

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

THORNE RESEARCH, INC. and THORNE HEALTHTECH, INC.,
Petitioners,

v.
CHROMADEX, INC.,
Patent Owner.

IPR2026-00400
U.S. Patent No. 12,252,506

PATENT OWNER'S PRELIMINARY RESPONSE

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EXHIBIT LIST

Exhibit	Description
2001	Conference and Scheduling Order, Case No. 2:26-cv-01758-RMG (D.S.C.)
2002	Complaint for Declaratory Judgment, Case No. 2:26-cv-01758-RMG (D.S.C.)
2003	Notice of Filing Proof of Service, Case No. 2:26-cv-01758-RMG (D.S.C.)
2004	U.S. Patent No. 11,981,698 to Migaud et al.
2005	U.S. Patent No. 11,584,770 to Migaud et al.
2006	U.S. Patent No. 10,815,262 to Migaud et al.
2007	U.S. Patent No. 10,000,519 to Migaud et al.
2008	U.S. Patent No. 10,815,262 File History
2009	U.S. Patent Publication No. 2018/0186824 to Migaud et al.
2010	Answer and Counterclaim, Case No. 2:26-cv-01758-RMG (D.S.C.)
2011	Declaration of Ron Bihovsky, Ph.D in support of Patent Owner's Preliminary Response
2012	Curriculum Vitae of Dr. Ron Bihovsky
2013	Clayden et al., Organic Chemistry (2 nd ed. 2012)
2014	U.S. Patent Application Publication No. 2005/0010603 A1

ChromaDex, Inc. (“Patent Owner”) submits this Patent Owner’s Preliminary Response to Thorne Research, Inc. and Thorne HealthTech, Inc.’s (collectively, “Petitioner”) petition seeking *inter partes* review (“IPR”) of U.S. Patent No. 12,252,506 (“the ‘506 patent”).

I. INTRODUCTION

Petitioner’s challenge sets forth no prior art that predates the ’506 Patent’s July 29, 2013 priority date. For that reason alone, the petition should be denied institution. Instead, the entire challenge relies on the flawed presumption that the ’506 Patent is not entitled to the priority date of its parent application which contains a nearly identical disclosure, GB 1313465.5 (EX1003).

The petition therefore rises or falls on a single premise: that the challenged claims are not entitled to any priority date earlier than April 26, 2023, the filing date of the application that issued as the ’506 patent, almost ten years after the priority date from the related parent application.

Petitioner’s theory is that R₆, R₇, and R₈ in the claimed compound of formula (IV) cannot be hydrogen because the priority documents purportedly only define those substituents as “hydroxyl-protecting groups.” This premise is demonstrably wrong.

First, the GB Priority Document itself shows that the inventors possessed compounds in which R₆, R₇, and R₈ are hydrogen. It discloses formula (I)—

structurally identical to formula (IV) with hydrogen at those positions—and Figure 1, which depicts nicotinamide riboside and related molecules with free hydroxyls, and it provides element-by-element support for every limitation of claim 1. Indeed, the Petition itself admits the shared specification “depicts its formula (I) having H at positions corresponding to R₆–R₈ of formula (IV)” Pet., 37. Under settled law, such disclosure through “words, structures, figures, diagrams, formulas” satisfies the written-description requirement and confirms possession. *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997). The challenged claims are therefore entitled to the July 29, 2013 priority date.

Second, the claim language is clear and recites no “logical impossibility.” Claim 1 provides that R₆, R₇, and R₈ “are each independently H or a hydroxyl-protecting group,” and the disjunctive “or” means each position may be either hydrogen or a protecting group—not both simultaneously. The purported “contradiction” exists only if one first accepts Petitioner’s false premise that the specification restricts these positions to hydroxyl-protecting groups. Petitioner does not once allege lexicography or disavowal, and the “as defined above” argument of the petition ignores explicit disclosures “above.” Instead, the Petitioner manufactures the “logical impossibility” argument by improperly importing an embodiment from the specification into the claims—the very approach the Federal Circuit has repeatedly condemned. *See, e.g., SuperGuide Corp. v. DirecTV Enters.*,

Inc., 358 F.3d 870, 875 (Fed. Cir. 2004). Because the claim language is broader than the working examples, and there are no “words or expressions of manifest exclusion or restriction,” the claims may not be confined to embodiments in which all three positions bear protecting groups.

Third, the '262 patent and its prosecution history confirm that R₆, R₇, and R₈ may each independently be hydrogen. The '262 patent—a great-grandparent of the '506 patent that shares an identical specification—claims formula (III) compounds in which those positions may each be H, and the USPTO allowed that claim without a new-matter rejection. That prosecution history refutes the Petition’s assertion that the '506 patent is the first patent in the family that discloses hydrogen at R₆, R₇, and R₈. The patent office has now twice confirmed the § 112 support for hydrogen at those positions.

At bottom, Thorne’s petition fails because neither the '184 Publication (published June 16, 2016) nor GRAS Notice 635 (2016) qualifies as prior art—in fact, they come nearly three years after the priority date of the '506 patent. Thorne’s attempt to break the priority chain of the '506 patent is internally inconsistent and contradicted by the intrinsic record. The Board should deny institution under 35 U.S.C. § 314(a).

II. BACKGROUND

Nicotinamide riboside (“NR”) is a form of vitamin B3 and a precursor to NAD⁺, a coenzyme involved in cellular metabolism. NAD⁺ levels naturally decline with age and metabolic stress, and NR supplementation has been reported to increase the body’s supply of NAD⁺, thereby supporting the cellular processes that depend on NAD⁺. Those processes include the conversion of food into usable cellular energy and the maintenance of mitochondrial function. Increased NAD⁺ availability has also been associated with activation of sirtuins, proteins linked to DNA repair, stress resistance, and other markers of healthy cellular aging, and clinical research has reported that NR supplementation may reduce certain inflammatory markers and cytokines in the blood. These reported benefits underscore why reliable methods for preparing NR and related compounds in suitable forms for nutritional use are important.

Academic scientists, including Dr. Charles Brenner, have made foundational discoveries that generated modern scientific interest in NR. ChromaDex built on that work by licensing defined university technologies, conducting NR-related research and development through its own scientists, and undertaking the development needed to translate laboratory science into reliable commercial products. In 2013, ChromaDex commercialized food-grade NIAGEN[®], its proprietary nicotinamide riboside chloride ingredient. ChromaDex supplies NIAGEN[®] to customers that

formulate dietary supplements, while Niagen Bioscience and its consolidated subsidiaries market and sell finished TRU NIAGEN[®] oral dietary supplements containing NIAGEN[®].

ChromaDex has also conducted NR research through its own scientists and supported independent investigators by supplying characterized materials and technical support. Its patent, licensing, manufacturing, regulatory, research, and supply activities form parts of the operating platform through which it has made NR products and defined NR technologies commercially available.

III. THE '506 PATENT

The '506 patent, titled “Methods of Preparing Nicotinamide Riboside and Derivatives Thereof,” issued on March 18, 2025, from Application No. 18/307,733 filed April 26, 2023. EX1001. The named inventors are Marie Migaud, Philip Redpath, Kerri Crossey, and Mark Doherty. EX1001 at (71), (73); EX1023.

The '506 patent claims priority through a chain of continuation applications to GB Patent Application No. 1313465.5, filed July 29, 2013 (the “GB Priority Document,” EX1003). Specifically, the '506 patent is a

[c]ontinuation of application No. 17/736,834, filed on May 4, 2022, now Pat. No. 11,981,698, which is a continuation of application No. 16/886,985, filed on May 29, 2020, now Pat. No. 11,584,770, which is a continuation of application No. 15/905,922, filed on Feb. 27, 2018, now Pat. No. 10,815,262, which is a continuation of application No. 14/908,831, filed as application No. PCT/EP2014/065971 on Jul. 24, 2014, now Pat. No. 10,000,519[, which claims priority to GB Patent Application No. 1313465.5, filed July 29, 2013].

See EX1001, cover page.

The technology disclosed in this family of applications concerns novel salts of nicotinamide riboside (“NR”) and related compounds, and methods of synthesis of these compounds and their salts.

Independent claim 1 of the ’506 Patent recites, in relevant part:

“A compound of formula (IV) . . . or the beta-anomer thereof, where: n is 0 and Y is absent; m is 1; R₁ is a substituted or unsubstituted primary amino; R₂-R₅ are each H; **R₆, R₇ and R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group**; or wherein R₆ is a phosphate; and X⁻ is an anion selected from [specified anion classes].” EX1001, claim 1 (emphasis added).

The disjunctive language—“each independently H *or* a hydroxyl-protecting group”—explains that each of R₆, R₇, and R₈ can independently be hydrogen or a hydroxyl-protecting group. Thorne’s entire challenge rests upon casting aside this disjunctive language and interpreting the ’506 specification such that (1) R₆, R₇, and R₈ are limited to hydroxyl-protecting groups and (2) that it is a “logical impossibility” for hydrogen to be a hydroxyl-protecting group. *See, e.g., Pet.*, 7–8.

IV. THE CITED REFERENCES

As detailed below, both of the references relied upon by Thorne postdate the July 29, 2013 earliest priority date by nearly three years. Neither qualifies as prior art. Thorne’s efforts to strip the ’506 patent of its priority claim based on alleged deficiencies in the same disclosure that Thorne contends anticipates the claims fall flat. And Thorne’s grounds fail for reasons set forth herein.

A. The '184 Publication (EX1022)

U.S. Pre-Grant Publication No. 2016/0168184 A1 (the "'184 publication") was published on June 16, 2016. EX1022. Critically, the '184 publication is the pre-grant publication corresponding to U.S. Patent 10,000,519, the first non-provisional application in the series of continuation applications to which the '506 patent claims priority. Thus, the '184 publication shares an essentially identical specification, including the same chemical structures, figures, and detailed description, and therefore has the same disclosure as the '506 patent itself.

B. GRAS Notice No. 635 (EX1017)

GRAS Notice No. 635 was filed with the FDA on March 29, 2016, and its review period closed on August 3, 2016. EX1017, EX1018. It concerns the use of nicotinamide riboside chloride as a dietary supplement ingredient and specifies certain manufacturing quality parameters. Thorne relies on this reference only for Ground 2 (obviousness of claims 29–30 and 32–33 relating to purity and solvent limits).

V. LEVEL OF ORDINARY SKILL IN THE ART

For purposes of this preliminary response only, Patent Owner applies the same skill level proposed by Petitioner. *See* Pet., 9.

VI. LEGAL STANDARDS

A. Claim Construction

Claim terms “are generally given their ordinary and customary meaning,” which is “the meaning that the term would have to a person having ordinary skill in the art in question at the time of the invention.” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc) (citations omitted). To determine that meaning, claims must “be read in view of the specification, of which they are a part.” *Id.* at 1315 (citations omitted). However, courts must not limit a claim based on limitations in the specification that are not part of the claim, and “as a general rule claims of a patent are not limited to the preferred embodiment ... or to the examples listed within the patent specification.” *Glaxo Wellcome, Inc. v. Andrx Pharms., Inc.*, 344 F.3d 1226, 1233 (Fed. Cir. 2003) (quoting *Dow Chem. Co. v. United States*, 226 F.3d 1334, 1342 (Fed. Cir. 2000)). Indeed, “a particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment. *SuperGuide*, 358 F.3d at 875.

The Federal Circuit has consistently held we “depart from the plain and ordinary meaning of claim terms based on the specification in only two instances: lexicography and disavowal.” *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1371 (Fed. Cir. 2014) (quoting *Thorner v. Sony Computer Ent. Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012)); *see also Luminara Worldwide, LLC v. Liown Elecs.*

Co., 814 F.3d 1343, 1353 (Fed. Cir. 2016). “The standards for finding lexicography and disavowal are exacting. ‘To act as its own lexicographer, a patentee must clearly set forth a definition of the disputed claim term other than its plain and ordinary meaning’ and must ‘clearly express an intent to redefine the term.’” *Hill-Rom*, 755 F.3d at 1371 (quoting *Thorner*, 669 F.3d at 1365).

Concerning the role of the preamble, the Federal Circuit has held that “when the claim drafter chooses to use both the preamble and the body to define the subject matter of the claimed invention, the invention so defined, and not some other, is the one the patent protects.” *Bell Commc’ns Rsch., Inc. v. Vitalink Commc’ns Corp.*, 55 F.3d 615, 620 (Fed. Cir. 1995) (citing *In re Paulsen*, 30 F.3d 1475, 1479, 31 USPQ2d 1671, 1673 (Fed.Cir.1994)).

The surrounding claims are also informative, with the Federal Circuit noting “[o]ther claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment as to the meaning of a claim term.” *Phillips*, 415 F.3d at 1314.

B. Priority

To establish priority, Patent Owner need only show that the earlier application discloses the claimed invention “in the manner provided by the first paragraph of section 112.” 35 U.S.C. § 120. Section 112 requires that “[t]he specification shall contain a written description of the invention, and of the manner and process of

making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same.” 35 U.S.C. § 112.

1. Written Description

As to written description, it is sufficient that the priority document “reasonably conveys to those skilled in the art that the inventor had possession” of the claimed subject matter. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). In the chemical arts, this showing may be made through “words, structures, figures, diagrams, formulas, etc.” *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d at 1566. Written-description support may be found in the specification as a whole, including the originally-filed claims, or any other portion of the originally-filed specification. *See In re Koller*, 613 F.2d 819, 823 (CCPA 1980); *see also In re Gardner*, 475 F.2d 1389, 1391 (CCPA 1973); *Application of Wertheim*, 541 F.2d 257, 264 (C.C.P.A. 1976).

2. Enablement

As to enablement, claims are enabled when, at the effective filing date of the patent, one of ordinary skill in the art could practice their full scope without undue experimentation. *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013). Factors relevant to whether a disclosure requires undue experimentation include: (1) quantity of experimentation necessary; (2) amount of direction or

guidance presented; (3) the presence or absence of working examples; (4) nature of the invention; (5) state of the prior art; (6) relative skill of those in the art; (7) predictability or unpredictability of the art; and (8) breadth of the claims. *Impax Labs., Inc. v. Aventis Pharms., Inc.*, 545 F.3d 1312, 1314–15 (Fed. Cir. 2008) (quoting *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)).

C. Anticipation

“Anticipation requires the presence in a single prior art disclosure of all elements of a claimed invention arranged as in the claim.” *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983) (citing *Soundsciber Corp. v. U.S.*, 360 F.2d 954, 960, 148 USPQ 298, 301 (Ct.Cl.1966)). In other words, a prior art reference anticipates “when the four corners of [that] ... document describe every element of the claimed invention, either expressly or inherently, such that a [POSITA] could practice the invention without undue experimentation.” *VirnetX Inc. v. Apple Inc.*, 665 F. App’x 880, 885 (Fed. Cir. 2016) (quoting *Spansion, Inc. v. Int’l Trade Comm’n*, 629 F.3d 1331, 1356 (Fed. Cir. 2010)).

VII. CLAIM CONSTRUCTION

Petitioner does not propose any terms for construction. Instead, Petitioner attempts to override the plain claim language by importing a purported definitional limitation from an example in the specification, arguing that R₆, R₇, and R₈ are limited to hydroxyl-protecting groups.

Patent Owner does not propose any terms for construction. Patent Owner and its expert have applied the plain and ordinary meaning of all claim terms in the analysis presented herein.

VIII. ARGUMENT

The Petition's two grounds of unpatentability rest exclusively on references published in 2016, after the July 29, 2013 priority date claimed by the '506 patent. The '184 Publication published on June 16, 2016 (EX1022); GRAS Notice 635 was filed March 29, 2016 (EX1017). Both references are prior art only if Petitioner can establish that the challenged claims are not entitled to any priority date before 2016. It cannot.

Thorne's IPR Petition is based on a very narrow reading of the '506 patent: (1) formula (IV) is defined in terms of an earlier structure referred to as formula (III) in the '506 Patent and all predecessor applications, and (2) formula (III) exclusively defines R₆–R₈ as hydroxyl protecting groups, not hydrogen. Pet., 12-15. However, this reading is both factually and legally flawed.

The Petition's sole theory for stripping priority is that the GB Priority Document and intermediate family members fail to enable and provide written description support for the recitation in claim 1 that R₆, R₇, and R₈ may be "H" because those documents purportedly only define R₆–R₈ as "hydroxyl-protecting

groups.” Pet., 13–14; EX1013, ¶¶ 43–78. This theory is wrong for multiple independent reasons.

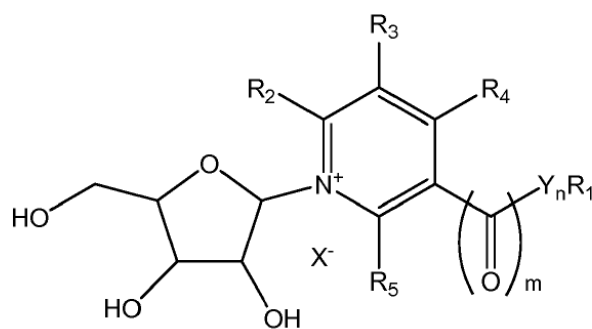
A. The GB Priority Document Supports and Enables R₆–R₈ May be H

The GB Priority Document, which antedates the ’184 publication, shows that the inventors of the ’506 patent were in possession of the claimed genus of compounds in the ’506 patent where R₆, R₇, and R₈ each may be hydrogen (H). For instance, the GB Priority Document (EX1003, p. 2)¹ discloses a generic structure of formula (I) which is a cationic pyridinium heterocycle with an optional carbonyl-containing group at the 3-position bonded to C1’ of ribofuranose:

¹ Pages cited in EX1003 refer to the native pagination contained in the document.

Summary of the Invention

According to the present invention, there is provided a method of preparing a compound of formula
 25 (I)



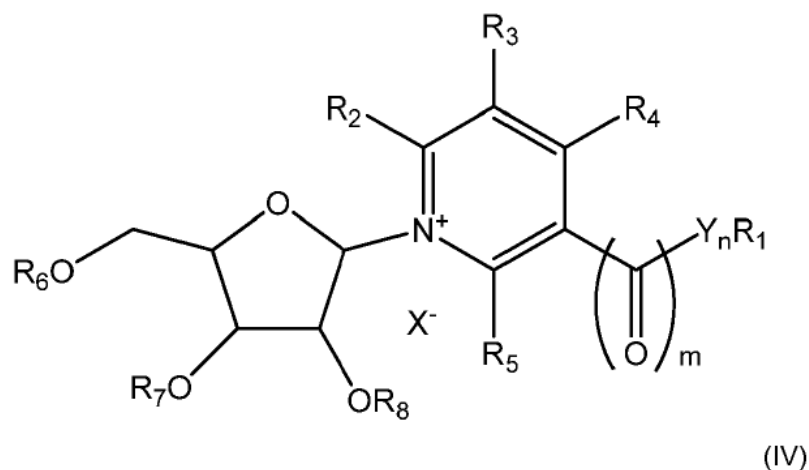
(I)

30 wherein

n is 0 or 1;

(EX1003, p. 2); EX2011 ¶ 63. The GB Priority Document (EX1003, p. 10) also discloses formula (IV) which retains the same pyridinium-ribose core but generalizes the three ribose hydroxyl positions, with R₆, R₇, and R₈ on the oxygen atoms bonded to the C2', C3', and C5' carbons:

30

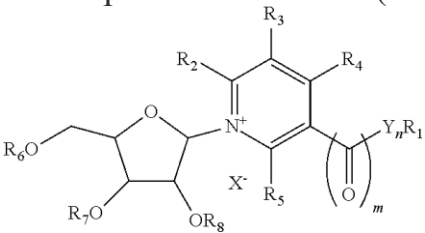
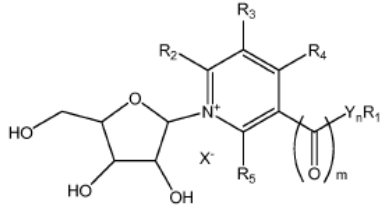
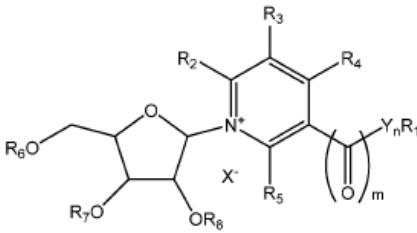


wherein

(EX1003, p. 10); EX2011 ¶¶ 64–65. A POSITA viewing these structures would immediately understand that the structure of formula (I) is equivalent to the structure of formula (IV) wherein R_6 , R_7 , and R_8 are each hydrogen atoms. EX2011 ¶¶ 62–65. As Dr. Bihovsky explains, formula (IV) is simply a class of structures that contains a smaller class of structures, formula (I). EX2011 ¶ 65. These formula (I) and formula (IV) structures in the GB Priority Document (EX1003, at 2, 10, Fig. 2) are equivalent to the formula (I) and formula (IV) structures disclosed in the ‘506 Patent (EX1001, at 4, 8, 11).

1. Element-by-element Support in the GB Priority Document

Every element of Claim 1 finds support in the GB Priority Document, including as described above:

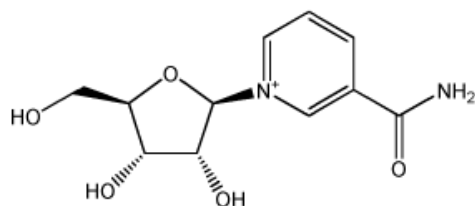
Claim 1 of '506 (EX1001)	GB Priority Document (EX1003)
A compound of formula (IV):  or the beta-anomer thereof, where:	Summary of the Invention According to the present invention, there is provided a method of preparing a compound (I)  (I)  (IV) EX1003 at 2, 10
n is 0 and Y is absent;	“n is 0 or 1” – EX1003, p. 2; Claim 1
m is 1;	“m is 0 or 1” – EX1003, p. 2; Claim 1
R ₁ is a substituted or unsubstituted primary amino;	“R ₁ is selected from . . . substituted or unsubstituted primary or secondary amino . . .” – EX1003, p. 2; Claim 1
R ₂ -R ₅ are each H;	“R ₂ -R ₅ , which may be the same or different, are each independently selected from H . . .” – EX1003, p. 2; Claim 1
R ₆ , R ₇ and R ₈ , which may be the same or different, are each independently	(see below)
H	formula (I) – EX1003, p. 2 (showing unprotected hydroxyls at C2', C3' and C5', R ₆ , R ₇ , and R ₈ are each H); Fig. 1 (nicotinamide riboside with free -OH groups at all three positions); p. 9 (R ₆ , R ₇ , and R ₈ may each <i>independently</i> be hydrogen because the specification discloses that optionally at least two of them are hydroxyl protecting groups);
or a hydroxyl-protecting group;	formula (IV) – EX1003, p. 9;

	(“Optionally, the R ₆ , R ₇ and R ₈ moieties are selected from substituted and unsubstituted acetyl, and substituted and unsubstituted benzoyl. Optionally, at least two of R ₆ , R ₇ and R ₈ are selected from unsubstituted acetyl or unsubstituted benzoyl.”)
or wherein R ₆ is a phosphate; and	Figure 1 – EX1003 (showing nicotinamide mononucleotide and nicotinate mononucleotide with phosphate); “Figure 1 shows the β-anomer forms of nicotinamide riboside, nicotinate riboside, nicotinamide mononucleotide and nicotinate mononucleotide, without counter ions” – EX1003, p. 16
X ⁻ is an anion selected from an anion of a substituted carboxylic acid, an anion of an unsubstituted carboxylic acid other than an anion of formic acid, an anion of a substituted or unsubstituted phosphate, an anion of a substituted or unsubstituted sulfate, an anion of a substituted or unsubstituted carbonate, and an anion of a substituted or unsubstituted carbamate.	“X ⁻ is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted sulfonate, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate” – EX1003, p. 3

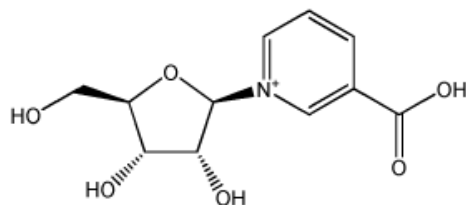
EX2011 ¶ 66. This element-by-element correspondence demonstrates that the GB Priority Document conveys possession of the claimed invention as recited in claim 1 of the '506 Patent. *Id.*; EX1001, Claim 1, 18:20-52. The claims of the '506 Patent are entitled to the July 29, 2013 priority date.

2. Figure 1 Discloses the Structure of Formula (IV) with R₆–R₈ = H

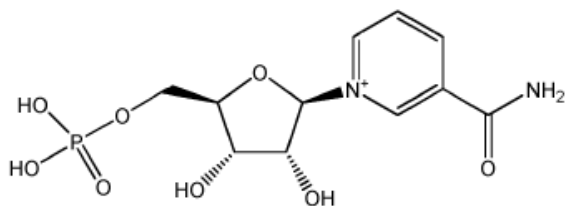
Figure 1 of the GB Priority Document depicts nicotinamide riboside and related structures (nicotinate riboside, nicotinamide mononucleotide, nicotinate mononucleotide) with free hydrogens at the R₆, R₇, and R₈ positions, as well as phosphates at the R₆ position:



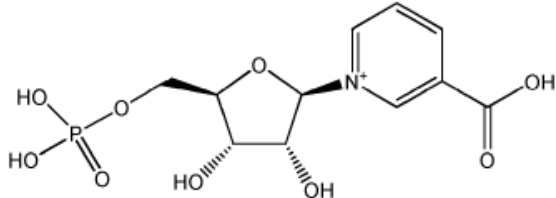
Nicotinamide riboside



Nicotinate riboside



Nicotinamide mononucleotide



Nicotinate mononucleotide

Figure 1

1/5

EX2011 ¶¶ 69–70; (EX1003, Figure 1). The '506 Patent contains an identical Figure 1 depicting the same molecules. (EX1001, p. 3). All four formulas depicted in Figure 1 are within the class of structures defined by formula (IV), while the first two

(nicotinamide riboside and nicotinate riboside) also fall within the class of structures defined by formula (I). EX2011 ¶¶ 69–74. Thus, a POSITA would understand that disclosures of formula (I) are also disclosures of formula (IV), wherein R_6 – R_8 are each H. *Id.* The Petition even confirms this understanding in its invalidity analysis, noting that the “’184 Publication depicts its formula (I) having H at positions corresponding to R_6 – R_8 of formula (IV).” Pet., 37.

As Dr. Bihovsky explains, a POSITA would understand that nicotinamide riboside could be described by either of the below recitations:

- A compound of formula (I) wherein n is 0, m is 1, R_1 is NH_2 , and R_2 – R_5 are H.
- A compound of formula (IV) wherein n is 0, m is 1, R_1 is NH_2 , and R_2 – R_5 are H, and R_6 – R_8 are H.

EX2011 ¶ 74. Put another way, these are two different ways to describe the same compound. *Id.* Likewise, a POSITA would understand that nicotinate riboside could be described by either of the below recitations:

- A compound of formula (I) wherein n is 1, m is 1, Y is O, and R_1 – R_5 are H.
- A compound of formula (IV) wherein n is 1, m is 1, Y is O, and R_1 – R_8 are H.

Id.

The disclosure of species compounds with all free hydroxyls bonded to the C2', C3', and C5' carbons of the riboside ring supports possession of the broader genus (formula (IV) where R_6 – R_8 may each independently be H or a protecting group). *See Ariad*, 598 F.3d at 1349-50 (“[A]n adequate written description of a

claimed 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.”).

B. There is no “Logical Impossibility” and the Full Scope of the Claims is Disclosed and Enabled

1. The Claim Language is Clear

The Petition incorrectly asserts that the claims “recite a logical impossibility” because they “require formula (IV), which by definition has R_6 – R_8 hydroxyl-protecting groups, yet also recite R_6 – R_8 as hydrogen” Pet., 7–8; EX2011 ¶¶76–77. Contrary to the arguments asserted in the Petition, the claims of the ’506 patent (e.g., claim 1) do *not* require that R_6 – R_8 be simultaneously hydrogen *and* a hydroxyl-protecting group. *Id.* That purported contradiction exists only if one first accepts Petitioner’s false premise that the specification restricts R_6 – R_8 to hydroxyl-protecting groups, which Petitioner then says conflicts with the ’506 patent claims’ express language allowing those same positions to be hydrogen. *Id.*

Furthermore, the claim language is clear in reciting that the functional groups R_6 – R_8 “may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R_6 is a phosphate.” EX1001, Claim 1. As Dr. Bihovsky explains, the specification of the ’506 patent, as well as its priority applications, provide support for this limitation. EX2011 ¶ 60. The claim uses the disjunctive “or”: each position is *independently* hydrogen **or** a hydroxyl-protecting group. EX1001,

Claim 1; EX2011 ¶ 76. There is no “impossibility” that requires R₆–R₈ to be simultaneously a hydroxyl-protecting group and hydrogen—only manufactured confusion set forth by Petitioner and Dr. Prestwich.

2. There is no Lexicography or Disavowal

Not once does the Petition identify where the ’506 patentee acts as a lexicographer and explicitly defines that R₆–R₈ must be a hydroxyl protecting group in formula (IV), because the patentee did no such thing. *See* EX2011 ¶¶ 77–79. Instead, pointing to disclosures of formula (III) and formula (IV) described explicitly as “optional” by the specification, the Petition argues:

The priority documents each explain that for formula (IV), “n, m, Y **R₁–R₈** and X[–] are *as defined above*” This, in turn, directs the POSA to the definition for R₁–R₈ immediately above formula (IV), which is the disclosure of formula (III). The priority documents uniformly describe formula (III) . . . “wherein n, m, Y, and R₁–R₅ are as defined above; and **R₆, R₇, and R₈**, which may be the same or different *are each independently a hydroxyl-protecting group*.”

Pet., 13–14. This hardly amounts to the *exacting* standard required for a determination that a patentee acted as its own lexicographer which the patentee “clearly express[es] an intent to redefine the term.” *Hill-Rom*, 755 F.3d at 1371; *see also Parkervision, Inc. v. Vidal*, 88 F.4th 969, 976 (Fed. Cir. 2023) (“The patentee’s use of the phrases “as used herein” and “refer to” conveys an intent for sentence 5 to be definitional.”). The language from the specification explained that

“*Optionally*, the compound of formula (III) is prepared by reacting a compound of formula (IV). EX2011 ¶¶ 79–81.

By contrast, the ’506 patent did plainly act as its own lexicographer for nine terms in the disclosure, as shown by the following excerpts:

- As used herein, the term “activated charcoal” is intended to mean a carbon containing material processed to be highly porous thereby increasing the surface area of the material. The term “activated charcoal” is intended to be synonymous with the term “activated carbon”. The activated charcoal may be in the form of powders and/or fibres and/or granules and/or pellets. (EX1001, 4:26–32).
- As used herein, the term “substituted” is intended to mean that any one or more hydrogen atoms is replaced with any suitable substituent, provided that the normal valency is not exceeded and the replacement results in a stable compound. (EX1001, 5:41–44).
- As used herein, the term “alkyl” is intended to mean a substituted or unsubstituted, saturated or unsaturated, optionally saturated, linear, branched or cyclic, aliphatic hydrocarbon, having from 1 to 12 carbon atoms, optionally from 1 to 10 carbon atoms, further optionally from 1 to 8 carbon atoms, still further optionally from 1 to 6 carbon atoms, even still further optionally 1 or 2 or 3 or 4 or 5 carbon atoms. (EX1001, 5:53–60).
- As used herein, the term “alkenyl” is intended to mean a substituted or unsubstituted, linear, branched or cyclic, aliphatic hydrocarbon, having at least one carbon-carbon double bond, and having from 2 to 12 carbon atoms, optionally from 2 to 10 carbon atoms, further optionally from 2 to 8 carbon atoms, still further optionally from 2 to 6 carbon atoms, even still further optionally 2 or 3 or 4 or 5 carbon atoms. (EX1001, 5:65–6:5).
- As used herein, the term “alkynyl” is intended to mean a substituted or unsubstituted, linear, branched or cyclic, aliphatic hydrocarbon, having at least one carbon-carbon triple bond, and having from 2 to 12 carbon atoms, optionally from 2 to 10 carbon atoms, further optionally from 2 to 8 carbon atoms, still further optionally from 2 to 6 carbon atoms, even still further optionally 2 or 3 or 4 or 5 carbon atoms. (EX1001, 6:7–13).

- As used herein, the term “aryl” is intended to mean a substituted, unsubstituted, monocyclic or polycyclic, aromatic hydrocarbon. Suitable aryls include, but are not limited to, substituted or unsubstituted phenyl, and substituted or unsubstituted heteroaryl. (EX1001, 6:16–20).
- As used herein, the term “ester-type protecting group” is intended to mean a protecting group that forms an ester bond for the purpose of hydroxyl protection and which may be substituted or unsubstituted. (EX1001, 7:22–25).
- As used herein, the term “ether-type protecting group” is intended to mean a protecting group that forms an ether bond for the purpose of hydroxyl protection and which may be substituted or unsubstituted. (EX1001, 7:29–32).
- As used herein, the term “silyl-type protecting group” refers to a protecting group that forms a silyloxy bond for the purpose of hydroxyl protection. (EX1001, 7:36–38).

These passages show that the '506 patentee clearly knew how to act as its own lexicographer when it wanted to do so. The absence of such clear definitional language in the passages relating to R_6 – R_8 in formulas (III) and (IV), along with the use of words such as “optionally,” indicate that the '506 patentee did not explicitly define R_6 – R_8 as Petitioner suggests. EX2011 ¶¶ 77–85.

Likewise, the Petition identifies no instances of disavowal in the prosecution history of the '506 Patent or any of its family members. As discussed in connection with the '262 Patent in Section VIII.B, the prosecution history of related patents actually contradicts the Petition's assertion that R_6 – R_8 may be hydrogen “did not appear in any of the pre-2023 patent applications to which the '506 patent claims priority.” Pet., 7–8.

3. Formula (IV) Compounds Are Not Limited By Embodiments of Formula (III) Compounds

Petitioner's lack of written-description argument, which is central to its attempt to break the priority chain of the '506 patent, rests on a premise the '506 patent specification does not contain any disclosure that R₆–R₈ can be hydrogen. According to Petitioner, because formula (III) compounds purportedly must have hydroxyl-protecting groups at R₆, R₇, and R₈, and because those compounds purportedly must be synthesized from formula (IV) compounds, formula (IV) must likewise have hydroxyl-protecting groups at those positions. But the specification never requires formula (III) compounds to be synthesized from formula (IV) compounds. EX2011 ¶¶ 80–82. As detailed below, Petitioner reaches that conclusion only by replacing the specification's permissive language with a mandatory limitation of its own making.

The specification states: “Optionally, the compound of formula (III) is prepared by reacting a compound of formula (IV)”. EX1001, 8:15-34. The word “optionally” cannot reasonably be read to mean “necessarily” or “exclusively” as Petitioner apparently urges. It identifies the conversion of formula (IV) to formula (III) as one disclosed route, not as a requirement that governs every formula (III) compound or restricts the universe of formula (IV) compounds. EX2011 ¶¶ 80–82. Petitioner's argument thus depends on deleting “optionally” from the specification and substituting a mandatory synthetic scheme that the inventors did not describe.

The specification's description of Figure 2 is even more explicit. It states that Figure 2 "depicts Scheme A," which illustrates "in general terms, that compounds of formula (IV) may be used to prepare compounds of formula (III), as described in Example 1." EX1001, 12:13–18. The specification then uses the same permissive formulation for the subsequent steps, explaining that formula (III) compounds "may be used" to prepare formula (II) compounds and that formula (II) compounds "may be used" to prepare formula (I) compounds. *Id.* at 12:16-20. The repeated phrase "may be used" describes possible synthetic pathways. EX2011 ¶¶ 79–82. It does not establish that formula (IV) compounds must serve as precursors to formula (III) compounds, much less that every formula (IV) compound must possess the structural features required for a formula (III) intermediate. *Id.*

Figure 2 therefore confirms that the formula (IV)-to-formula (III) conversion is a disclosed route through the specification's examples, not a universal definition of formula (IV). EX2011 ¶¶ 81–82. The specification introduces those examples in Figure 2 as "accompanying, non-limiting examples and drawings," further undercutting Petitioner's attempt to turn the illustrated route into a requirement that formula (III) compounds be exclusively synthesized from formula (IV) compounds. *Id.* at 12:7-9.

The petition further cites the priority documents' guidance that R₆, R₇, and R₈ "are required to be lipophilic *to the extent that* the reduced compound of formula

(III), once prepared, migrates into the organic phase of the bi-phasic reaction medium.” Pet., 24 (emphasis added); *see also* EX1001 at 8:66–9:4. But again, this is clearly one *example* set forth in the specification for an instance where an organic solvent is utilized for separation, not a recitation of what the invention *must* comprise. EX2011 ¶¶ 84–85. Indeed, as Dr. Bihovsky notes, there are other well-known methods of separation that would not require lipophilic protecting groups. EX2011 ¶ 85. The Petitioner’s attempt to break the priority chain by narrowly reading formula (IV) compounds in terms of optional embodiments of formula (III) should not stand.

4. Petitioner’s “As Defined Above” Argument Ignores the Specification’s Actual Structure and Depends on a Selective Reading of the Disclosure

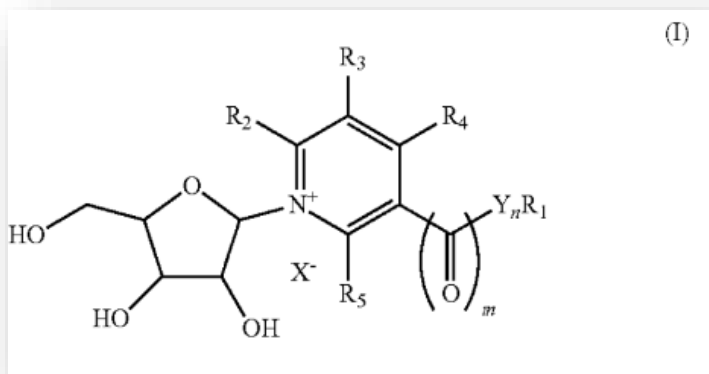
i. The Petitioner’s Narrow Reading of the Specification Should be Rejected

Petitioner’s written-description challenge hinges on a remarkably narrow—and self-serving—interpretation of a single phrase. According to Petitioner, when the specification introduces formula (IV) and states that “wherein n, m, Y, R₁–R₈ and X[–] are as defined above,” the phrase “as defined above” allegedly incorporates only the immediately preceding description of formula (III), which states that “R₆, R₇ and R₈, which may be the same or different, are each independently a hydroxyl-protecting group.” EX1001, 7:14-16, 8:14-30. From that premise, Petitioner argues

that formula (IV) compounds cannot have R_6 – R_8 equal to hydrogen. *See* Pet., 15–16.

The problem is that Petitioner reaches that conclusion only by ignoring virtually everything that appears above the formula (III) discussion. The phrase “defined above” does not say “defined in the immediately preceding section,” nor does it direct the reader to the formula (III) definition of R_6 – R_8 alone. Instead, it broadly references material previously disclosed in the specification. Petitioner’s argument succeeds only if the reader artificially begins the analysis at formula (III) and disregards the extensive disclosure that precedes it. There is no basis for doing so. *See* EX2011 ¶¶ 86–95.

Most notably, the specification first introduces formula (I), which expressly depicts the ribose hydroxyl groups as free hydroxyls where R_6 , R_7 , and R_8 are each hydrogen (H). EX1001, 2:31-52; EX2011 ¶ 93. Formula (I) is shown below:



The description of formula (I) unmistakably discloses embodiments in which the ribose positions corresponding to R₆, R₇, and R₈ are hydrogen. EX2011 ¶ 93.

Petitioner attempts to avoid this disclosure by treating the formula (III) definition as the exclusive meaning of “as defined above.” But there is no textual basis for that approach. When the specification introduces formula (III), it is describing a particular class of compounds and states that, for those formula (III) compounds, “R₆, R₇ and R₈ ... are each independently a hydroxyl-protecting group.” EX1001, 7:14-16. The specification then separately introduces formula (IV) compounds and states that “n, m, Y, R₁–R₈ and X⁺ are as defined above.” EX1001, 8:16-30. Nothing in that language instructs the reader to import every characteristic of formula (III) into formula (IV), much less to disregard earlier disclosures that are equally “above” the formula (IV) discussion. EX2011 ¶¶ 88–90.

In fact, Petitioner’s reading creates a glaring inconsistency with the specification as a whole. If “as defined above” were limited to the immediately preceding formula (III) disclosure, then formula (IV) would necessarily be constrained by features of formula (III) whenever common variables are used. But the specification repeatedly treats formulas (III) and (IV) as distinct classes of compounds. *See* EX1001, 8:15-18 (“Optionally, the compound of formula (III) is prepared by reacting a compound of formula (IV)”), and 12:13–16 (Figure 2 describes that compounds of formula (IV) “may be used” to prepare compounds of

formula (III)). A person of ordinary skill would understand that not every limitation applicable to formula (III) must automatically be imposed on formula (IV). EX2011 ¶ 88.

Ultimately, the phrase “as defined above” is the linchpin of Petitioner’s lack of written-description argument that seeks to break the priority chain of the ’506 patent. Yet Petitioner’s interpretation is not derived from the specification; it is imposed on the specification. By focusing exclusively on the immediately preceding formula (III) disclosure and ignoring the broader context of the ’506 patent, including formula (I), Petitioner manufactures a contradiction where none exists. The specification, read as a whole, does not support Petitioner’s selective reading of the ’506 patent specification. Rather, it repeatedly demonstrates that hydrogen is a disclosed and claimed option for R₆, R₇, and R₈ in formula (IV), and Petitioner’s contrary interpretation depends entirely on an unjustified and self-serving narrow reading of the phrase “as defined above.” EX2011 ¶ 86.

ii. Petitioner’s Argument That Formulas (I) and (II) Contain No “R-Groups” Fundamentally Misunderstands the Nature of Generic Chemical Formulas

In attempting to limit the description of R₆–R₈ in formula (IV) to hydroxyl-protecting groups described for formula (III), Petitioner argues that the disclosures associated with formulas (I) and (II) are irrelevant to the meaning of the phrase “as defined above.” Pet., 7. Petitioner justifies this because “R-groups do not appear on

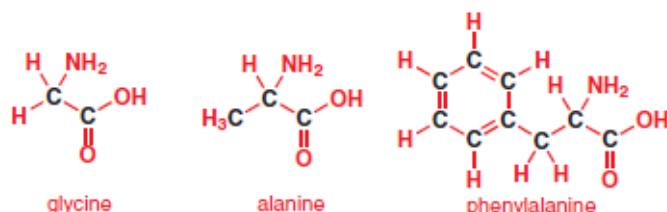
any of formulae (I) or (II), and thus there is no other definition ‘above’ in the specification.” *Id.* That argument rests on a basic misunderstanding of how a person of ordinary skill in the art interprets generic chemical formulas.

As Dr. Bihovsky explains, Petitioner’s argument fundamentally mischaracterizes the role of structural formulas in defining chemical compounds and the use of the symbol “R” which acts as a generic placeholder or wild card. EX2011 ¶¶ 90–93. Historically derived from the term “radical,” the use of “R” in a general formula is now generally understood as shorthand for “the rest of the molecule.” EX2011 ¶ 92. The use of R-groups is therefore a drafting convention used to identify positions of variability. EX2011 ¶¶ 92–93. Indeed, the next edition of the organic chemistry textbook relied on by Petitioner and Dr. Prestwich notes in its overview of organic structures:

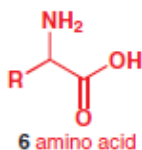
Hydrocarbon frameworks and functional groups

As we explained in Chapter 1, organic chemistry is the study of compounds that contain carbon. Nearly all organic compounds also contain hydrogen; most also contain oxygen, nitrogen, or other elements. Organic chemistry concerns itself with the way in which these atoms are bonded together into stable molecular structures, and the way in which these structures change in the course of chemical reactions.

Some molecular structures are shown below. These molecules are all amino acids, the constituents of proteins. Look at the number of carbon atoms in each molecule and the way they are bonded together. Even within this small class of molecules there's great variety—*glycine* and *alanine* have only two or three carbon atoms; *phenylalanine* has nine.



Before leaving carbon chains, we must mention one other very useful organic element symbol, R. R in a structure can mean *anything*—it's a sort of wild card. For example, structure 6 would indicate any amino acid, if R = H it is glycine, if R = Me it is alanine... As we've mentioned before, and you will see later, the reactivity of organic molecules is so dependent on their functional groups that the rest of the molecule can be irrelevant. In these cases, we can choose just to call it R.



EX2013 (Clayden) at 16, 24. The text provides that if R=H then the molecule is glycine, while if R=Me (methyl) then the molecule is alanine. *Id.* In each instance, the molecules are amino acids which fall within the identified structure 6—in the

same way formula (I) of the '506 patent falls within formula (IV). EX2011 ¶¶ 93–95.

A position of variability on a molecule does not cease to be position of variability merely because the disclosure provides a specific example where an R-group is labeled with a specific substituent *Id.*

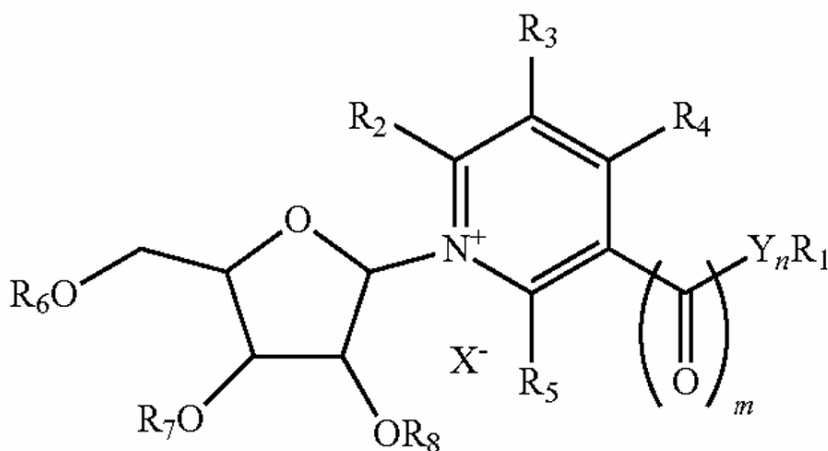
Dr. Bihovsky further explains that, instead of drawing entire molecules when discussing families of related compounds, POSITAs often use a “general formula” which is a single drawing in which a common core structure is shown in full, but certain positions are left as variables (e.g., R₁, R₂, R₃, etc.) to be filled in. EX2011 ¶¶ 91–95. In patent practice, when the variable positions of a general formula are limited to a set of allowed choices, the result is a Markush claim. *See* MPEP § 2117; *see also In re Harnisch*, 631 F.2d 716 (CCPA 1980). A single general formula with a few variable positions can therefore stand for a multitude of specific compounds, each corresponding to one particular combination of choices at the variable positions.

The key point, as Dr. Bihovsky explains, is that a general formula is deliberately open-ended at its variable positions. EX2011 ¶ 91. It is not a snapshot of one molecule, it is a template that describes many molecules simultaneously, with each specific compound that fits the template being a “species” and the whole family described by the template being a “genus.” EX2011 ¶¶ 91–95. The '506 patent, along

with many publications in this field, utilize this exact technique, employing a set of general formulas (I)–(IV), each of which describes a family of ribose-based compounds related to the nutritional supplement nicotinamide riboside. EX2011 ¶ 95.

Therefore, the preamble to claim 1 is not referencing any specific compound but rather orienting the reader to the class of compounds claimed, as specified by the rest of the claim:

1. A compound of formula (IV):



EX2011 ¶ 95.

Petitioner’s assertion that formulas (I) and (II) contain no R-groups because the labels “R₆,” “R₇,” and “R₈” do not literally appear in these formulas fundamentally mistakes nomenclature for chemistry. As Dr. Bihovsky explains, a

POSITA does not understand an R-group to be the literal text “R₆,” “R₇” or “R₈” printed on a diagram of the molecular structure. EX2011 ¶ 93. Rather, the R-group identifies a position on the molecular structure that may be occupied by different substituents. *Id.* Thus, when formula (I) depicts hydrogen at the three ribose positions corresponding to R₆, R₇, and R₈ in formula (IV), a POSITA recognizes that to be a disclosure that R₆, R₇, and R₈ may be hydrogen, even though they are no longer labeled with variable placeholders. *Id.*

Indeed, Petitioner’s own anticipation arguments expose the flaw in its reasoning. Throughout the Petition, Petitioner repeatedly relies on formula (I) of the ’184 publication to identify the positions corresponding to R₆–R₈ in formula (IV). For example, Petitioner repeatedly argues that formula (I) in the ’184 publication discloses hydrogen at positions “corresponding to R₆–R₈ of formula (IV).” *See, e.g.,* Pet., 37, 45, and 49. Petitioner cannot simultaneously argue that formulas (I) and (II) are irrelevant because they allegedly contain no R-groups, while also relying on those same formulas to identify positions “corresponding to R₆–R₈” when attempting to establish anticipation.

Furthermore, as Patent Owner explained in its Request for Discretionary Denial, the examiner of the earlier-filed ’262 patent (the great-grandparent of the ’506 patent) accepted the same reading of the shared specification that Patent Owner advances here. EX2011 ¶ 98. In its request for discretionary denial (Paper 006),

Patent Owner showed that the applicant supported amendments made during prosecution by citing paragraphs of the common disclosure that include formula (I), where the positions corresponding to R₆, R₇, and R₈ are hydrogen. Furthermore, the Patent Owner showed that the examiner accepted those citations and allowed claims directed to formula (III) compounds in which R₆, R₇, and R₈ are each H or are not all simultaneously H. EX1006 at claims 1, 2. That prosecution history is powerful intrinsic evidence because it shows that the Office previously read the same disclosure as supporting hydrogen at R₆, R₇, and R₈ based on formula (I), even though formula (I) does not explicitly contain any R-groups as printed in the specification. EX2011 ¶¶ 99–104.

In the end, Petitioner is not making a chemistry-based argument; it is asking the Board to disregard formula (I) based on the absence of printed R-group labels. Petitioner contends that formula (I) cannot inform the meaning of R₆–R₈ because the symbols “R₆,” “R₇,” and “R₈” do not physically appear on that structure. But that argument confuses the label with the underlying chemical position. Formula (I) depicts the same ribose positions that formula (IV) labels as R₆, R₇, and R₈, and it shows those positions occupied by hydrogen. Petitioner’s “no R-groups” point is therefore just an attempt to blind the Board to a directly relevant disclosure by insisting that only a structure printed with variable labels can show what substituents occupy the corresponding positions. But a POSITA would not read the specification

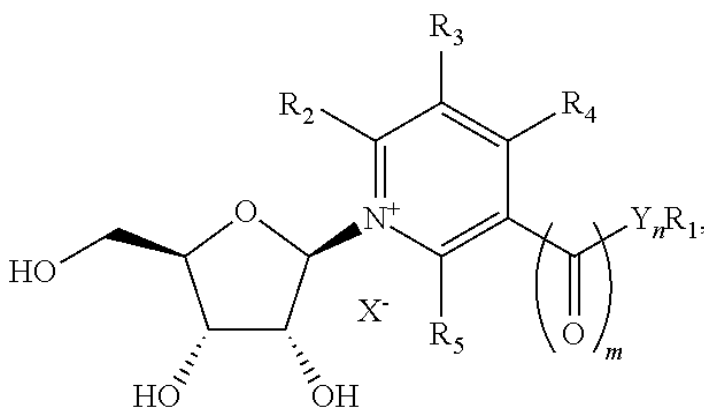
with blinders on. The disclosure of the underlying chemical positions does not disappear merely because the patent uses fixed substituents in one formula and variable placeholders in another. EX2011 ¶¶ 90–95.

5. The Language of the Surrounding Claims Shows the Inconsistencies in Petitioner’s Arguments

Petitioner’s argument is also refuted by the surrounding claims which, as the Federal Circuit noted in *Phillips*, can be “valuable sources of enlightenment as to the meaning of a claim term.” 415 F.3d at 1314. As discussed, the Petition relies entirely on the assumption that the examples in the patent that reference the structure of formula (IV) are controlling as to claim scope. But the dependent claims make clear that this is not the case.

For example, claims 8 and 26 which depend from claim 1 both claim:

The compound of claim 1 of formula:



EX1001, Claims 8, 26. Notably, this general formula depicts the beta-D-ribofuranosyl configuration of compounds having the same structure as formula (I), yet the claims depend from claim 1 and therefore fall within formula (IV) as recited

in claim 1. *See, e.g.*, EX1001, Fig. 2; EX2011 ¶ 97. These claims confirm that the claimed compounds of claim 1 are not explicitly limited to the examples of formula (IV) set forth in the specification.

6. Petitioner’s Argument Improperly Imports an Embodiment From the Specification Into the Claims

Petitioner’s argument depends entirely on limiting Claim 1 to only those embodiments in which R₆–R₈ are hydroxyl-protecting groups because of certain examples in the specification. But this is precisely the type of specification-to-claim importation the Federal Circuit has repeatedly condemned. *See, e.g., SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004) (“[A] particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment.”); *see also Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004) (“[T]he claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using ‘words or expressions of manifest exclusion or restriction.’”); *Tex. Instruments, Inc. v. U.S. Int’l Trade Comm’n*, 805 F.2d 1558, 1563 (Fed. Cir. 1986) (cautioning “against limiting the claimed invention to preferred embodiments or specific examples in the specification.”); *Phillips*, 415 F.3d at 1323 (“[A]lthough the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments.”).

Here, Claim 1 expressly recites the disjunctive wherein R_6 – R_8 are “each independently H or a hydroxyl protecting group; or wherein R_6 is a phosphate.” EX1001, Claim 1. The claim language is unambiguously broader than the working examples described in the specification, which Petitioner and Dr. Prestwich agree with. *See, e.g.*, Pet., 24; EX1013, ¶¶ 88-89. There is no lexicography or disavowal and no “words or expressions of manifest exclusion or restriction” limiting the claims to only those embodiments where all three positions bear protecting groups. The Petition’s attempt to restrict the claim scope based on selected specification passages is legally impermissible, in violation of black letter Federal Circuit law.

The proper written-description inquiry does not ask whether every embodiment describes R_6 – $R_8 = H$. It asks whether “the disclosure of the application [as] relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter.” *Ariad*, 598 F.3d at 1351. As demonstrated above, the formula (I) structure, Figure 1, and the ’262 patent’s claim language all convey possession of compounds falling within the structure of formula (IV) where R_6 , R_7 , and R_8 may each be hydrogen.

C. The ’262 Patent and its Prosecution History Confirm that R_6 – R_8 May be independently H or Other Functional Groups

Even accepting the Petition’s premise that formula (IV) is “defined in terms of” formula (III) (it is not, as explained below), the ’262 Patent (EX1006) conclusively refutes Petitioner’s contention that formula (III) limits R_6 – R_8 to

hydroxyl protecting groups. EX2011 ¶¶ 98–105. The '262 Patent as noted in Section III is a great-grandparent of the '506 Patent and shares an identical specification. Claim 1 of the '262 Patent is directed to compounds of formula (III) and requires, in part:

“**R₆, R₇ and R₈**, which may be the same or different, are each independently a hydroxyl protecting group **or are each H**, provided that when n is 1, m is 1, Y is O, R₁ is methyl, and R₂–R₅ are each H, then R₆, R₇, and R₈ are not all simultaneously H or unsubstituted acetyl”

EX1006, claim 1 (emphasis added). This clearly establishes that in the priority documents, R₆–R₈ are each capable of being H which directly refutes the Petition’s and Dr. Prestwich’s argument that the priority documents “uniformly describe formula (III)” as limited to hydroxyl-protecting groups in the R₆–R₈ positions. Pet., 13–14; EX2011 ¶¶ 98–99.

The prosecution history of the '262 Patent further confirms that R₆, R₇, and R₈ may each independently be H. As originally filed in the application that led to the '262 Patent (EX1006), claim 1 recited that R₆–R₈ “are each independently a hydroxyl protecting group or are each H,” and dependent claim 2 expressly recited that “R₆, R₇ and R₈ are each H.” EX2011 ¶¶ 100–103. During prosecution, the applicant added the “not all simultaneously H” provisos to claim 1 by amendment to overcome prior art rejections. *Id.*; EX2008 at 138 (Amendment dated May 27, 2020). During prosecution, applicant identified written-description support in the

pre-grant publication (US 2018/0186824 A1 or EX2009) at ¶¶ [0010]–[0014], [0016], [0055], [0077]–[0078]—which includes the formula (I) structure showing R₆–R₈ as hydrogen (free hydroxyls) and ¶ [0078] disclosing at least two of R₆–R₈ selected from acetyl or benzoyl (meaning the remaining position(s) could be H). EX2008 at 138 (Amendment dated May 27, 2020); EX2011 at ¶¶ 102–103. Notably, each of these amendments was accepted without a § 132 new matter rejection, meaning the examiner found written description support for that limitation.

Thus, both claim 1 and the prosecution history of the '262 Patent undermine Thorne's argument that formula (III) is necessarily limited to the situation where R₆–R₈ are hydroxyl protecting groups. Accordingly, it follows that even if formula (IV) in the challenged claims is defined in terms of formula (III), as Thorne contends, R₆–R₈ of formula (III) are not limited to hydroxyl protecting groups and may be hydrogen.

IX. CONCLUSION

For the above reasons, the Board should decline to institute inter partes review.

Date: September 22, 2026

Respectfully submitted,

KING & SPALDING LLP

BY: /s/Mikaela M. Stone

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CERTIFICATION OF WORD COUNT

The undersigned hereby certifies that the portions of the above-captioned PATENT OWNER'S PRELIMINARY RESPONSE specified in 37 C.F.R. § 42.24 includes 8,304 words and therefore complies with the 14,000-word limit set forth in 37 C.F.R. § 42.24. This word count was prepared using Microsoft Word 365 v.2607.

Date: September 22, 2026

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing **PATENT OWNER'S PRELIMINARY RESPONSE** and all supporting **EXHIBITS 2011-2014** were served by filing the documents through the Patent Trial and Appeal Case Tracking System (P-TACTS) as well as sent via Federal Express on September 22, 2026 and courtesy copies were also served via electronic mail, in their entireties on the following:

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Patent Owner's Preliminary Response
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Patent No. 12,252,506

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