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Filed on behalf of : AbbVie Biotechnology Ltd.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Coherus Biosciences Inc.,
Petitioner,

v.

AbbVie Biotechnology Ltd.,
Patent Owner.

Case IPR2017-00823
U.S. Patent No. 9,085,619

PATENT OWNER'S PRELIMINARY RESPONSE

TABLE OF CONTENTS

I. Introduction....1
II. Background....4
A. Gokarn ’011 And Gokarn Provisional....4
B. The State Of The Art....6
C. The ’619 Patent....8
III. Level Of Ordinary Skill In The Art....10
IV. Claim Construction....10
V. Petitioner Fails To Establish That Gokarn ’011 Is Entitled To The Earlier Filing Date Of Gokarn Provisional....10
A. Petitioner Fails To Establish Written Description Support For The Subject Matter Relied Upon In The Anticipation Challenge....11
1. Gokarn Provisional does not provide written description support for adalimumab....12
a. Petitioner improperly attempts to supplement Gokarn Provisional’s disclosure with extrinsic evidence....13
b. The Petition fails to establish that Gokarn Provisional describes a small genus of high-concentration antibodies....16
2. Gokarn Provisional does not provide written description support for concentrations from 50 to 200 mg/ml....20
3. Gokarn Provisional does not provide written description support for a “buffer-free” formulation....21
B. The Petition Fails To Establish That Gokarn Provisional Supports Claims 162 Or 165 Of Gokarn ’011....22
1. Petitioner fails to propose a claim construction for claims 162 or 165....23
2. Claim 162 lacks written description support....24
3. Claim 165 lacks written description support....26
C. The Petition Relies Solely On Priority To Gokarn Provisional....26

VI. Ground 1: Gokarn '011 Does Not Anticipate The Challenged Claims.....27
A. Gokarn Provisional Does Not Disclose Adalimumab.....29
B. The Petition's Anticipation Challenge Based On A Purported Small Genus Is Legally Flawed 30
C. Gokarn Provisional Does Not Disclose A Small Genus Of High-Concentration Antibodies 32
D. Petitioner's Cited *Petering* And *Ineos* Cases Are Inapposite 34
E. Gokarn Provisional Does Not Disclose Adalimumab At A Concentration Of 50 To 200 mg/ml 36
F. Gokarn Provisional Does Not Disclose An Adalimumab Formulation In Which The Formulation Lacks A Buffering System 37
VII. Conclusion 38

TABLE OF AUTHORITIES

CASES **PAGE**

AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.,
759 F.3d 1285 (Fed. Cir. 2014) 25

ArcelorMittal France v. AK Steel Corp.,
700 F.3d 1314 (Fed. Cir. 2012) 32, 33, 35

Ariad Pharm., Inc. v. Eli Lilly & Co.,
598 F.3d 1336 (Fed. Cir. 2010) (en banc) 15, 24

Atofina v. Great Lakes Chem. Corp.,
441 F.3d 991 (Fed. Cir. 2006) 37

Boston Sci. Corp. v. Johnson & Johnson,
647 F.3d 1353 (Fed. Cir. 2011) 13, 16, 18, 21, 26

Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.,
246 F.3d 1368 (Fed. Cir. 2001) 32

Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.,
800 F.3d 1375 (Fed. Cir. 2015) 22, 27

Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.,
471 F.3d 1369 (Fed. Cir. 2006) 29, 36

Ex parte Mann,
No. 2015-003571, 2016 WL 7487271 (P.T.A.B. Dec. 21, 2016) 11

Ex parte Morsa,
No. 2011-007576, 2014 Pat. App. LEXIS 1496 (B.P.A.I. Feb. 25, 2014) 30, 31

Forty Seven, Inc. v. Stichting Sanquin Bloedvoorziening,
No. IPR2016-01529, Paper 13 (P.T.A.B. Feb. 9, 2017).....21, 24, 26

Genise v. Desautels,
No. 104,834, 2003 WL 21979123 (B.P.A.I. Apr. 17, 2003).....12, 14, 31

Goeddel v. Sugano,
617 F.3d 1350 (Fed. Cir. 2010).....12, 14, 15

Helifix Ltd. v. Blok-Lok Ltd.,
208 F.3d 1339 (Fed. Cir. 2000).....30, 31

In re Arkley,
455 F.2d 586 (C.C.P.A. Feb. 17, 1972).....30, 33, 38

In re Fried,
312 F.2d 930 (C.C.P.A. Feb. 13, 1963).....13

In re LeGrice,
301 F.2d 929 (C.C.P.A. May 4, 1962).....30, 31

In re Magnum Oil Tools Int'l, Ltd.,
829 F.3d 1364 (Fed. Cir. 2016).....27

In re Meyer,
599 F.2d 1026 (C.C.P.A. June 7, 1979).....29

In re Petering,
301 F.2d 676 (C.C.P.A. Apr. 13, 1962).....34, 36

In re Ruschig,
379 F.2d 990 (C.C.P.A. June 22, 1967).....13

In re Schaumann,
572 F.2d 312 (C.C.P.A. Feb. 23, 1978).....34

Ineos USA LLC v. Berry Plastics Corp.,
783 F.3d 865 (Fed. Cir. 2015).....34, 35

Johns Manville Corp. v. Knauf Insulation, Inc.,
No. IPR2015-01633, Paper 10 (P.T.A.B. Jan. 4, 2016) 25

Lockwood v. Am. Airlines, Inc.,
107 F.3d 1565 (Fed. Cir. 1997) 14, 15, 18, 19

Net MoneyIN, Inc. v. VeriSign, Inc.,
545 F.3d 1359 (Fed. Cir. 2008) 38

Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.,
851 F.3d 1270 (Fed. Cir. 2017) 29, 30, 31

Novozymes A/S v. DuPont Nutrition Biosciences APS,
723 F.3d 1336 (Fed. Cir. 2013) 20

Regents of Univ. of Cal. v. Eli Lilly & Co.
119 f.3d 1559 (Fed. Cir. 1997) 24, 25

X2Y Attenuators, LLC v. ITC,
757 F.3d 1358 (Fed. Cir. 2014) 23

Zimmer Biomet Holdings, Inc. v. Four Mile Bay, LLC,
No. IPR2016-00011, Paper 8 (P.T.A.B. Apr. 1, 2016) 25

STATUTES

35 U.S.C. § 102 .....10, 11, 27, 30, 38

35 U.S.C. § 112 .....3, 12, 13

35 U.S.C. § 312 27

35 U.S.C. § 371 27

OTHER AUTHORITIES

37 C.F.R. § 42.22 27

37 C.F.R. § 42.65 25

PATENT OWNER EXHIBIT LIST

EXHIBIT	DESCRIPTION
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2022-2027	*Not Used*
2028	Rouet, et al., "Stability Engineering of the Human Antibody Repertoire," *FEBS Letters 588*, 269-277 (2014)
2029-2041	*Not Used*
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2043-2046	*Not Used*
2047	Wang, et al., "Antibody Structure, Instability, and Formulation," *J. Pharm. Sci. 96*(1), 1-26 (Jan. 2007)
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2051	Shire, "Formulation of Proteins and Monoclonal Antibodies (mAbs)," *Monoclonal Antibodies, Meeting the Challenges In Manufacturing, Formulation, Delivery and Stability of Final Drug Product, Woodhead Publishing Series in Biomedicine 77,* Chap. 4, 93-120 (Woodland Publishing, Cambridge, UK) (2015)
2052-2054	*Not Used*
2055	ZEVALIN® Label, Physicians' Desk Reference (Thomson PDR, Montvale, N.J., 60th ed.) (2006)

I. Introduction

In four separate Petitions, Coherus Biosciences ("Petitioner") challenges claims 16-19 and 24-30 of AbbVie Biotechnology Ltd.'s ("AbbVie") U.S. Patent No. 9,085,619 ("the '619 patent") directed to high concentration (50-200 mg/ml) aqueous pharmaceutical formulations comprising adalimumab (the active ingredient in HUMIRA®) without a buffering system. (IPR2017-00822, IPR2017-00823, IPR2017-01008, IPR2017-01009.) Each of the Petitions is flawed and should be denied for the reasons set forth in Patent Owner's respective preliminary responses.

Here, Petitioner presents a single proposed ground of unpatentability: anticipation by U.S. Patent Pub. No. 2016/0319011 ("Gokarn '011") (Ex. 1103) as of the June 14, 2005 filing date of U.S. Serial No. 60/690,582 ("Gokarn Provisional") (Ex. 1104; Pet., 1.) Petitioner asserts that Gokarn Provisional anticipates the claims and that Gokarn '011 "incorporates" the same disclosure as Gokarn Provisional. (*See, e.g.*, Pet., 36-45.) The Board should deny the Petition in its entirety because this sole ground presented is factually unsupported and legally deficient.

At the outset, the Petition does not establish that Gokarn '011 is entitled to the June 14, 2005 filing date of Gokarn Provisional. To obtain that effective date, Petitioner must show that Gokarn Provisional provides written description support

for both (1) the subject matter relied on in Gokarn '011 to allege anticipation and (2) at least one claim of Gokarn '011. (Pet., 22.) Petitioner does neither.[1]

Gokarn Provisional lacks written description support for the subject matter on which Petitioner attempts to rely in its anticipation challenge. Gokarn Provisional does not disclose adalimumab. Its generic disclosure of "proteins" and "antibodies" and two examples using a different antibody called "AMG412 (EMAB)" (also referred to as "EMAB") are insufficient to establish written description of adalimumab. Gokarn Provisional also fails to disclose the claimed concentration of 50 to 200 mg/ml of adalimumab in any formulation, let alone in a formulation without a buffering system. The only examples in Gokarn Provisional involve a *different antibody* (EMAB), in a *buffered* solution, at a concentration (46 mg/ml) *below* the claimed concentration (50-200 mg/ml). Gokarn Provisional evidences a failure to achieve even a 50 mg/ml concentration for the only antibody

[1] Importantly, Petitioner does not assert that Gokarn '011 is entitled to any other filing date within its chain of priority applications. Petitioner, for example, does not rely on material contained in any later application to allege anticipation. Consequently, Gokarn '011 is only entitled to its July 19, 2016 filing date, which is not prior art against the '619 patent.

Gokarn attempted to formulate. Because Gokarn Provisional does not disclose the subject matter Petitioner relies on for anticipation, Gokarn '011 is not prior art.

Gokarn '011 also is not prior art because Petitioner fails to show that Gokarn Provisional provides written description support for any claim of Gokarn '011. Petitioner alleges that Gokarn Provisional discloses "bufferless, high-concentration EMAB solutions" that support claims 162 and 165 of Gokarn '011. (Pet., 26.) But both EMAB examples in Gokarn Provisional *include buffers*. At most, Gokarn Provisional describes a research plan, which is inadequate under 35 U.S.C. § 112 to support either claim 162 or 165. For this independent reason, Gokarn '011 is not prior art.

But even if Gokarn '011 is considered to be prior art (which it is not), Petitioner fails to establish that it anticipates the challenged claims. The Petition relies exclusively on the disclosure of Gokarn Provisional, but Gokarn Provisional does not disclose adalimumab or any adalimumab-containing formulation ("bufferless" or otherwise). It fails to disclose the claimed concentration of 50-200 mg/ml of adalimumab or a formulation of adalimumab without a buffering system. And it does not disclose the combination of features required by the challenged claims. Each of these deficiencies in the disclosure of Gokarn Provisional, on its own, precludes any finding of anticipation based on Gokarn '011.

For these reasons, which are explained in more detail below, Petitioner has not shown that it is likely to prove that any challenged claim is unpatentable. The Board should therefore deny institution of the Petition.

II. Background

A. Gokarn '011 And Gokarn Provisional

Gokarn '011 was filed on July 19, 2016, and claims priority to Gokarn Provisional, filed June 14, 2005. (Ex. 1103.) Gokarn Provisional differs significantly from Gokarn '011 in part because Gokarn '011 includes different examples and a much lengthier specification. (*Compare* Ex. 1103 *with* Ex. 1104.) In its anticipation challenge, Petitioner relies on Gokarn Provisional, rather than any material added in Gokarn '011. (*See, e.g.*, Pet., 46-50; *id.*, 1 (contending Gokarn Provisional is incorporated by reference into Gokarn '011).)

Gokarn Provisional purports to describe an ongoing investigation into potential protein formulations. (Ex. 1104, 7, 16.)[2] It consists of three-pages of text, a short PowerPoint presentation, and one claim. (*See generally id.*; Pet., 24 n.2.) The text alleges very generally that potentially "self-buffering" formulations may be made using an incredibly broad and undefined class of pharmaceutical proteins,

[2] All citations herein refer to the exhibits' native page numbers, except IPR page numbers are used where the exhibits do not include native page numbers.

including "large, and small proteins, as well as different antibodies, naturally or non-naturally occurring peptides and proteins, including peptibodies, maxibodies, interbodies, etc." (*Id.*, 2:10-15.) Gokarn Provisional also states that an "active protein" may be the "primary source" of buffering, although "[o]ther traditional buffering agents may be present," such as acetate, citrate, and other buffers. (*Id.*, 1:9-25.) It states that a protein's potential for providing buffering capacity depends on "the presence of enough . . . charged amino acid residues including glutamic acid, aspartic acid, histidine, arginine, and lysine . . . ." (*Id.*, 2:18-23.) Gokarn Provisional states that this adequate buffer capacity requires the protein to be at "sufficiently high" concentration but reveals no specific concentration range. (*Id*., 1:5-9.)

Gokarn Provisional does not disclose adalimumab. It identifies only one specific protein, EMAB. (*Id.*, 4-5.) But it does not provide the structure, amino-acid sequence, or any other description of EMAB. (*See id.*)

Gokarn Provisional contains two examples in which buffered solutions of EMAB are prepared. (*Id*.) The first example describes *acetate-buffered* EMAB solutions. (*Id.*, 4.) The solutions were concentrated to 46 mg/ml, at which point they became "cloudy." (*Id.*) The second example describes the preparation of *succinate-buffered* EMAB solutions. (*Id.*, 5.) The solutions were concentrated to 45 mg/ml, at which point cloudiness appeared. (*Id.*)

Over the next several PowerPoint slides, Gokarn Provisional shows an attempt to extrapolate EMAB's buffering capacity by comparing the acetate- and succinate-buffered solution examples to an acetate buffer standard. (*Id.*, 6-13.) It states, however, that "[a] more accurate estimate of the buffer capacity from EMAB alone will have to be obtained from bufferless high concentration EMAB solutions." (*Id.*, 13.) Gokarn Provisional describes those investigations as "on-going." (*Id.*)

B. The State Of The Art

The buffered adalimumab formulation of HUMIRA was a breakthrough in the field of antibody therapeutics when it was approved in 2002. (Ex. 2042.) HUMIRA was the first commercialized high-concentration, liquid antibody formulation for subcutaneous administration. (*Id.*) HUMIRA was successfully formulated as a *buffered* pharmaceutical formulation and is one of the top selling drugs in the world. (Ex. 1105, 470; Ex. 2042, 1.) At the time of the invention of the '619 patent, HUMIRA was the only monoclonal antibody formulation approved for subcutaneous administration that was liquid rather than lyophilized—a testament to its remarkable formulation. (*See*, *e.g.*, Ex. 2047, 2-4 (Table 1).)

Like HUMIRA, all of the fifteen approved aqueous monoclonal antibody products available between 2003 and 2007 were provided with a buffering system.

(Ex. 2047, 2-4; Ex. 2055, 852.) The same held true as late as 2015. (Ex. 2051, 94-101 (Table 4.1); Ex. 2055, 852.)

At the time of the '619 patent invention, those skilled in the art used buffering systems because it was extremely difficult to make stable (*e.g.,* non-aggregated, non-fragmented, non-degraded, non-denatured, *etc.*), liquid pharmaceutical formulations of antibodies, particularly at high concentrations. (Ex. 2047, 5, 14; *see, e.g.*, Ex. 1101, 2:56-62 ("difficulties with the aggregation, insolubility, and degradation of proteins generally increase as protein concentrations in formulations are raised").) Even after HUMIRA's introduction, the scientific literature reported the use of buffering systems, such as citrate, to produce a successful formulation. (*See* Ex. 2028, 271.) The initial formulation of ERBITUX, for example, had antibody aggregation problems, which those skilled in the art addressed by empirically optimizing conditions and using citrate buffer. (*See id.*; *see also* Ex. 1101, 3:66-4:2 (stating that traditional formulations use buffering systems).)

The complexity and unpredictability of formulating antibodies resulted, at least in part, because a formulation designed for one antibody would not reasonably have been expected to be successfully applied to a different antibody. Indeed, it was well established by 2007 that antibodies had to be evaluated *individually* when developing a liquid formulation because of their differing

structures and properties. (Ex. 2047, 5, 14, 21.) This was true even for antibodies with similar sequences and among antibodies of the same class (*e.g.*, IgG or IgG1). (*Id.*; Ex. 2021, 690.)

C. The '619 Patent

The '619 patent details the surprising discovery that adalimumab formulated in water at high concentrations *without* a buffering system may be used as a pharmaceutical formulation. (*See* Ex. 1101, 3:29-33.) Contrary to the traditional approaches for monoclonal antibody formulation, the '619 patent describes and claims high concentration (50-200 mg/ml) aqueous pharmaceutical formulations comprising adalimumab without a buffering system. (*See, e.g.*, *id.*, 60:47-62:32, Table 12 & claims 16-18.)

While conducting experiments for a different but related purpose, the inventors made several observations that led them to use diafiltration techniques to produce adalimumab in pure water at concentrations ranging from 10 mg/ml to above 200 mg/ml. (*See, e.g.*, *id.*, 51:47-54:18, 60:47-62:32.) The '619 patent describes the resulting formulations as unexpectedly non-opalescent. (*See, e.g.*, *id.*, 60:6-16, 68:37-49.) That is, surprisingly, the formulations were clear, with no solution haziness or precipitation. (*Id.*, 44:47-57, 60:25-36.) The formulations were also "surprisingly stable," with only minimal protein aggregation even at adalimumab concentrations of 200 mg/ml, and "virtually no instability phenomena"

were observed. (*Id.*, 67:30-45, 68:52-55.) The '619 patent also discloses that adalimumab formulations without a buffering system had low viscosity at concentrations up to 200 mg/ml—a key property for a subcutaneously administered formulation. (*Id.*, 3:1-7, 60:17-20.) The patent contrasts the low viscosity of the adalimumab formulations without a buffering system with another protein (human serum albumin) formulation without a buffering system, which exhibited a six-fold *increase* in viscosity compared to a buffered formulation. (*Id.*, 65:1-10 (concluding that viscosity "may depend on the individual protein").)

The '619 patent claims are directed to the disclosed high-concentration adalimumab pharmaceutical formulations lacking a buffering system, which achieved the unexpected properties of low aggregation, low opalescence, low viscosity, and high solubility. (*Id.*, 151:9-152:65.) Independent claim 16 defines an aqueous pharmaceutical formulation comprising an antibody having the complementarity determining region (CDR) amino acid sequences of adalimumab, an antibody concentration of 50-200 mg/ml, and water, in which the formulation does not comprise a buffering system. (*Id.*, 152:15-32.)

At the time of AbbVie's invention, *no one* had successfully developed a commercial high concentration aqueous monoclonal antibody pharmaceutical formulation without a buffering system.

III. Level Of Ordinary Skill In The Art

For the limited purpose of this Preliminary Response, Patent Owner does not contest Petitioner's proposed level of ordinary skill in the art. (Pet., 20.)

IV. Claim Construction

Patent Owner believes that construction of the phrase "does not comprise a buffering system" is unnecessary at this stage. For purposes of this Preliminary Response only, Patent Owner does not dispute Petitioner's proposed construction: "contains no more than a *de minimis* amount of extrinsic buffer." (*Id.*, 20-21.)

V. Petitioner Fails To Establish That Gokarn '011 Is Entitled To The Earlier Filing Date Of Gokarn Provisional

Petitioner contends that Gokarn '011 is prior art to the challenged claims under 35 U.S.C. § 102(e) (pre-AIA) as of Gokarn Provisional's June 14, 2005 filing date. (Pet., 1, 21-32.) But as shown below, Petitioner fails to prove that Gokarn '011 qualifies as prior art.

Only two of Gokarn '011's related applications were filed before the '619 patent's earliest priority date (November 2007): Intl. Pub. No. WO 2006/138131 ("Gokarn PCT") (Ex. 1136) and Gokarn Provisional. (Ex. 1104.) Here, Petitioner relies *only* on Gokarn Provisional's filing date as the effective prior art date under

Section 102(e).[3] (Pet., 31-32.) To rely on this date, Petitioner must show that Gokarn Provisional provides written description support for both: (1) the subject matter relied on in Gokarn '011 to allege anticipation; and (2) at least one claim of Gokarn '011. *Ex parte Mann*, No. 2015-003571, 2016 WL 7487271, at *5-6 (P.T.A.B. Dec. 21, 2016). Petitioner fails to show this required support; thus, Gokarn '011 is not entitled to Gokarn Provisional's filing date.

A. Petitioner Fails To Establish Written Description Support For The Subject Matter Relied Upon In The Anticipation Challenge

Petitioner relies on an alleged disclosure in Gokarn Provisional of "50 mg/mL adalimumab in an aqueous, buffer-free formulation." (Pet., 36; *see also* Pet., 37, 39 (alleging "disclosure of 50 mg/mL adalimumab"), 43 ("Gokarn Provisional discloses a buffer-free formulation comprising 50 mg/mL adalimumab").) A threshold question, however, is whether Gokarn '011 is entitled to the date of Gokarn Provisional as to this subject matter. *Mann*, 2016 WL 7487271, at *5-6 (vacating Section 102(e) rejection because the examiner failed to

[3] In IPR2017-00822, Petitioner alleges that Gokarn PCT anticipates the claims of the '619 patent. This Petition would be entirely duplicative if it alleged anticipation based on matter added to Gokarn PCT.

demonstrate Section 112 support in an earlier provisional application for the subject matter relied on in the rejection). It is not.

Citing only anticipation case law, Petitioner never addresses whether Gokarn Provisional provides *written description* support for the subject matter upon which Petitioner relies. (*See* Pet., 31-32.) Gokarn '011 cannot be accorded priority to Gokarn Provisional's filing date because Petitioner failed to meet its burden of proving entitlement to that date under Section 112. *See Genise v. Desautels*, No. 104,834, 2003 WL 21979123, at *17 (B.P.A.I. Apr. 17, 2003) ("written description concerns what the specification shows as *being possessed by these particular inventors*, not what would have been obvious" in light of the specification)[4]; *Goeddel v. Sugano*, 617 F.3d 1350, 1355 (Fed. Cir. 2010).

1. Gokarn Provisional does not provide written description support for adalimumab

Gokarn Provisional contains only three pages of text, ten PowerPoint slides, and one claim. (Ex. 1104.) Its meager disclosure does not provide written description support for adalimumab because, critically, *Gokarn Provisional does not disclose adalimumab.* Instead it only vaguely mentions the extremely broad categories of "pharmaceutical proteins," "antibodies," and "peptibodies,

[4] In this paper, all emphases are added unless otherwise indicated.

maxibodies, interbodies, etc." (Ex. 1104, 2:10-15.) This generic and vague disclosure related to antibodies does not satisfy the written description requirement for the species adalimumab. *In re Ruschig*, 379 F.2d 990, 993-94 (C.C.P.A. June 22, 1967) (a generic chemical structure did not describe a chemical species); *Boston Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1367 (Fed. Cir. 2011) (a chemical genus did not describe a specific species or sub-genus).

The only antibody that Gokarn Provisional specifically identifies is EMAB, not adalimumab. (Ex. 1104, 4-5.) Gokarn Provisional does not define the structure of EMAB, and the Petition does not suggest that it is the same as adalimumab (which it is not), or even that it is similar. (*See* Pet., 37-40.) Accordingly, the disclosure of EMAB does not provide written description support for adalimumab. *In re Fried*, 312 F.2d 930, 936 (C.C.P.A. Feb. 13, 1963) (disclosure of one compound did not provide Section 112 support for a similar claimed compound that differed only as to a single substituent).

a. Petitioner improperly attempts to supplement Gokarn Provisional's disclosure with extrinsic evidence

Recognizing that Gokarn Provisional does not mention adalimumab at all, let alone in any concentration or in any formulation, Petitioner improperly attempts to read a "small genus" into Gokarn Provisional using hindsight. (Pet., 37.) Specifically, Petitioner contends that Gokarn Provisional discloses a small genus of

high-concentration antibodies—including the commercial HUMIRA formulation of adalimumab—that a "POSA would have known" and been able to "immediately envision[]." (*Id*., 39.) Petitioner's small genus theory, however, fails as a matter of law. *See Genise*, 2003 WL 21979123, at *17; *Goeddel*, 617 F.3d at 1355-56.

Gokarn Provisional does not disclose HUMIRA. But even assuming that persons skilled in the art would have been aware of the HUMIRA formulation of adalimumab at a 50 mg/ml concentration, HUMIRA was a *buffered* formulation. (Ex. 1105, 470, col. 2.) Thus, a skilled artisan reviewing Gokarn Provisional would have to first consult *extrinsic information* about the HUMIRA formulation (showing it to be buffered) and then *modify* that formulation to arrive at the subject matter relied upon in the Petition's anticipation challenge: "50 mg/mL adalimumab in an aqueous, buffer-free formulation." (Pet., 36.) Such obviousness-type reasoning is improper in a written description analysis. *See Goeddel*, 617 F.3d at 1356; *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1571-72 (Fed. Cir. 1997).

Indeed, in *Goeddel*, the Federal Circuit rejected the type of argument Petitioner presents here. 617 F.3d at 1355. In an interference proceeding, the Board held that one of ordinary skill "should have been able to envision" the subject matter of the count based on the specification of Sugano's application and a known amino acid sequence (as disclosed in a cited extrinsic reference), and awarded priority to Sugano. *Id*. The Federal Circuit reversed because even though the

count's subject matter could have been envisioned that did not establish constructive reduction to practice in the specification. *Id.* at 1356 (quoting *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc)).

Likewise, in *Lockwood*, the Federal Circuit held that it is not sufficient that a specification, "when combined with the knowledge in the art, would lead one to speculate as to "modifications that the inventor *might have envisioned, but failed to disclose*." 107 F.3d at 1572. Lockwood's claims were directed to an individual merchandising apparatus that contained a video disk player. *Id.* But his priority application only described a television set and a keypad. *Id.* The Federal Circuit affirmed summary judgment that Lockwood was not entitled to an earlier filing date, rejecting his argument that it would have been apparent to one skilled in the art that the inventor also envisioned using a terminal containing a video disk player. *Id.*

As in *Goeddel* and *Lockwood*, Petitioner's reliance on a combination of Gokarn Provisional with extrinsic knowledge of the HUMIRA formulation does not establish that Gokarn Provisional's inventor actually possessed and disclosed the subject matter Petitioner relies upon. *Lockwood*, 107 F.3d at 1571 ("It is the disclosures of the [specification] that count.").

b. The Petition fails to establish that Gokarn Provisional describes a small genus of high-concentration antibodies

The Petition also does not establish that Gokarn Provisional discloses any small genus of high-concentration antibodies that includes, among other things, adalimumab. (*See* Pet., 37-39.) Petitioner relies on Gokarn Provisional's statement that "antibodies at sufficiently high concentrations[] possess adequate buffering capacity in the pH range of 4.0 to 6.0." (*Id.*; Ex. 1104, 1:5-8.) This statement fails to provide the "precise definition" required to establish a genus, "such as by structure, formula, or chemical name." *Boston Sci.*, 647 F.3d at 1363 (citation omitted). The vague mention of "sufficiently high concentrations" does not point to any particular antibody concentration, to adalimumab, or to any other particular antibody. (Ex. 1104, 1:5-8.) Thus, Petitioner has failed to establish adequate disclosure of any genus within Gokarn Provisional. *Boston Sci.*, 647 F.3d at 1368-69 (holding that a specification's "meager disclosure" of "analogs" failed to disclose a narrower sub-genus of analogs "by name, by functionality, or even by implication").

Petitioner further seeks to define its alleged genus as including only antibodies that had *previously been formulated in the art* at concentrations above 30 mg/ml. (Pet., 38-39.) But Petitioner's attempt to establish a narrow genus is inconsistent with the disclosure of Gokarn Provisional, which states that the

"pharmaceutical proteins which are formulated according to the method of the present invention include large, and small proteins, as well as different antibodies, naturally or non-naturally occurring peptides and proteins, including peptibodies, maxibodies, interbodies, etc." (Ex. 1104, 2:10-15.) Gokarn Provisional does not limit its disclosed pharmaceutical proteins to antibodies, but rather attempts to encompass every possible category of protein. (*Id.*) It also does not exclude proteins that had not yet been—but potentially could be—formulated at higher concentrations. (*Id.*) Petitioner's small genus theory is further contradicted by the disclosure of Gokarn '011 itself, which contains nearly *sixty paragraphs* listing innumerable possible protein choices, many of which are not antibodies at all, much less previously known formulations of high-concentration antibodies. (Ex. 1103, [0216]-[0273].)

Additionally, Gokarn Provisional does not define any genus as having a protein concentration of 30 mg/ml or greater. Although Petitioner contends that "high concentration[]" refers to "around 30 mg/mL or higher," Gokarn Provisional contains no such disclosure. (*See* Pet., 38.) Instead, it merely reports 30 mg/ml as the concentration at which one specific antibody—EMAB—was theoretically

believed to provide an increased buffer capacity.[5] (Ex. 1104, 13.) Gokarn Provisional does not purport to extend the 30 mg/ml concentration to any other antibody, or to use 30 mg/ml to provide any "precise definition" of a broader genus of antibodies encompassing EMAB. (*Id.*); *Boston Sci.*, 647 F.3d at 1363. Petitioner's argument is again contradicted by the disclosure of Gokarn '011, which explains that one cannot make broad generalizations about any particular protein's buffering capacity. (Ex. 1103, [0206], [0215], [0389], [0392].)

Finally, a skilled person's alleged extrinsic knowledge of antibodies formulated at higher concentrations in *buffered formulations* cannot constitute a written description of a genus of the same antibodies formulated *without a buffering system* in Gokarn Provisional. *Lockwood*, 107 F.3d at 1571-72 (obviousness-type reasoning is insufficient for written description). The Petition cites extrinsic evidence of the formulations of, for example, the ATGAM, CAMPATH, HUMIRA, SYNAGIS, TYSABRI, AVASTIN, and VECTIBIX products. (Pet., 38-39.) These products, however, use buffering systems:

[5] There is no evidence in Gokarn Provisional that this protein is "self-buffering" at that concentration.

- CAMPATH: Phosphate buffering system. (Ex. 1161, 2 ("dibasic sodium phosphate" and "monobasic potassium phosphate").)
- HUMIRA: Phosphate and citrate buffering system. (Ex. 1105, 470, col. 2 ("monobasic sodium phosphate dehydrate," "dibasic sodium phosphate dehydrate," "sodium citrate," and "citric acid monohydrate").)
- SYNAGIS: Amino acid buffering system. (Ex. 1109, 1.)
- TYSABRI: Phosphate buffering system. (Ex. 1111, 1 ("sodium phosphate, monobasic, monohydrate" and "sodium phosphate, dibasic, heptahydrate").)
- AVASTIN: Phosphate buffering system. (Ex. 1110, 2 ("sodium phosphate (monobasic, monohydrate)" and "sodium phosphate (dibasic, anhydrous)").)
- VECTIBIX: Acetate buffering system. (Ex. 1149, 1 ("sodium acetate").)

Gokarn Provisional never mentions any of these antibody products, whether in their commercial buffered formulations or otherwise. Accordingly, Gokarn Provisional also does not provide any written description of *modified versions* of these pharmaceutical products that omit a buffering system from their formulations. *Lockwood*, 107 F.3d at 1572 (alleged "modifications that the inventor . . . failed to disclose" do not support written description).

Gokarn Provisional does not provide a written description of the subject matter Petitioner relies upon in its anticipation challenge—adalimumab. (Pet., 36.) Thus, Gokarn '011 is not entitled to the priority date of Gokarn Provisional.

2. Gokarn Provisional does not provide written description support for concentrations from 50 to 200 mg/ml

Gokarn Provisional also does not describe any adalimumab formulation having a concentration of 50-200 mg/ml. It provides only two examples, both containing EMAB, *not adalimumab*. (Ex. 1104, 4-5.) The first example concentrated EMAB to a maximum of 46 mg/ml, at which point the solution became "cloudy." (*Id.*, 4.) The second example prepared a 45 mg/ml EMAB formulation, again reaching the maximum concentration at which "cloudiness appear[ed]." (*Id.*, 5.) Neither Petitioner nor its declarant address EMAB's maximum concentrations being *below* 50 mg/ml. (*See* Pet., 9, 38, 40; *see also* Ex. 1102, ¶¶73-75, 91, 94.) While Gokarn Provisional attempts to predict by extrapolation the *buffering capacity* of an EMAB solution at 50 mg/ml (*id.* at 9), it never describes any EMAB solution capable of actually achieving a 50 mg/ml concentration, let alone up to 200 mg/ml. *Novozymes A/S v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336, 1349 (Fed. Cir. 2013) ("[I]f Novozymes had possessed a working [example] . . . it surely would have disclosed that [example] instead of, or at least along with, the nonfunctional [example] . . . ."). Thus, Gokarn Provisional does not provide written description support for an aqueous adalimumab formulation with a concentration of 50-200 mg/ml. Rather, it

describes a *failure* to achieve even 50 mg/ml for the only antibody for which formulation was attempted (EMAB). (*See* Ex. 1104, 4-5.)

3. Gokarn Provisional does not provide written description support for a "buffer-free" formulation

Gokarn Provisional also does not provide written description support for any formulation of adalimumab without a buffering system. Each of the two examples in Gokarn Provisional formulated EMAB *with a buffer*. (*Id.*, 4-5.) While Gokarn Provisional attempts to predict by extrapolation the buffering capacity of EMAB in solution, it concedes that "[a] more accurate estimate of the buffer capacity from EMAB alone will have to be obtained from bufferless high concentration EMAB solutions . . . ." (*Id.*, 13.) Gokarn Provisional does not show possession of any such "bufferless, high concentration EMAB solutions." (Pet., 26.) Instead, it states that such investigations were "on-going." (Ex. 1104, 13.)

A vague disclosure of so-called "on-going" experimentation does not satisfy the written description requirement. *Boston Sci.*, 647 F.3d at 1365-66 (specification describing claimed subject matter as "still under active investigation" provided inadequate written description support); *Forty Seven, Inc. v. Stichting Sanquin Bloedvoorziening*, No. IPR2016-01529, Paper 13 at 11 (P.T.A.B. Feb. 9, 2017) (denying petition because the provisional on which petitioner relied for priority only conveyed "a 'mere wish or plan' for obtaining the claimed invention")

(citation omitted). And here, the "on-going" investigation in Gokarn Provisional was not even directed to adalimumab.

In sum, Gokarn Provisional fails to provide written description support for adalimumab, let alone at concentrations from 50-200 mg/ml or in a formulation without a buffering system. Because Petitioner has failed to establish adequate support for the subject matter it relies upon—"50mg/mL adalimumab in an aqueous, buffer-free formulation"—the Petition should be denied. (Pet., 36.)

B. The Petition Fails To Establish That Gokarn Provisional Supports Claims 162 Or 165 Of Gokarn '011

Petitioner also fails to establish that Gokarn Provisional provides written description support for claims 162 or 165 of Gokarn '011, as it is legally required to do in order to rely on Gokarn Provisional's filing date. For this independent reason, Gokarn '011 is not entitled to the filing date of Gokarn Provisional. *See Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015).

Claims 162 and 165 of Gokarn '011 recite:

> 162. A pharmaceutical protein formulation comprising: an antibody in an amount sufficient for maintaining pH control; and a pharmaceutically acceptable excipient, wherein said pharmaceutical protein formulation is buffered by said antibody, and wherein the formulation lacks a buffer, apart from the antibody.

165. The pharmaceutical protein formulation of claim 162, wherein the antibody is epratuzumab.

(Ex. 1103, 37.)

1. Petitioner fails to propose a claim construction for claims 162 or 165

Petitioner acknowledges that for Gokarn Provisional to provide written description support for these claims, the four corners of Gokarn Provisional must disclose to one skilled in the art that the inventor possessed the *claimed* subject matter. (Pet., 23.) But to compare the disclosure of Gokarn Provisional to claims 162 and 165 of Gokarn '011, the Board must first determine the scope of those claims. *X2Y Attenuators, LLC v. ITC*, 757 F.3d 1358, 1365 (Fed. Cir. 2014) (written description analysis requires first construing the claims).

It is apparent from Petitioner's arguments and Dr. Radtke's testimony that the meaning of the phrase "wherein the formulation lacks a buffer" in claims 162 and 165 is important. Their discussions focus on whether Gokarn Provisional discloses "bufferless" or "buffer-free" formulations. (Pet., 23-32; Ex. 1102, ¶¶77-82.) *But neither Petitioner nor Dr. Radtke proposes a construction for the term "wherein the formulation lacks a buffer" or for any other term in either claim 162 or 165* of Gokarn '011. *See X2Y Attenuators*, 757 F.3d at 1365. This failure renders Petitioner's and Dr. Radtke's analyses deficient.

2. Claim 162 lacks written description support

Petitioner argues that claim 162 of Gokarn '011 has written description support because it is "similar" to claim 1 of Gokarn Provisional. (Pet., 24.) But claim 1 is broadly directed to preparing pharmaceutical formulations comprising an antibody in an amount sufficient for maintaining pH control and buffering the formulation. (*Id.*; Ex. 1104, 14.) Claim 1 does not include claim 162's language that "the formulation lacks a buffer, apart from the antibody." (Ex. 1104, 14.) Instead, claim 1 merely recites a broad genus of antibodies defined by their function (*e.g.*, "pH control"), and thus fails to support claim 162. (*Id.*)

Moreover, Petitioner cannot establish written description support by asserting that claim 162 of Gokarn '011 and claim 1 of Gokarn Provisional are "similar." *Ariad*, 598 F.3d at 1349-50 (an original claim may not support written description); *Forty Seven*, IPR2016-01529, Paper 13 at 10-11. Rather, Petitioner must show that Gokarn Provisional provides written description support for the full scope of claim 162. (*Id*.)

As the Board held in *Forty Seven*: "A sufficient description of a genus . . . requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." *Id.* at 11 (citations omitted) (quoting *Regents of Univ. of Cal. v. Eli Lilly &*

Co., 119 F.3d 1559, 1568-69 (Fed. Cir. 1997)); *see also AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1299 (Fed. Cir. 2014). Petitioner does not attempt to meet this test, identifying no representative species and no structural features common to members of the genus.

Instead, Petitioner asserts (1) that "a POSA would have understood that Gokarn Provisional also described buffer-free antibody formulations" and (2) "[a] POSA would readily conclude from the disclosure of Gokarn Provisional that Gokarn was in possession of antibody formulations without a buffer 'apart from the antibody,' as claimed in claim 162 of Gokarn '011 application." (Pet., 25-26.) The only support Petitioner provides for this statement is paragraphs 78-79 of Dr. Radtke's declaration. (Ex. 1102, 45-46.) But this testimony is just as conclusory as the Petition. (*Id.*, ¶¶ 78-79; Pet., 25-26.) Such conclusory expert statements should be accorded no weight. 37 C.F.R. § 42.65; *Zimmer Biomet Holdings, Inc. v. Four Mile Bay, LLC*, No. IPR2016-00011, Paper 8 at 11 (P.T.A.B. Apr. 1, 2016); *Johns Manville Corp. v. Knauf Insulation, Inc.*, No. IPR2015-01633, Paper 10 at 13 (P.T.A.B. Jan. 4, 2016).

Both Petitioner and Dr. Radtke allege that Gokarn Provisional includes actual "data" measuring the buffering capacity of EMAB solutions without an "extraneous buffer." (Pet., 25; Ex. 1102, ¶73.) This is incorrect. Gokarn Provisional discloses only two examples, both of which are *buffered*: "Acetate

Buffered EMAB" and "Low Succinate Buffered EMAB." (Ex. 1104, 4-5.) Its "Conclusion" states that "[a] more accurate estimate of the buffer capacity from EMAB alone *will have to be obtained* from bufferless high concentration EMAB solutions (on-going)." (*Id.*, 13.) Thus, Gokarn Provisional does not show possession of any "bufferless" EMAB solution.

Gokarn Provisional therefore does not provide written description support for claim 162 at least because it does not describe preparing or testing any "bufferless" antibody solution. (*Id.*) Instead, it at most describes *an "on-going" research plan*, which is insufficient. *See Boston Sci.*, 647 F.3d at 1365-66; *Forty Seven*, IPR2015-01529, Paper 13 at 11-13.

3. Claim 165 lacks written description support

Petitioner also asserts that Gokarn Provisional supports dependent claim 165 of Gokarn '011, which specifies that the antibody of claim 162 is EMAB. (Pet., 27-28.) But, as discussed above, Gokarn Provisional does not describe any "bufferless" EMAB solutions, and Gokarn Provisional's "*on-going" research plan* cannot support claim 165. (Ex. 1104, 13.) *See Boston Sci.*, 647 F.3d at 1365-66; *Forty Seven*, IPR2015-01529, Paper 13 at 11-13. Accordingly, Petitioner failed to establish that Gokarn '011 is entitled to claim priority to Gokarn Provisional.

C. The Petition Relies Solely On Priority To Gokarn Provisional

The Petition relies solely on Gokarn Provisional's filing date as the asserted

Section 102(e) prior art date, and makes *no attempt* to rely on the filing date of any other application in the priority chain of Gokarn '011. (*See* Pet., §§ IX(C), X.) And the Petition does not identify any disclosure in any later application that would provide written description support for its anticipation allegations. (*Id*.) Because the Petition fails to establish priority to Gokarn Provisional or rely on any other filing date, Petitioner has not shown that Gokarn '011 qualifies as a prior art reference before its 35 U.S.C. § 371(c) date of July 19, 2016. *Dynamic Drinkware*, 800 F.3d at 1381-82. The '619 patent was filed before that date and issued on July 21, 2015. (Ex. 1101.) Because Petitioner has not shown that Gokarn '011 qualifies as prior art to the '619 patent, the Petition should be denied. [6]

VI. Ground 1: Gokarn '011 Does Not Anticipate The Challenged Claims

Petitioner fails to establish a reasonable likelihood of proving anticipation of claims 16-19 and 24-30 of the '619 patent under Section 102(e). Each challenged

[6] Petitioner is not entitled to any intermediate filing date. If Petitioner intended to rely on additional disclosure from other applications not contained in Gokarn Provisional, it was required to explain its theory in the Petition such that Patent Owner could respond. *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1381 (Fed. Cir. 2016); 35 U.S.C. § 312(a)(3); 37 C.F.R. § 42.22(a)(2).

claim is directed to an aqueous pharmaceutical formulation comprising the antibody adalimumab at a concentration of 50-200 mg/ml, in which the formulation does not comprise a buffering system. (Ex. 1101, 152:15-65.) The anticipation challenge presented in Section X of the Petition relies only on the disclosure of Gokarn Provisional (Ex. 1104), which Petitioner contends is incorporated into Gokarn '011. (Pet., 32-50.) Yet Petitioner fails to identify any disclosure of the claimed combination of elements—or even of adalimumab itself—in Gokarn Provisional.[7] (*See id.*) Instead, Petitioner argues that one of ordinary skill would have (1) "immediately envisage[d]" the antibody adalimumab from the commercial *buffered* HUMIRA formulation, (2) recognized that HUMIRA was formulated at 50 mg/ml, (3) known that the HUMIRA formulation could be modified to remove the buffering system based on the disclosure of Gokarn Provisional, and (4) known how to perform (1)-(3) above without changing the 50 mg/ml adalimumab concentration of HUMIRA. (*Id.*)

[7] Petitioner concedes that its anticipation and priority analyses are identical. (Pet., 31-32 (pointing to Section X).) Thus, all of the deficiencies set forth above in Section V apply equally here.

This is not anticipation. Section 102 does not permit filling in missing elements simply because one of ordinary skill would allegedly "immediately envision" them. *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 851 F.3d 1270, 1274-75 (Fed. Cir. 2017). Rather, anticipation requires disclosure of each and every claim element within the four corners of a single prior art reference. *Id.*

A. Gokarn Provisional Does Not Disclose Adalimumab

As detailed above, the Petition fails to establish that Gokarn Provisional discloses adalimumab. Gokarn Provisional's vague mention of the broad classes of "pharmaceutical proteins," "antibodies," and "peptibodies, maxibodies, interbodies, etc." (Ex. 1104, 2:10-15) does not disclose the antibody species adalimumab. *In re Meyer*, 599 F.2d 1026, 1031 (C.C.P.A. June 7, 1979) (reversing anticipation because the genus "alkaline chlorine or bromine solution" did not disclose the species "alkali metal hypochlorite"). Moreover, Petitioner does not contend that the only antibody that Gokarn Provisional specifically identifies, EMAB, is the same as adalimumab, which it is not. (Ex. 1104, 4-5); *see Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 471 F.3d 1369, 1376-77 (Fed. Cir. 2006) (holding that a reference identifying compounds from the same family as the claimed compound did not anticipate). Because Gokarn Provisional does not disclose adalimumab, the Petition fails to establish any reasonable likelihood that Gokarn '011 anticipates.

B. The Petition's Anticipation Challenge Based On A Purported Small Genus Is Legally Flawed

Petitioner contends that a "POSA would have known" and been able to "immediately envision[]" from Gokarn Provisional a small genus of high-concentration antibodies including the commercial HUMIRA formulation of adalimumab. (Pet., 39.) Petitioner's small genus theory fails as a matter of law, however, because it requires improperly incorporating extrinsic evidence about the commercial HUMIRA formulation of adalimumab, which is nowhere mentioned in Gokarn Provisional. *Nidec*, 851 F.3d at 1273-75; *In re Arkley*, 455 F.2d 586, 589 (C.C.P.A. Feb. 17, 1972) ("We do not read into references things that are not there.").

Petitioner contends that its use of extrinsic evidence for anticipation is permissible because a reference anticipates "if a POSA could take its teachings in combination with the POSA's own knowledge of the particular art and be in possession of the invention." (Pet., 32 (citing *In re LeGrice*, 301 F.2d 929, 939 (C.C.P.A. May 4, 1962) and *Ex parte Morsa*, No. 2011-007576, 2014 Pat. App. LEXIS 1496, at *11 (B.P.A.I. Feb. 25, 2014)); *see also* Pet., 34-35 (citing *Helifix Ltd. v. Blok-Lok Ltd.*, 208 F.3d 1339, 1347 (Fed. Cir. 2000))). Petitioner is incorrect. The cited cases all invoked a skilled artisan's knowledge to determine whether an anticipatory reference was *enabled*, not to add elements missing from

an asserted Section 102 reference. *LeGrice*, 301 F.2d at 944; *Helifix*, 208 F.3d at 1348; *Morsa*, 2014 Pat. App. LEXIS 1496, at *11. Indeed, the Federal Circuit recently confirmed that Section 102 "does not permit the Board to fill in missing limitations simply because a skilled artisan would immediately envision them." *Nidec*, 851 F.3d at 1274-75 (reversing final written decision of anticipation).

Moreover, the Board has previously rejected Petitioner's view of anticipation law and distinguished Petitioner's cited *LeGrice* decision. *Genise*, 2003 WL 21979123, at *3 ("Genise appears to have the wrong idea as to what constitutes anticipation."). The Board confirmed that anticipation does not occur if a skilled artisan needs to fill in a missing element from a prior art reference with "with his own knowledge of the particular art [to] be in possession of the invention." *Id.* Rather, such allegations improperly assert an obvious-to-combine rationale. *Id.* The Board distinguished earlier cases, including those relied on by Petitioner, as directed to the requirement that an anticipatory reference be enabling, rather than permitting a skilled artisan's knowledge to fill in a reference's missing limitations. *Id.*; *see also Nidec*, 851 F.3d at 1274-75.

Accordingly, Petitioner's proposed anticipation ground rests on a legally deficient theory.

C. Gokarn Provisional Does Not Disclose A Small Genus Of High-Concentration Antibodies

Petitioner relies on Gokarn Provisional's statement that "antibodies at sufficiently high concentrations, possess adequate buffering capacity in the pH range of 4.0 to 6.0" as a disclosure of a small genus of high-concentration antibodies that includes adalimumab. (*See* Pet., 46; Ex. 1104, 1:5-8.) This statement fails, however, to disclose the "definite and limited class" required of an anticipatory small genus. *ArcelorMittal France v. AK Steel Corp.*, 700 F.3d 1314, 1323 (Fed. Cir. 2012) (citation omitted). Gokarn Provisional's vague mention of "sufficiently high concentrations" does not identify any particular antibody concentration. (Ex. 1104, 1.) Nor does this statement point to adalimumab or any other particular antibody. Thus, Petitioner has failed to establish disclosure of any small genus. *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1380 (Fed. Cir. 2001) (vacating anticipation where the reference disclosed "only the use of premedicants generally," not the specific classes of premedicants recited in the claims). *See also supra* Section V.A.1.b.

As discussed above, Petitioner's attempt to define its alleged genus as encompassing only antibodies that had *previously been formulated* at concentrations above 30 mg/ml contradicts Gokarn Provisional's disclosure of pharmaceutical proteins as including a large class of all types of proteins. (Pet., 38;

Ex. 1104, 2:10-15.) Gokarn Provisional also does not define any genus as having a protein concentration of 30 mg/ml or greater. Instead, it reports 30 mg/ml as the concentration at which EMAB was believed to provide an increased buffer capacity, but does not purport to extend the 30 mg/ml concentration to any other antibody or use 30 mg/ml to describe any "definite and limited class" of antibodies. (Ex. 1104, 13); *ArcelorMittal*, 700 F.3d at 1323.

Petitioner's small genus theory also invokes only an obvious-to-combine rationale, not anticipation. *Arkley*, 455 F.2d at 587-89. For example, even assuming that a skilled artisan would have been aware of the HUMIRA formulation of adalimumab at a 50 mg/ml concentration, HUMIRA was a *buffered* formulation. (Pet., 1; *see also* Ex. 1105, 470, col. 2.) Thus, a person reviewing Gokarn Provisional would have to recall extrinsic information about HUMIRA (showing it to be buffered) and then *modify* that formulation to arrive at the claimed subject matter. (Pet., 36.) The same is true for the commercial formulations (*e.g.*, the ATGAM, CAMPATH, SYNAGIS, TYSABRI, AVASTIN, and VECTIBIX products) cited by Petitioner. (Pet., 38-39; *see supra* V.A.1.b. (explaining that these products contain buffering systems.)) A skilled person's alleged extrinsic knowledge of antibodies formulated at higher concentrations in *buffered formulations* cannot disclose a small genus of antibodies formulated *without a buffering system*. *See Arkley*, 455 F.2d at 587-89.

Finally, Petitioner's reliance on the sole original claim of Gokarn Provisional is misplaced. (*See* Pet., 37-38.) While the C.C.P.A. cited an original claim as providing a narrowing disclosure towards a small genus in *In re Schaumann*, 572 F.2d 312, 316-17 (C.C.P.A. Feb. 23, 1978), the facts here are distinguishable. Claim 1 of Gokarn Provisional is directed to *any antibody*. (Ex. 1104, 14.) It is not limited to any particular class or type of antibodies. (*Id*.) It also does not limit the antibodies to those previously used in a "high concentration" formulation, let alone those previously formulated at a concentration of 30 mg/ml or greater. (*Id*.) Thus, original claim 1 further confirms that Gokarn Provisional is not directed to any alleged small genus of antibodies.

D. Petitioner's Cited *Petering* And *Ineos* Cases Are Inapposite

Petitioner relies on *In re Petering*, 301 F.2d 676 (C.C.P.A. Apr. 13, 1962) and *Ineos USA LLC v. Berry Plastics Corporation*, 783 F.3d 865 (Fed. Cir. 2015) to support its "small genus" theory. (Pet. 32-33, 38.) This reliance is misplaced. The broad disclosure of Gokarn Provisional is unlike the prior art at issue in those cases, which disclosed only a narrow genus of compounds identified by a preferred common structure. (*See id.*) In *Petering*, the reference's preferred generic structure encompassed only 20 identified compounds. 301 F.2d at 681. Similarly, in *Ineos*, a prior art reference disclosed a narrow genus of saturated fatty acid amides limited by a structure having 12 to 35 carbon atoms. 783 F.3d at 872. In view of the patent

owner's failure to present evidence concerning the size of this genus, the court held that it disclosed behenamide, which contains 22 carbon atoms and was therefore within the disclosed range of 12-35 carbon atoms. *Id.*

Unlike the prior art in *Petering* and *Ineos*, Gokarn Provisional does not describe any elements or features common to each member of any genus. (Ex. 1104, 2:10-15 (broadly disclosing vast categories encompassing all types of proteins).) It states that whether a protein can be formulated depends on the presence of "enough of the charged amino acid residues including glutamic acid, aspartic acid, histidine, arginine, and lysine . . . in high enough levels." (*Id.*, 2:18-23.) It further states that the "buffering ability of an antibody . . . arises mainly from its *solvent accessible*, polar charged amino acid residues." (*Id.*, 2:27-29.) But Petitioner fails to identify any disclosure in Gokarn Provisional explaining how many amino acid residues are sufficient, let alone any disclosure of whether, *for any given antibody*, its amino acid residues are solvent-accessible and capable of contributing to pH buffering of the formulation. There is also no evidence showing how one could determine whether antibodies contained sufficient amino acid residues compared to antibodies that did not. Accordingly, Gokarn Provisional does not disclose any "'definite and limited class' of suitable members," as required to define a small genus for anticipation. *See ArcelorMittal*, 700 F.3d at 1323 (holding that the prior art disclosure of a broad genus and single species did

not anticipate another species within that genus); *see also Zenith*, 471 F.3d at 1376 (affirming no anticipation and distinguishing *Petering* where the skilled artisan would need to selectively pick and choose elements from a genus to arrive at the claimed compounds).

Here, one would similarly have to resort to improper hindsight reasoning as well as evidence outside of the four corners of Gokarn Provisional to arrive at challenged claim 16 of the '619 patent. Compared to the deficient reference in *Zenith* that provided at least some guidance on possible chemical substituents, Gokarn Provisional provides *no guidance* on the number of amino acid residue substituents characterizing suitable antibodies, let alone which residues are solvent-accessible and therefore capable of contributing to pH control. (*See* Ex. 1104, 2:27-6:1.)

E. Gokarn Provisional Does Not Disclose Adalimumab At A Concentration Of 50 To 200 mg/ml

As addressed in *supra* Section V.A.2., Petitioner also fails to establish that Gokarn Provisional discloses any adalimumab formulation having a concentration of 50 to 200 mg/ml, as recited in claim 16. Indeed, the only concentrations disclosed for any formulation are in Gokarn Provisional's examples. (*See generally* Ex. 1104.) But each of these examples concentrated an EMAB formulation to a maximum of only 46 mg/ml or 45 mg/ml at which point the solutions became

"cloudy." (*Id.*, 4-5.) Thus, the maximum antibody concentration disclosed in Gokarn Provisional is somewhere below 46 mg/ml, not the claimed 50-200 mg/ml. Gokarn Provisional attempts, by theoretical extrapolation, to predict the *buffering capacity* of an EMAB solution at 50 mg/ml (*see, e.g., id.,* 9), but it never discloses any EMAB solution capable of achieving a 50 mg/ml concentration. *See Atofina v. Great Lakes Chem. Corp*., 441 F.3d 991, 999-1000 (Fed. Cir. 2006) (rejecting anticipation argument that undisclosed contact times could have been "typically and easily determined through calculation" by one of ordinary skill.) Thus, Gokarn Provisional does not disclose any adalimumab formulation with a concentration of 50-200 mg/ml.

F. Gokarn Provisional Does Not Disclose An Adalimumab Formulation In Which The Formulation Lacks A Buffering System

Petitioner also fails to establish that Gokarn Provisional describes a formulation of adalimumab that "does not comprise a buffering system," as recited in claim 16. (Ex. 1101, 152:31-22.) Gokarn Provisional's two examples provide EMAB—not adalimumab—in a solution with a *buffering system*. (Ex. 1104, 4-5.) Gokarn Provisional also states that "traditional buffering agents may be present in the formulation." (*Id.*, 1:18-19.) While Gokarn Provisional attempts to predict the buffering-capacity performance of an EMAB solution without a buffering system, it concedes that "[a] more accurate estimate of the buffer capacity from EMAB

alone will have to be obtained from bufferless high concentration EMAB solutions." (*Id.*, 13.) Gokarn Provisional, however, only states that such investigations were "on-going" and does not disclose any "bufferless, high concentration EMAB solutions," let alone an *adalimumab* formulation lacking a buffering system. (*Id.*) Accordingly, Gokarn Provisional's disclosure does not anticipate. *Arkley*, 455 F.2d at 587-89 (Section 102 rejections are proper only when the claimed subject matter is identically disclosed in the prior art).

Because Gokarn Provisional discloses different solutions of a different antibody, it does not support Petitioner's assertion that a skilled artisan would "immediately envision" adalimumab that was "buffer-free" from its disclosure. As a result, the Petition's proposed ground fails to comport with anticipation legal principles. *Arkley*, 455 F.2d at 587-89; *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1370-71 (Fed. Cir. 2008). The Petition should be denied.

VII. Conclusion

Petitioner does not establish that Gokarn '011 is prior art. Nor does Petitioner show that any challenged claim is anticipated. For these reasons, and those discussed above, Petitioner fails to establish a reasonable likelihood that any of the challenged claims are unpatentable. The Board should deny institution.

Dated: June 11, 2017

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

I, the undersigned, certify that the above Preliminary Response to Petition complies with the applicable type-volume limitations of 37 C.F.R. § 42.24(b)(1). Exclusive of the portions exempted by 37 C.F.R. § 42.24(a), this Preliminary Response, including footnotes, contains 8,010 words, as counted by the word count function of Microsoft Word. This is less than the limit of 14,000 words as specified by 37 C.F.R. § 42.24(a)(1)(i).

Dated: June 11, 2017

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), I certify that I caused to be served on the counsel for Petitioner a true and correct copy of the foregoing Patent Owner's Preliminary Response by electronic means on June 11, 2017 at the following email addresses of record:

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