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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PHARMACOSMOS A/S,
Petitioner,

v.

LUITPOLD PHARMACEUTICALS, INC.,
Patent Owner.

Case IPR2015-01490
Patent 7,754,702 B2

Before TONI R. SCHEINER, LORA M. GREEN, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

I. INTRODUCTION

A. Background

Petitioner, Pharmacosmos A/S ("Petitioner"), filed a Petition requesting *inter partes* review of claims 1–3, 10–15, 17, 23, 25–28, 30, 34, 41–43, and 47 ("the challenged claims") of U.S. Patent No. 7,754,702 B2 ("the '702 patent"). Paper 1 ("Pet."). Patent Owner, Luitpold Pharmaceuticals, Inc. ("Patent Owner"), filed a Patent Owner Preliminary Response. Paper 7. We determined that the information presented in the Petition and the Preliminary Response demonstrated that there was a reasonable likelihood that Petitioner would prevail in challenging claims 1–3, 10–15, 23, 25, 27, 28, and 41–43 as unpatentable under 35 U.S.C. § 102(b), and claims 17, 30, and 47 as unpatentable under § 103(a). Pursuant to 35 U.S.C. § 314, the Board instituted trial on January 8, 2016, as to claims 1–3, 10–15, 17, 23, 25, 27, 28, 30, 41–43, and 47 of the '702 patent. Paper 11 ("Institution Decision"; "Dec. Inst.") and Paper 13 (Erratum) (clarifying that trial was not instituted on claim 24).

Patent Owner filed a Response (Paper 23, "PO Resp."), a Motion to Amend (Paper 24), and a Corrected Motion to Amend (Paper 29, "Mot. Amend"). Petitioner subsequently filed a Reply (Paper 33, "Reply"), and an Opposition to Patent Owner's Motion to Amend (Paper 34, "Opp. Mot. to Amend"). Patent Owner filed a Reply to the Opposition to the Motion to Amend. Paper 38. Patent Owner filed also a Motion to Exclude (Paper 44), to which Petitioner filed an Opposition (Paper 47), and Patent Owner filed a Reply (Paper 48).

An oral hearing was held on September 22, 2016. The transcript of the hearing has been entered into the record. Paper 53 ("Tr."). Subsequent

to the hearing, Patent Owner also filed a Notice of Disclaimer disclaiming claims 28 and 29 of the '702 patent. Paper 52.

We have jurisdiction under 35 U.S.C. § 6. This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. Based on the record before us, we conclude that Petitioner has demonstrated by a preponderance of the evidence that claims 1–3, 10–15, 23, 25, 27, 30, and 41–43 of the '702 patent are unpatentable. We also determine that Patent Owner has not met its burden on its Motion to Amend regarding entry of proposed substitute claims. Accordingly, Patent Owner's Motion to Amend is *denied*. Patent Owner's Motion to Exclude is *denied-in-part* and *dismissed-in-part*.

B. Related Proceedings

Neither Petitioner nor Patent Owner identify any related district court proceedings. *See*, e.g. Pet. 1 ("There are no existing judicial or administrative matters that would affect, or be affected by, a decision in this proceeding."); Paper 6 ("Patent Owner's U.S. Patent No. 7,754,702 . . . is not involved in litigation."). However, Petitioner filed petitions for *inter partes* review of related patents U.S. Patent No. 8,431,549 B2 (IPR2015-01493) and U.S. Patent No. 8,895,612 B2 (IPR2015-01495). Pet. 1.

In IPR2015-01493, we instituted *inter partes* review of claims 1–5, 9, 12–14, 16, and 19 of the '549 patent. IPR2015-01493, Paper 11. We declined to institute *inter partes* review in IPR2015-01495. IPR2015-01495, Paper 11.

C. The '702 Patent (Ex. 1001)

The '702 patent issued on July 13, 2010, with Mary Jane Helenek, Marc L. Tokars, and Richard P. Lawrence as the listed co-inventors.

Ex. 1001. The '702 patent teaches that iron dextran, used for parenteral iron therapy, "has been associated with an incidence of anaphylactoid-type reactions," which "is believed to be caused by the formation of antibodies to the dextran moiety." *Id.* at 1:47–54. The '702 patent notes that other iron formulations that do not contain dextran have a markedly lower incidence of anaphylaxis. *Id.* at 1:55–57. Thus, the '702 patent relates to "methods of treating a disease, disorder, or condition characterized by iron deficiency or dysfunctional iron metabolism through the administration of at least 0.6 grams of elemental iron via a single unit dosage of an iron carbohydrate complex to a subject that is in need of such therapy." *Id.* at 2:32–37.

As taught by the '702 patent, "the method treats anemia . . . [such as] iron deficiency anemia." *Id.* at 2:38–39. In addition, as taught by the '702 patent, the "iron carbohydrate complexes [] can be administered parenterally at relatively high single unit dosages for the therapeutic treatment of a variety of iron-associated diseases, disorders, or conditions." *Id.* at 5:24–27.

According to the '702 patent:

> Applicants have discovered that certain characteristics of iron carbohydrate complexes make them amenable to administration at dosages far higher than contemplated by current administration protocols. Preferably, iron carbohydrate complexes for use in the methods described herein are those which have one or more of the following characteristics: a nearly neutral pH (e.g., about 5 to about 7); physiological osmolarity; stable carbohydrate component; an iron core size no greater than about 9 nm; mean diameter particle size no greater than about 35 nm, preferably about 25 nm to about 30 nm; slow and competitive delivery of the complexed iron to endogenous iron binding sites; serum half-life of over about 7 hours; low toxicity; *non-immunogenic carbohydrate component*; no cross reactivity with anti-dextran antibodies; and/or *low risk of anaphylactoid/hypersensitivity reactions*.

Id. at 10:58–11:5 (emphasis added).

In some embodiments of the '702 patent, "the iron carbohydrate complex is [an] iron carboxymaltose complex, iron mannitol complex, iron polyisomaltose complex, iron polymaltose complex, iron gluconate complex, iron sorbitol complex, [] iron hydrogenated dextran complex . . . [or] an iron polyglucose sorbitol carboxymethyl ether complex." *Id.* at 3:33–39. "In some preferred embodiments, the iron carboxymaltose complex is polynuclear iron (III)-hydroxide-4(R)-(poly-(1→4)-O-α-glucopyranosyl)-oxy-2(R),3(S),5(R),6-tetrahydroxy-hexanoate", which is also known as "VIT-45." *Id.* at 3:58–61; 5:16–18. The '702 patent teaches that as the iron carboxymaltose complex does not contain dextran, it does not react with anti-dextran antibodies, and, therefore, the risk of anaphylactoid/hypersensitivity reactions is low. *Id.* at 12:12–15. Moreover, as it has a nearly neutral pH (between 5 and 7), and physiological osmolarity, it is possible to administer higher single unit doses over shorter time periods than other iron-carbohydrate complexes. *Id.* at 12:15–19.

D. Illustrative Claim

This proceeding involves claims 1–3, 10–15, 17, 23, 25, 27, 28, 30, 41–43, and 47 of the '702 patent. Claim 1 is the only independent claim, is illustrative, and is reproduced below:

> *1.* A method of treating a disease, disorder, or condition characterized by iron deficiency or dysfunctional iron metabolism resulting in reduced bioavailability of dietary iron, comprising
>
> administering to a subject in need thereof an iron carbohydrate complex in a single dosage unit of at least about 0.6 grams of elemental iron;

wherein

the iron carbohydrate complex is selected from the group consisting of an iron carboxymaltose complex, an iron mannitol complex, an iron polymaltose complex, an iron gluconate complex, and an iron sorbitol complex; and

the iron carbohydrate complex has a substantially non-immunogenic carbohydrate component and substantially no cross reactivity with anti-dextran antibodies

wherein said disease, disorder or condition is not Restless Leg Syndrome.

E. Instituted Challenges

Claims	Basis	References
1–3, 10–13, 23, 25, 27, and 41–43	§ 102(b)	Geisser[1]
28[2]	§ 102(b)	Groman[3]
17 and 47	§ 103(a)	Geisser and Groman
1, 14, 15	§ 102(b)	van Zyl-Smit[4]
30	§ 103(a)	van Zyl-Smit and Funk[5]

[1] Geisser et al. ("Geisser"), WO 2004/037865 A1, published May 6, 2004 (Ex. 1002). Note that Ex. 1003 is the English language translation of Ex. 1002, and that US Patent No. 7,612,109 B2 (Ex. 1014) is the resulting patent of the U.S. National Stage application of Ex. 1002.

[2] Petitioner's challenge of claim 28 is now moot in view of Patent Owner's disclaimer of claims 28 and 29. Paper 52.

[3] Groman et al. ("Groman"), US 2003/0232084 A1, published Dec. 18, 2003 (Ex. 1004).

[4] R. van Zyl-Smit & J. A. Halkett ("van Zyl-Smit"), *Experience with the Use of an Iron Polymaltose (Dexrin) Complex Given by Single Total Dose Infusion to Stable Chronic Haemodialysis Patients*, 92 NEPHRON 316–323 (2002) (Ex. 1006).

[5] F. Funk, G. J. Long, D. Hautot, R. Büchi, I. Christl & P. G. Weidler ("Funk"), *Physical and Chemical Characterization of Therapeutic Iron Containing Materials: A Study of Several Superparamagnetic Drug Formulations with the ß-FeOOH or Ferrihydrite Structure*, 136 HYPERFINE INTERACTIONS 73–95 (2001) (Ex. 1026).

In addition, Petitioner relies on the Declaration of Dr. Robert Linhardt (Ex. 1005). Patent Owner relies on the Corrected Declaration Dr. Adriana Manzi (Ex. 2080).[6]

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the specification of the patent in which they appear. *See* 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016) (upholding the use of the broadest reasonable interpretation standard). Under that standard, we presume that a claim term carries its "ordinary and customary meaning," which "is the meaning that the term would have to a person of ordinary skill in the art in question" at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007); *see also Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1062 (Fed. Cir. 2016) ("Under a broadest reasonable interpretation, words of the claim must be given their plain meaning, unless such meaning is inconsistent with the specification and prosecution history."). Any special definition for a claim term must be set forth in the specification with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner offers explicit constructions of several claim terms (Pet. 11–14), as does Patent Owner (PO. Resp. 5–15). We determine only the

[6] The corrected Declaration of Dr. Manzi was filed also by Petitioner as Exhibit 1053. Note that Exhibit 1053 differs from the corrected Declaration of Dr. Manzi of Exhibit 2080 at least at paragraph 43, as Exhibit 1053 has hand-written changes made to the text of the Declaration.

following claim term requires explicit construction for purposes of this Decision. *See, e.g.*, *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'") (quoting *Vivid Techs, Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

1. "substantially non-immunogenic carbohydrate component"

The challenged claims require that "the iron carbohydrate complex has a substantially non-immunogenic carbohydrate component." Petitioner argues that the broadest reasonable interpretation of "substantially non-immunogenic carbohydrate component" is a carbohydrate component resulting in a "low risk of anaphylactoid/hypersensitivity reactions." Pet. 13 (citing Ex. 1001, 11:5, 15:16–44). Petitioner asserts that this "does not necessarily mean that the iron carbohydrate complex is also substantially non-immunogenic in view of the specification, which consistently considers separately the immunogenicity of the carbohydrate and the iron complex of which it is a part." *Id.* (citing Ex. 1001, 3:17–24, 10:58–11:5).

Patent Owner responds that in the related proceeding, IPR2015-01493 (Paper 11, 7), we construed this term as "a carbohydrate component resulting in a 'low risk of anaphylactoid/hypersensitivity reactions.'" PO Resp. 6–7. Patent Owner asserts, however, that our construction does not indicate the meaning of "low risk." *Id.* at 7.

Patent Owner interprets "the term 'substantially nonimmunogenic' as requiring an incidence of adverse events lower than iron dextran." *Id.* Relying on Fishbane,[7] which was cited in the '702 patent, Patent Owner

[7] S. Fishbane ("Fishbane"), *Safety In Iron Management*, 41 AM. J. KIDNEY DIS. S18–S26 (2003) (Ex. 2012).

argues that "the term 'substantially non-immunogenic' should mean an incidence level of adverse events lower than that exhibited by iron dextran, i.e., lower than 0.6%." *Id.* at 7–8 (citing Ex. 2080 ¶ 21–22).

Petitioner argues that Patent Owner's construction of "low risk" is based on the complex as a whole, rather than just the carbohydrate component, as Fishbane related to iron dextran complexes. Reply 10. We agree with Petitioner that the language of the term "substantially non-immunogenic carbohydrate component" itself only requires an assessment of the immunogenicity of the carbohydrate component, and disagree with Patent Owner that the claims require an assessment of the immunogenicity of the iron carbohydrate complex as a whole.

In that regard, we note that the Specification of the '702 patent supports our construction that the "substantially non-immunogenic carbohydrate component" is limited to the carbohydrate component as opposed to the iron carbohydrate complex as a whole. Specifically, the Specification teaches in the background section that previously available iron dextran products suffered from a "high incidence of anaphylactoid reactions . . . believed to be caused by the formation of antibodies to the dextran moiety," while "[o]ther parenteral iron products (e.g., iron sucrose and iron gluconate) do not contain the dextran moiety, and the incidence of anaphylaxis with these products is markedly lower." Ex. 1001, 1:53–57; *see also id.* at 11:3–4 ("non-immunogenic carbohydrate component; no cross reactivity with anti-dextran antibodies"). Moreover, the language of independent claim 1 itself does not require a non-immunogenic complex, but only specifies that the "iron carbohydrate complex has a substantially non-immunogenic carbohydrate component."

Moreover, we decline to limit the term "substantially non-immunogenic carbohydrate complex" to require an incidence level of lower than 0.6%. Rather, what is supported by the claim language and the Specification is a low risk such that the incidence of adverse events of the carbohydrate complex is lower than dextran. *See, e.g.*, Tr. 53–54 (counsel for Patent Owner acknowledging that Fishbane was not incorporated by reference, and that it was only cited as a "see generally").

Patent Owner argues further that the term "substantially non-immunogenic carbohydrate component" requires administration to "a cohort large enough to reveal adverse events." PO Resp. 9–10. Patent Owner contends that "to learn whether . . . an iron carbohydrate complex has a 'substantially non-immunogenic carbohydrate component' requires administration to a sample size sufficient to reveal adverse immune effects were they to arise." *Id.* at 9. Thus, Patent Owner construes "the term 'substantially nonimmunogenic carbohydrate component' as a carbohydrate component having an 'incidence rate of anaphylactoid/hypersensitivity reactions lower than that for dextran, when administered to a cohort large enough to reveal adverse events.'" *Id.* at 10.

Petitioner contends that "there are no working examples supporting most of the carbohydrates listed in the '702 patent claims, let alone a 'large cohort.'" Reply 10–11.

We decline to construe "substantially non-immunogenic carbohydrate complex" as requiring administration to a large enough cohort to reveal adverse effects, as there is nothing in the Specification of the '702 patent that teaches or suggests that a minimum sample size in order to determine whether the iron carbohydrate complex has a substantially non-

immunogenic carbohydrate component. *See also* Tr. 56 (counsel for Patent Owner acknowledging that a required cohort size "is not discussed by the Specification").

Thus, we construe "substantially non-immunogenic carbohydrate component" as a "carbohydrate component resulting in a low risk of anaphylactoid/hypersensitivity reactions, wherein a low risk is an incidence of adverse events lower than dextran."

B. Level of Ordinary Skill in the Art

Petitioner asserts that the ordinary artisan "would hold at least a bachelor's level degree in chemistry or biochemistry with some related post-graduate experience (academic or industrial) in the area of carbohydrates and their metal complexes." Pet. 14 (citing Ex. 1005 ¶ 6).

Patent Owner disagrees with Petitioner's characterization of the level of skill in the ordinary artisan, contending that "some related post-graduate experience" may only be "a year or two or three working in an academic or industrial environment." PO Resp. 4–5 (quoting Ex. 2056, 24:8–10). Patent Owner argues that as the challenged claims are drawn to a method of treatment, the ordinary artisan would have some relevant academic or industry experience in the production or administration of biologics. *Id.* at 5 (citing Ex. 2080 ¶ 17).

We do not find a significant different between the requirements for the ordinary artisan proposed by Petitioner and Patent Owner. We agree with Petitioner (Pet. 14) that the best evidence of the level of skill in the art are the references themselves, *see Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001), and, thus, we need not explicitly adopt either Petitioner's or Patent Owner's characterization of the level of skill in the art.

Moreover, we note that the result of the analysis regarding the patentability of the claims would be the same under the requirements for the ordinary artisan proposed by either Petitioner or Patent Owner.

C. Patentability

1. Principles of Law

To prevail on its challenges to the patentability of claims, Petitioner must prove unpatentability by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). That is, in an *inter partes* review, the burden of persuasion is on the petitioner to prove unpatentability, and that burden never shifts to the patent owner. *See* 35 U.S.C. § 316(e); *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015).

a. Anticipation

In order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. *In re Schreiber,* 128 F.3d 1473, 1477 (Fed. Cir. 1997). We must analyze prior art references as a skilled artisan would. *See Scripps Clinic & Res. Found. v. Genentech, Inc.,* 927 F.2d 1565, 1576 (Fed. Cir. 1991), *overruled on other grounds by Abbott Labs. v. Sandoz, Inc.,* 566 F.3d 1282 (Fed. Cir. 2009) (stating that to anticipate, "[t]here must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention").

b. Obviousness

A claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). The level of ordinary skill in the art usually is evidenced by the references themselves. *See In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995); *In re Oelrich*, 579 F.2d 86, 91 (CCPA 1978).

Prior art references must be "considered together with the knowledge of one of ordinary skill in the pertinent art." *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994) (quoting *In re Samour*, 571 F.2d 559, 562 (CCPA 1978)). Moreover, "it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom." *In re Preda*, 401 F.2d 825, 826 (CCPA 1968). That is because an obviousness analysis "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR*, 550 U.S. at 418; *see In re Translogic Tech., Inc.*, 504 F.3d. at 1259.

2. Anticipation of Claim 1 under 35 U.S.C. § 102(b) Over Geisser

Petitioner contends that claims 1–3, 10–13, 23, 25–27, and 41–43 are unpatentable as being anticipated by Geisser. Pet. 22–39. With the exception of claim 26, we instituted trial on this basis for each of these claims. Dec. Inst. 6–11; 19.

Petitioner sets forth claim charts demonstrating where each element of the claims is taught by the reference (Pet. 26–39), and relies on the Declaration of Dr. Robert Linhardt (Ex. 1005) to support its anticipation challenge.

Patent Owner disagrees with Petitioner's assertions (PO Resp. 15–18), and relies on the Corrected Declaration of Dr. Adriana Manzi (Ex. 2080) as evidence that each limitation of the challenged claims is not taught by Geisser.

a. Geisser (Ex. 1002, Ex. 1003 (as translated))

Geisser discloses "a water-soluble iron-carbohydrate complex obtained from an aqueous iron(III)-salt solution and an aqueous solution of the product obtained by oxidizing one or several maltodextrins with an aqueous hypochlorite solution at an alkaline pH value" and "a method for the production of said complex and medicaments for the treatment and prophylaxis of iron deficiencies." Ex. 1003, Abstract.

As taught by Geisser, medications containing iron carbohydrate complexes "are suitable . . . in the prophylaxis or therapy of iron-deficiency anemia" and are "particularly suitable for parenteral use." *Id.* at 1:5–8.[8] Geisser discloses that such iron carbohydrate complexes have the advantage of "low toxicity and a reduced risk of anaphylactic shock." *Id.* at 8:9; *see also id.* at 1:27–28 (noting that the preparation "is supposed . . . to prevent the dangerous anaphylactic shocks that can be induced by dextran."). Geisser teaches also that, in view of the stability of the iron carbohydrate

[8] Unless otherwise indicated, the page numbers of the Exhibits refer to the page numbers of the exhibit itself, and not the page numbers added by the parties.

complexes, it is possible to administer medications containing the complexes as a single dose of 500 mg to 1000 mg, over the course of an hour. *Id.* at 8:16–17.

b. Analysis

Petitioner asserts that Geisser discloses all the limitations of independent claim 1. Pet. 22–27. Specifically, Petitioner contends that Geisser teaches iron carboxymaltose complexes, and their use in treating iron deficiency anemia. *Id.* at 23 (citing Ex. 1003, Abstract, 1:4–7, 2:4–9, 7:30–31). Moreover, Petitioner contends that Geisser teaches administering iron carbohydrate complexes as a single dose of 500–1000 mg of iron, and teaches that the complexes have low toxicity and a reduced danger of anaphylactic shock. *Id.* at 23 (citing Ex. 1003, 1: 26–2:1, 8:7–10, 8:14–17).

One of the specific iron carbohydrate complexes recited in claim 1 is an "iron carboxymaltose complex," which Petitioner contends is disclosed by Geisser, despite "the term 'carboxymaltose' [] not [being] used by Geisser." *Id.* at 17. Petitioner asserts that "Geisser teaches iron carboxymaltose as disclosed and claimed in the '702 patent" because "the '702 patent describes, as a preferred embodiment, the preparation of iron carboxymaltose via oxidation of maltodextrins using language that tracks (almost verbatim) that of Geisser (without referencing Geisser)." *Id.* at 17–18 (citing Ex. 1005 ¶ 10).

In his Declaration, Dr. Robert Linhardt considers "Geisser to disclose carboxymaltose, iron carboxymaltose complexes, and methods for making iron carboxymaltose complexes." Ex. 1005 ¶ 9. In the Declaration, Dr. Linhardt considers "an iron carboxymaltose complex to be a complex between carboxymaltose and iron." *Id.* ¶ 8. Dr. Linhardt further considers

"the carboxymaltose as defined in the '702 patent a maltose or maltodextrin, comprised of maltose type units, in which the aldehyde group of the reducing sugar end has been oxidized to form a carboxylic acid group." *Id.* Patent Owner's expert, Dr. Manzi, agrees with Dr. Linhardt's description of carboxymaltose. Ex. 2080 ¶ 32.

Petitioner notes further that the U.S. equivalent of Geisser, U.S. Patent No. 7,612,109 B2 (Ex. 1014), is cited along with the '702 patent "in the F.D.A. Orange Book as covering Injectafer® (a.k.a. VIT-45)." *Id.* at 17 (citing Ex. 1012). In his Declaration, Dr. Linhardt notes that "Geisser describes, in [the] working examples, the way to make and use iron carboxymaltose having the chemical name . . . as recited in claim 27" of the '702 patent. Ex. 1005 ¶ 13. The chemical species recited in claim 27 of the '702 patent is also known as "VIT-45." Ex. 1001, 5:16–18, 11:37–40.

Regarding the properties of Geisser's iron carbohydrate complexes, Petitioner asserts that "Geisser discloses that the iron carbohydrate complexes have low toxicity and reduced danger of anaphylactic shock." Pet. 23 (citing Ex. 1003, 3:26–4:1). In the Declaration, Dr. Linhardt "consider[s] the iron carboxymaltose complexes described in Geisser to be identical or nearly identical to iron carboxymaltose complex embodiments of the '702 patent, both in terms of synthetic methods and chemical properties." Ex. 1005 ¶ 10. In the Declaration, Dr. Linhardt further considers that because "anti-dextran antibodies [] specifically recognize dextran (a primarily α-1-6 linked oligomer or polymer of glucose), [he] would not expect an anti-dextran antibody to cross-react with iron carboxymaltose, in which the carbohydrate is a primarily α-1-4 linked oligomer or polymer of glucose." *Id.* at ¶ 8.

Dr. Linhardt notes further that "the iron carboxymaltose complexes described by Geisser fall within" the molecular weight ranges disclosed in the '702 patent, and that "Geisser describes a general synthetic method that is nearly identical to the method described in the '702 patent." *Id.* at ¶ 10.

Thus, for the reasons discussed in this Decision and as set forth in the Petition (Pet. 22–27), we find that Petitioner has demonstrated by a preponderance of the evidence that Geisser teaches all the limitations of claim 1, either inherently or explicitly. That is, we agree with Petitioner that Geisser teaches a method of treating a disease characterized by an iron deficiency, specifically iron deficiency anemia (Pet. 23; Ex. 1003, Abstract, 1:4–7, 2:4–7, 9:30–31). We further agree that Geisser teaches a method of administering an iron carbohydrate complex, that is, iron carboxymaltose, in a single dosage form of at least 0.6 grams of elemental iron, as Geisser teaches administering iron carbohydrate complexes as a single dose of 500–1000 mg of iron. Pet. 23 (citing Ex. 1003, 1:26–4:1, 8:7-10, 10:14–17).

In that regard, we credit the testimony of Dr. Linhardt that Geiser discloses iron carboxymaltose, and that Geisser describes a general synthetic method that is nearly identical to the method described in the '702 patent. Ex. 1005 ¶¶ 8–10, 13.

In addition, as Geisser teaches one of the iron carbohydrate complexes explicitly recited by claim 1, that is, iron carboxymaltose, it would inherently meet the limitation that the carbohydrate component is substantially non-immunogenic and would have substantially no cross-reactivity with anti-dextran antibodies. *In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990) ("Products of identical chemical composition can not have mutually exclusive properties."). The teachings of Geisser support that

finding, as Geisser specifically teaches that the complexes have low toxicity and a reduced danger of anaphylactic shock. Pet. 23 (citing Ex. 1003, 1:26–2:1, 8:7–10); *see also* Ex. 1001, 12:12–14 (noting that as "[t]he iron carboxymaltose complex (e.g., VIT-45) generally does not contain dextran and [it] does not react with dextran antibodies.").

We have considered Patent Owner's arguments in finding that Petitioner has demonstrated by a preponderance of the evidence that challenged claim 1 is anticipated by Geisser, but do not find them persuasive for the reasons discussed below.

Patent Owner contends that Petitioner has not demonstrated that Geisser teaches an iron carbohydrate complex having "a substantially non-immunogenic carbohydrate component and substantially no cross reactivity with anti-dextran antibodies" as recited in independent claim 1. PO Resp. 15–17. Patent Owner argues that "Geisser does not specifically discloses these properties" and that "Petitioner has not sufficiently demonstrated how the complexes of Geisser would have a 'substantially non-immunogenic carbohydrate component'." *Id.* at 15, 17.

We are not persuaded by Patent Owner's argument. Patent Owner does not dispute that Geisser discloses an iron carboxymaltose complex, and as we noted in our Decision instituting *inter partes* review, a disclosure of a specific iron carbohydrate complex such as iron carboxymaltose is likewise a disclosure of its inherent properties. Dec. Inst. 8. In contrast, as discussed above, Petitioner has pointed to Geisser's teachings regarding the properties of the iron carbohydrate complexes taught therein, which would necessarily include the claimed iron carboxymaltose complex. Specifically, Geisser's complexes exhibit "reduced toxicity and [] prevent[] the dangerous

anaphylactic shocks that can be induced by dextran." Ex. 1003, 1:26–28. Petitioner has also identified similarities between Geisser's process of preparing iron carboxymaltose and that which is disclosed in the '702 patent, noting that the process disclosed in the '702 patent specification for "the preparation of iron carboxymaltose via oxidation of maltodextrins [uses] language that tracks (almost verbatim) that of Geisser (without referencing Geisser)." Pet. 17–18. Petitioner also has pointed to the working examples of Geisser which disclose methods for making and using an iron carboxymaltose having the same chemical name as that which is recited in claim 27 of the '702 patent. *Id*. at 18 (citing Ex. 1005 ¶¶ 12–13). Moreover, Petitioner's expert notes that "the iron carboxymaltose complexes described by Geisser fall within" the molecular weight ranges disclosed in the '702 patent. Ex. 1005 ¶ 10. Thus, a preponderance of the evidence of record supports our finding that Geisser's iron carboxymaltose complex meets the limitation of an "iron carboxymaltose complex . . . [having] a substantially non-immunogenic carbohydrate component" as recited in challenged claim 1 of the '702 patent.

Patent Owner contends further that Petitioner "argues that the listing of Geisser in the FDA's Orange Book for Injectafer® would render it an anticipatory reference", thereby "conflating the standards for listing a patent in the Orange Book and anticipating a claim." PO Resp. 15–16. Specifically, Patent Owner asserts that "Geisser may claim a genus encompassing the iron carboxymaltose species and is thereby sufficient for listing in the Orange Book", but Petitioner has failed to identify "where Geisser's disclosure is such that the [iron carboxymaltose] species . . . would be 'at once envisaged' from [Geisser's] disclosure." *Id.* at 16.

We do not find Patent Owner's argument persuasive. First, we note that Petitioner's anticipation challenge does not rest solely on the mere listing of Geisser's US equivalent (Ex. 1014) in the Orange Book as covering the iron carboxymaltose complex Injectafer. We also note that although Patent Owner asserts "Petitioner has not met its burden of demonstrating that Geisser necessarily discloses iron carboxymaltose as claimed" (PO Resp. 16), Patent Owner does not dispute that Geisser discloses an iron carboxymaltose complex. We additionally note this line of argument does not even address the Declaration testimony by Dr. Linhardt that Geisser describes the way to make and use the iron carboxymaltose complex according to claim 27 of the '702 patent, which is also known as "VIT-45", or Injectafer®. Ex. 1005 ¶ 13. Further, as observed by Petitioner, "the claims under consideration are not directed specifically to VIT-45, but rather to the genus iron carboxymaltose." Reply 14.

Patent Owner does not make any separate arguments regarding the patentability of claims 2, 3, 10–13, 23, 25, 27, and 41–43 over Geisser. We find that Petitioner has established also that those claims are anticipated by Geisser (Pet. 27–39), and we adopt that analysis as our own.

c. Conclusion

After considering Petitioner's and Patent Owner's positions, as well as their supporting evidence, we determine that Petitioner has shown by a preponderance of the evidence that claims 1–3, 10–13, 23, 25, 27, and 41–43 are anticipated under 35 U.S.C. § 102(b) by Geisser.

3. Obviousness of claims 17 and 47 under 35 U.S.C. § 103(a) Over Geisser and Groman

Petitioner contends that claims 17, 34, and 47 are unpatentable as being obvious over Geisser and Groman. Pet. 44–50. We instituted trial on this basis for claims 17 and 47 only. Dec. Inst. 13–16.

Petitioner sets forth claim charts demonstrating where each element of claims 17 and 47 is taught by the references (Pet. 46–47, 50), and relies on the Declaration of Dr. Robert Linhardt (Ex. 1005) to support its obviousness challenge.

Patent Owner disagrees with Petitioner's assertions (PO Resp. 22–29), and relies on the Corrected Declaration of Dr. Adriana Manzi (Ex. 2080) to support its arguments.

a. Groman (Ex. 1004)

Groman is drawn to a method of administering a composition containing "an iron oxide complex with a polyol, [such as] for example dextran". Ex. 1004 ¶ 8. Such compositions "can serve as an iron supplement for patients suffering from anemia." *Id.* ¶ 82.

As taught by Groman:

> An embodiment of the invention provides a reduced polysaccharide iron oxide complex, wherein the reduced polysaccharide is derivatized, for example, the reduced derivatized polysaccharide is a carboxyalkyl polysaccharide. The carboxyalkyl is selected from the group consisting of carboxymethyl, carboxyethyl and carboxypropyl. Further, the reduced polysaccharide can be a reduced dextran, for example, the reduced dextran can be a reduced carboxymethyl dextran.

Id. ¶ 31.

Groman teaches that "[i]n a more particular embodiment, the reduced derivatized polysaccharide is an ether polysaccharide, more particularly a

carboxyalkylether polysaccharide selected from the group consisting of carboxymethylether, carboxyethylether, and carboxypropylether polysaccharide." *Id*. ¶ 38.

Groman teaches:

> Other embodiments in accordance with the present invention include an improved pharmacological composition of the type employing an iron oxide complex with a polyol or polyether, wherein the improvement comprises a polyol or polyether iron oxide complex composition prepared at concentrations of between about 1 mg/kg of body weight to about 4 mg/kg of body weight in a total volume of biocompatible liquid from about 1 mL to about 15 mL and for a total single dose from about 50 mg to about 600 mg, wherein the pharmacological composition is capable of being parenterally administered to a subject at a rate substantially greater than 1 mL/min, or alternatively at a rate of about 1 mL/sec, and wherein the iron oxide complex provides upon administration minimal detectable free iron in the subject and minimal incidence of anaphylaxis.

Id. ¶ 16.

b. Analysis

Claim 17 depends from claim 1 and requires that "the single dosage unit of elemental iron is administered in about 15 minutes or less." Petitioner asserts that Geisser anticipates claim 1, and that Groman teaches certain iron carbohydrate complexes "in a time interval that includes about 15 minutes or less." Pet. 45, 47 (citing Ex. 1004 ¶ 16). Petitioner contends that "[a]lthough Geisser does not explicitly disclose administration of the iron carboxymaltose complex in 15 minutes or less, [the ordinary artisan] would have combined the teachings of Geisser with Groman rendering it obvious to administer the iron carbohydrate complexes of Geisser at the administration rates disclosed in Groman." *Id.* at 45–46 (citing Ex. 1005 ¶ 22). Petitioner contends that "[t]he carboxymethylated [reduced] dextran

disclosed in Groman is structurally analogous to the carboxymaltose disclosed in Geisser, and used for essentially the same purpose." *Id.* at 46 (citing Ex. 1005 ¶¶ 20–22). Petitioner contends further that "[t]he carboxy groups of both carboxymethylated reduced dextran according to Groman and carboxymaltose according to Geisser would be expected to form tight, stable complexes with iron" and that administration of either such complex "would be unlikely to produce undesirable toxic effects." *Id.* Petitioner further contends that in view of these similarities, "it would have been obvious that the iron carboxymaltose complexes of Geisser could also be administered at rates disclosed in Groman." *Id.*

Claim 47 depends from claim 42 and requires that "the iron carbohydrate complex is intravenously injected as a bolus." Petitioner asserts that "Geisser anticipates [c]laim 42" and that "Groman discloses injecting the iron-polyglucose sorbitol carboxymethyl ether complexes as a bolus." Pet. 49 (citing Ex. 1004 ¶¶ 27, 28, 51, 52, 167, 169). Petitioner contends that in view of the "structural similarities" and "alleged improved safety of the compounds of both Geisser and Groman, it would have been obvious to one of ordinary skill in the art that the iron carboxymaltose complex of Geisser could be administered as a bolus." Pet. 49–50.

Patent Owner disagrees with Petitioner's assertions, and relies on the Corrected Declaration of Dr. Adriana Manzi (Ex. 2080) as evidence that the challenged claims are not obvious. PO Resp. 22–29. Patent Owner contends that "Geisser does not disclose that the iron carbohydrate complex can be administered at a rate of 'about 15 minutes or less' as required by claim 17," "[r]ather, Geisser discloses that the 'single dose . . . can be applied over the course of 1 hour.'" *Id.* at 27. Moreover, Patent Owner

contends that "Groman and Geisser relate to different iron carbohydrate complexes" (*id.* at 23), and "Petitioner's 'structurally analogous' arguments. . . are not based on any evidence or scientific basis" (*id.* at 25). According to Patent Owner,

> The carbohydrate component of Groman is different from the carbohydrate component of Geisser. As acknowledged by the Petitioner, Geisser's carbohydrates are derived from maltodextrin, which has **α-1-4** linkages between glucose monomers. Petition, p. 25; Ex. 1005, ¶ 8; Ex. 2080, ¶ 50. In contrast, the carbohydrates in Groman are derived from dextran, which has **α-1-6** linkages between glucose monomers.

Id. at 23–24.

Patent Owner notes further that in a separate proceeding (IPR2015-01495) challenging U.S. Patent No. 8,895,612, this tribunal "agreed with Patent Owner's position regarding the lack of motivation to combine Geisser and Groman." *Id.* at 23 n.1.

Petitioner responds by pointing to the Neiser[9] article published in 2015, which, according to Petitioner, "discloses that ferric carboxymaltose and ferumoxytol have equivalent iron binding properties" despite their differences in structure. Reply 17–18. Thus, according to Petitioner, "the compounds of Geisser and Groman are structurally analogous[,] and [a skilled artisan] would have believed them to be so on the effective filing date of the '702 patent," and "would have reasonably expected that the use of iron carboxymethyl dextran according to Groman could inform the use of iron carboxymaltose according to Geisser." *Id.* at 18. Petitioner responds

[9] Neiser et al. ("Neiser"), *Physico-Chemical Properties of the New Generation IV Iron Preparations Ferumoxytol, Iron Isomaltoside 1000 and Ferric Carboxymaltose*, BIOMETALS 1–21 (2015) (Ex. 1035).

further that the Board's non-institution of trial in IPR2015-01495 is distinguishable from the current proceeding. *Id.* at 19. Specifically, in IPR2015-01495, "Groman was applied by Petitioner as a primary reference that inherently disclosed administration of a rate of 15 minutes or less", whereas in the current proceeding, "inherency is not invoked, but rather the rate [of elemental iron administration] is properly deemed obvious over Groman." *Id.*

After considering the parties' respective positions and evidence, we do not find Petitioner's contentions persuasive. Specifically, although Geisser does teach that a high application speed is made possible by its invention (Ex. 1003, 1:30–2:1), Geisser teaches also that, in view of the stability of the iron carbohydrate complexes, it is possible to administer medications containing the complexes as a single dose of 500 mg to 1000 mg, over the course of an hour. *Id.* Petitioner has not provided sufficiently persuasive evidence as to why, in view of that teaching of Geisser, it would have been obvious for one of ordinary skill in the art to choose, from all the variables disclosed in Groman, those parameters that would result in administering at least about 0.6 grams of elemental iron in less than fifteen minutes, much less administering the elemental iron as a single bolus. Moreover, Petitioner does not explain sufficiently why the ordinary artisan would have used the rate of Groman, when Geisser specifically teaches that its compounds are administered over one hour. *See* Ex. 1003, 8:16–17.

c. Conclusion

After considering Petitioner's and Patent Owner's positions, as well as their supporting evidence, we determine that Petitioner has not shown by a

preponderance of the evidence that claims 17 and 47 are rendered obvious by the combination of Geisser and Groman.

4. Anticipation of claims 1, 14, and 15 under 35 U.S.C. § 102(b) Over van Zyl-Smit

Petitioner contends that claims 14 and 15 are unpatentable as being anticipated by van Zyl-Smit. Pet. 50–54. We instituted trial on this basis for each of these claims, as well as for claim 1, from which claims 14 and 15 depend. Dec. Inst. 16–17.

Petitioner sets forth claim charts demonstrating where each element of the claims is taught by the reference (Pet. 52–54), and relies on the Declaration of Dr. Robert Linhardt (Ex. 1005) to support its anticipation challenge.

Patent Owner disagrees with Petitioner's assertions (PO Resp. 29–35), and relies on the Corrected Declaration of Dr. Adriana Manzi (Ex. 2080) as evidence that each limitation of the challenged claims is not taught by van Zyl-Smit.

a. van Zyl-Smit (Ex. 1006)

van Zyl-Smit discloses the administration of an iron polymaltose complex for the treatment of iron deficiency anemia. Ex. 1006, Abstract. The iron complex was administered at a total dose infusion (TDI) of 900–3,200 mg of iron, which was diluted in 500 ml of normal saline, and infused over a four hour period during a dialysis session. *Id.* at 317.

van Zyl Smit reported:

> No anaphylactoid and no delayed reactions such as pyrexia, arthralgia, or myalgia were seen. Hypotensive episodes were more difficult to assess as these occur frequently during the course of normal haemodialysis. At no stage did the clinicians responsible for the care of these patients feel that any of these

> episodes were related to the iron infusions, none of the infusions had to be stopped and no thrombophlebitis occurred.

Id. at 321.

According to van Zyl-Smit:

> Anti-dextran antibodies are largely responsible for the high prevalence of side effects, including anaphylaxis, to dextran containing compounds. With compounds such as iron sucrose and iron gluconate, side effects seem to be mostly related to the rate of iron release. It has therefore been suggested that for patients on haemodialysis, maximum single doses of these compounds should be limited to about 300 and 125 mg respectively. The iron polymaltose (dextrin) preparation (Ferrimed) used in this study releases iron more slowly and allows the use of TDI. In this respect it is similar to the dextran containing compounds which also have minimal free iron related side effects with high doses used with TDI.

Id. at 322 (references omitted).

Thus, van Zyl-Smit teaches "TDI with iron polymaltose (dextrin) is a safe and effective way of correcting iron deficiency." *Id.* at 323.

b. Analysis

Petitioner relies on van Zyl-Smit for disclosing "administration of iron polymaltose complex, Ferrimed®, for treating iron deficiency." Pet. 51 (footnote omitted) (citing Ex. 1006, 316–317). Petitioner relies on van Zyl-Smit for disclosing also the "administration of iron polymaltose at a total dose infusion of 900-3200 mg," and for disclosing "that the administration of the complex does not result in anaphylactoid and delayed reactions such as pyrexia, arthralgia or myalgia." *Id.* at 51–52 (citing Ex. 1006, 317, 321). Thus, Petitioner contends, as van Zyl-Smit taught that the administration of the complex did not result in anaphylactoid and delayed reactions, the carbohydrate complexes are substantially non-immunogenic. *Id.* at 52

(citing Ex. 1005 ¶ 23). Moreover, Petitioner contends, as the complexes of van Zyl-Smit do not contain dextran, the ordinary artisan would expect the complexes to "inherently ha[ve] substantially no cross reactivity with anti-dextran antibodies." *Id.* (citing Ex. 1005 ¶ 23).

For the reasons set forth in the Petition (Pet. 50–54), we find Petitioner has demonstrated by a preponderance of the evidence that van Zyl-Smit teaches all the limitations of claim 1, either inherently or explicitly. We agree with Petitioner that van Zyl-Smit teaches a method of treating a disease characterized by an iron deficiency. *See* Pet. 51; Ex. 1006, 316–317). van Zyl-Smit teaches a method of administering one of the iron carbohydrate complex specifically recited by challenged claim 1, that is, iron polymaltose, in a single dosage form of at least 0.6 grams of elemental iron, as van Zyl-Smit teaches administering iron carbohydrate complexes as a single dose of 900-3200 mg of iron. *See id.*

In addition, we find that as van Zyl-Smit teaches that the administration of the complex did not result in anaphylactoid and delayed reactions (Ex. 1006, 321), the ordinary artisan would understand that the carbohydrate complexes are substantially non-immunogenic. Moreover, we agree with Petitioner that as the complexes of van Zyl-Smit do not contain dextran, the ordinary artisan would expect the complexes to inherently have substantially no cross reactivity with anti-dextran antibodies.

We have considered Patent Owner's arguments in finding that Petitioner has demonstrated that challenged claim 1 is anticipated by van Zyl-Smit, but do not find them persuasive for the reasons discussed below.

Specifically, Patent Owner contends that "van Zyl-Smit does not ever disclose the administration or testing of the carbohydrate polymaltose

separate from its complexation to iron" and "[t]hus, van Zyl-Smit does not teach a 'substantially non-immunogenic carbohydrate component' consistent with the Board's interpretation for this term." PO Resp. 29–30 (citing Ex. 2056, 79:6–10; Ex. 2080 ¶ 35). Patent Owner contends further that "Petitioner has not shown that the polymaltose *by itself* would be substantially non-immunogenic" and thus, "van Zyl-Smit does not disclose that the polymaltose (dextrin) carbohydrate component is a 'substantially non-immunogenic carbohydrate component' as this term is construed by the Board." *Id.* at 31 (citing Ex. 2080 ¶¶ 34–37).

As noted by Dr. Lindhart (Ex. 2056, 83:16–84:21), van Zyl-Smit teaches that "[a]nti-dextran antibodies are largely responsible for the high prevalence of side effects, including anaphylaxis due to dextran-containing compounds" (Ex. 1006, 322). Given that teaching, as well as the fact that van Zyl-Smit specifically teaches one of the iron complexes of claim 1 (an iron polymaltose complex), and that no anaphylactoid or delayed reactions were seen, we agree with Petitioner (Reply 21) that a preponderance of the evidence of record supports the finding that the carbohydrate component taught by van Zyl-Smit is substantially non-immunogenic and has substantially no cross-reactivity with anti-dextran antibodies. As we noted above with respect to Geisser's disclosure of iron carboxymaltose, a disclosure of a specific iron carbohydrate complex, such as iron polymaltose, is likewise a disclosure of its inherent properties, regardless of whether the immunogenicity or reactivity of a given complex should be determined on the basis of the carbohydrate component individually or the complex as a whole. It is, therefore, reasonable to conclude that that the iron

polymaltose disclosed in van Zyl Smit has a substantially non-immunogenic carbohydrate component in the same manner as the claimed species.

Patent Owner contends further that "the 62-patient sample size in van Zyl-Smit . . . is too small to conclude that the lack of adverse events in that sample is indicative of the polymaltose (dextrin) being 'substantially non-immunogenic' as required by claim 1." PO Resp. 33 (citing Ex. 2080 ¶¶ 38, 39).

As noted above in the discussion of claim construction, we decline to adopt Patent Owner's proposed construction of "substantially non-immunogenic carbohydrate complex" as requiring administration to a large enough cohort to reveal adverse effects. Again, there is nothing in the '702 patent that teaches or suggests that a minimum sample size must be evaluated in order to determine whether the iron carbohydrate complex has a substantially non-immunogenic carbohydrate component.

Patent Owner argues also that the disclosure of an iron polymaltose (dextrin) complex is not "generalizable to iron polymatose." PO Resp. 33 (emphasis removed). Specifically, Patent Owner contends that a commercial product, Ferrosig, includes warning regarding immune effects, stating that "[p]arenterally administered iron preparations can cause allergic or anaphylactoid reactions." *Id.* at 33–34 (quoting Ex. 2003, 4[10]) (citing Ex. 2080 ¶ 41). That warning, Patent Owner asserts, is "evidence that a product having the same name (Ferrosig, 'iron polymaltose') can cause immunogenic reactions." *Id.* at 34 (citing Ex. 2080 ¶ 41). The Ferrosig data sheet, however, does not support Patent Owner's position because even for

[10] The numbering referred to for Exhibit 2003 is the numbering added by Patent Owner to the Exhibit.

that other iron polymaltose formulation, the data sheet indicates only that "[a]dverse reactions to parenteral FERROSIG have only been reported *infrequently*," and that "[s]ystemic reactions after [intramuscular injection] are *rare* but may include anaphylaxis." Ex. 2003, 4 (emphasis added).

We note that the language of claim 1 requires only a "substantially non-immunogenic carbohydrate component," and there is no indication in the '702 patent that adverse reactions in all patients in all conditions must be prevented. Thus, the fact that there may still be a risk of some immunogenic reaction with certain iron polymaltose products does not exclude methods of administering those products from the scope of claim 1. Moreover, as noted by Petitioner (Pet. 51–52), van Zyl-Smit specifically teaches that administration of the complex did not result in anaphylactoid and delayed reactions (Ex. 1006, 321), and thus, we determine that a preponderance of the evidence supports Petitioner's position that van Zyl-Smit's iron polymaltose complex meets the claimed requirement of having a "substantially non-immunogenic carbohydrate component".

Claims 14 and 15 ultimately depend from claim 1 and, according to Petitioner, "modify only the amount of elemental iron provided by the single dosage unit." Pet. 51. Patent Owner does not make any separate arguments regarding the patentability of claims 14 and 15 over van Zyl-Smit. We find Petitioner's evidence and arguments persuasive as to those claims (Pet. 50–54), and we adopt that analysis as our own.

c. Conclusion

After considering Petitioner's and Patent Owner's positions, as well as their supporting evidence, we determine that Petitioner has shown by a

preponderance of the evidence that claims 1, 14, and 15 are anticipated under 35 U.S.C. § 102(b) by van Zyl-Smit.

5. Obviousness of claim 30 under 35 U.S.C. § 103(a) Over van Zyl-Smit and Funk

Petitioner contends that claim 30 is unpatentable as being obvious over van Zyl-Smit and Funk. Pet. 55–57. We instituted trial on this basis. Dec. Inst. 18.

Petitioner sets forth claim charts demonstrating where each element of claim 30 is taught by the references (Pet. 56–57), and relies on the Declaration of Dr. Robert Linhardt (Ex. 1005) to support its obviousness challenge.

Patent Owner disagrees with Petitioner's assertions (PO Resp. 35–40), and relies on the Corrected Declaration of Dr. Adriana Manzi (Ex. 2080) to support its arguments.

a. Funk (Ex. 1026)

Funk discloses that "[t]he effectiveness of therapeutically used iron compounds is related to their physical and chemical properties." Ex. 1026, Abstract. Funk looked at "a series of iron(III) oxyhydroxide complexes which are kept in solution as colloidal particles by protection with different carbohydrate coatings." *Id.* at 74. Specifically, Funk looked at the following iron compounds:

> Ferrum Hausmann® intramuscular (iron(III) hydroxide dextran complex, Dexfer®; lots 375009A1, solution sample, and 521119M, powder sample), in the following called iron dextran; Ferrum Hausmann® intramuscular (high molecular weight iron(III) hydroxide complex with polymaltose, Amylofer®; lots 545009A1, solution sample, and 612209M, powder sample), called iron dextrin; Maltofer® (low molecular weight iron(III) hydroxide complex with polymaltose; lots 654009M, drops

> solution sample, and 512219M, powder sample), called iron polymaltose; and Ferrum Hausmann® i.v. (iron(III) hydroxide sucrose complex, Venofer®; lot 630209, solution sample), called iron sucrose. Human apo-transferrin was purchased from Sigma Chemicals Co., St. Louis, MO, USA.

Id. at 74–75.

Table III of Funk provides several structural parameters of the iron compounds, and is reproduced below:

Parameter	Iron sucrose	Iron poly-maltose	Iron dextran	Iron dextrin
diameter from XRD (nm)	≈1	1.9	1.8	4.1
volume from XRD (nm^3)	0.5	3.6	3.1	36.1
blocking temperature, T_B (K)	55	65	115	215
relative volume from T_B (nm^3)	8.4	11.0	19.3	36.1
relative diameter from T_B (nm)	2.5	2.8	3.3	4.1
point of zero charge	6.9 ± 0.5	6.7 ± 0.5	7.6 ± 0.3	7.5 ± 0.7
XRD surface area ($m^2\ g^{-1}$)	1690	890	940	410
BET surface area ($m^2\ g^{-1}$)	–	0.5	1.5	1.6

Id. at 90.

Funk teaches that "larger and more crystalline particles of iron dextrin exhibit a stronger resistance to dissolution than the smaller and more disordered particles of iron dextran and especially iron polymaltose and iron sucrose." *Id.*

b. Analysis

Claim 30 depends from claim 1 and further requires that "the iron carbohydrate complex comprises an iron core with a mean iron core size of no greater than about 9 nm." Petitioner asserts that, as discussed with the anticipation challenge over van Zyl-Smit, van Zyl-Smit teaches all of the limitations of claim 1. Pet. 55. In addition, Petitioner notes that van Zyl-Smit teaches that iron carbohydrate complexes that are used as supplements

"should be stable and release iron slowly, to minimize free iron concentration in the blood." *Id.* (citing Ex. 1006, 322). Petitioner acknowledges, however, that "van Zyl-Smit does not explicitly disclose the physical characteristics of the iron polymaltose complex." *Id.*

Petitioner relies on Funk for its disclosure that "iron carbohydrate complexes have an iron core size of 1.9 nm to 4.1 nm." *Id.* (citing Ex. 1026 Abstract, 74–75, 80, and 90 (Table III)). In particular, Petitioner notes that iron dextrin, that is, iron polymaltose, demonstrated the greatest stability and the least lability. *Id.* (citing Ex. Ex. 1026, 90).

Petitioner contends, therefore, that "it would have been obvious to one of ordinary skill in the art to use the iron dextrin having a particle size of 4.1 nm disclosed in Funk for the treatment of iron deficiency as disclosed in van Zyl-Smit" in view of van Zyl-Smit's disclosure "that administration of iron polymaltose (i.e., iron dextrin) of low lability and high stability *in vivo* is desirable to achieve long-lasting iron supplementation with low toxicity and side effects." *Id.* at 55–56 (citing Ex. 1005 ¶¶ 25–27).

For the reasons set forth in the Petition (Pet. 55–57), we find that Petitioner has demonstrated by a preponderance of the evidence that the combination of van Zyl-Smit and Funk renders obvious the method of claim 30. As discussed above, we find that Petitioner has demonstrated van Zyl-Smit teaches all of the limitations of challenged claim 1, from which challenged claim 30 depends. van Zyl-Smit does not teach the size of the iron core, but as noted by Petitioner (Pet. 55), van Zyl-Smit teaches that the iron carbohydrate complexes should be stable and release iron slowly, to minimize free iron in the blood. Ex. 1006, 322.

Funk teaches that "[t]he effectiveness of therapeutically used iron compounds is related to their physical and chemical properties." Ex. 1026, Abstract. Funk looked at iron carbohydrate complexes, all of which had an iron core with a mean iron core size of no greater than about 9 nm. Ex. 1029, 90. Thus, we agree with Petitioner that the ordinary artisan would have used an iron core with a mean iron core size of no greater than about 9 nm with a reasonable expectation of success, such as the 4.1 nm for iron dextrin taught by Funk, as that iron carbohydrate complex demonstrated the greatest stability and the least lability. *Id.* In addition, the fact that all of the iron carbohydrate complexes of Funk had a mean iron core size of no greater than about 9 nm provides a further reasonable expectation of success of using that mean iron core size in the iron carbohydrate complexes specifically recited by challenged claim 1.

We have considered Patent Owner's arguments in concluding that the combination of van Zyl-Smit and Funk renders challenged claim obvious, but do not find them persuasive for the reasons discussed below.

Specifically, Patent Owner contends that "the combination of van Zyl-Smit and Funk does not teach or suggest every element of claim 30." PO Resp. 35. Specifically, Patent Owner argues that Funk's "measurements correspond to the size of the entire particle, *not the iron core*", and that "Funk does not provide any measurements for the iron core" of the four iron carbohydrates. *Id.* at 36 (citing Ex. 2080 ¶ 43). Specifically, Patent Owner asserts that Petitioner's expert, Dr. Linhardt, testified during his deposition that "all of the iron carbohydrate complexes of Funk have an iron (III) hydroxide core," and thus there is no indication that the difference in properties is due to differences in core sizes. *Id.* (citing Ex. 2056, 148:7–

20). Patent Owner further contends that Funk contains a disclosure that "shows that iron dextrin and iron polymaltose are not equivalent species." *Id.* at 37 (citing Ex. 2080 ¶ 47; 2056, 139:15–21). According to Patent Owner, "[g]iven van Zyl-Smit's use of the phrase 'iron polymaltose (dextrin), [the ordinary artisan] would have no basis to pick any particular dissolution rate from Funk and derive any teachings therefrom. *Id.* at 39 (citing Ex. 2080 ¶¶ 47, 48).

We are not persuaded by Patent Owner's arguments. As noted by Petitioner in its Reply, although Dr. Manzi stated in her original Declaration that the measurements of Funk "correspond to the size of the entire particle, and not the iron core (Ex. 2080 ¶ 43), she stated in her corrected Declaration that [i]t is unclear from Funk if these measurements correspond to the size of the entire particle or the iron core" (Ex. 1053 ¶ 43). Reply 24. Further, as noted by Petitioner (Reply 24), Dr. Manzi acknowledged that Funk's X-ray diffraction technique could be used to measure iron core size, and that a publication that references Funk, Neiser, refers to Funk as teaching iron core size. Ex. 1054, 82:16–83:4, 85:12–20, Ex. 1035, 9.[11] Thus, we agree with Petitioner that a preponderance of the evidence "favors Funk teaching iron core size." Reply 24.

We agree also with Petitioner (Reply 24) that Patent Owner's argument as to which iron polymaltose corresponds to the iron polymaltose of van Zyl-Smit is irrelevant, as all the core sizes disclosed by Funk, i.e.,1.0, 1.9, 1.8, and 4.1 nm, are less than 9 nm. In that regard, we note that the prior art need not teach an advantage over other possible alternatives in

[11] The page number of Exhibit 1035 refers to the page number added by Petitioner to the bottom of the Exhibit.

order to render the claimed combination obvious. *See, e.g.*, *In re Mouttet*, 686 F.3d 1322, 1334 (Fed. Cir. 2012) ("[J]ust because better alternatives exist in the prior art does not mean that an inferior combination is inapt for obviousness purposes.").

Patent Owner contends further that "[t]here was no motivation to combine van Zyl-Smit and Funk and the combination offers no reasonable expectation of success." PO Resp. 39 (emphasis removed). Patent Owner asserts that the teachings of Funk regarding dissolution rate and iron complex lability are related to the carbohydrate complex of the core, rather than the iron core itself. *Id.* Thus, Patent Owner asserts, "[b]ecause Funk has no particular teachings regarding iron core size, and Funk separately characterizes iron dextrin and iron polymaltose with two very different dissolution properties, [the ordinary artisan] would not have been motivated to combine the disclosure of Funk with van Zyl-Smit." *Id.* at 39–40 (citing Ex. 2080 ¶ 46).

Again, we agree with Petitioner that there is a reason "to combine Funk and van Zyl-Smit" in the manner proposed because "van Zyl-Smit raises free iron and toxicity as a concern [and] this concern is addressed by Funk." Reply 24–25. Moreover, all of the iron core sizes disclosed by Funk (Ex. 1026, 90 (Table III)) meet the limitation added by challenged claim 30 of "a mean iron core size of no greater than about 9 nm." Funk is, therefore, evidence that such core sizes are appropriate with a variety of carbohydrate complexes, and would be understood as such by the ordinary artisan. The Supreme Court has emphasized that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative

steps that a person of ordinary skill in the art would employ." *KSR,* 550 U.S. at 418. "If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. *Id.* Finally, we note that "'[o]bviousness does not require absolute predictability of success . . . *all that is required is a reasonable expectation of success.*'" *In re Kubin*, 561 F.3d 1351, 1360 (quoting *In re O'Farrell*, 853 F.2d 894, 903–904 (Fed. Cir. 1988)).

c. Conclusion

After considering Petitioner's and Patent Owner's positions, as well as their supporting evidence, we determine that Petitioner has shown by a preponderance of the evidence that claim 30 is unpatentable as obvious under 35 U.S.C. § 103(a) over the combination of van Zyl-Smit and Funk.

D. Patent Owner's Corrected Contingent Motion to Amend (Paper 29)

Patent Owner filed a Contingent Motion to Amend (Paper 24) on March 29, 2016, and a Corrected Contingent Motion to Amend (Paper 29) on April 25, 2016. In its Corrected Contingent Motion to Amend (Paper 29), Patent Owner presents a proposed set of substitute claims, stating that "[i]f issued claim 1 is found unpatentable based on Grounds 1 or 4, Luitpold requests cancelling claim 1 and replacing it with substitute claim 58," "[i]f issued claims 2, 3, 10–13, 23, 25, 27, and 41–43 are found unpatentable on Ground 1, Luitpold requests cancelling these claims and replacing them with proposed substitute claims 56–64 and 67–72," [i]f issued claims 14 and 15 are found unpatentable on Ground 4, Luitpold requests cancelling these claims and replacing them with proposed substitute claims 65 and 66," "[i]f issued claim 1 or claim 30 is found unpatentable on Ground 5, Luitpold requests cancelling these claims and replacing claim 1 with claim 58, which incorporates the limitations of claim 30." Mot. Amend 1. Patent Owner

further states that "[i]f issued claim 17 or issued claim 47 is found unpatentable on Ground 3, Luitpold requests cancelling the claim deemed unpatentable and replacing it with the corresponding substitute claim: claim 74 for claim 17 and claim 73 for claim 47." *Id.* at 1–2.[12]

1. Proposed Substitute Claims

Proposed substitute independent claim 58 is reproduced below, with underlined text indicating material inserted relative to claim 1, and brackets indicating material removed relative to that claim:

> 58. A method of treating a disease, disorder, or condition characterized by iron deficiency or dysfunctional iron metabolism resulting in reduced bioavailability of dietary iron, comprising administering to a subject in need thereof an iron carbohydrate complex in a single dosage unit of at least about 0.6 grams of elemental iron; wherein the iron carbohydrate complex is selected from the group consisting of an iron carboxymaltose complex, an iron mannitol complex, **[**an iron polymaltose complex,**]** an iron gluconate complex, and an iron sorbitol complex; and the iron carbohydrate complex has a substantially non-immunogenic carbohydrate component and substantially no cross reactivity with anti-dextran antibodies wherein said disease, disorder or condition is not Restless Leg Syndrome, and wherein the iron carbohydrate complex comprises an iron core with a mean iron core size of no greater than about 9 nm.

Mot. Amend 3–4.

As the moving party, Patent Owner bears the burden of proof to establish that it is entitled to the relief requested. 37 C.F.R. § 42.20(c). The proposed amendment is not entered automatically, but only upon Patent Owner having demonstrated the patentability of those substitute claims. A

[12] Patent Owner made a further contingent request regarding the cancellation of claim 28 on Ground 2. We do not reach this contingent request, however, in view of Patent Owner's disclaimer of claim 28 in Paper 52.

motion to amend may be denied if it "seeks to enlarge the scope of the claims of the patent or introduce new subject matter." 37 C.F.R. § 42.121. Thus, a motion to amend must set forth where support may be found for the claim as amended. *Id.*

2. Analysis

a. No Broadening of Scope

Proposed substitute claims may not enlarge the scope of the original patent claims. 35 U.S.C. § 316(d)(3); 37 C.F.R. § 42.121(a)(2)(ii). We determine that proposed substitute claim 58 further limits claim 1. Accordingly, no issue exists with regard to the prohibition against broadening original patent claims.

b. Written Description Support

Proposed claim 58 removes a member of the Markush group of iron carbohydrate complexes, and adds the limitation of original claim 30. In addition, Patent Owner points to where support for proposed amended claim 58 may be found in priority application, U.S. Application Serial No. 60/757,119, as well as the disclosure as originally filed. Mot. Amend. 10–12. Thus, we determine that proposed claim 58 does not introduce new subject matter.

c. Patentability

An *inter partes* review is neither a patent examination proceeding nor a patent reexamination proceeding. The substitute claims proposed in a motion to amend are not entered automatically and then subjected to examination. Rather, the proposed substitute claims will be added directly to the patent, without examination, *if* the patent owner's motion to amend is granted. In a motion to amend, the patent owner is not rebutting a rejection

in an office action, as though this proceeding were a patent examination or a reexamination. Instead, the patent owner, as the movant, bears the burden of establishing the patentability of the proposed substitute claims.

In its Motion to Amend, Patent Owner addresses the patentability of proposed substitute claim 58 over the prior art. Mot. Amend 12–21. In its Opposition to the Motion to Amend, Petitioner contends that the proposed substitute claims are rendered obvious by the combination of Geisser, van Wyck,[13] optionally with Groman and/or Funk. Opp. Mot. Amend 12–18.

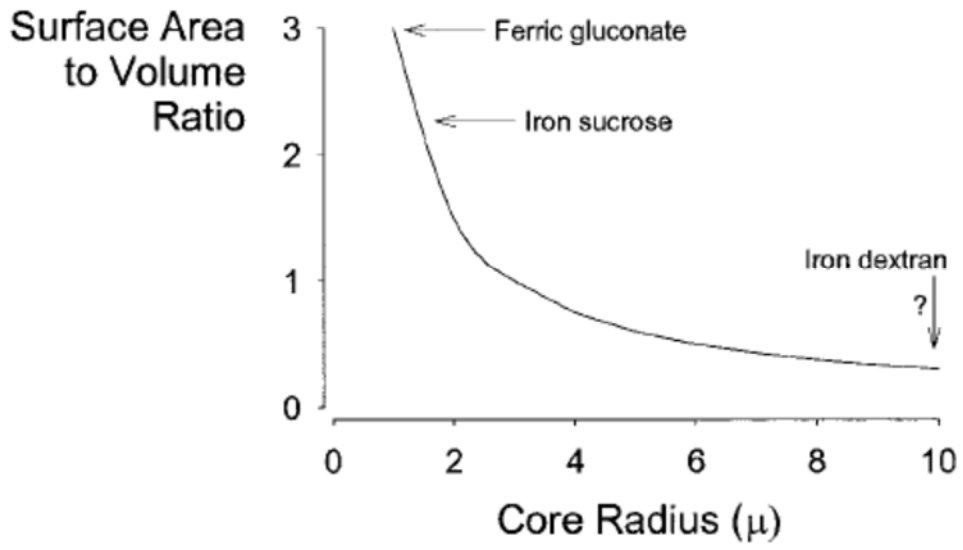
The teachings of Geisser, Groman, and Funk are discussed above. As to the use of intravenous ("IV") iron compounds, van Wyck teaches:

> No IV iron compounds generate detectable free iron. All IV iron agents release biologically available or labile iron. The rate of labile iron release in each agent is inversely related to the size of its iron core. The clinical consequences of labile iron release have little significance at low iron doses but limit the maximum tolerated single dose and rate of infusion of each IV iron agent.

Ex. 2049, 1.

van Wyck teaches further that "all agents share the same core chemistry, [thus,] the rate of iron release per unit surface area likely would be similar among agents (differing, perhaps, only by the strength of the carbohydrate ligand-core iron bond)." *Id.* at 5. Figure 1 of van Wyck is reproduced below:

[13] Note that Van Wyck, Ex. 2049, includes two related papers. David B. Van Wyck, Bo. G. Danielson, George R. Aronoff, *Making Sense: A Scientific Approach to Intravenous Iron Therapy*, 15 J. AM. SOC. NEPHROL. S91–S92 (2004); David B. van Wyck, *Labile Iron: Manifestations and Clinical Implications*, 15 J. AM. SOC. NEPHROL. S107–S111 (2004). The numbering to Exhibit 2049, therefore, refers to the numbering added by Patent Owner to the bottom of the page.



Id. at 6. Figure 1 shows the relationship between core radius and surface area to volume ratio. *Id.* According to van Wyck, "[i]f labile iron can cause a free-iron-like reaction and free-iron-like reactions are dose limiting and, if so, then the maximum tolerated dose and rate of administration would be inversely related to labile iron fraction and follow the sequence ID("iron dextran")>IS ("iron sucrose")>SFGC ("ferric gluconate")." *Id.*

Petitioner relies on Geisser as discussed above in the anticipation challenge of original claim 1 over Geisser. Opp. Mot. Amend 12. As to the added limitation that the iron carbohydrate complex comprises an iron core with a mean iron core size of no greater than about 9 nm, Petitioner asserts:

> The '702 patent sets this 9 nm threshold as a boundary defining the iron core, and provides, as its rationale, that "[g]enerally, the rate of labile iron release in each agent is inversely related to the size of its iron core," citing van Wyck, Ex. 2049. The '702 patent set forth the range of iron core sizes most broadly as 'less than about 9 nm but greater than about 1 nm, about 2 nm . . .' Ex. 1001, 14:54–59. There is no data suggesting that these boundaries were derived through Patent Owner's experimentation, and van Wyck is, appropriately, credited.

Id. at 13.

Relying on Figure 1 of van Wyck (Ex. 2049, 6), Petitioner asserts that the curve plateaus for core radii greater than 4 or 5 nm, that is, core diameters greater than 8 or 10 nm. *Id.* Petitioner asserts further van Wyck discloses that ferric gluconate and iron sucrose are associated with high levels of labile iron. *Id.* Petitioner contends, therefore, that the ordinary artisan would have chosen iron core sizes greater than 2 but less than 9 nm "with a reasonable expectation that it would have low labile iron-associated toxic effects and therefore could be used at high doses." *Id.* at 14. Petitioner asserts that the ordinary artisan would have had a reason to combine Geisser and van Wyck because Geisser teaches that high doses require increased stability and van Wyck teaches the characteristics that promote stability. *Id.* at 14.

Moreover, according to Petitioner, at the time of invention the ordinary artisan would have been aware of other iron carbohydrate complexes that had favorable "labile iron" properties wherein the iron core size was less than 9 nm. *Id.* at 15–16. Petitioner specifically refers to ferumoxytol, which was referenced by the '702 patent, as having a core size between 6.2 and 7.3 nm (citing Ex. 1001, 13:33–50; Groman '498[14]), and iron dextrin, which Funk teaches has a core size of about 4.1 nm (citing Ex. 1026, 90 (Table 1)). *Id.* at 15–16. Petitioner contends that the ordinary artisan would have understood from van Wyck that core size is relevant to labile iron release, and would have looked to iron core sizes found in the prior art, such as those taught by Groman '498 and Funk, which have low

[14] Groman et al., U.S. Patent No. 6,599,498 B1, issued July 29, 2003 (Ex. 1017) ("Groman '498).

free iron toxicity and could be used at high doses. *Id.* at 16. Petitioner contends, therefore, that the ordinary artisan would have chosen iron core sizes greater than 2 but less than 9 nm "with a reasonable expectation that it would have low labile iron-associated toxic effects and therefore could be used at high doses." *Id.* at 14.

We agree with Petitioner that Patent Owner has not demonstrated that proposed substitute claim 58 is patentable over the prior art. Specifically, we agree with Petitioner that the combination of Geisser, van Wyck, Groman and Funk renders proposed substitute claim 58 obvious.

In that regard, we note that as discussed above with the anticipation challenge, that Geisser teaches all of the limitations of proposed claim 58, except that Geisser does not teach a mean core size for its iron core. Proposed claim 58 adds the limitation that the "iron carbohydrate complex comprises an iron core with a mean core size no greater than about 9 nm."

As noted by Petitioner (Opp. Mot. Amend 13), the Specification of the '702 patent refers to van Wyck for the proposition that "[g]enerally, the rate of labile iron release in each agent is inversely related to the size of its core." Ex. 1001, 14:25–28. In addition, we agree with Petitioner ((Opp. Mot. Amend 13) that Figure 1 of Van Wyck, reproduced above, the line plateaus for core radii greater than 4 or 5 nm, that is, core diameters greater than 8 or 10 nm.

As for the reason to combine and a reasonable expectation of success, we agree with Petitioner (Opp. Mot. Amend 14) that the ordinary artisan would have had a reason to combine Geisser and van Wyck as described by Petitioner because Geisser teaches that high doses require increased stability

(Ex. 1003, 1–2, 8) and van Wyck (Ex. 2049, 1, 6) teaches the characteristics that promote stability.

Moreover, Van Wyck teaches that all agents share the same core chemistry, and, thus, the rate of iron release per unit surface area would be similar among agents (Ex. 2049, 5), and Groman '498 and Funk are evidence that core sizes less than about 9 nm are appropriate with a variety of carbohydrate complexes, and would be understood as such by the ordinary artisan. The ordinary artisan would have, therefore, had a reasonable expectation of success of using an iron core with a mean iron core size of no greater than about 9 nm. We have carefully considered Patent Owner's arguments to the contrary in coming to this conclusion, but do not find those arguments to be persuasive for the reasons set forth below.

In its Corrected Motion to Amend, Patent Owner distinguishes Geisser on the basis that it "does not offer any explicit teaching that the carbohydrate component of its iron carbohydrate complex is substantially non-immunogenic," asserting that Geisser does not provide any examples of administration of the complex. Mot. Amend. 14. Patent Owner contends further that Geisser is silent on the properties of the iron in the iron carbohydrate complex, and thus, Geisser does not provide any reason to alter the core size "to contravene dosing conventions in the art (as identified by the '702 patent)." *Id.*

As Patent Owner notes, however, Geisser is silent as to core size. Thus, the ordinary artisan would have looked to formulations known in the art, such as those Groman '498 and Funk, to determine an appropriate core size. Moreover, van Wyck, as discussed above, provides a reason as to why the ordinary artisan would have used a core size less than about 9 nm.

Patent Owner also addresses van Wyck in its Motion to Amend. Mot. Amend. 20. Specifically, Patent Owner argues that van Wyck does not teach administration of a high dose of the iron carbohydrate complexes required by proposed substitute claim 58. *Id.* That argument is not persuasive as van Wyck teaches the considerations that go into selection of a core size, and Geisser teaches the administration of a high dose of the iron carbohydrate complexes required by proposed substitute claim 58.

Patent Owner contends further that van Wyck does not teach a core size less than about 9 nm, but in fact is drawn to maximizing core size, which van Wyck teaches is "inversely proportional to labile iron release." Reply. Opp. Mot. Amend 9 (citing Ex. 2049, 6). According to Patent Owner, van Wyck in fact teaches that its preferred core size is 10 nm, which is greater than the "less than about 9 nm required by the substitute claims." *Id.* (citing Ex. 2049, 6). Patent Owner relies also on the testimony of its expert, Dr. Manzi, who declares that teachings related to iron dextran cannot be extrapolated to other carbohydrate species, and, thus, the ordinary artisan would not apply iron dextran properties to the iron carbohydrate of Geisser. *Id.* (citing Ex. 1053 ¶ 70).

According to Patent Owner, Petitioner provides no reason as to why the ordinary artisan "would combine van Wyck with 'iron carbohydrate complexes [aside from those addressed in van Wyck] with favorable 'labile iron' properties that happened to be smaller than about 9 nm.'" *Id.* at 9–10 (alteration original) (quoting Opp. Mot. Amend 15). Moreover, Patent Owner argues, Petitioner points to no disclosure in Funk or Groman '498 that relates to the species of the iron carbohydrate complex of Geisser. *Id.* at

10 (citing Ex. 1053 ¶ 64 (Dr. Manzi testifying as to Baile that there is "little consistency within the class of iron carbohydrate complexes.")).

Funk, Patent Owner asserts, in fact teaches that the dissolution characteristics of iron carbohydrate complexes areultimately carbohydrate dependent. *Id.* (citing Ex. 1026, 92–93). Patent Owner cites *Pharmacosmos A/S v. Luitpold Pharmaceuticals Inc.*, IPR2015-01495, Paper 11, p. 17-18 (PTAB January 8, 2016), noting that the "Board rejected the combination of Geisser and Groman due to the distinctions in structure of the carbohydrate complexes." *Id.*

We do not find Patent Owner's argument persuasive in this regard. Initially, we note that Patent Owner does not provide a construction for the claim term "less than about 9 nm," and does not explain why the ordinary artisan would understand "about" as excluding a core size of 10 nm.

Moreover, we have reviewed page 6 of Exhibit 2049, and do not find an explicit teaching by van Wyck that a core size of 10 nm is preferred. At best, van Wyck teaches "[i]f labile iron can cause a free-iron-like reaction and free-iron-like reactions are dose limiting . . . then the maximum tolerated dose and rate of administration would be inversely related to labile iron fraction and follow the sequence ID>IS>SFGC." Ex. 2049, 6. van Wyck, in that statement, is ordering the data points in its Figure 1. Patent Owner does not address Petitioner's contention that, as shown in Figure 1, the curve plateaus for core radii greater than 4 or 5 nm, that is, core diameters greater than 8 or 10 nm. That teaching, along with known complexes, such as those in Funk and Groman '498, provide a reason as to why the ordinary artisan would have chosen a core size "less than about 9 nm."

As to Dr. Manzi's testimony, Dr. Manzi states:

> Due to this well-known association between immunogenic effects and dextran, [the ordinary artisan] in January 2006 would not have believed that teachings relating to iron dextran complex specific references could be reliably combined with the teachings related to another iron carbohydrate complex, let alone yield a reasonable expectation of success.

Ex. 1053 (Dr. Manzi Corrected Declaration) ¶ 70. Dr. Manzi is discussing the immunogenic effects, which, Geisser teaches are induced by dextran, that is, the carbohydrate component of an iron dextran complex. Thus, it is unclear how this testimony relates to the properties of the iron core. Moreover, as taught by van Wyck, all agents share the same core chemistry, and, thus, the rate of iron release per unit surface area would be similar among agents. Ex. 2049, 5. van Wyck is evidence, therefore, that the ordinary artisan would have looked to the core size of other known iron agents in determining an appropriate iron core size for the iron carbohydrate complex of Geisser.

3. Conclusion

For the reasons set forth above, we conclude that Patent Owner has failed to demonstrate the patentability of proposed substitute claim 58.[15] In addition, Patent Owner does not separately argue the patentability of the remainder of the proposed substitute claims. We, therefore, *deny* patent Owner's Motion to Amend.

[15] In this regard, we further conclude that Petitioner has demonstrated by a preponderance of the evidence the unpatentability of proposed substitute claim 58 over the combination of Geisser, van Wyck, Groman and Funk.

E. Motion to Exclude (Paper 44)

Patent Owner seeks to exclude Petitioner's Exhibits 1055, 1056, 1057, 1059, 1060, 1061, 1063, and portions of Exhibit 1054. Paper 44, 1.

As to Exhibit 1054, Patent Owner contends that Petitioner has mischaracterized and improperly used Dr. Manzi's testimony. *Id.* at 13. Patent Owner asserts, therefore, that Dr. Manzi's testimony from 68:19–70:10 should be excluded, as should any portions of Petitioner's Opposition to the Motion to Amend relying on that testimony. *Id.* (citing Opp. Mot. Amend 24).

We conclude that Patent Owner's contentions go to the weight of the testimony and argument, and not whether the testimony and the portions of Petitioner's Opposition to the Motion to Amend relying on that testimony should be excluded. Moreover, we note that we did not rely on that portion of Exhibit 1054 in this Decision.

We note further that we did not rely on Exhibits 1055, 1056, 1057, 1059, 1060, 1061, and 1063 in this Decision. Thus, we dismiss the Motion to Exclude as to those Exhibits as moot.

III. CONCLUSION

Petitioner has shown by a preponderance of the evidence that claims 1–3, 10–13, 23, 25–27, and 41–43 are unpatentable as anticipated by Geisser under 35 U.S.C. § 102(b).

Petitioner has not shown by a preponderance of the evidence that claims 17 and 47 are unpatentable as obvious over Geisser and Groman under 35 U.S.C. § 103(a).

Petitioner has shown by a preponderance of the evidence that claims 1, 14, and 15 are unpatentable as anticipated by van Zyl-Smit under 35 U.S.C. § 102(b).

Petitioner has shown by a preponderance of the evidence that claim 30 is unpatentable as obvious over van Zyl-Smit and Funk under 35 U.S.C. § 103(a).

In view of Patent Owner's disclaimer of claims 28 and 29, we dismiss as moot Petitioner's anticipation challenge of claim 28.

Patent Owner's Motion to Amend is denied.

IV. ORDER

Accordingly, it is hereby:

ORDERED that Petitioner has shown by a preponderance of the evidence that claims 1–3, 10–15, 23, 25, 27, 30, and 41–43 of the '702 patent are unpatentable;

FURTHER ORDERED that Petitioner has failed to show the unpatentability of claims 17 and 47 by a preponderance of the evidence,

FURTHER ORDERD that claims 28 and 29 are cancelled;

FURTHER ORDERED that Petitioner's Motion to Amend is *denied*;

FURTHER ORDERED that Patent Owner's Motion to Exclude is *denied* as to Exhibit 1054, and *dismissed* as moot as to Exhibits 1055, 1056, 1057, 1059, 1060, 1061, and 1063 ; and

FURTHER ORDERED that, because this is a final written decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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