 5%" at least encompasses formulations having up to 5.9% w/w ethanol.

### C. Formulated for spot-on delivery

Petitioner further submits that the broadest reasonable interpretation of the term "formulated for spot-on delivery" in claim 17 of the '038 patent is a formulation that can be deposited onto the skin of an animal by local point application. This construction is guided by the term's ordinary meaning and is consistent with the term's use in the specification of the '038 patent, and its use in the prior art. (*See*, *e.g.*, Exh. 1015, ¶ 40; Exh. 1002, col. 4, ll. 36–42 and 60–62; Exh. 1007, col. 4, ll. 37–39; Exh. 1008, ¶ [0012]; Exh. 1029, col. 6, ll. 51–54.)

For the remaining terms of the challenged claims, Petitioner submits that they have well understood ordinary meanings (Exh. 1015, ¶ 41) and/or do not need to be construed for purposes of this petition.

## VI. Identification of Challenge (37 C.F.R. § 42.104(b))

*Inter partes* review of claims 1–21 of the '038 patent is requested based on the following grounds:

Ground 1: Claims 1, 3–5 and 7–17 are anticipated by Freehauf.

Ground 2: Claim 6 is rendered obvious by Freehauf in view of Jeannin or Young.

Ground 3: Claims 1–3 and 7–19 are anticipated by Etchegaray.

Ground 4: Claims 1–3 and 7–21 are rendered obvious in view of Etchegaray or the FRONTLINE® TOP SPOT References.

Ground 5: Claims 4–6 are rendered obvious by Etchegaray in view of Maddison, Jeannin, or Young.

Ground 6: Claims 1–3, 9 and 18–19 are anticipated by Pan.

The declarations of Dr. Witchey (Exh. 1015), Saijun Gong (Exh. 1017), Dr. Clark (Exh. 1013), Randy Sheppard (Exh. 1011), and Morris M. Jackson (Exh. 1032) are submitted herewith in support of the proposed grounds.

Dr. Witchey's declaration provides the state of art at the earliest possible effective filing date of the '038 patent and explains why the claimed formulations

lack novelty or inventiveness in view thereof. (Exh. 1015.) Because certain components of the prior art formulations are described in terms of "volume/volume" percentage ("v/v"; $cm^3$ per 100 $cm^3$ of the formulation) or "weight/volume" percentage ("w/v"; gram per 100 $cm^3$ of the formulation) instead of "weight/weight" percentage ("w/w"; gram per 100 grams of the formulation) as used in the claims of the '038 patent, Dr. Witchey also relies on a series of formulation experiments that replicated certain prior art formulations to determine the inherent w/w percentages of various components, thereby demonstrating that these formulations anticipate the claims of the '038 patent. (Exh. 1015, ¶ 9 and Apps. B, E, G and I.) These formulation experiments are described in the Gong Declaration (Exh. 1017).

Dr. Clark explains why, contrary to the Examiner's Reason for Allowance, the patentee failed to demonstrate any results that would have been unexpected to a POSA. (Exh. 1013.) Specifically, Dr. Clark explains why the Petrick Declaration—submitted during prosecution of the '003 application and appearing to be the only basis of the Examiner's Reason for Allowance—does not support any alleged unexpected results.

The Sheppard Declaration demonstrates, *inter alia*, that the FRONTLINE® TOP SPOT MSDS (Exh. 1020) was publicly available more than one year prior to the earliest effective filing date of the '038 patent. (Exh. 1011.)

Finally, the Jackson Declaration demonstrates that certain non-patent literature was publicly available more than one year prior to the earliest effective filing date of the '038 patent. (Exh. 1032.)

### A. Ground 1: Claims 1, 3–5 and 7–17 are anticipated by Freehauf

Freehauf was published on March 5, 2009, prior to March 18, 2009, the earliest possible priority date of the '038 patent. Freehauf, therefore, is prior art under pre-AIA 35 U.S.C. § 102(a). Freehauf is an International PCT application publication, which designated the United States, was published in English, and has an international filing date of August 29, 2008. Freehauf, therefore, is also prior art under pre-AIA 35 U.S.C. § 102(e). Freehauf was not before the Examiner during prosecution of the '038 patent.

#### 1. Claim 1 is anticipated by Freehauf

The claim chart below compares limitation-by-limitation claim 1 of the '038 patent to Freehauf's disclosure. As shown, Freehauf expressly discloses every element of claim 1. (*See* Exh. 1015, ¶ 43–46, 94.)

| Claim 1 | Disclosure of Freehauf |
|---|---|
| A parasiticidal formulation comprising: | Freehauf teaches: "The present invention provides improved fipronil formulations useful in controlling ectoparasites on a domestic animal." (Exh. 1008, ¶ [0006].) |
| from about 8 to about 12 % by weight Fipronil, or a veterinary acceptable derivative thereof; | Freehauf teaches: "The formulation will typically comprise fipronil at a concentration of about 10% (w/v)." (Exh. 1008, ¶ [0006].)<br><br>Freehauf discloses an embodiment that contains |

| Claim 1 | Disclosure of Freehauf |
|---|---|
| | 10% by weight fipronil: "fipronil: 10%; Cosmetic Fluid CF-76: 20%; isopropyl alcohol: 20%; dipropylene glycol monomethyl ether: q.s. to 100%." (Exh. 1008, ¶ [0050].) |
| less than about 5% by weight of the formulation of ethanol; and | The Freehauf embodiment contains no ethanol.[1] (Exh. 1008, ¶ [0050].) |
| at least one organic solvent which is not ethanol. | The Freehauf embodiment contains dipropylene glycol monomethyl ether. (Exh. 1008, ¶ [0050].) |

### 2. Claims 3–5 and 7–17 are anticipated by Freehauf

Freehauf also anticipates dependent claims 3–5 and 7–17 as shown in the claim chart below. (*See* Exh. 1015, ¶ 43–46, 95–99.)

| Claims | Disclosure of Freehauf |
|---|---|
| Claim 3: The formulation of claim 1, wherein the Fipronil or a veterinarily acceptable derivative thereof is Fipronil. | The Freehauf embodiment contains 10% by weight fipronil. (Exh. 1008, ¶ [0050]) |
| Claim 4: The formulation of claim 1, which further comprises an insect growth regulator (IGR). | Freehauf teaches: "In some embodiments, other components are included in the formulation. The other component may be a second active ingredient, for example, a pesticide. Useful pesticides include insect growth regulators." (Exh. 1008, ¶ [0028]) |
| Claim 5: The formulation of claim 4, wherein the IGR is S-methoprene. | Freehauf teaches that methoprene, among others, can be used as IGR. (Exh. 1008, ¶ [0031].) |

[1] As discussed above, a formulation having no ethanol meets the broadest reasonable construction of "less than about 5% by weight of the formulation of ethanol." (*See supra* § V.)

| | |
|---|---|
| | "Methoprene" refers to the racemic mixture of two enantiomers (R and S) and therefore includes S-methoprene. (Exh. 1015, ¶ 76, n. 11.) |
| Claim 7: The formulation of claim 1 wherein the at least one organic solvent which is not ethanol is *diethylene glycol monoethyl ether*, ethylene glycol monoethyl ether, dipropylene glycol n-butyl ether, *dipropylene glycol monomethyl ether*, or combinations thereof. | Freehauf discloses an embodiment that contains dipropylene glycol monomethyl ether. (Exh. 1008, ¶ [0050]; *see also id.*, ¶ [0027] (disclosing diethylene glycol monoethyl ether as a suitable solvent).) |
| Claim 8: The formulation of claim 7 wherein the at least one organic solvent which is not the ethanol is diethylene glycol monoethyl ether. | Freehauf teaches formulations that consist essentially of fipronil and a veterinarily acceptable carrier, (*Id.*, ¶ [0006]), which can be "diethylene glycol monoethyl ether." (*Id.*, ¶ [0027].) |
| Claim 9: The formulation of claim 1 further comprising at least one antioxidant. | Freehauf teaches: "The formulation may further comprise additional components such as a second active ingredient, a colorant, *an antioxidant*, a light stabilizer, or a combination thereof." (*Id.*, ¶ [0006] (emphasis added).) |
| Claim 10: The formulation of claim 9 comprising at least two antioxidants. | Freehauf teaches: "Useful antioxidants include, for example, *butylhydroxyanisole*, *butylhydroxytoluene*, ascorbic acid, sulphites, metabisulphites, or thiosulphates (e.g. sodium thiosulphate, sodium metabisulphite, potassium metabisulphite, etc.), propyl gallate, and/or tocopherol, *or a mixture of not more than two of these agents*." (*Id.*, ¶ |
| Claim 11: The formulation of claim 9 wherein the at least one antioxidant is selected from the group consisting of *butylated hydroxylanisole*, *butylated hydroxyltoluene*, alpha tocopheral [*sic*], ascorbic acid, ascobyl palmitate, fumeric acid, malic acid, citric acid, sodium ascorbate, sodium | |

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|---|---|
| metabisulfate, n-propyl gallate, and monothioglycerol. | [0033] (emphasis added).)[2] |
| Claim 12: The formulation of claim 10 wherein the at least two antioxidants are independently selected from the group consisting of *butylated hydroxylanisole*, *butylated hydroxyltoluene*, alpha tocopheral [*sic*], ascorbic acid, ascobyl palmitate, fumeric acid, malic acid, citric acid, sodium ascorbate, sodium metabisulfate, n-propyl gallate, and monothioglycerol. | |
| Claim 13: The formulation of claim 11 wherein the at least one antioxidant is butylated hydroxylanisole or butylated hydroxyltoluene. | |
| Claim 14: The formulation of claim 13 wherein the at least one antioxidant is butylated hydroxylanisole. | |
| Claim 15: The formulation of claim 13 wherein the at least one antioxidant is butylated hydroxyltoluene. | |
| Claim 16: The formulation of claim 12 wherein the at least two antioxidants are butylated hydroxyltoluene and butylated hydroxylanisole. | |
| Claim 17: The formulation of claim 1, wherein the formulation is formulated | Freehauf teaches: "The 'local topical formulation' may be referred to herein as |

[2] "Butylhydroxyanisole," also known as "butylated hydroxylanisole" and as "butylated hydroxylanisole," is abbreviated as "BHA." "Butylhydroxytoluene," also known as "butylated hydroxyltoluene" and "butylated hydroxytoluene," is abbreviated as "BHT." (Exh. 1015, note 2.)

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| for spot-on delivery. | 'the formulation of the present invention,'" which is a "fluid formulation . . . such as pour-on formulations, *spot-on formulations* and spray-on formulations." (Exh. 1008, ¶ [0010] (emphasis added).) |

### B. Ground 2: Claim 6 is rendered obvious by Freehauf in view of Jeannin or Young

U.S. Patent No. 6,096,329 ("Jeannin"; Exh. 1029) issued on August 1, 2000, and Young, *et al*., *Veterinary Parasitology*, 125: 397–407 (2004) ("Young"; Exh. 1033) was published in 2004, both more than one year prior to March 18, 2009, the earliest possible effective filing date of the '038 patent. Thus, both Jeannin and Young are prior art under pre-AIA 35 U.S.C. § 102(b). (Exh. 1015, ¶ 75 and 86 and Exh. 1032, ¶ 10–12.) Like Freehauf, neither Jeannin nor Young were considered during the prosecution of the '038 patent.

Claim 6 depends from claim 5, which depends from claim 4, which in turn depends from independent claim 1. As discussed above, Freehauf anticipates claims 1, 4 and 5. Claim 6 merely adds that the amount of S-methoprene is from about 5% to about 25% by weight of the formulation.

Although Freehauf does not expressly disclose S-methoprene in the amount of about 5%–25% w/w, formulations containing S-methoprene within this range were well-known in the art as evidenced by Jeannin and Young. (Exh. 1015, ¶ 142–50.) Specifically, Jeannin expressly describes an insecticidal combination to

control fleas in small mammals, which includes fipronil with an IGR. (Exh. 1029, Abstract.) Jeannin further teaches that the IGR is preferably methoprene, which can be present in a proportion of from 1 to 20% (w/v), significantly overlapping with the claimed range of between 5%–25% w/w. (Exh. 1029, col. 3, l. 59, col. 9, ll. 32–36; Exh. 1015, ¶ 75, 148.) Young also relates to the development of parasiticidal formulations, and teaches that a formulation combining fipronil with S-methoprene in an amount that falls between 5%–25% by weight (*i.e.* 9% w/v) is efficacious. (*See* Exh. 1033; Exh. 1015, ¶ 145–46.)

As Freehauf, Jeannin, and Young are in the same field of endeavor and are directed to similar parasiticidal formulations as the ’038 patent, it would have been obvious to a POSA to combine the teachings of Freehauf with Jeannin or Young and to modify the formulations disclosed in Freehauf to include S-methoprene in the claimed amounts to improve the formulations’ efficacy, thereby rendering claim 6 obvious. (Exh. 1015, ¶ 151–53.)

### C. Ground 3: Claims 1–3 and 7–19 are anticipated by Etchegaray

Etchegaray issued on May 28, 2002, more than one year prior to March 18, 2009, the earliest possible effective filing date of the ’038 patent. Thus, Etchegaray is prior art under pre-AIA 35 U.S.C. § 102(b).

Etchegaray teaches spot-on fipronil containing compositions for treating and protecting domestic animals from parasites such as fleas and ticks. (Exh. 1007)

Etchegaray teaches that the compositions contain four components: (a) an insecticidal active ingredient, such as fipronil (b) a crystallization inhibitor, such as polyethylene glycols, (c) an organic solvent, such as diethylene glycol monoethyl ether ("DGME") and (d) an organic co-solvent, which can be ethanol, isopropanol, methanol. (Exh. 1007, col. 4, ll. 15–18, col. 5, ll. 2–3, col. 5, l. 28, col. 4, ll. 63–65, col. 6, ll. 9–10; Exh.1015, ¶ 47–48.) Etchegaray teaches that the compositions can also include antioxidants, and provides a list of optional antioxidants, such as BHA and/or BHT. (Exh. 1007, col. 4, ll. 33–35, col. 6, ll. 11–15; Exh.1015, ¶ 49.).

Etchegaray also provides 24 example formulations. (Exh.1015, ¶ 59; Exh. 1007, col. 6–7, Table.) One such example formulation, Example No. 14 of Etchegaray, contains 12.08% w/w fipronil, 5.77% w/w ethanol, DGME, Polyvinylpyrrolidone, polysorbate 80, BHA, and BHT. (Exh. 1017, ¶ 16–26 and App. D; Exh.1015, ¶ 61–62.)

Although Etchegaray was considered during the prosecution of the '038 patent, the Examiner apparently was not made aware that Etchegaray discloses the limitation "less than about 5% by weight of the formulation of ethanol." Further, for the reasons explained in sections D(1)(b)(i)–(vi) below, the Petrick Declaration apparently misled the Examiner into believing that "the [claimed] composition is unexpectedly effective in controlling parasites with a decreased amount of ethanol," and "[t]here is neither motivation, nor reason given by the prior art to

[decrease the amount of ethanol] to arrive at the instant composition, nor a reasonable expectation of success in doing so." (Exh. 1004, p. 13.) To the contrary, there was nothing unexpected about the claimed formulations, and, indeed, Etchegaray discloses, either expressly or inherently, each limitation of independent claim 1 and dependent claims 2–3 and 7–19 of the '038 patent.

### 1. Claim 1 is anticipated by Etchegaray

Example No. 14 of Etchegaray teaches all of the limitations of claim 1 of the '038 patent. (Exh. 1007, col. 6, l. 43 –col. 7, l. 35; col. 7, l. 57–col. 8, l. 24; and Table; Exh. 1017, ¶ 16–26 and App. D; Exh.1015, ¶ 100–03.)

As explained in the Witchey and Gong Declarations, an experiment was performed to replicate Example 14 of Etchegaray to determine the inherent amount of ethanol present in the formulation in terms of a weight percentage of the formulation. (Exh. 1015, ¶ 101; Exh. 1017, ¶ 16–26.) As explained in those declarations, the formulation in Example 14 of Etchegaray inherently contains 12.08% w/w fipronil and 5.77% formulation w/w ethanol. (Exh. 1015, ¶ 101–02; Exh. 1017, ¶ 26, App. D.) Because "less than about 5%" includes 5.77% under the term's broadest reasonable interpretation (*see supra* § V), Etchegaray meets this claim limitation. This limitation is also met because Etchegaray expressly teaches ethanol is an optional cosolvent, which can be replaced by, for example,

isopropoanol, resulting in a formulation with 0% ethanol. (*See* Exh. 1007, col. 6, ll. 9–10; Exh. 1015, ¶ 103.) Thus, claim 1 is anticipated by Etchegaray.

The claim chart below compares limitation-by-limitation claim 1 of the '038 patent to the disclosure of Etchegaray. As shown, Etchegaray satisfies all of the limitations of claim 1.

| **Claim 1** | **Etchegaray** |
|---|---|
| A parasiticidal formulation comprising: | The formulation of Example No. 14 is an example of a "novel antiparasitic compositions for the treatment and protection of animals." (Exh. 1007, col. 1, ll. 45–47; col. 6, l. 43 –col. 7, l. 35; col. 7, l. 57–col. 8, l. 24; and Table.) |
| from about 8 to about 12 % by weight Fipronil, or a veterinarily acceptable derivative thereof; | The formulation of Example No. 14 has 12.08% w/w fipronil. (Exh. 1007, col. 6, l. 43 –col. 7, l. 35; col. 7, l. 57–col. 8, l. 24; and Table; Exh. 1017, ¶ 26; App. D.) |
| less than about 5% by weight of the formulation of ethanol; and | The formulation of Example No. 14 has 5.77% w/w ethanol. (Exh. 1007, col. 6, l. 43 –col. 7, l. 35; col. 7, l. 57–col. 8, l. 24; and Table; Exh. 1017, ¶ 26; App. D.)<br>The co-solvent ethanol can also be replaced with isopropanol or methanol, resulting in zero ethanol in the formulation. (Exh. 1007, col. 6, ll. 9–10.) |
| at least one organic solvent which is not ethanol. | The formulation of Example No. 14 has DGME as an organic solvent. (Exh. 1007, col. 6, l. 43 –col. 7, l. 35; col. 7, l. 57–col. 8, l. 24; and Table; Exh. 1017, ¶ 24 and App. D.) |

### 2. Claims 2–3 and 7–19 are anticipated by Etchegaray

Etchegaray also anticipates dependent claims 2–3 and 7–19 as shown in the claim chart below.

| Claims | Etchegaray |
|---|---|
| Claim 2: The formulation of claim 1, further comprising one or more crystallization inhibitor. | Etchegaray teaches that the composition contains component (b), a crystallization inhibitor. (Exh. 1007, col. 2, ll. 65–67.)<br>In Example No. 14, the formulation contains 10 g crystallization inhibitor (5 g polyvinylpyrrolidone and 5 g polysorbate 80). (Exh. 1007, col. 6–7, Table.) |
| Claim 3: The formulation of claim 1, wherein the Fipronil or a veterinarily acceptable derivative thereof, is Fipronil. | In Example No. 14, the formulation contains fipronil. (Exh. 1007, col. 6–7, Table.) |
| Claim 7: The formulation of claim 1 wherein the at least one organic solvent which is not ethanol is *diethylene glycol monoethyl ether*, ethylene glycol monoethyl ether, dipropylene glycol n-butyl ether, dipropylene glycol monomethyl ether, or combinations thereof. | In Example No. 14, the formulation contains diethylene glycol monoethyl ether. (Exh. 1007, col. 6–7, Table.) |
| Claim 8: The formulation of claim 7 wherein the at least one organic solvent which is not the ethanol is diethylene glycol monoethyl ether. | In Example No. 14, the formulation contains diethylene glycol monoethyl ether. (Exh. 1007, col. 6–7, Table.) |
| Claim 9: The formulation of claim 1 further comprising at least one antioxidant. | Etchegaray teaches: "The composition may also comprise an antioxidant intended to inhibit aerial oxidation." (Exh. 1007, col. 4 ll. 33–35.) |
| Claim 10: The formulation of claim 9 comprising at least two antioxidants. | In Example No. 14, the formulation contains two antioxidants, butylated hydroxyanisole and butylated hydroxytolune. (Exh. 1007, col. 6–7, Table.) |
| Claim 11: The formulation of claim 9 wherein the at least one antioxidant is selected from the group consisting of *butylated hydroxylanisole, butylated hydroxyltoluene,* alpha tocopheral [*sic*], ascorbic acid, ascobyl palmitate, fumeric acid, malic acid, citric acid, sodium | |

| Claims | Etchegaray |
|---|---|
| ascorbate, sodium metabisulfate, n-propyl gallate, and monothioglycerol. | |
| Claim 12: The formulation of claim 10 wherein the at least two antioxidants are independently selected from the group consisting of *butylated hydroxylanisole, butylated hydroxyltoluene*, alpha tocopheral [*sic*], ascorbic acid, ascobyl palmitate, fumeric acid, malic acid, citric acid, sodium ascorbate, sodium metabisulfate, n-propyl gallate, and monothioglycerol. | |
| Claim 13: The formulation of claim 11 wherein the at least one antioxidant is butylated hydroxylanisole or butylated hydroxyltoluene. | |
| Claim 14: The formulation of claim 13 wherein the at least one antioxidant is butylated hydroxylanisole. | |
| Claim 15: The formulation of claim 13 wherein the at least one antioxidant is butylated hydroxyltoluene. | |
| Claim 16: The formulation of claim 12 wherein the at least two antioxidants are butylated hydroxyltoluene and butylated hydroxylanisole. | |
| Claim 17: The formulation of claim 1, wherein the formulation is formulated for spot-on delivery. | Etchegaray teaches: "The compositions according to the invention . . . are generally applied by deposition on the skin ('spot on' or 'pour on' application)." (Exh. 1007, col. 4, ll. 37–39.) |
| Claim 18: The formulation of claim 2, wherein the one or more crystallization inhibitor is selected from the group consisting of polyethylene glycols, polyethylene glycol hydrogenated castor oil, *polyvinylpyrrolidone,* polyvinyl | In Example No. 14, the formulation contains 10 g crystallization inhibitor, which includes 5 g polyvinylpyrrolidone and 5 g polysorbate 80. (Exh. 1007, col. 6–7, Table.) |

| Claims | Etchegaray |
|---|---|
| alcohols, copolymers of vinyl acetate, invylpyrrolidone [sic], benzyl alcohol, mannitol, glycerol, sorbitol, polyoxyethylenated soribtan esters, ploy oxyethylenated [sic] hydrogenated castor oil, lecithin, sodium carboxymethylcellulose, methacrylates and combinations thereof. | |
| Claim 19: The formulation of claim 18 wherein the at least one crystallization inhibitor is polyethylene glycol, polyethylene glycol hydrogenated castor oil, or combinations thereof. | Etchegaray teaches: "As crystallization inhibitor b) which can be used in the invention, mention may be made in particular of: . . . polyethylene glycols . . . and polyoxyethylenated derivatives of castor oil." (Exh. 1007, col. 4, l. 66–col. 5, l. 29.) |

Accordingly, and for the reasons discussed above with regard to claim 1, claims 2–3 and 7–19 are anticipated by Etchegaray.

### D. Ground 4: Claims 1–3 and 7–21 are rendered obvious by Etchegaray or the FRONTLINE® TOP SPOT References

As Dr. Witchey explains, the FRONTLINE® TOP SPOT product sold by Merial Inc.—the formulation of which is described in the 2001 FRONTLINE® TOP SPOT MSDS (Exh. 1020), Dudley, *Whole Dog J.*, 2002:18–22, 19 (2002) ("Dudley") (Exh. 1028), and Mackley, *et al.*, *Dermatitis*, 16(3):149–50 (2005) ("Mackley"; Exh. 1022) (collectively "the FRONTLINE® TOP SPOT References")—is an embodiment of Etchegaray. (Exh. 1015, ¶ 66, App. K.) Mackley and Dudley were both published and publicly available at least more than one year prior to March 18, 2009, the earliest possible effective filing date of

the ’038 patent. (Exh. 1032, ¶ 7–9 and 16–18.) As demonstrated by the Sheppard Declaration and further evidenced by Mackley (Exh. 1022, p. 149–50), Dudley (Exh. 1028, p. 19) and AU Patent No. 2007341647 (Exh. 1036, p. 1, ll. 27–28), the 2001 FRONTLINE® TOP SPOT MSDS (Exh. 1020) was also published and publicly available at least more than one year prior to March 18, 2009. (Exh. 1011, ¶ 6–13; Exh. 1015, ¶ 67.) Thus, the FRONTLINE® TOP SPOT References are prior art under pre-AIA 35 U.S.C. § 102(b). As evidenced by the FRONTLINE® TOP SPOT References, the FRONTLINE® TOP SPOT formulation contained 9.7% w/w fipronil, 7.7% w/w ethanol, polyvinylpyrrolidone, butylhydroxytoluene, hydroxyanisole, and DGME. (Exh. 1015, ¶ 68; Exhs.1020, 1022 and 1028.)

### 1. Claim 1 is rendered obvious by Etchegaray or the FRONTLINE® TOP SPOT References

The only possible point of difference between the formulation of claim 1 and the prior art is the “less than about 5% by weight of the formulation of ethanol” limitation. As provided above, the formulations disclosed in Example 14 of Etchegaray and the FRONTLINE® TOP SPOT References have 5.77% w/w and 7.7% w/w ethanol, respectively. (Exh. 1015, ¶ 114–115.) Thus, even if claim1 were construed to require no more than exactly 5% w/w ethanol, the amounts of ethanol in the formulations described in Etchegaray and the FRONTLINE® TOP SPOT References would differ from the claimed formulation by only 0.77% or 2.7% w/w ethanol, respectively. Such minor differences in the percentages of ethanol—

a component known to be non-essential for the efficacy of fipronil-containing parasiticidal formulations—does not make claim 1 patentably distinct from the prior art formulations. (*Id.,* ¶ 114–136.)

Pursuant to pre-AIA 35 U.S.C. § 103, "[a] patent for a claimed invention may not be obtained . . . if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains." 35. U.S.C. § 103 (pre-AIA).

#### (a) Claim 1 is *prima facie* obvious in view of Etchegaray or the FRONTLINE® TOP SPOT References

The concept of *prima facie* obviousness determines who has the burden of production of evidence. If a *prima facie* case is established, the burden of production falls upon the patentee to come forward with evidence on secondary considerations. *Galderma Labs. v. Tolmar, Inc.*, 737 F.3d 731, 738 (Fed. Cir. 2013). Here, claim 1 is *prima facie* obvious for at least the following reasons.

##### (i) The overlap and closeness between the claimed ethanol content and that disclosed in Etchegaray and the FRONTLINE® TOP SPOT References render the claim *prima facie* obvious

The Federal Circuit has consistently held that "[i]n cases involving overlapping ranges, . . . even a slight overlap in range establishes a *prima facie*

case of obviousness" if not anticipation. *E.g.*, *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003); *In re Woodruff*, 919 F.2d 1575, 1578 (Fed. Cir. 1990) (holding that a claimed range of "more than 5% to about 25%" was rendered obvious by a prior art range of "about 1–5%"); *In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997) (holding that a claimed range of 100–600 Angstroms was rendered *prima facie* obvious by a prior art range of 50–100 Angstroms); *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1379 (Fed. Cir. 2008) (noting "the long standing precedent of this court and our predecessor . . . that 'discovery of an optimum value of a variable' in a known . . . composition is 'usually obvious." (citations omitted)).

Even if the claimed range and the prior art range do not precisely overlap, a claimed range is still *prima facie* obvious if it is so close to the prior art range that a POSA would have expected them to exhibit the same properties. *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 783 (Fed. Cir. 1985) ("The proportions are so close that prima facie one skilled in the art would have expected them to have the same properties."); *Ortho-McNeil Pharm., Inc. v. Teva Pharms. Indus*., 344 Fed. Appx. 595, 600 (Fed. Cir. 2009) (holding a claim to be *prima facie* obvious "[b]ecause the difference between 1:7.1 and 1:10 is so slight")

Here, claim 1 is *prima facie* obvious over Etchegaray or the FRONTLINE® TOP SPOT References because of the overlap between the claimed range of "less than about 5%" with the ranges taught in Etchegaray (*i.e.* 0–32.7% w/v), and

because of the closeness between the claimed range and the ethanol levels in the specific, disclosed embodiments (5.77% w/w in Example No. 14 of Etchegaray and 7.7% w/w in the FRONTLINE® TOP SPOT References). As Dr. Witchey explains, Etchegaray teaches that the cosolvent (*e.g.* ethanol) can range between 0–32.7% (w/v), which overlaps with the claimed range of "less than about 5%" by weight. (Exh. 1015, ¶ 48–54, Table I.) In particular, an example formulation prepared according to the teaching in Etchegaray was determined to have 4.31% w/w ethanol, evidencing the overlap between the Etchegaray range and claimed range. (Exh. 1017, ¶ 15, App. B; Exh. 1015, ¶ 58.)

**(ii) A POSA would have arrived at the claimed formulations from the prior art by implementing a predictable variation**

As the Supreme Court explained in *KSR International Co. v. Teleflex Inc.*, "[i]f a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability." 550 U.S. 398, 417 (2007). Indeed, it has long been held that a mere modification to the concentration of an ingredient in the prior art is not patentable unless the modification "produce[s] a new and unexpected result which is different in kind and not merely in degree from the results of the prior art." *In re Aller*, 220 F.2d 454, 456 (C.C.P.A. 1955).

Here, a POSA would have arrived at the claimed formulation (less than about 5% w/w ethanol) from Example 14 of Etchegaray (5.77% w/w) or from the

FRONTLINE® TOP SPOT formulation (7.7% w/w) by slightly reducing the ethanol amount, *i.e.* by 0.77% or 2.7%, which, as Dr. Witchey explains, is a predictable variation of a known element, and any asserted difference between the claimed formulations and the prior art formulations at most constitutes "an obvious minor variation of an element known to be non-essential for the efficacy of the formulation, and of which a similar variation was known to have little effect on the efficacy of the formulation." (Exh. 1015, ¶ 118, 127–31). Such variation is not patentable under § 103. *See KSR International Co*., 550 U.S. at 417; *In re Aller*, 220 F.2d at 456; *Ortho-McNeil Pharm., Inc.*, 344 F. App'x at 602; *Tokai Corp. v. Easton Enterprises, Inc.*, 632 F.3d 1358, 1372 (Fed. Cir. 2011).

First, Etchegaray teaches that ethanol is an optional co-solvent that can be replaced by, for example, isopropanol. (Exh. 1007, col. 6, ll. 9–10.) Thus, as Dr. Witchey explains, a POSA could simply replace ethanol in the disclosed formulations, in whole or in part, to arrive at the claimed range and reasonably predict that such minor variations to have little discernible impact on the efficacy of the formulations. (Exh. 1015, ¶ 128–29.)

As Dr. Witchey observes, Etchegaray expressly teaches variations of ethanol content similar to those that allow a POSA to arrive at the claimed formulation, and that such variations did not impact the efficacy of the formulations. (Exh. 1015, ¶ 125.) Specifically, Etchegaray provides 24 examples with various amounts

of ethanol (7.5 $cm^3$, 10 $cm^3$, and 15 $cm^3$), and teaches the reduction of ethanol from 15% v/v to 7.5% v/v did not affect the efficacy of the formulation over a period of 13 weeks. (Exh. 1015, ¶ 60; Exh. 1007, col. 6–7.)

Furthermore, a number of references published before March 18, 2009, the earliest possible priority date of the '038 patent, demonstrate that the cosolvent, either ethanol or any $C_1$-$C_6$ alcohol, is not essential to the efficacy of a spot-on parasiticidal formulation. (Exh. 1015, ¶ 75–80.) For example, European Patent No. EP 1066854 (Exh. 1012), published on January 10, 2001, teaches that "[p]our-on or spot-on formulations may be prepared by dissolving the active ingredients in an acceptable liquid carrier vehicle . . . with or *without* addition of a volatile component such as isopropanol [or ethanol]." (*Id.*, p. 3, ll. 42–44 (emphasis added).) Likewise, U.S. Patent No. 6,426,333 (Exh. 1027), which issued on July 30, 2002, discloses a formulation containing fipronil, which "comprises a pharmaceutically or veterinary acceptable organic solvent and *optionally* an organic cosolvent." (*Id.*, col. 10, ll. 43–45 (emphasis added).) Similarly, as discussed above, Freehauf discloses effective spot-on formulations with fipronil as the sole active ingredient that do not contain ethanol or any other $C_1$-$C_6$ alcohol. (*Supra* § VI.A.1.) Clearly, ethanol or any other $C_1$-$C_6$ alcohol cosolvent, was known to be non-essential for the efficacy of a fipronil parasiticidal formulation, further evidencing that a 0.77–2.7% reduction of ethanol level in Etchegaray or

FRONTLINE® TOP SPOT formulations to arrive at the claimed formulation constitutes, at best, a predictable variation of a known element in prior art. (Exh. 1015, ¶ 88–90, 124–26.)

**(iii) A POSA would have been motivated to modify the prior art formulations to arrive at the claimed formulation with a reasonable expectation of success**

The Supreme Court explained in *KSR International Co.*:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

550 U.S. at 402.

Here, claim 1 is also *prima facie* obvious in view of Etchegaray or the FRONTLINE® TOP SPOT References because there was a design need to modify the prior art formulations, as well as a finite number of identified, predictable solutions, which would have led a POSA to the anticipated success by pursuing the known options within his or her technical grasp.

JILL E. MADDISON, ET AL., SMALL ANIMAL CLINICAL PHARMACOLOGY (2002) ("Maddison"; Exh. 1034), a textbook published more than one year before March 18, 2009 (Exh. 1032, ¶ 13–15), cautions that spot-on parasiticidal products might

cause "skin lesions at the site of application" and that "products with flammable vehicles" in particular might have a "temporary risk of ignition." (*Id.*, p. 185.) As Dr. Witchey explains in her declaration, the design needs to reduce any flammable risk of the formulations or any dryness and irritation of the pet's skin at the spot of application, for example, would have motivated a POSA to reduce ethanol in the FRONTLINE® TOP SPOT formulation and the Etchegaray formulations. (Exh. 1015, ¶ 119–26.) Indeed, the '038 patent admits in the Background section that a design need existed to create formulations with higher flashpoints. (*See* Exh. 1002, col. 1, ll. 40–51).) The patentee should be held to this admission. *See*, *e.g.*, *Pharmastem Therapeutics, Inc. v. ViaCell*, *Inc.*, 491 F.3d 1342, 1362 (Fed. Cir. 2007) ("Admissions in the specification . . . are binding on the patentee for purposes of a later inquiry into obviousness.")

The slight adjustment of ethanol in the prior art formulations would be a predictable solution within a POSA's technical grasp. As explained by Dr. Witchey, formulation scientists "commonly create and screen several sample formulations in which the amount of one component is varied to see what effect, if any, it may have on any desired characteristic of the formulation." (Exh. 1015, ¶ 125.) By way of example, Etchegaray provides a grid of 24 formulations with various levels of different components, including ethanol, and confirms the efficacies of all 24 formulations. (*Id.*; Exh. 1007, col. 6–7, Table, col. 7, l. 57–col.

8, l. 24.) The option to reduce ethanol in the prior art formulations would have been one of a finite number of identified, predictable solutions to meet the design needs mentioned above because ethanol was known as a drying agent and a flammable ingredient. (Exh. 1015, ¶ 122; Exh. 1020, p. 1; Exh. 1023, p. 21.)

Finally, a POSA would have implemented this option with anticipated success because, as explained above, ethanol was known to be non-essential for the efficacy of parasiticidal formulations, and similar variations were known to produce no discernible impact on efficacy. (*Supra* §VI.D.1.(a).(ii).)

In view of the foregoing, it is "the product not of innovation but of ordinary skill and common sense" for a POSA to reduce the ethanol content in the FRONTLINE® TOP SPOT formulation or the Etchegaray formulations to arrive at claim 1. *See KSR International Co.*, 550 U.S. at 402. Thus, to the extent that Etchegaray does not anticipate the "less than about 5%" limitation, at a minimum, Etchegaray and the FRONTLINE® TOP SPOT References, viewed either independently or in combination, render claim 1 *prima facie* obvious.

**(b) The *prima facie* case of obviousness is not overcome by secondary considerations**

Because claim 1 is *prima facie* obvious, "the burden of production falls upon the patentee to come forward with evidence that (1) the prior art taught away from the claimed invention; (2) there were new and unexpected results relative to the prior art; or (3) there are other pertinent secondary considerations." *Galderma*

*Labs*., 737 F.3d at 738. The prosecution history shows that the Examiner allowed the challenged claims based on alleged unexpected results. Specifically, the Reasons for Allowance provide that "the composition is unexpectedly effective in controlling parasites with a decreased amount of ethanol." (Exh. 1004, p. 13.)

The Examiner, however, was mistaken, and the *prima facie* case of obviousness is not overcome by any unexpected results. The only evidence produced by the patentee regarding unexpected results was the Petrick Declaration (Exh. 1006), which purported to show an unexpected effectiveness for the claimed formulations.[3] This evidence fails to overcome the strong *prima facie* case of obviousness at least because: (1) the studies in the Petrick Declaration did not compare the claimed formulation with the closest prior art; (2) the studies in the Petrick Declaration are not commensurate in scope with the protection sought by the claims; (3) the alleged "unexpected" results reported in the Petrick Declaration would, in fact, have been expected by a POSA; (4) the Petrick Declaration fails to show that the claimed ethanol range was superior or critical over the overlapping

[3] As explained by Dr. Witchey, it would have been expected that reducing the ethanol concentration of the prior art formulations would result in higher flashpoints. (Exh. 1015, ¶ 122.) Thus, the results described in Example 4 of the '038 patent would not have been unexpected. (*Id*.)

prior art ranges; (5) the studies in the Petrick Declaration fail to link any alleged unexpected property to the alleged patentable distinction, *i.e.*, the ethanol content; and (6) the alleged unexpected results constituted at best minor differences in degree.

**(i) The studies in the Petrick Declaration did not compare the claimed formulation with the closest prior art**

"[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art." *In re Baxter Travenol Labs*., 952 F.2d 388, 392 (Fed. Cir. 1991); *In re De Blauwe*, 736 F.2d 699, 705 (Fed. Cir. 1984) ("[A]n applicant relying on comparative tests to rebut a prima facie case of obviousness must compare his claimed invention to the closest prior art.").

Here, the Petrick Declaration compared the claimed formulation with an alleged FRONTLINE™ product that allegedly contained 10% ethanol by weight based on a third party analysis (Exh. 1006, p. 2, ¶ 10). This formulation was not the closest prior art. Because the patentee relied on the "less than about 5% by weight of the formulation of ethanol" limitation to show unexpected results, Dr. Petrick should have compared the claimed formulation to prior art formulations having closest to "less than about 5% by weight of the formulation of ethanol" while meeting the other limitations of the claims. As previously shown,

Etchegaray teaches a formulation that contains 5.77% w/w ethanol, and the FRONTLINE® TOP SPOT References teach a formulation that contains 7.7% w/w ethanol, both meeting the other limitations of claim 1. (*See supra* § VI.D.1.) Accordingly, both Etchegaray and the FRONTLINE® TOP SPOT References are closer art than the formulations used in Dr. Petrick's studies, which purportedly had 10% ethanol.

As Dr. Petrick did not compare the claimed formulation to the closest prior art, his Declaration cannot overcome the *prima facie* obviousness of the claims.

**(ii) The studies in the Petrick Declaration were not commensurate in scope with the protection sought by the claims**

For a showing of unexpected results to overcome a *prima facie* case of obviousness, the evidence submitted must be commensurate in scope with the degree of protection sought by the claims. *In re Harris*, 409 F.3d at 1344 ("Even assuming that the results were unexpected, Harris needed to show results covering the scope of the claimed range."); *see also In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983); *In re Clemens*, 622 F.2d 1029, 1035 (C.C.P.A. 1980). Here, Dr. Petrick's studies only examined the efficacy of claimed formulations having 5% w/w ethanol and nothing less (Exh. 1006, p. 9–10); but the claims of the '038 patent seek protection for formulations ranging anywhere from 0% to about 5%

w/w ethanol. Therefore, Dr. Petrick's studies fail to show unexpected results commensurate in scope with this entire range.

Dr. Petrick stated in conclusory fashion that "based on the results of these experiments [which tested the efficacy of formulations with 5% ethanol] and my 32 years of experience in veterinary product development, formulations similar to [these formulations but] containing less than 5% ethanol would be expected to have similar results." (Exh. 1006, p. 3, ¶ 31.) As an initial matter, this conclusory assertion, unsupported by any evidence, should be disregarded. *Phillips v. AWH Corp*., 415 F.3d 1303, 1318 (Fed. Cir. 2005) (en banc) ("[C]onclusory, unsupported assertions by experts . . . are not useful to a court."); *Telemac Cellular Corp. v. Topp Telecom, Inc*., 247 F.3d 1316, 1329 (Fed. Cir. 2001) ("Broad conclusory statements offered by [the patentee's] experts are not evidence . . . .").

More importantly, this conclusory assertion is inconsistent with Dr. Petrick's assertion in the same declaration that "a person of skill in the art would have expected that a decrease in the amount of [ethanol] from about 10% to 5% would have . . . substantially decreased the efficacy of the formulation." (Exh. 1006, p. 1,

¶ 6–7.) Dr. Petrick provided no justification for these two incongruous assertions.[4] (Exh.1013, ¶ 27.)

Because Dr. Petrick's unsupported and contradictory assertions should be given no weight, and do not cure the patentee's failure to provide evidence of unexpected results that are commensurate in scope with the claims, the results in Petrick Declaration cannot overcome the *prima facie* obviousness of the claims.

**(iii) The alleged "unexpected" results reported in the Petrick Declaration would, in fact, have been expected by a POSA**

"[I]n order to properly evaluate whether a superior property was unexpected, the [trier of fact] should . . . consider[] what properties were expected." *Id.* at 1371. The proponent of unexpected results must provide sufficient evidence to show what would have been expected by a skilled artisan. *Id.* ("Pfizer's evidence must fail because the record is devoid of any evidence of what the skilled artisan would have expected.").

Here, the studies contained in the Petrick Declaration fail to establish unexpected results because the record is devoid of any evidence demonstrating that the alleged "unexpected" results were indeed unexpected. Dr. Petrick merely

[4] As discussed *infra* § VI.D.1(b)(iii), a POSA would not in fact have expected a decrease from 10% to 5% to affect efficacy.

asserted without support that a POSA would have "expected that a decrease in the amount of drying agent (ethanol) from 10% to 5% would have also substantially decreased the efficacy of the formulation." (Exh. 1006, ¶ 6–7.) After discussing the results of individual studies, Dr. Petrick then concluded that the tested claimed formulations "have equivalent or, in some cases, greater efficacy than FRONTLINE™ products despite having a lower ethanol content of 5% compared to FRONTLINE™ products' 10%," which was "surprising and unexpected." (*Id*., ¶ 29–30.)

Not only was the premise relied on by Dr. Petrick unsupported and incorrect, the studies in the Petrick Declaration fail to support the alleged "higher efficacy" of the claimed formulation, or provide any results that would have been "surprising and unexpected" to a POSA.

Contrary to Dr. Petrick's unsupported assertions, a POSA would not have expected such a minor decrease in ethanol (*i.e.*, from 10% to 5%) to produce any discernible impact on efficacy of the formulation, let alone a "substantial" impact. As explained by Dr. Witchey, ethanol, a drying agent, while helping enhance the animal's coat appearance, was known to be non-essential for the efficacy of a parasiticidal formulation. (Exh. 1015, ¶ 118, 134–36.) Additionally, Etchegaray expressly teaches that ethanol could be either reduced from 15% v/v to 7.5% v/v without producing any discernible impact on efficacy, or actually entirely replaced

by, for example, isopropanol. (Exh. 1015, ¶ 60, 118; Exh. 1007, col. 6–7, Table) Thus, contrary to Dr. Petrick's assertion, a POSA would have expected the tested claimed formulations with 5% ethanol to be equally efficacious as formulations with 10% ethanol.

In any event, the studies in the Petrick Declaration fail to support the alleged higher efficacy of the claimed formulations. As Dr. Petrick concedes, the majority of his studies only support that embodiments of the claimed formulations are, at best, merely as efficacious as, *i.e.*, not superior to, the prior art FRONTLINE™ formulations he tested. (Exh. 1006, ¶ 30.) Specifically, of all the studies provided, those in Exhibits 4–6, 9, 11–13, and 15–16 did not show any difference in efficacy. (Exh. 1006, p. 12–33, Exhibits 4–16.) In fact, none of the studies establish that claimed formulations Formulations A2 and B2 are more efficacious than the prior art formulations, and the Petrick declaration does not assert otherwise. (Exh. 1013, ¶ 30.)

It was only for a handful of the studies (Exhibits 7, 8, 10, and 14 of the Petrick Declaration) that the Petrick Declaration even contends support an increase in efficacy for certain of the claimed formulations. (*Id*., ¶ 32.) However, as explained by Dr. Clark, a close review of these studies reveals multiple defects and that the reported results cannot reasonably support any alleged increase in efficacy. (*Id*., ¶ 28–49.)

The studies involving the claimed Formulations A1, A3, and B1 (which the Petrick Declaration asserts have greater efficacy than the prior art FRONTLINE™ formulations) are flawed and the data unreliable. (*Id*., ¶ 28–41.) As Dr. Clark explains, the majority of the data points for these studies at best show that there are no differences in efficacy between the claimed formulations and the FRONTLINE™ formulations. (*Id*., ¶ 41.) Indeed, it was only in a few of the assays, against only a subset of the challenged ectoparasites, and then only at sporadic late time points that any differences were allegedly observed. (*Id*., ¶ 32.) As Dr. Clark explains, the alleged differences are more likely the result of expected experimental variation rather than any meaningful difference in efficacy. (*Id.*) The sporadic data points cited in the Petrick Declaration as allegedly showed increased efficacy are more likely just artificial results of outliers in these test groups that skewed the results. (*Id.*)

In addition, some data in certain studies are indecipherable, and the calculations appear to be incorrect. (*Id.*, ¶ 34–36.) There are also multiple inconsistencies in the experimental descriptions, including inconsistent references to the tested ectoparasites or tested animals, inconsistent references to the tested formulations and inconsistencies in data interpretation, which further undermine any conclusions from these studies. (*Id.*, ¶ 42–49.)

In sum, the studies in the Petrick Declaration do not support the alleged higher efficacy of the claimed formulations with 5% ethanol compared to prior art formulations with 10% ethanol. At best, they demonstrate that the decrease in ethanol had no impact on efficacy at all, which would have been well expected by a POSA.

**(iv) The studies in the Petrick Declaration fail to link the alleged unexpected property to the alleged patentable distinction, *i.e.*, the ethanol content**

To overcome a *prima facie* case of obviousness, the showing of unexpected results must be linked within a reasonable certainty to the feature that distinguished the claimed invention from the prior art. *See Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356, 1363 (Fed. Cir. 2012) (holding that the referenced studies do not establish an unexpected cooling effect for the claimed combination because the tested products "differed from the [prior art products] in a number of other ways"); *In re Dunn*, 349 F.2d 433, 439 (C.C.P.A. 1965) ("We cannot attach particular significance as showing nonobviousness to those examples since the procedures followed in the two examples do not [show that] . . . the improved results can be traced, within a reasonable certainty, to the solvent alone."). Studies comparing the claimed formulations to the prior art formulations need to be "truly comparative," as otherwise "[t]he cause and effect sought to be proven is lost here in the welter of unfixed variables." *Id.*

Here, the Petrick studies are not "truly comparative" because, as Dr. Clark explains, the formulations tested by Dr. Petrick differed from the prior art formulations in aspects beyond the feature that allegedly distinguished the claims from the prior art, *i.e.*, the ethanol content. (Exh.1013, § VI. D.1.) As a result, it is impossible to draw any conclusions as to whether any alleged differences in efficacy are attributable a variation in ethanol content as opposed to some other ingredient. (*Id*., ¶ 50.)

For example, the FRONTLINE™ and FRONTLINE™ Plus formulations both contained PVP K 17 and Polysorbate 80, which were not in the claimed formulations to which they were compared. Moreover, these FRONTLINE™ formulations did not contain Polyethylene glycol ("PEG") 1000 and PEG 60 hydrogenated castor oil that were included in the Formulations A1–A3 to which they were compared. (Exh.1013, ¶ 51–52; Exh. 1006, p. 9–11.)

Because of the multiple unfixed variables, a POSA would not be able to attribute any differences in efficacy to any differences in ethanol content. *See Wm. Wrigley Jr. Co.*, 683 F.3d at 1363; *see also In re Dunn*, 349 F.2d at 439. As discussed in Dr. Clark's declaration, comparing the results of the claimed formulations against one another, it is more likely that any differences in efficacy were actually caused by the presence or absence of these other ingredients, than by the difference in ethanol levels. (Exh.1013, ¶ 54.) Specifically, three of the four

studies that purportedly showed any difference in efficacy tested the A Formulations, whereas the studies testing the B Formulations consistently showed no difference. Thus, any alleged efficacy differences between FRONTLINE™ and the A formulations more likely resulted from the presence of the additional ingredients in the A Formulations that were not in the FRONTLINE™ formulation or the B Formulations, than from the small differences in the ethanol content. (*Id*., ¶ 53.)

For example, whereas Formulation A1 allegedly showed greater efficacy than the FRONTLINE™ formulation against controlling ticks, Formulation B1 did not. (Exh. 1006, p. 3, ¶ 20 and 23.) Both Formulations A1 and B1, however, contained the same amounts of fipronil (9.7%) and ethanol (5%). (*Id*., p. 9–10.) Their formulations differed only in that Formulation A1—but not Formulation B1— further contained PEG 1000 and PEG 60 hydrogenated castor oil. (*Id*.) As Dr. Clark explains, because both Formulations A1 and B1 had the same ethanol content, but only A1 allegedly had a higher efficacy than the FRONTLINE™ formulation to which they were compared, the alleged higher efficacy of Formulation A1 could only be attributed to presence of PEG 1000 and PEG 60 hydrogenated castor oil in that formulation, and not to any difference in the amount of ethanol. (Exh. 1013, ¶ 54.)

Furthermore, as Dr. Clark explains, it is against common judgment of a POSA to attribute the alleged differences in efficacy to the minor variation of ethanol, because that ethanol is a drying agent that evaporates shortly after administration, and that the alleged evidence of greater efficacy in the Petrick Studies did not appear until weeks after administration. (*Id.*, ¶ 56–59.)

In sum, because the studies involved unfixed variables and were not "truly comparative," and because it is against a POSA's common judgment to link the differences in efficacy observed weeks after administration to the minor reduction of ethanol level, the Petrick studies do not support the patentee's assertion that "decreasing the amount of ethanol of ethanol to 5% *results in* compositions that are more efficacious against particular parasites" (Exh. 1005, p. 100 (emphasis added)). Thus, the Petrick Declaration cannot overcome the *prima facie* obviousness of the claims.

**(v) The Petrick Declaration fails to show that the claimed range was superior or critical over the overlapping prior art ranges**

The Federal Circuit has emphasized that "the law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims," and that "in such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range." *In re*

*Woodruff*, 919 F.2d at 1578 (citing *Gardner v. TEC Sys., Inc*., 725 F.2d 1338 (Fed.Cir. 1984)); *see, e.g.*, *In re Boesch*, 617 F.2d 272 (C.C.P.A. 1980); *In re Ornitz*, 351 F.2d 1013 (C.C.P.A. 1965); *In re Aller*, 220 F.2d 454 (C.C.P.A. 1955).

Here, to overcome the *prima facie* case of obviousness the patentee must establish that the claimed range is critical, or superior, over the ranges taught in Etchegaray, which it fails to do. As explained by Dr. Clark, even if one were to assume *arguendo* that the experiments described in the Petrick Declaration had been properly designed and the results were taken at face value, a POSA would not be able to conclude that the tested claimed formulations are more efficacious than the FRONTLINE™ formulations. (*Supra* § VI.D.1.(b).(v); Exh. 1013, ¶ 29.)

Also, since a POSA would have expected the reduction of ethanol—a known flammable ingredient in the prior art formulations—would result in higher flashpoints, the results described in Example 4 of the '038 patent also does not establish any unexpected superior property of the claimed formulations.

In sum, the studies in the Petrick Declaration do not support the alleged higher efficacy of the claimed formulations, or establish any other unexpected superior properties of the claimed formulation compared to prior art. Because the Petrick Declaration fails to show any unexpected superiority—let alone criticality—of the claimed range as compared to the prior art, it fails to establish the unexpected results necessary to overcome the *prima facie* case of obviousness.

### (vi) The alleged unexpected results constituted at best minor differences in degree

Ultimately, the alleged unexpected results cannot overcome the *prima facie* case of obviousness because they would constitute, at best, only a minor difference in degree, rather than a difference in kind. Unexpected results that are probative of nonobviousness are those that are "'different in kind and not merely in degree from the results of the prior art.'" *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004) (citation omitted); *see also In re Harris*, 409 F.3d at 1344 (holding a "32–43% increase in stress-rupture life, however, does not represent a 'difference in kind' that is required to show unexpected results"). In particular, "where an unexpected increase in efficacy is measured by a small percentage, as here, and the evidence indicates that skilled artisans were capable of adjusting the percentage, the result constitutes a difference in degree, not kind." *Galderma Labs.*, 737 F.3d at 739.

Here, even accepting *arguendo* that the decrease of ethanol from 10% to 5% was expected to result in a decrease in efficacy, the failure of any such expected decrease to materialize would only constitute a difference in degree, not in kind. *See id.* Accordingly, the results are not probative of nonobviousness and do not overcome the *prima facie* case of obviousness.

### 2. Claims 2–3 and 7–19 are rendered obvious by Etchegaray

As demonstrated in § VI.C.2 above, Etchegaray teaches each of the limitations added by dependents claims 2–3 and 7–19, all of which depend from claim 1. Thus, to the extent that Etchegaray renders obvious independent claim 1, Etchegaray also renders obvious dependent claims 2–3 and 7–19.

### 3. Claims 20–21 are rendered obvious by Etchegaray

As stated above, Etchegaray anticipates and/or renders obvious claim 19. Claim 20 depends from claim 19 and requires the crystallization inhibitors to be PEG and PEG hydrogenated castor oil. Claim 21 depends from claim 20 and additionally requires the amount of PEG and PEG hydrogenated castor oil to be about 5% by weight of the formulation each.

Although Etchegaray does not expressly teach an antiparasitic formulation having the specific combination of PEG and PEG hydrogenated castor oil as the crystallization inhibitors, such a combination would have been obvious to a POSA in view of Etchegaray. Regarding the crystallization inhibitors, Etchegaray teaches that "the combination of a film-forming agent of polymer type and a surfactant" is preferred (Exh. 1007, col. 5, ll. 35–37), and that the surfactant is preferably a nonionic surfactant (Exh. 1007, col. 5, ll. 45–46). Further, Etchegaray provides a list of the film-forming agents of polymer type, which includes PEG (Exh. 1007, col. 5, ll. 2–3), and a list of the nonionic surfactants, which includes

polyoxyethylenated derivatives of castor oil (Exh. 1007, col. 5, l. 28). It was well known in the art that PEG hydrogenated castor oil was a polyoxyethylenated derivative of castor oil suitable for antiparasitic formulations. (Exh. 1002, col. 3, ll. 12–14 and Exh. 1031[5], ¶ [0038] (teaching that "[s]uitable surfactants include . . . polyoxyl castor oil derivatives" and "[p]referred are . . . polyethylene glycol hydrogenated castor oil. . . ."). Accordingly, claim 20 would have been obvious to a POSA, because PEG and PEG hydrogenated castor oil is a preferred combination of crystallization inhibitors taught in Etchegaray. (Exh. 1015, ¶ 139)

Furthermore, Etchegaray teaches that "[t]he film-forming agent and the surfactant may in particular be incorporated in similar or identical amounts," (Exh. 1007, col. 5, ll. 50–51), and provides exemplified formulations that include 5% polyvinylpyrrolidone and 5% polysorbate 80 by weight (Exh. 1007, col. 6–7, Table). It would have been obvious to a POSA to substitute polyvinylpyrrolidone with PEG, both exemplary film-forming agents in Etchegaray, and polysorbate 80 with PEG hydrogenated castor oil, both exemplary nonionic surfactant in Etchegaray, to arrive at the formulation of claim 21. (Exh.1015, ¶ 140–41.)

The following claim chart summarizes the relevant teachings of Etchegaray.

[5] U.S. Patent Publication No. 2007/0265171, published on November 15, 2007, is prior art under pre-AIA 35 U.S.C. § 102 (b).

| Claims | Disclosure of Etchegaray |
|---|---|
| Claim 20: The formulation of claim 19, wherein the at least one crystallization inhibitor is a polyethylene glycol and polyethylene glycol hydrogenated castor oil. | Etchegaray teaches that "the combination of a film-forming agent of polymer type and a surfactant" is preferred (Exh. 1007, col. 5, ll. 35–37), and that the surfactant is preferably a nonionic surfactant (Exh. 1007, col. 5, ll. 45–46).<br><br>Etchegaray provides a list of the film-forming agents of polymer type including PEG (Exh. 1007, col. 5, ll. 2–3), and a list of the nonionic surfactants including polyoxyethylenated derivatives of castor oil (Exh. 1007, col. 5, l. 28). |
| Claim 21: The formulation of claim 20, wherein the amount of polyethylene glycol is about 5% by weight of the formulation and the amount of polyethylene glycol hydrogenated castor oil is about 5% by weight of the formulation. | Etchegaray teaches that crystallization inhibitor can be present in a proportion of from 1 to 20% by weight, preferably from 5 to 15% (Exh. 1007, col. 2, ll. 65–67.)<br><br>Etchegaray teaches specific formulations (Ex. 1–12) containing 5% polyvinylpyrrolidone and 5% polysorbate 80 by weight. (Exh. 1007, col. 6–7, Table.) |

### E. Ground 5: Claims 4–6 are rendered obvious by Etchegaray in view of Maddison, Jeannin or Young

As previously explained, Etchegaray, Maddison, Jeannin, and Young are all § 102(b) prior art. Claims 5 and 6 both depend from claim 4, which in turn depends from independent claim 1. Claim 4 requires the formulation to contain an IGR. Claims 5 and 6 additionally require that the IGR is S-methoprene in the amount of about 5%–25% w/w.

As discussed above, Etchegaray teaches all of the elements of claim 1. Although Etchegaray does not disclose a formulation combining fipronil and an

IGR, a POSA would have known to combine an IGR such as methoprene with fipronil to improve efficacy of parasiticide formulations.

Specifically, Maddison shows that it was in the common knowledge of those in the field to prepare spot-on pesticide products for pets containing a variety of active ingredients, including a combination of fipronil and S-methoprene. (Exh. 1034, pp. 185, 187, and 190; Exh. 1015, ¶ 143) Likewise, Jeannin expressly describes an insecticidal combination to control mammal fleas, in particular on cats and dogs, which includes fipronil with an IGR, preferably methoprene. (Exh. 1029, col. 1, l. 63–col. 2, l. 54; col. 3, ll. 41–44 and 50–60; and col. 6, ll. 8–9; Exh. 1015, ¶ 144.) Jeannin further teaches that methoprene can be present in a proportion of from 1 to 20% (w/v) (Exh. 1029, col. 9, ll. 32–36), which significantly overlaps with the claimed range of between 5%–25% by weight.

Young relates to the development of parasiticidal formulations, and demonstrates the efficacy of a formulation combining fipronil with S-methoprene in an amount that falls between 5%–25% by weight (*i.e.* 9% w/v). (Exh. 1033; Exh. 1015, ¶ 145–46.) Additionally, Young provides that:

> With the addition of (S)-methoprene to fipronil, the resulting combination spot-on now provides a single product to (1) break the cat flea life cycle under field conditions in spite of the lack of compliance to regular/monthly applications, (2) reinforce the efficacy of fipronil against adult fleas, and (3) provide long-term stewardship

of the fipronil molecule since the combination of two different modes of action is will delay the development of flea resistant strains to fipronil. (Exh. 1033, p. 407.)

Accordingly, Maddison, Jeannin or Young would have provided both the motivation and a basis for a reasonable expectation success for a POSA to modify Etchegaray to arrive at the formulations of claims 4–6. (Exh. 1015, ¶ 142–50.) The following claim chart summarizes the relevant teachings of Jeannin and Young.

| **Claims** | **Jeannin** | **Young** |
|---|---|---|
| Claim 4: The formulation of claim 1, which further comprises an insect growth regulator (IGR). | Jeannin describes an insecticidal combination to control mammal fleas, in particular fleas on cats and dogs, which includes fipronil with an IGR. (Exh. 1029, col. 1, l. 63–col. 2, l. 54; col. 3, ll. 41–44.) | Young teaches parasiticidal formulations combining fipronil with the IGR s-methoprene. (Exh. 1033, p. 397, Abstract.) |
| Claim 5: The formulation of claim 4, wherein the IGR is S-methoprene. | Jeannin teaches that IGR is preferably methoprene.[6] (Exh. 1029, col. 6, ll. 8–9.) | Young teaches a parasiticidal formulation containing fipronil and (S)-methoprene. (Exh. 1033, p. 397, Abstract.) |
| Claim 6: The formulation of claim 5 wherein the amount of S-methoprene is from about 5%–25% by weight of the | Jeannin teaches that methoprene can be present in a proportion of from 1 to 20% (w/v). (Exh. 1029, col. 9, ll. 32–36.) | Young teaches a parasiticidal formulation containing "the combination spot-on of 10% (w/v) fipronil and 9% (w/v) (S)-methoprene." (Exh. 1033, |

[6] "Methoprene" inherently includes S-methoprene. (Exh. 1015, ¶ 76, n. 11.)

| | | |
|---|---|---|
| formulation. | | p. 397, Abstract.) |

### F. Ground 6: Claims 1–3, 9 and 18–19 are anticipated by Pan

Pan was published on February 27, 2008, more than one year before March 18, 2009, the earliest possible effective filing date of the ’038 patent. Thus, Pan is prior art under pre-AIA 35 U.S.C. § 102(b). Pan was not before the examiner during prosecution of the ’038 patent.

#### 1. Claim 1 is anticipated by Pan

Pan teaches “a pharmaceutical composition containing fipronil as well as its application in preparing a medicament for killing auricular mites in animals.” (Exh. 1030, p. 2, Abstract.) The claim chart below shows a limitation-by-limitation comparison between claim 1 of the ’038 patent and the disclosure of Pan.

In Embodiment 4 of Pan, the components of the formulation are described by either weight per volume (g/100 ml), or volume per volume (ml/100 ml). In order to obtain the equivalent w/w percentage for the components, Pan’s Embodiment 4 was replicated and determined to inherently contain 9.50% w/w fipronil, 3.74% w/w ethanol, and the non-ethanol organic solvent N, N-dimethyl formamide. (Exh. 1015, ¶ 71–74; Exh. 1017, ¶ 38–46, App. H.) Thus, Pan’s Embodiment 4 meets every limitation of claim 1.

| **Claim 1** | **Pan: Embodiment 4 (Exh. 1030, p. 14)** |
|---|---|
| A parasiticidal formulation comprising: | Pan teaches that Embodiment 4 is a parasiticidal pharmaceutical composition. |

| | |
|---|---|
| from about 8 to about 12 % by weight Fipronil, or a veterinarily acceptable derivative thereof; | "Measure 10 g of fipronil" in a 100 ml formulation (Exh. 1030, p. 14), which equals 9.50% w/w fipronil. (Exh. 1017, ¶ 46, App. H.) |
| less than about 5% by weight of the formulation of ethanol; and | "then add 5 ml of ethanol" in the 100 ml formulation (Exh. 1030, p. 14), which equals 3.74% w/w ethanol. (Exh. 1017, ¶ 46, App. H) |
| at least one organic solvent which is not ethanol. | "35 ml of N, N-dimethyl formamide" (Exh. 1030, p. 14) |

### 2. Claims 2–3, 9 and 18–19 are anticipated by Pan

In addition to independent claim 1, Pan also anticipates dependent claims 2–3, 9 and 18–19 as shown in the claim chart below.

| **Claims** | **Disclosure of Pan** |
|---|---|
| Claim 2: The formulation of claim 1, further comprising one or more crystallization inhibitor.[7] | Pan teaches that "other assisting agents may be added into the preparation, such as . . . stabilizer," (Exh. 1030, p. 9), which can be "selected from the group consisting of hydrogenated castor oil, *polyethylene glycol,* aluminum stearate and pyrrolidone." (Exh. 1030, p. 11 (emphasis added).) |
| Claim 3: The formulation of claim 1, wherein the Fipronil or a veterinarily acceptable derivative thereof is Fipronil. | Embodiment 4 contains fipronil. (Exh. 1030, p. 14.) |

[7] The '038 patent teaches that crystallization inhibitors include vinylpyrrolidone, polyvinylpyrrolidone, polyethylene glycols, polyoxyethylenated hydrogenated castor oil (e.g. PEG-60 hydrogenated castor oil), etc. (Exh. 1002, col. 3, ll. 9–16.)

| Claims | Disclosure of Pan |
|---|---|
| Claim 9: The formulation of claim 1 further comprising at least one antioxidant. | Embodiment 4 contains vitamin K, an antioxidant. (Exh. 1030, p. 14.)[8] |
| Claim 18: The formulation of claim 2, wherein the one or more crystallization inhibitors is selected from the group consisting of *polyethylene glycols*, polyethylene glycol hydrogenated castor oil, polyvinylpyrrolidone, polyvinyl alcohols, copolymers of vinyl acetate, invylpyrrolidone [sic], benzyl alcohol, mannitol, glycerol, sorbitol, polyoxyethylenated soribtan esters, ployoxyethylenated [sic] hydrogenated castor oil, lecithin, sodium carboxymethylcellulose, methacrylates and combinations thereof. | Pan teaches that "other assisting agents may be added into the preparation, such as . . . stabilizer," (Exh. 1030, p. 9), which can be "selected from the group consisting of hydrogenated castor oil, *polyethylene glycol,* aluminum stearate and pyrrolidone." (Exh. 1030, p. 11 (emphasis added).) |
| Claim 19: The formulation of claim 18 wherein the at least one crystallization inhibitor is *polyethylene glycols,* polyethylene glycol hydrogenated castor oil, or combinations thereof. | Pan teaches that "other assisting agents may be added into the preparation, such as . . . stabilizer," (Exh. 1030, p. 9), which can be "selected from the group consisting of hydrogenated castor oil, polyethylene glycol, aluminum stearate and pyrrolidone." (*Id.*, p. 11.) |

## VII. The Prior Art References and Grounds of Challenge Are Not Redundant

The Petition cites to three primary references, namely, Freehauf, Etchegaray and Pan, and challenges claims 1–21 of the '038 patent on six grounds. These

[8] Pan teaches that antioxidant can be selected from "ascorbic acid, vitamin K, dithioglycerol, dithiooxamide and thiourea." (Exh. 1030, p. 11.)

prior art references and grounds of challenges are not redundant of each other for the following reasons.

Claim 1 is the only independent claim of the ’038 patent. As stated above, during prosecution, the limitation that the claimed parasiticidal formulation has “less than about 5% by weight of the formulation of ethanol” was relied on for patentability. Freehauf discloses a specific parasiticidal formulation that contains *zero* ethanol and satisfies all other limitations of claim 1. Freehauf is not redundant at least because it serves as the only novelty defeating reference for claims 4–5, which depend from claim 1 and include additional limitations related to an “insect growth regulator.”

Etchegaray is not redundant with Freehauf. First, Etchegaray discloses a specific formulation (Example 14) that contains 5.77% w/w ethanol, which falls within the claimed range of “less than *about* 5%.” Petitioner submits that the broadest reasonable interpretation of the term “less than about 5%” includes zero. With this construction, Freehauf anticipates claims 1, 3–5 and 7–17. Should the Board construe the term to exclude 0% and conclude that Freehauf does not teach this limitation, however, Example 14 of Etchegaray would, by containing 5.77% w/w ethanol. Etchegaray is not redundant with Freehauf also because it teaches the additional elements of claims 2 and 18–21, which are not challenged based on Freehauf here.

Ground 3 (anticipation) and Ground 4 (obviousness) are non-redundant, alternative grounds based on Etchegaray depending on the claim construction adopted by the Board. Petitioner submits that the broadest reasonable interpretation of the term "less than about 5%" includes at least 5.9% as the upper limit. Accordingly, Etchegaray anticipates claims 1–3 and 7–19 of the '038 patent. However, should the Board construe the term to mean less than exactly 5%, instead of anticipating, Etchegaray would still render claims 1–3 and 7–19 obvious to a POSA. Additionally, claims 20–21 are only challenged in Ground 4 of this Petition.

Pan is not redundant with either Freehauf or Etchegaray because Pan discloses a specific formulation (Embodiment 4) that contains 3.8% w/w ethanol, which defeats any alleged novelty of claim 1 under any reasonable construction of the term "less than about 5%." Pan also does not render Freehauf or Etchegaray redundant because in this Petition, a number of dependent claims (*i.e.*, claims 4–8, 10–17 and 20–21) are challenged based on Freehauf and/or Etchegaray, but not on Pan.

Accordingly, Petitioner respectfully requests the Board to consider all cited references and institute *Inter Partes* Review on all six grounds.

## VIII. Conclusion

As explained in the foregoing and the accompanying declarations, claims 1–21 of the '038 patent are anticipated and/or rendered obvious by the prior art cited herein. Petitioner has established a reasonable likelihood of prevailing on each of the asserted grounds for unpatentability, and resolution of this Petition in Petitioner's favor is respectfully requested.

The Patent Office is authorized to charge the $25,600 Petition Fee (request fee: $9,200 (one claim over 20) and post-institution fee: $16,400 (6 claims over 15)), along with any deficiencies in fees related to this Petition, to Deposit Account 50-1432, ref: 078907-695092.

Respectfully Submitted,

Date: June 10, 2016

/s/ J. Patrick Elsevier, Ph.D.

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## Certificate of Compliance

I, the undersigned, certify that the above Petition complies with the applicable type-volume limitations of 37 C.F.R. **§** 42.24 (a)(i). Exclusive of the portions exempted by 37 C.F.R. **§** 42.24(a), this Petition, including footnotes, contain 13,999 words, as counted by the word count function of Microsoft Word. This is less than the limit of 14,000 words as specified by 37 C.F.R. § 42.24(a)(i).

Date: June 10, 2016

/s/ J. Patrick Elsevier, Ph.D.

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## Certificate of Service

Pursuant to 37 C.F.R. §§ 42.6(e)(4) and 42.205(b), the undersigned certifies that a copy of the foregoing Petition for *Inter Partes* Review of U.S. Patent No. 8,829,038 and all supporting exhibits were served on the patent owner on June 10, 2016, at the correspondence address of record via overnight delivery to the counsels of record for the patent owner at the following address:

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