

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERIAL LIMITED,
Petitioner,

v.

VIRBAC,
Patent Owner.

Case IPR2014-01279
Patent 8,501,799 B2

Before FRED E. McKELVEY, JAMES T. MOORE, and LINDA M. GAUDETTE,
Administrative Patent Judges.

McKELVEY, *Administrative Patent Judge.*

DECISION
Rehearing Granted—Institution of Inter Partes Review
37 C.F.R. § 42.108

I. INTRODUCTION

Petitioner filed an original Petition (Paper 1), and thereafter a Revised Petition (Paper 8), seeking entry of an order instituting an *inter partes* review of claims 1–15 (all the claims) of U.S. Patent No. 8,501,799 B2 (“the ’799 patent”, Ex. 1001). 35 U.S.C. §§ 311–319; 37 C.F.R. § 42.104.

On 22 January 2015, an order was entered declining to institute an *inter partes* review. Paper 13.

The order declined to institute an *inter partes* review as to all three grounds urged by Petitioner.

Petitioner timely filed a Request for Rehearing (“Pet. Reh’g”). Paper 14.

On 20 February 2015, the Board invited Patent Owner to file a Response to the Request for Rehearing. Paper 16.

Patent Owner timely filed a Response (“Resp.”). Paper 17.

Petitioner seeks rehearing only as to Ground 1 and Ground 2, both of which rely on Huet ’333.

In the Petition for Rehearing, Petitioner maintains that we misapprehended or overlooked the disclosure in Huet ’333 describing the use of a cosolvent as being optional, i.e., not required. Pet. Reh’g. 4.

We agree with Petitioner that we overlooked the significance of that portion of Huet ’333 indicating that use of a cosolvent is optional.

Upon consideration of the Petition for Rehearing¹ and the Response, we grant the Petition for Rehearing and order institution of an *inter partes* review.

¹ Familiarity with the Revised Petition (Paper 8), Preliminary Response (Paper 10), and Order Declining to Institute (Paper 13) is assumed.

II. BACKGROUND

A. The '799 Patent

The '799 patent relates to antiparasitic pharmaceutical compositions said to be useful for treating flea infestation on pets, particularly dogs and cats. Ex. 1001, 3:36–37, 3:55.

Independent claim 1 reads:

A liquid pharmaceutical composition, comprising:

[1] as active principle, 5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-(trifluoromethylsulfinyl)-1H-pyrazole-3 carbonitrile (fipronil),

[2] at least 5% (weight/volume) of benzyl alcohol and

[3] at least 50% (weight/volume) of an organic solvent chosen from

- [a] propylene glycol monomethyl ether,
- [b] dipropylene glycol n-butyl ether,
- [c] ethylene glycol monomethyl ether,
- [d] ethylene glycol monoethyl ether,
- [e] diethylene glycol monomethyl ether and
- [f] propylene glycol, and
- [g] mixtures thereof,

[4] it being understood that said composition is free of C₁-C₄ alcohol.

Ex. 1001, 11:16–27 (lettering, numbering in brackets, and indentation added).

The significant limitation in issue is that identified as paragraph [4] in claim 1, as reproduced above.

B. Analysis—Claim 1

One element of the Huet '333 composition is a pharmaceutically or veterinary acceptable liquid carrier vehicle, identified as element “(2).” Ex. 1005, 5:29–30.

Huet '333 teaches that the liquid carrier vehicle (2) can be a combination of a solvent and a cosolvent:

(2) The liquid carrier vehicle comprising [1] a solvent and [2] a cosolvent where

[1] the solvent is selected from the group consisting of *acetone*, *acetonitrile*, *benzyl alcohol*, *butyl diglycol*, *dimethylacetamide*, *dimethylformamide*, *dipropylene glycol n-butyl ether*, *ethanol*, *isopropanol*, *methanol*, *ethylene glycol monoethyl ether*, *ethylene glycol monomethyl ether*, *monomethylacetamide*, *dipropylene glycol monomethyl ether*, *liquid polyoxyethylene glycols*, *propylene glycol*, *2-pyrrolidone*, in particular *N-methylpyrrolidone*, *diethylene glycol monoethyl ether*, *ethylene glycol*, *diethyl phthalate fatty acid esters*, such as the *diethyl ester* or *diisobutyl adipate*, and a mixture of at least two of these solvents and

[2] the cosolvent is selected from the group consisting of *absolute ethanol*, *isopropanol* or *methanol*.

Ex. 1005, 6:5–20 (indentation, matter in brackets, and emphasis added).

Huet '333 further teaches:

These formulations comprise a composition of an effective amount of compound A [including *fipronil* (col. 2:57)] and/or compound B dissolved in a pharmaceutical or veterinary acceptable carrier vehicle where a crystallization inhibitor is optionally present. Compound of (A) can advantageously be present in this formulation in a proportion of about 1 to about 20%, preferably of about 5 to about 15% (percentages as weight by volume = W/V). The liquid carrier vehicle comprises a

pharmaceutically or veterinary acceptable organic solvent and *optionally* an organic cosolvent.

The organic solvent for the liquid carrier vehicle will preferably have a dielectric constant of between about 10 and about 35, preferably between about 20 and about 30, the content of this solvent in the overall composition preferably representing the remainder to 100% of the composition. *It is well within the skill level of the practitioner to select a suitable solvent on the basis of these parameters.*

The organic cosolvent for the liquid carrier vehicle will preferably have a boiling point of less than about 100 °C., preferably of less than about 80 °C., and will have a dielectric constant of between about 10 and about 40, preferably between about 20 and about 30; this cosolvent can advantageously be present in the composition according to a weight/weight (W/W) ratio with respect to the solvent of between about 1/15 and about 1/2; the cosolvent is volatile in order to act in particular as drying promoter and is miscible with water and/or with the solvent. *Again, it is well within the skill level of the practitioner to select a suitable solvent on the basis of these parameters.*

The organic solvent for the liquid carrier includes the commonly acceptable organic solvents known in the formulation art. These solvents may be found, for example, in Remington Pharmaceutical Science, 16th Edition (1986). These solvents include, for example, *acetone*, ethyl acetate, *methanol*, *ethanol*, *isopropanol*, dimethylformamide, dichloromethane or diethylene glycol monoethyl ether (Transcutol).

Ex. 1005, 10:36–11:5 (emphasis added).

Based on (1) documents in the record, (2) information found from the internet, and (3) the HANDBOOK OF CHEMISTRY AND PHYSICS, CRC Press

(62nd ed. 1981), we believe the solvents described by Huet '333 have the dielectric constants and boiling points shown in Table 1.²

Table 1			
Solvent	Dielectric Constant ϵ	B.p. °C	Meet criteria for cosolvent
Acetone	20.7	56	Yes
Acetonitrile	37.5	82	Yes
Benzyl alcohol	12	205.3	No
Butyl diglycol		230	No
Dimethylacetamide	37.8	166	No
Dimethylformamide	36.7	152	No
Dipropylene glycol n-butyl ether		230	No
Ethanol	24.6	78.5	Yes
Isopropanol (2-hydroxy-propane)	17.9	65	Yes
Methanol	32.7	65	Yes
Ethylene glycol mono-ethyl ether (2-ethoxy-ethanol)		135	No
Ethylene glycol mono-methyl ether (2-methoxy-ethanol; Methyl Cellosolve®)		125	No
Monomethylacetamide		205	No
Dipropylene glycol mono-methyl ether		190	No
Liquid polyoxyethylene glycols ³			
Propylene glycol (1,2-propane diol)		188.2	No
2-pyrrolidone	28.18	245	No

² We invite the parties to comment on the data in Table 1, prepared from the three listed sources, in presenting any Patent Owner's merits response and any Petitioner's reply.

³ Description is too broad and generic to allow for a determination of a specific dielectric constant or boiling point.

Table 1			
Solvent	Dielectric Constant ϵ	B.p. °C	Meet criteria for cosolvent
N-methyl pyrrolidone	9.08	202	No
Diethylene glycol mono-ethyl ether ((2-ethoxyethoxy)ethanol)		196	No
Ethylene glycol	68	37.7	No
Diisobutyl adipate		183	No

Petitioner emphasizes the “optional” nature of the cosolvent, a matter we overlooked in entering our order declining to institute an *inter partes* review trial.

Huet ’333 also teaches that a crystallization inhibitor may be present:

(3) a crystallization inhibitor selected from the group consisting of an anionic surfactant, a cationic surfactant, a non-ionic surfactant, an amine salt, an amphoteric surfactant or polyvinylpyrrolidone, polyvinyl alcohols, copolymers of vinyl acetate and vinylpyrrolidone, polyethylene glycols, *benzyl alcohol*, mannitol, glycerol, sorbitol, polyoxyethylenated sorbitan esters; lecithin, sodium carboxy-methylcellulose, and acrylic derivatives, or a mixture of these crystallization inhibitors.

Ex. 1005, 6:21–30 (emphasis added).

The crystallization inhibitor may be present in a proportion of about 1 to about 20% (w/v), preferably about 5 to about 15%. Ex. 1005, 11:58–60.

Patent Owner has several responses to the Petition for Rehearing.

First, Patent Owner maintains that “[t]he abuse of discretion standard of review is the same heightened standard federal appeals courts use to review district court factual findings.” Resp. 1 (citation omitted). In the context of Article III

proceedings, however, federal appeals courts review district court findings under a clearly erroneous standard and jury findings under a substantial evidence standard. The “abuse of discretion” standard applicable to requests for rehearing of decisions not to institute is based on the Director’s rule (37 C.F.R. § 42.71(c)), and not necessarily Article III practice. *See FirstHealth of the Carolinas, Inc. v. CareFirst of Maryland, Inc.*, 479 F.3d 825, 829 (Fed. Cir. 2007) (the TTAB has discretion to interpret reasonably the meaning of “excusable neglect” in the context of its own regulations). In our view, when we recognize that we have misapprehended or overlooked a significant fact, the necessary abuse of discretion required by Rule 42.71(c) has been established.

Second, Patent Owner maintains that a mere disagreement with a Board determination is not a proper basis for a rehearing. Resp. 2. In this case, there could not have been a “mere disagreement” because in our initial order we never addressed the “optional” nature of the cosolvent.

Third, Patent Owner concedes that there is precedent to the effect that “disclosing **optional** inclusion of a particular component teaches compositions that both do and do not contain that component.” Resp. 4 (citing *Upsher-Smith Labs. v. PamLab, LLC*, 412 F.3d 1319, 1322–23 (Fed. Cir. 2005)). However, according to Patent Owner, “the *Upsher-Smith* rule is not inflexible, and its application depends on the nature and content of the prior art’s disclosure.” Resp. 4 (citing *Allergan, Inc. v. Apotex, Inc.*, 754 F.3d 952 (Fed. Cir. 2014)). Patent Owner states that:

the disclosure in the cited prior art [in *Allergan*] was “**too sparse and ambiguous for a person of ordinary skill to comprehend** [the prior art’s disclosure] as anticipating” the asserted claim [limitation].”

Resp. 5 (citation omitted).

In the case before us, we believe “optional” in Huet ’333 means that the cosolvent may be present or it may not be present.

An analysis of Huet ’333 confirms why.

It is true that in column 6, Huet ’333 characterizes the “liquid carrier vehicle” as comprising [1] a solvent and [2] a cosolvent. Ex. 1005, 6:5–6, 6:18–20. However, in subsequently describing its invention in broader terms, Huet ’333 explicitly states that an organic cosolvent is optional: “optionally an organic cosolvent.” Ex. 1005, 10:45.

One reason a *cosolvent* would not be necessary is that Huet ’333 describes the *solvent* itself may include ethanol, isopropanol, and/or methanol. *Id.* at 6:10.

To the extent that the *cosolvent* is limited to ethanol, isopropanol, and methanol (*id.* at 6:19), other solvents listed as suitable solvents, and having the desired properties of the cosolvent, include acetone and acetonitrile. *Id.* at 6:7.

Acetone and acetonitrile (1) are not “alcohols” within the meaning of element [4] of claim 1 of the ’799 patent; (2) have dielectric constants within the required range of about 10 to about 40 (Ex. 1005, 10:56), with acetone having a dielectric constant with the preferred range of between about 20 and about 30 (Ex. 1005, 10:57); and (3) have boiling points of “less than about 100 °C.” (Ex. 1005, 10:54).

The solvent described by Huet ’333 includes “a mixture of at least two of these solvents.” Ex. 1005, 6:18.

One possible mixture is (1) dipropylene glycol n-butyl ether, or ethylene glycol monomethyl ether, or “in particular” ethylene glycol monoethyl ether (Ex. 1005, 6:9, 6:12–13, 6:14–16, 11:4–5), *and* (2) acetone or acetonitrile. Alternatively, a solvent mixture can include benzyl alcohol. Ex. 1005, 6:7–8.

Likewise, the crystallization inhibitor can be benzyl alcohol. Ex. 1005, 6:26, 12:13. The crystallization inhibitor generally is present in a proportion of about 1 to about 20% (w/v), preferably about 5 to about 15%, the latter being within the scope of element [2] of claim 1 as reproduced above. Ex. 1005, 11:58–60.

The composition, as described by Huet '333 appears to embrace (i.e., is generic to,) the claimed composition, as becomes manifest from the following claim chart.

Claim Chart	
Claim limitation	Description in Huet '333
A liquid pharmaceutical composition, comprising:	The invention relates to a pharmaceutically or veterinary acceptable liquid carrier vehicle. Ex. 1005, 1:23–29
as active principle, 5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-(trifluoromethylsulfinyl)-1H-pyrazole-3 carbonitrile (fipronil),	Active ingredient (A) is fipronil (Ex. 1005, 6:44–45; <i>see</i> 10:6–8, 14:4, 14:26)
at least 5% (weight/volume) of benzyl alcohol	A crystallization inhibitor may be present (Ex. 1005, 10:39–40) preferably in a proportion of about 5 to about 15% (w/v) (Ex. 1005, 11:58–60).
at least 50% (weight/volume) of an organic solvent	The active ingredient is present in an amount of preferably 5 to 15% (w/v) (Ex. 1005, 10:40–43) The crystallization inhibitor is present in a proportion preferably of 5 to 15% (w/v) (Ex. 1005, 11:58–60) The solvent makes up the remainder (Ex. 1005, 10:50). When a crystallization inhibitor is present, the minimum preferred amount of solvent is $100 - (15 + 15) = 70$ w/v; the maximum preferred amount of solvent is $100 - (5 + 5) = 90$ w/v.

chosen from [a] propylene glycol monomethyl ether, [b] dipropylene glycol n-butyl ether, [c] ethylene glycol monomethyl ether, [d] ethylene glycol monoethyl ether, [e] diethylene glycol monomethyl ether and [f] propylene glycol, and [g] mixtures thereof,	The solvent selected from the group consisting <i>inter alia</i> of [b] dipropylene glycol n-butyl ether (Ex. 1005, 6:9), [c] ethylene glycol monomethyl ether (Ex. 1005, 6:11), [d] ethylene glycol monoethyl ether (Ex. 1005, 6:10–11), and [g] mixtures thereof (Ex. 1005, 6:18),
it being understood that said composition is free of C₁-C₄ alcohol.	There is no requirement that the solvent must include any C₁-C₄ alcohol. The cosolvent, which can be absolute ethanol, isopropanol, or methanol (Ex. 1005, 6:19–20), is optional (Ex. 1005, 10:45).

We recognize in circumstances similar to those present in this case that it often is questioned why one skilled in the art would “pick and choose” particular ingredients (solvents and crystallization inhibitors in this case) where a reference describes several alternatives. There is an answer.

First, the entire disclosure of Huet ’333 is in the public domain. One skilled in the art should be free to use any combination described by Huet ’333 in proportions that Huet ’333 characterizes as being within the skill of the art. Claim 1 of the ’799 patent presumptively removes from that public domain a portion of what is described by Huet ’333. Absent some unexpected result obtained by the subgenus of claim 1 of the ’799 patent vis-à-vis the broader genus

described by Huet '333, it is likely that the subject matter of claim 1 of the '799 patent would have been obvious within the meaning of 35 U.S.C. § 103(a). Patent Owner, in responding on the merits, is free to present evidence of unexpected results.

Second, absent an unexpected result, it would be fair to say that it was the named inventors of the '799 patent who, in effect, ended up picking and choosing among the various options that happen to have been in the public domain.

Ground 1 also relies on Saito. What Saito reveals is that ethanol, isopropanol, and benzyl alcohol possibly are equivalent or interchangeable solvents. Ex. 1015 ¶ 70. Insofar as the Huet '333 solvent is concerned, Saito is consistent with Huet '333—revealing that the solvent may be *inter alia* absolute ethanol, isopropanol, or benzyl alcohol. Benzyl alcohol would not be an equivalent insofar as the Huet '333 cosolvent is concerned given its boiling point above 100 °C. See Table 1, above.

Ground 2 also relies on Sirinyan (Ex. 1017A) and Ex. 1018A (English language equivalent). Sirinyan describes spot-on compositions free of C₁–C₄ alcohols. However, nothing in Huet '333 requires the presence of a C₁–C₄ alcohol given that a cosolvent of absolute ethanol, isopropanol or methanol is “optional” and there is no requirement that the solvent comprise absolute ethanol, isopropanol or methanol albeit the solvent may comprise one or more of these three alcohols.

We prefer to let the parties further develop on the record the relevance or non-relevance of Saito and/or Sirinyan even though we believe Petitioner has shown a reasonable likelihood that claim 1 of the '799 patent is unpatentable under 35 U.S.C. § 103(a) over Huet '333 alone.

C. Other Claims

Claim 2—fipronil represents from 1% to 20% (w/v). Ex. 1005, 10:41–43 (about 1 to about 20%, preferably about 5 to about 15% (w/v)).

Claim 3—fipronil represents from 5% to 15% (w/v). *Id.*

Claim 4—benzyl alcohol represents 25% to 35% (w/v). *Id.* at 6:7–8, 10:46–48, 10:51–52 (benzyl alcohol can be one component in a mixture of solvents and one skilled in the art would have known how to select a suitable solvent, including the amounts of various individual solvents within a mixture of solvents).

Claim 5—organic solvent is diethylene glycol monoethyl ether. *Id.* at 6:15–16.

Claim 6—composition includes an excipient chosen from surfactants, thickeners, dyes, fragrances, and antioxidants. *Id.* at 12:5–8 (formulation can include an antioxidant), 13:5–9.

Claim 7—antioxidant can be butylhydroxytoluene. *Id.* at 13:7 (butylated hydroxytoluene); other antioxidants common with those of claim 7 also described at 13:6–8.

Claim 8—antioxidant represents from 0.005% to 2% (w/v). *Id.* at 12:7–8 (antioxidant present in an amount of from about 0.005 to about 1%, preferably of about 0.01 to about 0.05%).

Claim 9—composition comprises one or more additional antiparasitic active principles.⁴ *Id.* at 6:31–34 (preferred are spot-on formulations wherein both compounds of formula I (e.g., fipronil) and a macrocyclic lactone antihelmintic or antiparasitic agent are present).

⁴ We interpret the word “principles” to mean “material” or “ingredient.”

Claim 10—where additional antiparasitic active principles can be an endoparasiticide. *Id.* at 10:1 (at least one endectocidal compounds (B)).

Claim 11—method of prevention or treatment of flea infestations comprising applying a composition of claim 1 to an animal in need thereof. *Id.* at 9:15–29 (describing application for formulation).

Claim 12—method where animal is a cat or dog. *Id.* at 9:64–66 (dogs and cats).

Claim 13—method where animal is a dog and amount administered ranges from 0.3 to 6 ml. *Id.* at 13:18–21 (amount applied is on the order of about 0.3 to about 3 ml for dogs).

Claim 14—method wherein the dose of fipronil ranges from 5 to 15 mg per kg of body weight. *Id.* at 10:12–15 (the effective amount in a dose is, for the fipronil, preferably from about 1 to about 50 mg per kg of weight of animal).

III. ORDER

Upon consideration of the Revised Petition, the Preliminary Response, the Petition for Rehearing and the Response to the Petition for Rehearing, and for the reasons given above, it is

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review trial is hereby instituted on the following grounds.

Ground 1: claims 1–15 of the '799 patent as unpatentable under § 103(a) over Huet '333 and Saito.

Ground 2: claims 1–15 of the '799 patent as unpatentable under § 103(a) over Huet '333 and Sirinyan.

FURTHER ORDERED that *inter partes* review of the '799 patent is hereby instituted commencing on the date of this DECISION. 35 U.S.C. § 314(a).

FURTHER ORDERED that notice is hereby given of the institution of an *inter partes* review trial. 35 U.S.C. § 314(c); 37 C.F.R. § 42.4.

FURTHER ORDERED that the trial is limited to the grounds and claims identified above.

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