IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

ERFINDERGEMEINSCHAFT UROPEP GbR,	§	
	§	
Plaintiff,	§	
	§	
v.	§	Case No. 2:15-CV-1202-WCB
	§	
ELI LILLY AND COMPANY,	§	
	§	
Defendant.	§	

MEMORANDUM OPINION AND ORDER

In this patent infringement case, the plaintiff Erfindergemeinschaft UroPep GbR ("UroPep"), a German association of urology researchers and physicians, sued the defendant Eli Lilly and Company ("Lilly") for infringement of U.S. Patent No. 8,791,124 ("the '124 patent"). Claim 1 of the '124 patent is to a method of administering an effective amount of a compound known as an inhibitor of the enzyme phosphodiesterase ("PDE") V, in order to treat the condition of benign prostatic hyperplasia ("BPH"). UroPep alleged that Lilly induced infringement of claim 1 by marketing and selling the drug Cialis for the treatment of BPH. Lilly denied infringement and asserted various invalidity defenses. After a trial, a jury found the '124 patent infringed and not invalid. The jury awarded damages in the amount of $20 million.

Pursuant to Rules 50(b) and 59, Fed. R. Civ. P., Lilly now moves for judgment as a matter of law or, in the alternative, a new trial. Dkt. No. 375. The motion is denied.

BACKGROUND

I. The Invention of '124 Patent

UroPep owns the '124 patent, entitled "Use of Phosphordiesterase [sic] Inhibitors in the Treatment of Prostatic Diseases." The disclosure was originally filed as part of a PCT application on July 9, 1997—the undisputed priority date of the '124 patent. The application under 35 U.S.C. § 371 ("the 371 application") was filed in April 2000 and later abandoned. The 371 application, in turn, gave rise to a continuation application that issued as U.S. Patent No. 8,106,061 ("the '061 patent) in January 2012. The '124 patent is a continuation of the patent application that matured into the '061 patent. '124 patent, col. 1, ll. 5-8.

The original specification filed in July 1997 begins by describing BPH, a condition in which the benign growth of the prostate gland in older males causes constriction of the neighboring urethra and results in lower urinary tract symptoms, including difficulties in urinating. See id., col. 1, ll. 9-24. One prior art treatment method for BPH was surgery to reduce the size of the prostate. Id., col. 1, ll. 14-15. Another prior art method was the administration of drugs, such as alpha-receptor blockers or drugs that interfere with hormonal regulation of the prostate, to induce relaxation of human prostatic muscle. Id., col. 1, ll. 20-28. Those drugs, however, were not particularly effective and had significant side effects. Id., col. 1, ll. 24-31; id., col. 1, line 67 through col. 2, line 2.

The inventors of the '124 patent identified a new drug target: phosphodiesterase ("PDE") enzymes. '124 patent, col. 1, ll. 32-35. At that time, it was known that smooth muscle cells contain molecules called cyclic adenosine monophosphate ("cAMP") and cyclic guanosine monophosphate ("cGMP"), which promote the relaxation of smooth muscle. Id., col. 1, ll. 39-42. It was also known that PDE enzymes break down cAMP and cGMP. Id., col. 1, ll. 43-44.

Finally, it was known that inhibitors of PDEs prevent the breakdown of cAMP and cGMP, which promotes smooth muscle relaxation. Id., col. 1, ll. 44-52.

Those skilled in the art had studied PDEs and knew that PDEs come in different types (subesterases), including PDE1 through PDE5.[1] '124 patent, col. 1, ll. 53-60. Publications reported that those PDE types are distributed differently throughout the body's organs and organ systems, and that the activity of those PDE types varies depending on where they are located. Id., col. 1, ll. 60-65; see also, e.g., Dkt. No. 342, Trial Tr. at 307-08 (a particular PDE type may not be present in a particular tissue; or, even if the PDE type is present in that tissue, the PDE type may not be functionally relevant in that tissue because other conditions in the tissue render the activity of the PDE meaningless).

The prior art also identified compounds that selectively inhibit specific PDE types, i.e., compounds that suppress the activity of a specific PDE type. '124 patent, col. 1, ll. 44-52; see also id., col. 1, ll. 66-67; id., col. 7, ll. 35-40, 43-45. In particular, hundreds of selective inhibitors of PDE5 were known at that time, including the selective PDE5 inhibitor tadalafil, which is the active ingredient in Lilly's product Cialis. Dkt. No. 344, Trial Tr. at 1254 (UroPep's expert describes the advanced state of the art regarding selective PDE5 inhibitors); Dkt. No. 343, Trial Tr. at 791-93 (Lilly's expert acknowledges that tadalafil, as well as 118 other compounds disclosed in a document published in 1995, were known PDE5 inhibitors before the priority date of the '124 patent).

The inventors of the '124 patent performed several experiments. See Dkt. No. 342, Trial Tr. at 316-17 (referencing experiments described in patent disclosure). The first set of

[1] The PDE subesterases were initially identified by Roman numerals, the convention followed in the '124 patent (e.g., PDE V). It is now more common to use Arabic numerals (e.g., PDE5). For consistency, except where quoting record materials, the modern convention will be used throughout.

experiments revealed that PDE1, PDE4, and PDE5 were present and had significant activity in human prostatic tissue. '124 patent, col. 2, ll. 6-11. The second set of experiments showed that compounds that selectively inhibit PDE1, PDE4, and PDE5 caused the relaxation of strips of human prostatic tissue. Id., col. 7, ll. 11-34. Based on those results, the inventors determined that compounds that selectively inhibit those three PDEs would treat BPH. See id., col. 7, ll. 35-37; id., col. 8, ll. 5-16. The disclosure identifies a number of "preferred selective inhibitors of PDE I, IV, and V," including 10 discrete chemical compounds and two classes of chemical compounds. Id., col. 2, line 28 through col. 4, line 46.[2] For convenience, those "preferred selective inhibitors of PDE I, IV, and V" will be referred to as "the identified preferred selective inhibitors." Tadalafil is not among those identified preferred selective inhibitors.

The disclosure also describes and incorporates "known methods" to determine whether any particular compound is a "selective inhibitor" of a specific PDE type. '124 patent, col. 7, line 35 through col. 8, line 16. If a compound is a selective inhibitor of one of the identified PDE types (PDE1, PDE4, or PDE5), then that compound is "suitable for the purpose according to the invention," id., col. 7, ll. 35-37—namely, for the prophylaxis and treatment of BPH and other prostatic diseases, id., col. 2, ll. 17-27.

In the original Patent Cooperation Treaty ("PCT") application, the patentees claimed the "[u]se of [any of the identified preferred selective inhibitors] in the prophylaxis and treatment of prostatic diseases, in particular benign prostatic hyperplasia" and others. PCT Application, at 4 (claim 1); see also id. at 5 (claim 2 covers "medicaments for" the prophylaxis and treatment of BPH and other prostatic diseases using any of the identified preferred selective inhibitors); id. at

[2] The disclosure also identifies, as "preferred selective inhibitors of PDE I, IV, and V," the "pharmacologically compatible salts" of those 10 compounds and two classes of compounds. '124 patent, col. 4, line 47.

6 (claim 3 covers the use of the identified preferred selective inhibitors "in the preparation of medicaments for the prophylaxis and treatment of" BPH and other prostatic diseases). The '061 patent, filed in May 2003, claims "[a] method of treating" BPH or prostatism by "administering a selective inhibitor of [PDE] IV and/or [PDE] V," selected from a group of six of the identified preferred selective inhibitors. '061 patent, col. 8, ll. 4-26 (independent claim 1); see also id., col. 8, ll. 29-53 (independent claim 3 is to a method of "relaxing prostatic muscles" by administering, to someone with BPH or prostatism, a selective inhibitor of PDE4 and/or PDE5 selected from a group of nine of the identified preferred selective inhibitors).

In the 1980s and 1990s, some drug companies were investigating PDE5 inhibitors for the treatment of other conditions, such as erectile dysfunction. See, e.g., Dkt. No. 342, Trial Tr. at 314-16 (Pfizer was investigating the PDE5 inhibitor sildenafil (Viagra) in the 1980s and 1990s). Lilly was one of them: Lilly developed Cialis (with tadalafil as the active ingredient) as a drug for erectile dysfunction, and Lilly sought approval of Cialis in the United States and Europe for that indication in mid-2001. See Dkt. No. 343, Trial Tr. at 955. Then, in December 2001, Lilly began discussing other possible indications for Cialis, including whether to develop Cialis as a treatment for BPH. See id., Trial Tr. at 958, 996. Lilly decided to engage in that development and obtained FDA approval for the BPH indication in 2011. Id., Trial Tr. at 1003. Lilly then began marketing and selling Cialis for the treatment of BPH.

The '061 patent was in effect at that time. The claims of the '061 patent, however, do not cover Cialis, because tadalafil is not one of the identified preferred selective inhibitors required by the claims of the '061 patent.

In December 2011, the patentees filed a continuation application that later issued as the '124 patent. During prosecution, the examiner rejected the claims on the basis of nonstatutory

double-patenting over the '061 patent. See Dkt. No. 106-8, at 63-64. The patentees then amended claim 1 to exclude many of the identified preferred compounds required in the claims of the '061 patent. See Dkt. No. 106-8, at 115.[3] Claim 1 of the issued '124 patent recites:

> A method for prophylaxis or treatment of benign prostatic hyperplasia comprising administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of
>
> > dipyridamole,
> >
> > 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline,
> >
> > 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate.
> >
> > 4((3,4-(methylendioxy)benzyl)amino)-6,7,8-trimethoxy-quinazoline,
> >
> > 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,
> >
> > 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole,
> >
> > 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one,
> >
> > 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chronan-4-one,
> >
> > and pharmacologically compatible salts thereof.

'124 patent, col. 8, ll. 18-41 (duplicate compound removed).[4] Those eight compounds excluded from claim 1 are all among the identified preferred selective inhibitors. Thus, claim 1 of the '124 patent on its face includes selective PDE5 inhibitors such as tadalafil, which is not among the identified preferred selective inhibitors.

[3] After that amendment, the examiner rejected the claims as anticipated by the claims of the '061 patent. The patentees entered a terminal disclaimer with respect to the '061 patent, and the examiner then allowed the claims of the '124 patent. See Dkt. No. 106-8, at 121-28.

[4] Claim 1, as set forth in the '124 patent, contains a duplicate listing of 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one.

The ’124 patent issued in July 2014. In October 2014, UroPep notified Lilly by letter of potential infringement of the ’124 patent. Lilly received the letter but did not respond. In July 2015, UroPep filed this action for infringement.

II. The Trial

At trial, the parties introduced evidence from several sets of competing experts, including physicians skilled in urology, medicinal chemists skilled in drug development, and economists. In addition, UroPep called one of the named inventors of the ’124 patent, Dr. Stefan Ückert, to testify about the invention. Lilly called employees Dr. Lars Viktrup and Janelle Sabo to speak about Lilly’s development of Cialis for the BPH indication.

In its Rule 50 and Rule 59 motions, Lilly has not challenged the sufficiency of the evidence of infringement. UroPep introduced ample evidence that the administration of Cialis for BPH infringed claim 1 of the ’124 patent. The Court construed claim 1 of the ’124 patent to require that an effective amount of a “selective PDE5 inhibitor”—i.e., a compound that is at least 20 times more selective for PDE5 than for PDE1 through PDE4—be administered to treat an individual suffering from BPH. See Dkt. No. 149, at 27; Dkt. No. 234, at 16. At trial, UroPep introduced the Cialis drug label approved by the U.S. Food & Drug Administration (“FDA”). That drug label expressly identifies tadalafil, the active ingredient in Cialis, as an inhibitor more than 20 times more selective for PDE5 than for PDE1, PDE2, PDE3, and PDE4. The label also states that five milligrams of Cialis is an effective amount to treat BPH, and the label directs physicians to prescribe Cialis as a treatment for individuals suffering from BPH. Dkt. No. 341, Trial Tr. at 216, 218. UroPep’s expert urologist, Dr. Anthony Sliwinski, went through the Cialis label and explained how it met each of the limitations of claim 1. Id., Trial Tr. at 222-23; see also Dkt. No. 342, Trial Tr. at 323-24, 327 (UroPep’s expert medicinal chemist, Dr. Andrew

Bell, did the same). Dr. Sliwinski also testified about his medical practice, in which he diagnoses patients with BPH and prescribes Cialis for the treatment of that condition. Dkt. No. 341, Trial Tr. at 216-18.[5]

Second, UroPep provided evidence that Lilly had induced infringement by marketing Cialis for the treatment of BPH. For example, the Cialis label, which is addressed to physicians and patients, counsels the administration of Cialis for the treatment of BPH. See Dkt. No. 341, Trial Tr. at 216-19. UroPep also introduced numerous advertisements, brochures, coupons, and other marketing materials that Lilly has distributed to physicians and consumers regarding the use of Cialis as a treatment for BPH. See Dkt. No. 341, Trial Tr. at 223-27; see also Dkt. No. 342, Trial Tr. at 394-95 (evidence that Lilly spent over $100 million to run one television advertisement regarding the use of Cialis for BPH and erectile dysfunction); id., Trial Tr. at 396-97 (same message regarding the administration of Cialis for BPH and erectile dysfunction on Lilly's websites). In addition, Dr. Sliwinski testified about his receipt of such materials, Cialis drug samples, and visits from Lilly pharmaceutical representatives, all of which caused him and the partners in his practice to prescribe Cialis for BPH. See Dkt. No. 341, Trial Tr. at 206-07, 220, 223-27.

Lilly presented four primary invalidity defenses: lack of written description under 35 U.S.C. § 112, ¶ 1; lack of enablement under that same provision; anticipation under 35 U.S.C.

[5] Lilly's only challenge to the evidence of infringement was the suggestion that doctors may prescribe Cialis to treat BPH without correctly diagnosing the patients' condition as BPH, i.e., lower urinary tract symptoms resulting from an enlarged prostate. See Dkt. No. 346, Trial Tr. at 1482 (Lilly's closing argument on noninfringement: "Did they prove an enlarged prostate? I'll leave that to you."). Dr. Sliwinski, however, explained how he appropriately diagnoses BPH before prescribing Cialis. See, e.g., Dkt. No. 341, Trial Tr. at 218-19 (explaining that, before prescribing Cialis for BPH, he rules out all other possible causes of the patient's symptoms to conclude that the patient in fact suffers from BPH). In the absence of contrary evidence, the jury could reasonably infer that his experience was representative.

§ 102; and obviousness under 35 U.S.C. § 103. Although the jury rejected each defense, Lilly argues that each is a ground for judgment as a matter of law or, in the alternative, a new trial. Lilly also contends that the Court improperly rejected Lilly's argument that claim 1 of the '124 patent is indefinite and that the Court's claim constructions are erroneous, requiring judgment as a matter of law or a new trial. Finally, according to Lilly, the Court gave several erroneous jury instructions and made several erroneous evidentiary rulings, each of which requires a new trial.

DISCUSSION

Lilly asserts that the Court should enter judgment in Lilly's favor pursuant to Rule 50(b) based on (1) any one of Lilly's invalidity defenses asserted at trial, (2) indefiniteness of the claim term "inhibitor of phosphodiesterase (PDE) V," and (3) any of the rejected claim constructions. Lilly also argues that it is entitled to a new trial pursuant to Rule 59 on any of those grounds, or based on (4) the Court's jury instruction on enablement, (5) the Court's failure to give an instruction based on 35 U.S.C. § 101, (6) the exclusion of certain evidence based on untimely disclosures, or (7) the assertedly improper impeachment of one of Lilly's experts.

I. Legal Standard

Fifth Circuit law determines what legal standards apply to a motion for judgment as a matter of law under Rule 50(b) and a motion for a new trial under Rule 59. Wi-Lan, Inc. v. Apple, Inc., 811 F.3d 455, 461 (Fed. Cir. 2016). A motion for judgment as a matter of law "is a challenge to the legal sufficiency of the evidence supporting the jury's verdict." Dresser-Rand Co. v. Virtual Automation Inc., 361 F.3d 831, 838 (5th Cir. 2004); see also Vadie v. Miss. State Univ., 218 F.3d 365, 372 (5th Cir. 2000) ("A jury verdict must be upheld unless 'there is no legally sufficient evidentiary basis for a reasonable jury to find' as it did.") (quoting Fed. R. Civ. P. 50). The court must "draw[] all reasonable inferences and resolv[e] all credibility

determinations in the light most favorable to the non-moving party." Dresser-Rand, 361 F.3d at 838. The court "grants great deference to a jury's verdict and will reverse only if, when viewing the evidence in the light most favorable to the verdict, the evidence points so strongly and overwhelmingly in favor of one party that the court believes that reasonable jurors could not arrive at any contrary conclusion." Id.; accord Wi-Lan, 811 F.3d at 461 (applying Fifth Circuit law).

As for the alternative motion for a new trial, Lilly must show that "it is reasonably clear that prejudicial error has crept into the record or that substantial justice has not been done." Laxton v. Gap Inc., 333 F.3d 572, 586 (5th Cir. 2008) (internal quotation marks omitted). In making that determination, the "court weighs all of the evidence," but the court "need not view [the evidence] in the light most favorable to the nonmoving party." Id. The court, however, may not grant a new trial "unless the verdict is against the great weight of the evidence." Dresser-Rand, 361 F.3d at 838; accord Wi-Lan, 811 F.3d at 461 (applying Fifth Circuit law); see also Laxton, 333 F.3d at 586 ("A new trial is warranted if the evidence is against the great, and not merely the greater, weight of the evidence.").

II. Written Description

The written description requirement of 35 U.S.C. § 112, ¶ 1 provides, in pertinent part:

> The 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 (2006). For purposes of written description, that clause has been interpreted to require that the specification "describe the invention sufficiently to convey to a person of skill in the art that the patentee had possession of the claimed invention at the time of the application,

i.e., that the patentee invented what is claimed." Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1345 (Fed. Cir. 2010) (en banc).

Both parties offered expert testimony and numerous exhibits addressed to the written description issue. The primary point of contention was whether the disclosure supports the claim term "an inhibitor of phosphodiesterase (PDE) V," construed as "a selective inhibitor of PDE5, which is at least 20 times more effective in inhibiting PDE5 as compared to PDE1 through PDE4." See Dkt. No. 346, Trial Tr. at 1412-13. Lilly's theory at trial was that the disclosure is inadequate to describe the genus encompassed by that claim term as construed. In response, UroPep presented evidence that the disclosure described both a sufficient number of representative species within the scope of that genus and structural features common to the members of the genus. See Ariad, 598 F.3d at 1351.

Over UroPep's objection, the Court adopted Lilly's proposed instruction regarding the written description requirement. Compare Dkt. No. 344, Trial Tr. at 1357 (Lilly "suggest[s] 'a sufficient number of representative compounds'") with Dkt. No. 346, Trial Tr. at 1427 (Court instructs jury that written description must include "a sufficient number of representative compounds or a common structural feature so that a person of ordinary skill in the art would understand, from reading the patent, that the inventor invented the full scope of the claimed method."); see also Dkt. No. 346, Trial Tr. at 1397-98 (Court rejects UroPep's proposed reference to "one or more representative compounds"). Under Lilly's proposed instruction, the jury found that Lilly had failed to prove invalidity by clear and convincing evidence.

A. Written Description Support for the Claim Limitation of a Selective Inhibitor of PDE5

In its post-trial motion, Lilly argues that the evidence introduced at trial shows that Lilly is entitled to a judgment of invalidity for lack of an adequate written description of a selective inhibitor of PDE5, or a new trial. The Court disagrees.

According to Lilly, the claim term describes a genus using functional language—that is, "a selective inhibitor of PDE5" is defined by its function as a compound that selectively inhibits PDE5. Lilly contends that no reasonable jury could find that the disclosures contained within the "four corners" of the specification describe a sufficient number of representative species within the scope of the genus, or structural features common to the members of the genus. See Dkt. No. 375, at 15 (quoting Ariad, 598 F.3d at 1351); see also Dkt. No. 393, at 6-7 (Lilly argues that UroPep is restricted to the "four corners" of the patent and cannot rely upon "that which is undescribed but allegedly obvious from the art.").

Lilly proceeds from the wrong premise. As the Federal Circuit explained in Ariad, the possession inquiry is not limited to what is expressly described within the "four corners" of the specification. Instead, the possession inquiry is an objective one that is viewed from the perspective of a person of ordinary skill in the art:

> The term "possession" . . . has never been very enlightening. It implies that as long as one can produce records documenting a written description of a claimed invention, one can show possession. But the hallmark of written description is disclosure. Thus, "possession as shown in the disclosure" is a more complete formulation. Yet whatever the specific articulation, the test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art. Based on that inquiry, the specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed.

598 F.3d at 1351.

Because "the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before . . . it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention . . . ." LizardTech, Inc. v. Earth Res. Mapping, Inc., 424 F.3d 1336, 1345 (Fed. Cir. 2005). The level of detail required to satisfy the written description requirement therefore "varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology." Ariad, 598 F.3d at 1351; see also Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005) (what is required "varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence").

Under the proper legal standard, Lilly cannot establish that it is entitled to the requested relief. As the Federal Circuit has emphasized, in written description cases, "[t]he primary consideration is *factual* and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure." Union Oil Co. of Cal. v. Atl. Richfield Co., 208 F.3d 989, 996 (Fed. Cir. 2000); see also ScriptPro, LLC v. Innovation Assocs., Inc., 762 F.3d 1355, 1359 (Fed. Cir. 2014) (sufficiency of the written description is a question of fact). There was sufficient evidence for the jury to find that Lilly did not prove by clear and convincing evidence that the '124 patent failed to disclose "either a representative number of species falling within the scope of the genus or structural features common to members of the genus so that one of skill in the art [could] 'visualize or recognize' the members of the genus." Ariad, 598 F.3d at 1350.

1. Representative Number of Selective PDE5 Inhibitors

A reasonable jury could have found that Lilly failed to show that the disclosure lacked a sufficient number of representative compounds falling within the scope of the genus of selective PDE5 inhibitors. The specification describes a number of "preferred selective inhibitors of PDE I, IV, and V." '124 patent, col. 2, line 28. Those "preferred selective inhibitors" include 10 discrete compounds (a) through (j), and two classes of compounds (k) and (l). Id., col. 2, line 29 through col. 4, line 47. The patent identifies those compounds and classes of compounds by chemical name and, in most cases, structural drawings. Id.

The evidence at trial showed that many of the compounds identified in the '124 patent as "preferred selective inhibitors of PDE I, IV, and V" were known to be selective PDE5 inhibitors in July 1997. Based on his expert knowledge and pointing to printed publications, UroPep's expert Dr. Andrew Bell testified that the compounds identified as (a), (c), (d), and (g) in the '124 patent were publicly known as selective PDE5 inhibitors before July 1997. See Dkt. No. 342, Trial Tr. at 314-15 (sildenafil, MY5445, and zaprinast—compounds (a), (c), and (g) in the specification—were known selective PDE5 inhibitors); Dkt. No. 344, Trial Tr. at 1260-61, 1265-66 (compound E4021—compound (d) in the specification—was a known selective PDE5 inhibitor). Experts called by Lilly also testified as to the known PDE5 activity of those compounds in July 1997. Dr. Nicholas Terrett noted that the scientific literature showed that a number of quinazoline compounds—within the class of compounds (k) in the specification—were known to inhibit PDE5. Dkt. No. 343, Trial Tr. at 710-11. Lilly's expert Dr. David Rotella explained that sildenafil (compound (g)) is a pyrazolopyrimidone and within the class of compounds (l) in the specification. Id., Trial Tr. at 740; see also id., Trial Tr. at 723 (Dr. Rotella admits sildenafil was a known selective PDE5 inhibitor in July 1997).

In addition to the compounds expressly disclosed in the '124 patent, the jury heard undisputed evidence that hundreds of PDE5 inhibitors were known by July 1997. Dr. Bell testified about the advanced state of the art regarding selective PDE5 inhibitors in July 1997: "There were hundreds of known inhibitors, selective inhibitors of PDE5 known at that time. This was a pretty mature area." Dkt. No. 342, Trial Tr. at 318; see also Dkt. No. 344, Trial Tr. at 1254 (explaining that hundreds of selective PDE5 inhibitors were known by July 1997); id., Trial Tr. at 1267-68 (explaining that skilled artisans were aware of hundreds of other selective PDE5 inhibitors beyond those expressly named in a 1995 review article). Lilly's expert Dr. Rotella admitted that tadalafil, as well as 118 other compounds in one sample paper published in 1995, were known PDE5 inhibitors before July 1997. Dkt. No. 343, Trial Tr. at 792-93. There was also evidence that at least two selective PDE5 inhibitors—in particular, sildenafil and zaprinast—had been subjected to human clinical testing long before July 1997, albeit for conditions other than BPH. Dkt. No. 344, Trial Tr. at 1293-94; see also Dkt. No. 342, Trial Tr. at 315-18 (Dr. Bell describes Viagra clinical trials in 1980s and 1990s).

Given the evidence of the knowledge of a person of skill in July 1997 regarding PDE5 inhibitors, including tadalafil, a reasonable jury could have found that the specification disclosed a sufficient number of representative species of selective PDE5 inhibitors. Written description is a question of fact, and "[f]or generic claims, [there are] a number of factors for evaluating the adequacy of the disclosure, including 'the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.'" Ariad, 598 F.3d at 1351 (quoting Capon v. Eshhar, 418 F.3d at 1359). UroPep presented evidence as to all of those factors, much of which Lilly failed to rebut. The jury was entitled to credit UroPep's evidence and find that Lilly failed to meet its burden.

Lilly nevertheless contends that the disclosure of several species of selective PDE5 inhibitors in the '124 patent is insufficient, because Lilly's evidence showed that the genus of selective PDE5 inhibitors is large. For example, one witness put on by Lilly testified that the chemical class of quinazolines—identified as preferred in the '124 patent—contains "billions of compounds." Dkt. No. 341, Trial Tr. at 182-83. Although far fewer compounds within that class of quinazolines are selective PDE5 inhibitors such that they would fall within the claimed genus, Dkt. No. 342, Trial Tr. at 342, it was generally undisputed that the claimed genus is nonetheless very large. UroPep's expert testified that hundreds of PDE5 inhibitors, including tadalafil, were known in 1997, and that at least tens of thousands have been developed since then. See Dkt. No. 342, at 332, 341-42.

That evidence, however, is not dispositive. There is no "bright-line rule governing the number of species that must be disclosed to describe a genus claim, as this number necessarily changes with each such invention, and it changes with progress in a field." Ariad, 598 F.3d at 1351; see also Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1368 (Fed. Cir. 2006) ("where . . . accessible literature sources clearly provided, as of the relevant date, [the species falling within the claimed genus], satisfaction of the written description requirement does not require either the recitation of or incorporation by reference of such [species].") (parentheticals omitted). The specification of the '124 patent alone discloses at least four discrete compounds that were known to be selective PDE5 inhibitors, as well as two compound classes that were known to contain selective PDE5 inhibitors. That express disclosure was in the context of a mature field in which skilled artisans knew what PDE5 inhibitors were and had already discovered hundreds of them. Those representative species would indicate to a skilled artisan at the time of the invention that

selective PDE5 inhibitors such as tadalafil, well known in the mature field in 1997, would work in the claimed invention.

The Federal Circuit has rejected a rule that at least one representative compound is always needed to satisfy the written description requirement. See Capon v. Eshhar, 418 F.3d 1349, 1356-1358 (Fed. Cir. 2005) (rejecting the interpretation of "controlling precedent" from the Federal Circuit as "requir[ing] inclusion in the specification of the complete nucleotide sequence of 'at least one' chimeric gene"—i.e., one representative species—because the prior art may supply that understanding); cf. Eli Lilly, 119 F.3d at 1569 ("'Mention of representative compounds encompassed by generic claim language clearly is not required by § 112 or any other provision of the statute. But where no explicit description of a generic invention is to be found in the specification[,] . . . mention of representative compounds may provide an implicit description upon which to base generic claim language.'") (quoting In re Robins, 429 F.2d 452, 456-57 (C.C.P.A. 1970)). The identification of a large number of representative compounds is one way to meet the written description requirement, but not the only way. See, e.g., In re Herschler, 591 F.2d 692, 701 (C.C.P.A. 1979) (specification's disclosure of a single example species was sufficient because numerous species were known to skilled artisans); In re Fuetterer, 319 F.2d 259, 265 (C.C.P.A. 1963) (Rich, J.) (disclosure of four species was sufficient even for huge genus that was not fully known at the time of the invention); see also In re Angstadt, 537 F.2d 498, 502-03 (C.C.P.A. 1976) (patentees "are not required to disclose *every* species encompassed by their claims even in an unpredictable art") (quoted in Regents of the Univ. of Cal. v. Eli Lilly & Co., 119 F.3d 1559, 1569 (Fed. Cir. 1997)).

For example, in Capon, the claimed chimeric genes were "prepared from known DNA sequences of known function." 418 F.3d at 1358. Both parties "explain[ed] that th[e] invention

does not concern the discovery of gene function or structure." Id. Both parties also "explain[ed] that the[] invention is not in discovering which DNA segments are related to the immune response, for that is in the prior art, but in the novel combination of the DNA segments to achieve a novel result." Id. The Federal Circuit ruled that the Board of Patent Appeals and Interferences "erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes." Id.; see also Unocal, 208 F.3d at 997 (written description requirement was satisfied because evidence at trial showed that skilled artisans were aware of the properties of raw petroleum sources and knew, upon reading the disclosure, how to vary those sources in combination to achieve a final product with desired characteristics; given the background knowledge of persons of skill in the art, the patentees were not required to "describe the exact chemical component of each combination that falls within the range claims of the" patent).

As in Capon, it was undisputed at trial that hundreds of selective PDE5 inhibitors, as well as their function, were known in the art at the time of the invention. See '124 patent, col. 1, ll. 36-65. It was also clear that selective PDE5 inhibitors were not themselves the invention. '124 patent, col. 2, ll. 17-20 (describing the invention as the use of selective inhibitors of PDE1, PDE4, and PDE5 in the prophylaxis and treatment of prostatic diseases, including BPH); see also Dkt. No. 341, Trial Tr. at 174-78 (Lilly's counsel clarifying that the inventor did not claim the discovery of PDEs, PDE inhibitors, alpha-blockers, or the mechanism of action of cAMP and cGMP in relaxing prostatic muscle); Dkt. No. 344, Trial Tr. at 1295 (Dr. Bell: a person of skill does not "need to discover brand-new PDE5 inhibitors to use the '124 patent invention"); id. at 1283 (Dr. Bell confirming that the UroPep inventors did not "discover PDE5 inhibitors"). The

disclosure does not describe the "novel result" of inhibiting PDE5. Ariad, 598 F.3d at 1349. Such compounds were already well known and the effect of inhibiting PDE5 already achieved; instead, the invention was to use a group of compounds well known in the art, including tadalafil, in a novel method of treating BPH.

It is often the case that a patent claiming the invention of a new genus, or the use of a new genus, must provide more detail regarding that genus, such as disclosing a number of representative species or a structural feature by which to recognize the new genus. See, e.g., Ariad, 598 F.3d 1336, 1357-58 (claiming methods of using new "molecules potentially capable of reducing NF-κB activity," where no such molecules had been completely synthesized but were merely "prophesized"); Rochester, 358 F.3d 916, 923 (claiming use of new COX-2 inhibitors that were merely "hypothesized"); Eli Lilly, 119 F.3d 1559, 1567 (claiming cDNA for human insulin that had never been characterized); Fiers v. Revel, 984 F.2d 1164, 1171 (Fed. Cir. 1993) (claim to DNA that was of unknown structure); Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991) (claims directed to unknown gene encoding human erythropoietin, where gene was not adequately characterized); see also Boston Sci. Corp. v. Johnson & Johnson, 647 F.3d 1353, 1364-65 (Fed. Cir. 2011) (claiming use of new "macrocyclic lactone analogs of rapamycin" where none were disclosed, only a small number were known in the prior art, very little was known about their function, and no guidance was provided to determine which, if any, would work in the invention). As in Ariad, when one purports to have "invented a genus," the written description should "disclose a variety of species that accomplish the result," because "'[t]he description requirement of the patent statute requires a description of the invention, not an indication of a result that one might achieve if one made the invention.'" 598 F.3d at 1350 (quoting Eli Lilly, 119 F.3d at 1568). Otherwise, a person of skill in the art

would not be aware of what makes up the new genus, and the claimed invention would not be sufficiently described.

On the other hand, when a genus is well understood in the art and not itself the invention but is instead a component of the claim, background knowledge may provide the necessary support for the claim. For example, in Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1319 (Fed. Cir. 2003), the invention was the production of recombinant erythropoietin (a hormone). The method claims included the use of vertebrate or mammalian host cells to produce the recombinant erythropoietin. Id. at 1322. In response to a written description challenge based on the generic terms "mammalian cell" and "vertebrate cell," the Federal Circuit ruled that the disclosure did not need to identify specific representative species or common structural characteristics of the genera of vertebrate and mammalian cells, "because the claim terms at issue here ["vertebrate cells" and "mammalian cells"] are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend." Id. at 1332 (distinguishing Eli Lilly, 119 F.3d 1559, and Enzo Biochem v. Gen-Probe Inc., 323 F.3d 956 (Fed. Cir. 2002)).

As another example, the Court of Claims and Patent Appeals determined that an application disclosing one example of a physiologically active steroidal agent provided sufficient written description to support claims directed to a novel method of using dimethyl sulfoxide in combination with such steroidal agents for delivery of those agents through topical administration. In re Herschler, 591 F.2d at 701. In that case, numerous steroidal agents were known in the art at the time of the invention. Id. As the court noted, "[w]ere th[e] application drawn to novel 'steroidal agents,' a different question would be posed." Id.; see also Rochester, 358 F.3d at 928 (discussing Herschler).

That principle applies equally to the chemical arts, despite Lilly's suggestion to the contrary. See Dkt. No. 393, at 9 (Lilly states that "decided cases have long recognized [that the field of pharmaceutical chemistry and drug development] is highly unpredictable."). Rochester, which Lilly cites in support, in fact states that such distinctions are "irrelevant; the statute applies to all types of inventions." 358 F.3d 916, 925; see also Ariad, 598 F.3d at 1352 (noting that the principles underlying the written description requirement "ha[ve] not just been applied to chemical and biological inventions.") (citing LizardTech, 424 F.3d at 1343-47). Although certain aspects of the chemical arts may be unpredictable, that does not mean that the chemical arts always require the identification of representative species to support a claimed genus, even when there is substantial knowledge in the field regarding the genus.

In a hypothetical case involving the chemical arts, for example, a claim might be directed to the novel use of a particular salt, where the salt must be dissolved in a "solubilizing agent." The broad genus of "solubilizing agents" would not require representative species if persons of skill knew of many solvents that could dissolve the salt, and thereby serve as a "solubilizing agent" in that invention. Patents in the chemical field may often involve claims that include well-understood genera. See, e.g., Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1371-72 (Fed. Cir. 2001) (independent claims to methods for treating patients with taxol-sensitive tumors by administering taxol within a fixed range along "with a medicament that reduces or eliminates hypersensitivity reactions," and dependent claims specifying that such "medicaments" are chosen from the broad genera of "steroids, antihistamines, H_2 receptor antagonists, and combinations thereof.").

None of the cases cited by Lilly support Lilly's argument that a disclosure must include some absolute number of species to support any patent claim to a genus. Those cases instead

show that patent claims may be invalidated based on the failure to disclose any, or more than one, species in a nascent area where knowledge of the art has nothing to add to the disclosure. E.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 918, 923 (Fed. Cir. 2004) (patent claims directed to COX-2 inhibitors were invalidated for lack of adequate written description because the existence of such inhibitors was merely "hypothesized"; no such inhibitors were yet known and none were described in the patent); AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc., 759 F.3d 1285, 1300-01 (Fed. Cir. 2014) (affirming verdict of invalidity for lack of written description because the patent disclosed only one very limited subgenus within a diverse claimed genus); Ariad, 598 F.3d 1336, 1355, 1357-58 (holding invalid claims directed to "molecules potentially capable of reducing NF-κB activity," where the disclosure contained "no working or even prophetic examples of methods that reduce NF-κB activity, and no completed synthesis of any of the molecules prophesized to be capable of reducing NF-κB activity," and where the prior art "was primitive and uncertain" and had not identified even a single example inhibitor).

Boston Scientific Corp. v. Johnson & Johnson, 647 F.3d 1353 (Fed. Cir. 2011), on which Lilly relies, also does not support Lilly's position. There, the Federal Circuit affirmed the grant of summary judgment of invalidity "[g]iven the absence of information regarding structural characteristics of [the claimed] macrocylic lactone analogs or examples of macrocylic lactone analogs in the specification, the unpredictability of the art and the nascent state of using drug-eluting stents to inhibit restenosis." 647 F.3d at 1366-67. Although the patentee argued that the mechanism of action was known in the art and supplied the necessary description, the court noted that the specification expressly "refutes any conclusion that the structural elements of rapamycin and its mechanism of action and biological activity was known." Id. at 1366. For

that reason, although "a patentee may rely on information that is 'well-known in the art' for purposes of meeting the written description requirement," the patentee in Boston Scientific could not rely on such information to overcome the express disclosures of the patent. 647 F.3d at 1366; see also id. ("when the four corners of the specification directly contradict information that the patentee alleges is 'well-known' to a person of skill at the effective filing date, no reasonable jury could conclude that the patentee possessed the invention.").

Where representative compounds are necessary to satisfy the written description requirement, the number of such compounds that must be disclosed depends on the context, including the knowledge already available in the art. Unlike the patent at issue in Boston Scientific, the '124 patent expressly provides that the field of PDE5 inhibitors and their mechanism of action was well known before July 1997. '124 patent, col. 1, ll. 36-65; see also id., col. 7, ll. 35-45. UroPep also provided substantial extrinsic evidence corroborating that proposition, such as testimony and documents showing that hundreds of selective PDE5 inhibitors, including tadalafil, were known at the time of the invention. The patentees were not required to include those hundreds of compounds in the disclosure, and in fact the law makes it clear that it is preferable that they not do so. See Falko-Gunter Falkner v. Inglis, 448 F.3d 1357, 1368 (Fed. Cir. 2006) ("As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution. Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification."). Lilly does not say what number of compounds would be sufficient; even if the Court assumes that Lilly's position is that the number required must be at least one more than the number of compounds disclosed in the '124 patent, Lilly has not demonstrated that Lilly is entitled to relief under governing law in light of the evidence at trial.

Lilly highlights other evidence, but none of that evidence warrants judgment as a matter of law or a new trial on the written description issue.

1. According to Lilly, it is unclear which of all possible compounds within the genus will selectively inhibit PDE5 and effectively treat BPH. Dkt. No. 375, at 16. Lilly's argument ignores the claim construction and incorrectly assumes that the genus includes all PDE5 inhibitors, whereas the genus in claim 1 includes only selective PDE5 inhibitors. Id. at 17 (citing Dr. Terrett's testimony that it is "impossible to say" whether all PDE5 inhibitors—as opposed to all selective PDE5 inhibitors—would treat BPH). Lilly has not pointed to any evidence, much less clear and convincing evidence, that an effective amount of a selective PDE5 inhibitor would not treat BPH. Compare Dkt. No. 342, Trial Tr. at 338-39 (Dr. Bell testifies that he does not know whether a 10 milligram (relatively small) dose of the selective PDE5 inhibitor zaprinast would effectively treat BPH) with Dkt. No. 375, at 17 (Lilly suggests that Dr. Bell testified that he does not know whether zaprinast is capable of effectively treating BPH).[6]

2. Lilly argues that the evidence shows that a person of skill would not know definitively, simply by looking at the structure of any particular compound, whether that compound would selectively inhibit PDE5 and effectively treat BPH. Dkt. No. 375, at 16-17. Such a high standard has never been required for written description. If Lilly's standard were

[6] Lilly contends that UroPep's experts "condemn[]" the potency and selectivity of zaprinast, a selective PDE5 inhibitor noted in the '124 patent. Dkt. No. 393, at 9. For support, however, Lilly highlights in its motion portions of trial exhibits regarding zaprinast that were not presented to the jury during trial. Compare id. at 8 (relying on reported results regarding zaprinast in plaintiff's exhibits 183 and 239) with Dkt. No. 344, Trial Tr. at 1250-51 (UroPep used plaintiff's exhibit 183 to show Dr. Bell's work on sildenafil, not zaprinast) and id., Trial Tr. at 1266-67 (UroPep used plaintiff's exhibit 183 to show prior art knowledge of the potency of E4021). Lilly failed to make those points to the jury at trial, and those points cannot be used to show that the jury acted unreasonably in finding against Lilly. In any event, the results (and error margins) reported in those exhibits are insufficient to prove Lilly's invalidity case, particularly given the substantial evidence that persons of skill understood, and other publications reported, that zaprinast is a selective PDE5 inhibitor.

required for written description, there would be no need to consider, in the context of enablement, whether any experimentation was undue or merely routine. See AK Steel Corp. v. Sollac, 344 F.3d 1234, 1244 (Fed. Cir. 2003) ("That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art."); see also Dkt. No. 375, at 31 (Lilly argues that the '124 patent is not enabled because "[t]he quantity of experimentation just to . . . identif[y] selective PDE V inhibitors is exceedingly high, considering that the specification of the '124 patent fails to describe any specific compound as a selective PDE V inhibitor and fails to disclose a representative number of claimed species. . . ."). Furthermore, the Ariad standard may be satisfied by either a representative number of species or a common structural feature. It is the latter, not the former, that requires recognition of the compound as a member of the genus upon looking at the compound's chemical structure.

It is also important to note that tadalafil was a known selective PDE5 inhibitor by July 1997. Therefore, to the extent that preferred selective PDE5 inhibitors were disclosed and understood by skilled artisans to work in the claimed invention due to their activity, tadalafil would be known by skilled artisans and understood to work in the claimed invention because it was known to have the same activity.

In any event, UroPep introduced testimony by Dr. Bell discussing how tadalafil shares a core chemical structure with compound E4021 (compound (d) in the specification). Dkt. No. 344, Trial Tr. at 1259-63. Lilly's expert Dr. Rotella gave a general opinion that the chemical structure of tadalafil is "distinct from the other chemical classes and compounds that were

presented" in the '124 patent. Dkt. No. 343, at 760; see also id. at 758 (stating that "[t]adalafil is miles away from these structures [compounds (a)-(j) in the '124 patent] . . . in a structural sense."). The jury was entitled to credit Dr. Bell's testimony. Furthermore, Dr. Bell's testimony was more specific than—and, in that regard, undisputed by—Dr. Rotella's testimony. Lilly introduced expert testimony that PDE5 inhibitors in general have diverse structures, but Lilly did not produce evidence distinguishing between tadalafil and E4021.[7]

3. Lilly contends that eight of the preferred compounds in the specification cannot serve as representative species because those eight compounds are excluded from claim 1 of the '124 patent. Lilly cites no support for that proposition, and the Court sees no merit to it. Patentees may choose to exclude from the claims some embodiments supported by the disclosure. Inphi Corp. v. Netlist, Inc., 805 F.3d 1350, 1355 (Fed. Cir. 2015) ("It is for the inventor to decide what bounds of protection he will seek."). In fact, a patentee may choose to exclude some embodiments in order to avoid double patenting problems, as happened in this case. See, e.g., In re Johnson, 558 F.2d 1008, 1019 (C.C.P.A. 1977) (written description was adequate where two specific compounds were omitted from a claim "to avoid having [the claim] read on a lost interference count"). But the compounds' exclusion from the claims does not mean that those individual compounds are no longer representative of other, non-excluded compounds covered by claim 1.

Even if it were the case that those eight compounds could not serve as representative species, Lilly would not be entitled to relief. For one thing, zaprinast and MY5445—compounds

[7] Lilly's reference to a portion of Defendant's Trial Exhibit 1347 (a 2007 review by Dr. Rotella) to show that a PDE4 inhibitor shares that core structure is not evidence on that point. The portion of the exhibit that Lilly cites was not discussed at trial. Rather, the exhibit was used for an entirely different purpose. See Dkt. No. 343, Trial Tr. at 807-10 (showing that Dr. Rotella referenced Dr. Ückert's 2001 publication to support a statement that PDE5 inhibitors may be used to treat BPH); see also id. at 863.

(a) and (c) in the specification—are not excluded from claim 1, and both were identified by sufficient evidence at trial as selective PDE5 inhibitors. The jury was entitled to find that Lilly failed to show that MY5445 and zaprinast are not representative species that fall within the genus, and the great weight of the evidence does not support Lilly's position on that point.

2. Common Structural Features

A reasonable jury also could have found that Lilly failed to prove by clear and convincing evidence that the written description did not disclose "structural features common to the members of the genus." Ariad, 598 F.3d 1336, 1351. While the disclosure does not expressly discuss the common structural features of PDE5 inhibitors, UroPep presented evidence at trial that persons of skill in the art would recognize such shared features. The jury was entitled to credit that evidence and find that the knowledge of persons of skill in the art satisfied the written description requirement.

UroPep's expert Dr. Bell gave a lengthy description of the core chemical structure found in a number of selective PDE5 inhibitors, including tadalafil and compound E4021 (compound (d) in the '124 patent), as well as a number of other prior art compounds. Dkt. No. 344, Trial Tr. at 1262-63; see generally id., Trial Tr. at 1259-68. The patent's disclosure of E4021 is therefore the disclosure of a species with a chemical structure shared by tadalafil. The jury was entitled to credit that testimony over the contrary testimony of Lilly's expert. Dkt. No. 343, Trial Tr. at 758-60.

Lilly contends that Ariad requires the disclosure of a structural feature common to all members of the genus. The Court disagrees. A patent's specification might identify three different structural features each found in one of three subgenera (or the same structural features may already be known in the art). The patent may claim an invention that includes a limitation

to a genus made up of those three subgenera. Under those circumstances, a person of skill in the art would be able to "'visualize or recognize' the members of the genus" by looking for any one of those three structural features. Ariad, 598 F.3d 1336, 1350.

In any event, UroPep presented unrebutted evidence that PDE5 inhibitors all share a common structural feature. According to Dr. Bell, PDE5 inhibitors may not all share a common "chemical" structure like the core chemical structure found in tadalafil and E4021, but all PDE5 inhibitors share a common "physical" structure. Dkt. No. 344, Trial Tr. at 1280-81. In three dimensions, that physical structure resembles an envelope: it contains a flat section, typically made up of two or more fused rings, and an attached section directed upwards. Id. at 1280. That physical structure fits into the active site of the PDE5 enzyme, inhibiting the enzyme's activity. Id. at 1281. UroPep's evidence indicated that skilled artisans may then add to that core physical structure to increase the PDE5 inhibitor's potency and selectivity. See id. at 1264.

As Lilly points out, that testimony regarding PDE5 inhibitors does not establish whether those common physical structures "will cause such an interaction [with PDE5] to occur either potently or selectively." Dkt. No. 393, at 5. UroPep, however, presented sufficient evidence that a skilled artisan would be aware of a common physical structure shared by the members of that genus, and that a skilled artisan could make modifications to increase potency and selectivity. The jury was entitled to rely on that evidence, particularly in light of the fact that Lilly failed to rebut it in any meaningful way. Lilly therefore failed to meet its burden to prove invalidity on that ground by clear and convincing evidence.

B. Permissible Breadth of the Disclosure

Lilly also notes that the disclosure describes the use of selective inhibitors of PDE1, PDE4, and PDE5 for the treatment or prophylaxis of BPH and a number of other conditions

related to the prostate. Lilly argues in its motion, for the first time, that the disclosure is too broad to support the narrow scope of claim 1 of the '124 patent—i.e., the use of selective PDE5 inhibitors for the treatment or prophylaxis of BPH.

1. Lilly has waived that argument. The Court will not grant a Rule 50(b) motion based on a theory that Lilly neither gave notice of in the pretrial order nor presented at trial.[8] See Dkt. No. 251 (pretrial order mentioned only the general written description defense); Dkt. Nos. 341-44, 346 (at no time during trial did Lilly raise such an argument in support of its written description defense). Lilly's silence deprived UroPep at trial of any opportunity to respond to that theory and develop a record in support. See Fujifilm Corp. v. Motorola Mobility LLC, 182 F. Supp. 3d 1014, 1038 (N.D. Cal. 2016) (denying motion for judgment of invalidity as matter of law and motion for a new trial based on an obviousness theory purportedly supported by the evidence because the defendant waived that theory by not presenting it at trial); see also Fractus, S.A. v. Samsung Elecs. Co., 876 F. Supp. 2d 802, 838 (E.D. Tex. 2012) (defendant waived affirmative defense in post-trial motion by not explicitly presenting that defense at trial, "depriv[ing] [plaintiff] of any opportunity to substantively respond with its own testimony or evidence"); Allergan v. Barr Labs., Inc., 808 F. Supp. 2d 715, 735 (D. Del. 2011) (because "defendants clearly present a different theory of obviousness post-trial than was presented at trial," that new argument was waived; defendants could not "switc[h] horses by combining pieces of testimony . . . into new obviousness theories," thereby depriving plaintiff of the opportunity "to mount a defense at trial to the [new obviousness] theories"). Lilly has waived that argument as a basis for the current motion, and as a basis for appeal. See Interactive Gift Exp., Inc. v. Compuserve Inc., 256 F.3d 1323, 1346-47 (Fed. Cir. 2001) ("[A] party's argument

[8] Nor did Lilly make that argument in its earlier motion for summary judgment based on lack of written description. See Dkt No. 120.

should not be a moving target" but "should be consistent, thereby ensuring a clear presentation of the issue to be resolved, an adequate opportunity for response and evidentiary development by the opposing party, and a record reviewable by the appellate court that is properly crystallized around and responsive to the asserted argument.").

Lilly complains that its failure to raise that defense was due to the Court's having urged Lilly to make its oral Rule 50(a) arguments "in bite-size form." Dkt. No. 346, Trial Tr. at 1391. The Court, however, did not cut counsel off nor prevent Lilly from raising its new theory. Cf. Blackboard, Inc. v. Desire2Learn, Inc., 574 F.3d 1371, 1380 (Fed. Cir. 2009) (noting that the defendant's Rule 50(a) motions were cursory and the court quickly took them under advisement, but that the defendant preserved the arguments because "it [was] clear from the context that neither the court nor [the plaintiff's] attorneys needed any more enlightenment about [the defendant's] position on those issues."). Even though Lilly had given no indication at trial that it was relying on any theory of invalidity based on an overbroad disclosure, Lilly nonetheless chose to move on its written description defense based solely on the statement: "The Rule 50 motion would be also on written description, that the evidence meets the clear and convincing evidentiary standard to show that the inventors did not possess the full scope of the claim." Dkt. No. 346, Trial Tr. at 1392. Although Rule 50(b) is construed liberally, such a general statement is not sufficient to provide notice to UroPep of Lilly's entirely new theory. See Navigant Consulting, Inc. v. Wilkinson, 508 F.3d 277, 288 (5th Cir. 2007) (court "may excuse 'technical noncompliance' when the purposes of [Rule 50(a)] are satisfied," which are "to enable the trial court to re-examine the question of evidentiary insufficiency as a matter of law if the jury returns a verdict contrary to the movant, and to alert the opposing party to the insufficiency before the case is submitted to the jury."); see also Blackboard, 574 F.3d at 1379-80 (purpose of Rule 50(a)

is "to alert the court to the party's legal position and to put the opposing party on notice of the moving party's position as to the insufficiency of the evidence.") (citing Navigant, 508 F.3d at 288-89). Lilly therefore waived its post-trial argument that the disclosure is too broad to support claim 1.

2. Setting aside the waiver issue, Lilly's argument fails on the merits. According to Lilly, the patentees did not appreciate the utility of using selective PDE5 inhibitors to treat BPH in July of 1997; therefore, the patentees failed to adequately disclose that narrowed invention, which is the subject of claim 1 of the '124 patent. Specifically, Lilly complains that the disclosure does not differentiate among the utility of inhibiting PDE1, PDE4, or PDE5 for any of the listed conditions, including BPH. See Dkt. No. 393, at 13. Lilly is wrong.

The original disclosure—shared by the PCT application, the '061 patent, and the '124 patent—describes the invention as the use of selective inhibitors of PDE1, PDE4, or PDE5 for treating BPH and other prostatic diseases. The first two paragraphs describe the condition of BPH and prior art methods of treatment. '124 patent, col. 1, ll. 9-31. The next two paragraphs set forth the biological mechanism of inducing smooth muscle relaxation in the prostate, which prior art methods had unsuccessfully targeted. Id., col. 1, ll. 32-52. The disclosure then explains how PDEs work in the body generally, and posits that targeting PDEs may prove successful if such PDEs are present and functional in the prostate. Id., col. 1, line 53 through col. 2, line 5. Finally, the subsequent two paragraphs discuss the inventors' work in discovering that PDE1, PDE4, and PDE5 are present and functional in the prostate; that selective inhibitors of those PDEs would allow for relaxation of prostatic tissue; and therefore that selective inhibitors of those PDEs would be effective for the prophylaxis and treatment of BPH and other prostatic

diseases. Id., col. 2, ll. 6-28; see also id., col. 7, ll. 11-34 (describing experiments showing the effectiveness of the use of selective inhibitors of PDE1, PDE4, and PDE5).

Lilly points to a later portion of the specification, where the patentees lay out multiple embodiments of the invention:

> Surprisingly, it has now been found that [PDE1], [PDE4] and [PDE5] are of particular importance in human prostatic muscles. . . . A well-aimed inhibition of those [PDE1, PDE4, and PDE5] isoenzymes will result in relaxation of the prostatic muscles even when minute doses of a specific inhibitor are administered, with no appreciable effects in other organ strips, in particular vessels, being observed. Therefore, [those PDE] isoenzymes have an excellent efficiency in the treatment of prostatic diseases.
>
> Therefore, the subject matter of the invention is the use of specific inhibitors of [PDE1], [PDE4] and [PDE5] in the prophylaxis and treatment of prostatic diseases, in particular benign prostatic hyperplasia [BPH], the so-called urge symptoms, pollacuria (frequent micturition), nycturia (nocturnal micturition), weakened urine jet, urge incontinence (involuntary discharge of urine), prostatism, instabilities of the bladder muscles, [and] impotence.

'124 patent, col. 2, ll. 11-24. Lilly complains that the written description requirement is not satisfied because the original disclosure does not "provide sufficient detail to identify and describe the invention later claimed"—i.e., the use of selective PDE5 inhibitors (versus selective PDE1 or PDE4 inhibitors) for the treatment of BPH (versus other prostatic diseases). Dkt. No. 375, at 12. Thus, Lilly contends, the disclosure does not provide sufficient "blaze marks" directing the choice of PDE5 inhibitors to treat BPH. See Boston Sci. Corp. v. Johnson & Johnson, 647 F.3d 1353, 1367 (Fed. Cir. 2011) ("[I]n the absence of blaze marks 'as to what compounds other than those disclosed as preferred, might be of special interest[,] . . . simply describing a large genus of compounds is not sufficient to satisfy the written description requirement as to particular species or sub-gen[era].") (internal quotation mark omitted).

It is enough that the disclosure specifically identifies, among other various options, the use of selective PDE5 inhibitors for the prophylaxis or treatment of BPH.[9] For that reason, the disclosure in this case is unlike the disclosures in any of the cases cited by Lilly. See Novozymes A/S v. DuPont Nutrition Bioscis. APS, 723 F.3d 1336, 1348 (Fed. Cir. 2013) (specification "contained no disclosure of any variant that actually satisfies the claims, nor is there anything to suggest that [the patentee] actually possessed such a variant at the time of filing."); Boston Sci. Corp., 647 F.3d 1353, 1367-69 (disclosure did not support claims to subgenus of "macrocyclic triene analogs of rapamycin," because the disclosure identified only the larger genus of "analogs of rapamycin," did not mention or provide any guidance toward the subgenus, and the knowledge of skilled artisans did not fill in the gaps, as no such analogs were known in the art); Fujikawa v. Wattanasin, 93 F.3d 1559, 1570-71 (Fed. Cir. 1996) (claim to a subgenus was not adequately supported by the disclosure of a larger genus, without mention of or guidance toward the subgenus); In re Ruschig, 379 F.2d 990, 994 (Fed. Cir. 1967) (disclosure encompassed over half a million compounds but never identified, nor provided guidance toward, the one particular compound specifically named in a later-added claim).

It is common for patentees to disclose a range of possible embodiments, as the '124 patent's disclosure does. Contrary to Lilly's contention, a patentee need not indicate that one embodiment is "of special interest" in order to claim it. Dkt. No. 375, at 14; see also Dkt. No. 393, at 11 (Lilly complains that disclosure does not establish "primacy" of PDE5). Indeed, UroPep might have added other claims directed to the use of selective PDE1 inhibitors for the treatment of BPH, or to the use of selective PDE4 inhibitors for the treatment of another prostatic

[9] The disclosure goes much farther than that. The specification singles out BPH by extensively describing that condition and explaining how specific PDE inhibitors, in particular, may be used to effectively treat BPH by relaxing the prostatic muscles. See '124 patent, col. 1, line 9 to col. 2, line 16.

disease. A patentee is free to selectively claim one particular embodiment without running afoul of the written description requirement.

Lilly makes much of the fact that the disclosure does not expressly identify a selective inhibitor of PDE5 (an inhibitor 20 times more selective for PDE5 than for PDE1 through PDE4), and the fact that "the disclosure does not describe actually using any such selective [PDE5] inhibitors to effectively treat BPH specifically." Dkt. No. 393, at 11. Neither fact is fatal, however, because the disclosure describes both selective PDE5 inhibitors and their effect in relaxing prostatic tissue to treat BPH.

The specification lists "[p]referred selective inhibitors" of PDE1, PDE4, and PDE5, and the undisputed evidence at trial demonstrated that at least four compounds in that list were known before July 1997 to be selective PDE5 inhibitors. Dkt. No. 342, Trial Tr. at 314-15 (sildenafil, MY5445, and zaprinast—compounds (a), (c), and (g) in the specification—were known selective PDE5 inhibitors); Dkt. No. 344, Trial Tr. at 1260-61, 1265-66 (compound E4021—compound (d) in the specification—was a known selective PDE5 inhibitor); see also Dkt. No. 343, Trial Tr. at 710-11 (a number of quinazoline compounds—within the class of compounds (k) in the specification—were known to inhibit PDE5); Dkt. No. 343, Trial Tr. at 723, 740 (sildenafil was a known selective PDE5 inhibitor and is a pyrazolopyrimidone that falls within the class of compounds (l) in the in the specification). It was also undisputed that a person of skill in the art at the time of the invention would know of hundreds of selective PDE5 inhibitors, and that several PDE5 inhibitors were already in human clinical trials, see Dkt. No. 342, Trial Tr. at 315-318; Dkt. No. 343, Trial Tr. at 792-93; Dkt. No. 344, Trial Tr. at 1254, 1293-94.

The specification also discusses experiments that showed that selective inhibitors of PDE1, PDE4, and PDE5 in fact relaxed prostatic tissue. '124 patent, col. 7, ll. 11-34 (describing experiments and conclusions); see also id., col. 7, ll. 35-37 & col. 8, ll. 5-16 (explaining that an inhibitor must be 20 times as selective for the PDE of interest—e.g., PDE5—to be "suitable for the purpose according to the invention."). Those experiments therefore demonstrated that selective inhibitors of PDE1, PDE4, and PDE5 could be used to effectively treat BPH. See id., col. 1, ll. 20-24 (noting that prior art showed that BPH can be treated by inducing relaxation of prostatic muscle cells); id., col. 2, ll. 11-16 ("A well-aimed inhibition of these isoenzymes [PDE1, PDE4, and PDE5] will result in relaxation of the prostatic muscles"; "therefore, [those selective inhibitors] have an excellent efficiency in the treatment of prostatic diseases" such as BPH.).

Lilly does not explain why the specification must describe the use of a PDE5 inhibitor for the treatment of BPH in a human clinical trial in order to satisfy the written description requirement, and the Court sees no reason to hold that it must. The evidence at trial indicates otherwise. See Dkt. No. 342, Trial Tr. at 527-38 (in the context of enablement, Lilly's expert admits that "[h]uman studies would not be necessary" for a person of skill to practice the full scope of the invention); Dkt. No. 344, Trial Tr. at 1295 (UroPep's expert says the same); see also id. at 1297-98 (human clinical data was available in 1997 for the selective PDE5 inhibitors sildenafil and zaprinast, although not for the treatment of BPH). More importantly, in addition to the lack of evidence presented by Lilly on that score, there was sufficient evidence that a person of skill, upon reading the disclosure, would understand that the administration of selective PDE5 inhibitors could be used to treat BPH by relaxing the prostatic muscle tissue. See '124 patent, col. 1, ll. 20-24; id., col. 2, ll. 11-16; id., col. 7, ll. 11-37; id., col. 8, ll. 5-16; see also Dkt. No.

341, Trial Tr. at 166-68 (describing tissue bath experiments showing prostate tissue relaxation reported in the '124 patent). Even if the jury had been presented with Lilly's waived argument, the jury could reasonably have determined that Lilly failed to meet the high standard of clear and convincing evidence for finding claim 1 of the '124 patent invalid based on the lack of an adequate written description of the invention.

C. Exclusion of Eight Compounds from Claim 1

Lilly next argues that the patent is invalid because the disclosure does not explain why particular compounds were expressly excluded from claim 1, while other compounds were not. According to Lilly, the disclosure must explain any negative limitation in a claim, and a failure to do so renders the patent invalid for lack of an adequate written description.[10] That is not the law.

As discussed previously, patentees are free to claim certain embodiments while excluding others. Inphi, 805 F.3d at 1355 ("It is for the inventor to decide what bounds of protection he will seek."). One reason a patentee may choose to exclude particular compounds is to avoid a double patenting rejection, and the patentee is not required to explain that reason in the disclosure. E.g., In re Johnson, 558 F.2d at 1019 (excluding two compounds from the claim to avoid reading on a lost interference count, without explaining as much in the patent); see also Inphi, 805 F.3d at 1355 (a disclosure does not need to explain the reason; it is enough that the specification "properly describ[e] alternative features of the patented invention" to indicate that the patentees "are merely excising the inventions of another, to which they are not entitled."). As the prosecution history makes clear, the patentees expressly excluded eight compounds from

[10] The Court has already addressed that argument in detail in a post-trial memorandum opinion. See Dkt. No. 359, at 10-13.

claim 1 of the '124 patent in order to avoid a double-patenting rejection based on the inventors' earlier '061 patent. See Dkt. No. 106-8, at 63-64.

Lilly next contends that avoidance of a double-patenting rejection cannot be the reason for the negative limitation in claim 1 of the '124 patent, because claim 3 of the '061 patent includes zaprinast, which is not excluded from claim 1 of the '124 patent.[11] Lilly complains that "there is no explanation for why zaprinast was not excluded." Dkt. No. 375, at 26. According to Lilly, the failure to exclude zaprinast shows that claim 1 is an "arbitrary dissection of a unitary invention [that] the written description requirement prohibits." Id. at 27.

The written description requirement contains no such prohibition. See Inphi, 805 F.3d at 1355; see also, e.g., Santarus, 694 F.3d at 1351 ("Th[e] exclusion narrowed the claims, as the patentee is entitled to do.") (citing MPEP § 2173.05(i)); In re Johnson, 558 F.2d at 1019. What is prohibited is a negative limitation that is contrary to the thrust of the invention. For example, in In re Bimeda Research & Development Ltd., 724 F.3d 1320, 1323 (Fed Cir. 2013), the invention was a "non-antibiotic approach"—no use of anti-infectives—to preventing mastitis, or udder inflammation, in cows. Claim 32 specifically excluded the anti-infective agent acroflavine, suggesting that other similar anti-infectives could be used instead of acroflavine. That suggestion made no sense, since the invention was to avoid the use of anti-infectives. See id. (disclosure was "generally inconsistent with a formulation which, like claim 32, excludes acriflavine but could include antibiotics," i.e., other anti-infectives).

[11] The prosecution history clearly disproves Lilly's theory. After the examiner's rejection, the patentees responded that the double-patenting "rejection is overcome by the instant amendment, which excludes from the present claims [of the application issued as the '124 patent] every compound (i.e., PDE inhibitor) recited in the patented claims [of the '061 patent] for 'treating . . . benign prostatic hyperplasia.'" Dkt. No. 106-8, at 115.

By contrast, the exclusion of the eight compounds in claim 1 of the '124 patent suggests that other PDE5 inhibitors could be used. That is consistent with the disclosure and exactly what the patentees intended. Moreover, UroPep presented expert testimony that a person of skill would not be confused by those specific exclusions. See Dkt. No. 344, Trial Tr. at 1283-84.

The point is that a patentee can choose to claim any particular embodiments identified in the specification and exclude others, without explanation, as long as the claim does not indicate to persons of skill that it covers embodiments inconsistent with, and therefore unsupported by, the disclosure. As stated by the court in In re Johnson, 558 F.2d at 1019:

> The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of § 112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute.

For those reasons, the negative limitation in claim 1 does not entitle Lilly to judgment as a matter of law or the grant of a new trial.

III. Enablement

The enablement requirement of 35 U.S.C. § 112, ¶ 1 derives from the same provision as the written description requirement:

> The 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 (2006). For purposes of enablement, that clause has been interpreted to require that a person of skill in the art, upon reading the disclosure, be able to practice the full scope of the claim without undue experimentation. Alcon Research Ltd. v. Barr Labs., Inc., 745 F.3d 1180, 1188 (Fed. Cir. 2014); Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d 1342, 1359-60 (Fed. Cir. 1998); In re Wands, 858 F.2d 731, 736-37 (Fed. Cir. 1988). Like the written

description requirement, the enablement requirement is viewed from the perspective of one of ordinary skill in the art. See Johns Hopkins, 152 F.3d at 1360 ("[I]t is imperative when attempting to prove lack of enablement to show that *one of ordinary skill in the art* would be unable to make the claimed invention without undue experimentation."). "'Furthermore, the test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention.'" Id. (quoting PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564 (Fed. Cir. 1996)) (alteration in original). "Factors to be considered in determining whether a disclosure would require undue experimentation . . . include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim[]." In re Wands, 858 F.2d 737.

Whether a disclosure fails to satisfy the enablement requirement is a question of law based on underlying factual findings. Alcon Research, 745 F.3d at 1188. It is the challenger's burden to prove lack of enablement by clear and convincing evidence. Id.

In its motion, Lilly essentially reargues the disputed case that was tried to the jury. Lilly's primary contention is that the jury should not have credited UroPep's expert's testimony regarding the routine nature of the experimentation referred to in the patent that would be required to determine whether a compound is 20 times more selective for PDE5 as compared to PDE1 through PDE4, and whether that compound could be administered to an individual to treat

BPH. But Dr. Bell's testimony was detailed, credible, and supported by published research. His testimony was also supported by personal experience: Dr. Bell worked at Pfizer and discovered the selective PDE5 inhibitor sildenafil in the 1980s. See Dkt. 342, Trial Tr. at 293. The jury was entitled to credit his opinion over that of Lilly's expert.

For example, in determining whether a group of promising compounds were selective PDE5 inhibitors, Dr. Bell testified that it took a few weeks to screen half a million compounds. Dkt. 344, Trial Tr. at 1282-83. He also explained that drug companies, including Pfizer, would "routinely" screen their massive collections for such purposes. Id.; see also Dkt. No. 343, Trial Tr. at 729 (Lilly's expert, Dr. Rotella, identified the same screening he did at Bristol-Myers Squibb). Furthermore, Dr. Bell testified that the field was mature, and that a skilled artisan would not necessarily need to conduct any screening but could "use their own [PDE5 inhibitor] if they've got one already." Dkt. No. 344, Trial Tr. at 1295; see also id., Trial Tr. at 1283 (stating that Pfizer did not need to screen its collection of compounds in 1997 "because we already had sildenafil").

Dr. Bell also discussed the methods expressly incorporated in the '124 patent to separate PDE isoenzymes and discern inhibitor selectivity. He testified that Pfizer used those methods of determining selectivity, termed "fractionation methods," when working on sildenafil. Dkt. No. 344, Trial Tr. at 1284-85 (referring to the Galwan and Nicholson articles in the '124 patent, col. 7, ll. 38-39). In addition, Dr. Bell pointed to other publications using those fractionation methods. See, e.g., Dkt. No. 344, Trial Tr. at 1285. He stated that "[i]t was the standard method that was being used particularly in the [pharmaceutical] industry at the time." Id.

Lilly argues that those selective PDE5 inhibitors may not be sufficiently potent or otherwise effective to treat BPH (for example, by being insufficiently bioavailable). Dkt. No.

375, at 32, 34-35. But Dr. Bell testified that the methods described in the '124 patent to identify potent and selective PDE5 inhibitors "are very common and are commonly used throughout the industry." Dkt. No. 344, Trial Tr. at 1284 (referring to the '124 patent, col. 7, line 11 through col. 8, line 16); see also Dkt. No. 344, Trial Tr. at 1274 (explaining that the standard industry practice to determine potency was to measure the so-called IC_{50} values, the same values referred to in the '124 patent, col. 8, ll. 5-7).

Beyond selectivity and potency, Lilly contends that the claim limitation regarding an effective amount of a PDE5 inhibitor to treat BPH is not enabled. But Dr. Bell clarified that skilled artisans would "simply have to do what we call routine dose ranging" in order "to determine what effective amount of a PDE5 inhibitor was needed to treat BPH." Dkt. No. 344, Trial Tr. at 1294; see also Eli Lilly & Co. v. Actavis Elizabeth LLC, 435 F. App'x 917, 923 (Fed. Cir. 2011) ("Enablement is not negated if a reasonable amount of experimentation is required to establish dosages and formulation of an active ingredient."). Meanwhile, Lilly presented no competing evidence at trial that "any potent PDE5 inhibitor [was] dose-range studied and [did] not effectively treat[] BPH." Dkt. No. 344, Trial Tr. at 1298; see also Eli Lilly & Co. v. Actavis Elizabeth LLC, 435 F. App'x at 922 (no enablement problem where "[t]here was no evidence that known procedures for determination of dosages and formulation did not apply," and distinguishing ALZA Corp. v. Andrx Pharmaceuticals LLC, 603 F.3d 935 (Fed. Cir. 2010), where "the field of ascending release dosage forms [w]as 'not mature' and 'a breakaway' from the prior art") (quoting ALZA Corp., 603 F.3d at 941).

Finally, Lilly points to testimony from its experts, Drs. Rotella and Roehrborn, that the patent's working examples of oral formulations and injections "are confused, nonsensical and almost certainly non-workable to demonstrate enablement of an effective amount of a selective

[PDE5] inhibitor to treat BPH." Dkt. No. 375, at 35. The jury, however, was entitled to accept Dr. Bell's testimony over that of Lilly's experts. See Dkt. No. 344, Trial Tr. at 1297 (Dr. Bell: In general, oral formulation in drug development was routine and "probably one of the most easy formulations to achieve"; in particular, skilled artisans would already know of available oral formulations of PDE5 inhibitors and published data, as some inhibitors were already in clinical trials.).[12]

In attacking the '124 patent's disclosure, Dr. Bell's testimony, and UroPep's other evidence, Lilly makes several fundamental errors regarding the enablement requirement. Lilly argues that undue experimentation would be required for one artisan to synthesize all members of the genus of selective PDE5 inhibitors. Dkt. No. 375, at 31-32. That is not the correct inquiry. A patent must enable a skilled artisan to practice the full scope of the invention; it does not need to ensure that a skilled artisan can practice the entire scope of the invention within a short period of time. See In re Wands, 858 F.2d 731, 739 (noting that "[t]he nature of monoclonal antibody technology is that it involves screening hybridomas to determine which ones secrete antibody with desired characteristics," among other process steps, and that the patentee's success in developing candidates through this procedure "indicates that . . . the amount of effort needed to obtain such antibodies is not excessive"). Such a rule would invalidate all broad claims for lack of enablement.

Lilly also fails to appreciate the distinction between what is required to practice the invention and what is required for FDA approval of a selective PDE5 inhibitor as a drug to treat BPH. See Kemin Foods, L.C. v. Pigmentos Vegetales Del Centro S.A. de C.V., 464 F.3d 1339,

[12] Indeed, Lilly's expert Dr. Roehrborn published articles about the efficacy of PDE5 inhibitors to treat BPH, relying on the work of one of the inventors, Dr. Ückert. See Dkt. No. 342, Trial Tr. at 609 (Dr. Roehrborn's article cites Dr. Ückert's 2001 article, which reports results from the tissue strip experiments referenced in the '124 patent).

1350 (Fed. Cir. 2006) (rejecting the argument that the claim term "'no traces of toxic chemicals' should be interpreted as limiting the claim to products in which the levels of all chemicals are below the toxic thresholds set by the [FDA]," because "[n]either the patent nor our claim construction . . . makes any reference to toxicity thresholds, whether promulgated by the FDA or otherwise."); see also Mitsubishi Chem. Corp. v. Barr Labs., Inc., 435 F. App'x 927, 934-35 (Fed. Cir. 2011) (refusing to limit a claim covering a pharmaceutical composition "to those compositions that are 'safe, effective, and reliable for use in humans'" because "[t]he specification does not require this restrictive construction, nor is this property necessary for patentability."); In re '318 Patent Infringement Litig., 583 F.3d 1317, 1324 (Fed. Cir. 2009) ("human trials are not required for a therapeutic invention to be patentable"). In its motion, Lilly repeatedly refers to the work that Lilly did to develop Cialis and obtain FDA approval. But that amount of experimentation, whether "undue" or not, is far beyond the amount of experimentation required to practice the scope of claim 1 of the '124 patent. See Dkt. No. 344, Trial Tr. at 1295 (Dr. Bell's opinion that claim 1 does not require the amount of experimentation necessary to satisfy FDA approval standards).

More generally, Lilly argues that the '124 patent does not include a variety of other tests and data showing that the invention works. See Dkt. No. 375, at 33-36. But the standard for enablement does not require a particular kind of confirmatory evidence or, depending on the facts of the case, any confirmatory evidence at all. See Alcon Research, 745 F.3d at 1189-90 ("[W]e have rejected enablement challenges based on the theory that there can be no guarantee that the prophetic examples actually work"; "it is irrelevant here, as a legal matter, whether the . . . patents contain data proving that PECOs enhance the chemical stability of prostaglandins."). The patentees do not need to disclose data showing that any particular selective PDE5 inhibitor

treats BPH; rather, the patentees merely need to enable a skilled artisan to practice the invention of using a PDE5 inhibitor to treat BPH. And while Lilly complains that its experts testified that BPH "is indisputably 'complex,' 'poorly defined,' 'highly variable,' and 'complicated,'" Dkt. No. 393, at 16, the jury was not required to credit that testimony. The '124 patent's disclosure specifies the mechanism by which PDE inhibitors work, how those inhibitors may be used to relax smooth muscle tissue, and how relaxation of prostatic smooth muscle tissue to treat BPH was known in the prior art. '124 patent, col. 1, line 9 through col. 2, line 5. Given that evidence, a reasonable jury could have found that claim 1 was sufficiently enabled regarding the use of PDE5 inhibitors to treat BPH.

UroPep points out in its response that there was evidence at trial supporting each of the factors identified in In re Wands, 858 F.2d at 728, that bears on enablement. UroPep's evidence showed that the quantity of experimentation necessary was routine; that the specification provided direction and guidance in light of the description, incorporated references, and the knowledge of persons of skill in the art; that the specification provides working examples; that the nature of the invention was the administration through traditional means of well-understood compounds as a novel method of treatment; that the state of the prior art was well developed and far out of its infancy; that the level of skill of those in the art was high; that the art showed that the mechanism of PDEs was known, that the research field regarding selective PDE5 inhibitors was mature, and that the relaxation of prostatic tissue would predictably treat BPH; and that claim 1 of the '124 patent, although broad, was nonetheless narrowed to a particular embodiment. See Dkt. No. 385, at 26-36.

Lilly makes the additional argument that this case is controlled by Wyeth v. Abbott Laboratories, 720 F.3d 1380 (Fed. Cir. 2013), in which the Federal Circuit held certain claims

invalid for lack of enablement. But Lilly's comparison of the facts in this case to the facts in Wyeth is faulty, as Lilly assumes facts that the jury was not required to find. For one, Lilly states that PDE5 inhibitor research was "an unpredictable and poorly understood field." Wyeth, 720 F.3d at 1386. UroPep presented ample evidence to the contrary. Lilly then states that the '124 patent provides no guidance as how to treat BPH and evaluate that treatment. Dkt. No. 375, at 30-31. UroPep, however, introduced evidence that such guidance was found both in the patent and in the prior art, and that procedures for such measurements were both incorporated in the patent and well understood—indeed, routine—in the art. Finally, Lilly argues that running the assays for a single compound would take weeks and thus constituted "undue experimentation" under the court's decision in Wyeth. 720 F.3d at 1386. In that regard, Lilly notes that it spent 10 years to obtain FDA approval for Cialis. But, once again, FDA approval is not required to enable a patent claim to a medicinal compound or a method of treatment. And, as the court in Wyeth observed, "[u]ndue experimentation is a matter of degree. Even a considerable amount of experimentation is permissible as long as it is merely routine or the specification provides a reasonable amount of guidance regarding the direction of experimentation." Id. at 1385-86 (internal citations and quotation marks omitted). In the context of a disclosure and a field that provides no guidance, aimless plodding through systematic experimentation of a single compound that would take weeks may be undue. See id. at 1386. By contrast, the '124 patent guides a practitioner to preferred selective PDE5 inhibitors and routine methods of evaluating and developing other inhibitors, in the already well-developed field of PDE5 inhibitor research.

Lilly has not shown it is entitled to judgment as a matter of law, nor has it shown that the "great weight of the evidence" is in its favor on the issue of enablement such as to justify the grant of a new trial.

IV. Obviousness

Lilly contends (in some tension with its position on the written description requirement and enablement) that everything of substance that was disclosed in the ’124 patent was known in the prior art, and that claim 1 of the patent must be held invalid for obviousness as a matter of law. In particular, Lilly notes that it was known before the ’124 patent that relaxing smooth muscle tissue in the prostate can help ameliorate urination difficulties and that PDE inhibitors can relax smooth muscle tissue by reducing the digestion of cAMP and cGMP by PDE enzymes. According to Lilly, it would have been obvious to a person of skill in the art, knowing what was known in the prior art at the time of the invention, to conclude that a PDE5 inhibitor would be useful in the treatment or prophylaxis of BPH.

In light of the burden on Lilly to show obviousness by clear and convincing evidence, the jury was entitled to find from the evidence at trial that claim 1 of the ’124 patent would not have been obvious. Dr. Ückert testified (and Lilly does not dispute) that the inventors discovered PDE1, PDE4, and PDE5 in the prostate. After conducting experiments designed to identify the functional relevance of PDE enzymes in the prostate, the inventors determined that PDE5 inhibition relaxes prostatic smooth muscle tissue, and that PDE5 inhibitors could treat the signs and symptoms of BPH. Dkt. No. 341, Trial Tr. at 162-70; see also Dkt. No. 342, Trial Tr. at 309.

In addition to Dr. Ückert’s testimony, Dr. Bell testified that it was impossible to predict in advance which PDEs would be present in which organ, or what role, if any, a particular PDE would play in that organ. Dkt. No. 344, Trial Tr. at 1285. The jury also heard objective evidence of non-obviousness relating to the commercial success that flowed from the use of PDE5 inhibitors to treat BPH.

In its argument to the contrary, Lilly contends that in view of the state of the art at the time of the invention, a reasonable jury would have been compelled to find the invention invalid for obviousness. That is particularly so, according to Lilly, because the '124 specification discloses that the prior art had discovered the mechanism of PDEs in smooth muscle, the role of PDE inhibitors, and the fact that relaxing smooth muscle would treat BPH.

The problem with that argument is that Lilly has failed to show that it was obvious to use a selective inhibitor of PDE5 to treat BPH. At the time of the invention, it was not known that PDE5 was even present in the prostate. See Dkt. No. 341, Trial Tr. at 161-62. Furthermore, other research showed that PDE5 was not particularly relevant in the bladder, which, like the prostate, is part of the urogenital tract. See id., Trial Tr. at 161. It was the inventors of the '124 patent who performed experiments and discovered that PDE5 was present and functionally relevant in prostatic tissue. Based on that discovery, they used the knowledge in the prior art to come up with a novel method of treating BPH.

Given what was known in the prior art, Lilly did not show that it would have been obvious to consider using PDE inhibitors to relax prostatic tissue, and that it would have been obvious to use selective inhibitors of PDE5 to treat BPH. Moreover, the prior art reference on which Lilly principally relies for its obviousness argument, a 1995 article by Arthur L. Burnett, DX 1245, did not describe the use of a selective PDE5 inhibitor to treat BPH, that PDE5 was found in the prostate, or even that PDE5 should be investigated. See Dkt. No. 342, Trial Tr. at 507. In fact, Dr. Bell testified at trial that the Burnett article taught away from the presence and role of PDE5 in the prostate. Dkt. No. 344, Trial Tr. at 1290-92. Dr. Bell explained that the analysis in the article pointed to PDE3 inhibition, rather than PDE5 inhibition, as being potentially relevant in the prostate.

Lilly invokes the Federal Circuit's decision in PharmaStem Therapeutics, Inc. v. ViaCell, Inc., 491 F.3d 1342 (Fed. Cir. 2007), in support of its obviousness argument, but that case is quite different from this one. In PharmaStem, the prior art references had inferred that the concentration of stem cells in umbilical cord blood was much greater than in adult blood. The court therefore rejected the patent holder's argument that the inventors had discovered that stem cells are present in high concentrations in cord blood. The inventors merely provided experimental confirmation of what the prior art references had inferred. The court held that to be insufficient to avoid a finding of obviousness. 491 F.3d at 1362-63. In this case, there was no equivalent finding or suggestion in the prior art that PDE5 was found in the prostate or what functional role PDE5 would play in the prostate. Given the state of the evidence as to what was taught and what was not taught in the prior art, the Court concludes that substantial evidence supports the jury's conclusion that Lilly failed to prove by clear and convincing evidence that the claimed invention would have been obvious to a person of skill in the art as of the priority date of the '124 patent.

V. Anticipation

Continuing its march through each of the defenses recognized by title 35, Lilly next argues that the jury improperly rejected its defense that claim 1 of the '124 patent was anticipated by a prior art reference that was introduced at trial. In making that argument, Lilly again faces an exacting standard: It must show that a rational jury could not have found that Lilly failed to prove the factual defense of anticipation by clear and convincing evidence. Orion IP, LLC v. Hyundai Motor Am., 605 F.3d 967, 975 (Fed. Cir. 2010). The evidence Lilly points to does not come close to satisfying that standard.

The putatively anticipating reference is a monograph by Dr. C.S. Cheung, a practitioner of traditional Chinese medicine. Brian LaForgia, one of Dr. Cheung's associates, testified at trial that Dr. Cheung made his monographs available to interested persons through a catalog that was mailed to acupuncturists and other persons interested in Dr. Cheung's work. Dkt. No. 343, Trial Tr. 885-87. Lilly made no showing that Mr. LaForgia, or acupuncturists in general (absent other training or experience), qualify as persons of skill in the art for purposes of the '124 patent. Id., Trial Tr. at 898.

The reference Lilly highlighted at trial was a self-published 107-page monograph entitled "TCM Management Benign Prostate Hyperplasia Long Bi (Prostatism)," which pertained to the treatment of BPH. Dkt. No. 343, Trial Tr. at 882-85. Mr. LaForgia testified that the monograph was listed in Dr. Cheung's catalogs from 1995 and 1996, and that in late 1994 or early 1995 he saw the monograph in the library of an organization known as the American College of Traditional Chinese Medicine in San Francisco. Mr. LaForgia said that the American College of Traditional Chinese Medicine had been formed by Dr. Cheung and two other doctors. Id., Trial Tr. at 886-91. Mr. LaForgia admitted that he had no idea how books were cataloged in that library. Id., Trial Tr. at 900-01. In fact, there was no evidence at trial that the books were cataloged at all.

Lilly's theory of anticipation was based on the portion of 35 U.S.C. § 102(b) that relates to an anticipating printed publication. See 35 U.S.C. § 102(b) (2006). That portion of the statute reads as follows: "A person shall be entitled to a patent unless—the invention was patented or described in this or a foreign country . . . more than one year prior to the date of the application

for patent in the United States."[13] The Court allowed the anticipation defense to go to the jury, but the jury found that the Cheung monograph did not anticipate claim 1 of the '124 patent.

In order to satisfy the requirements of section 102(b), a party challenging a patent on "printed publication" grounds must show that the allegedly invalidating publication contains "each and every element of [the] claimed invention." Lewmar Marine, Inc. v. Barient, Inc., 827 F.2d 744, 747 (Fed. Cir. 1987); see generally PIN/NIP, Inc. v. Platte Chem. Co., 304 F.3d 1235, 1243 (Fed. Cir. 2002). In addition, the printed publication must have been in the public domain more than a year before the priority date of the application, which in this case means before July 9, 1996. See SRI Int'l, Inc. v. Internet Sec. Sys., Inc., 511 F.3d 1186, 1194 (Fed. Cir. 2008). The Court concludes that it was reasonable for the jury to reject Lilly's anticipation defense in this case, based on findings either (1) that the evidence did not establish that the Cheung reference contained all the limitations of claim 1 of the '124 patent, or (2) that the Cheung reference was not in the public domain before July 9, 1996.

A. Anticipation by Cheung

The Cheung monograph contains a brief report of a study (not conducted by Dr. Cheung) in which 34 subjects were administered a "basic formula" containing a variety of herbs, including Horny Goat Weed. Horny Goat Weed, also known as epimedii, is an herb that contains a small amount of icariin, a known PDE5 inhibitor. Lilly contends that the Cheung reference described all 34 subjects as having been given Horny Goat Weed and that the study proved that the Horny Goat Weed ingested by the subjects was responsible for an improvement

[13] In 2011, section 102(b) was amended and recodified as part of the Leahy-Smith America Invents Act ("AIA"). Because the application that matured into the '124 patent was filed prior to March 16, 2013, the pre-AIA version of section 102(b) applies to this case. See AIA, 125 Stat. 284, 293 (2011).

in BPH symptoms in most of the subjects. The Cheung reference, however, is not at all clear on that point, for several reasons.

First, in the reported study the subjects were given a variety of herbs. It was therefore unclear that icariin was the component that was responsible for the improvement in symptoms reported by most of the subjects. Lilly's expert, Dr. Claus Roehrborn, conceded that "it is possible that there are some compounds in the other herbs having an effect on the prostate or the symptoms." Dkt. No. 342, Trial Tr. at 573.

Second, the description of the composition given to the subjects did not make it clear that all of the subjects received icariin, since it appears from the Cheung reference that Horny Goat Weed was an optional, not a mandatory, ingredient in the formulation given to the subjects. Dr. Roehrborn testified that the fact that Horny Goat Weed was listed as an ingredient in one of the two formulations that were administered to subjects in the study reported by Cheung indicates that at least some of the subjects received a formulation containing Horny Goat Weed. While that may be true, Dr. Roehrborn did not testify, and the evidence did not clearly establish, that Horny Goat Weed was found in the formulation that was given to any of the subjects who reported favorable results; so far as the evidence shows, Horny Goat Weed (and thus icariin) could have been contained only in the formulations given to the subjects who did not report an improvement in their symptoms.

Finally, evidence offered by UroPep at trial showed that icariin is a far less potent PDE5 inhibitor than tadalafil. See Dkt. No. 344, Trial Tr. at 1249 (5 milligrams of tadalafil is equivalent to 8120 milligrams of icariin). In addition, the evidence showed that Horny Goat Weed contains, by generous estimate, only 0.5% icariin. Id. at 1247. Based on that evidence, UroPep's witness, Dr. Bell, testified that a patient would have to eat approximately 1.6 kilograms

(3.5 pounds) of Horny Goat Weed to get the same effect as a 5 milligram dose of Cialis. Id. at 1250. Yet the Cheung study indicated that the amount of Horny Goat Weed ingested by the subjects of that study was only 15 grams. See DX 1551, at 80 (listing 15 grams of "Hb. Epimedii" as part of one of the two basic formulations used in the reported study). Based on that evidence, the jury could have concluded that the small amount of icariin in the Horny Goat Weed administered to some of the subjects in the reported study would not have been enough to have a measurable effect on the subjects' BPH symptoms, and thus would not have satisfied the "effective amount" limitation of the '124 patent.

In support of its anticipation argument, Lilly cites Rasmusson v. SmithKline Beecham Corp., 413 F.3d 1318 (Fed. Cir. 2005), which Lilly characterizes as "a case remarkably similar to this one." Dkt. No. 393, at 22. In fact, Rasmusson is not at all like this case. In Rasmusson, the prior art reference at issue taught the same method for administering the same drug that was claimed in the patent in dispute. The appellee argued that the prior art reference did not anticipate because it presented data showing that the method did not have anti-tumor effects, while the patent contained data showing the opposite. 413 F.3d at 1326. The court held that for anticipation it was enough that the prior art reference disclosed the invention, even though the reference may not have recognized the effectiveness of the invention for the purpose later identified in the patent. This case presents a very different scenario. Based on the evidence before it, the jury could readily have found that the administration of Horny Goat Weed discussed in the Cheung monograph differed materially from the administration of PDE5 inhibitors claimed in the '124 patent in a way that prevented the Cheung composition from satisfying the limitation requiring the administration of an "effective amount" of a PDE5 inhibitor.

In light of the evidence at trial summarized above, a reasonable jury could readily have concluded that Lilly failed to prove anticipation because the Cheung reference did not entail the ingestion of enough Horny Goat Weed to have a therapeutic effect on patients' BPH. In that event, the Cheung reference would not satisfy the "effective amount" limitation of claim 1 of the '124 patent.

B. Printed Publication

As a second ground for rejecting Lilly's anticipation defense, the jury could have found that the evidence failed to show that the Cheung reference qualified as a "printed publication." To satisfy that element of section 102(b), a reference must have been "disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence, can locate it." Kyocera Wireless Corp. v. Int'l Trade Comm'n, 545 F.3d 1340, 1350 (Fed. Cir. 2008).

The jury could readily have found that the Cheung reference was not made available to the public by July 1996 in a manner that would have made it accessible to persons of skill in the art. Mr. LaForgia's testimony—the only evidence regarding the distribution of the Cheung monograph—did not establish that the publication was distributed or cataloged in a way that would have made it reasonably available to a person of skill in the pertinent art. Instead, his testimony indicated only that a catalog containing an advertisement of the publication—not the publication itself—was sent to persons who had expressed an interest in Dr. Cheung's work, not persons of skill in the art, and that Mr. LaForgia found the monograph in the library of Dr. Cheung's organization, the American College of Traditional Chinese Medicine. Mr. LaForgia did not know whether, or how, the publication was cataloged in that library; there was no evidence that the publication could be found in any other locations or obtained from any source

except directly from Dr. Cheung; and there was no evidence that persons of skill in the relevant art frequented, or even were aware of the American College of Traditional Chinese Medicine.[14] In light of the infirmities in the "printed publication" evidence offered through Mr. LaForgia, a reasonable jury could readily have concluded that Lilly failed to prove that element of the defense of anticipation by clear and convincing evidence. See Applied Med. Res. Corp. v. U.S. Surgical Corp., 147 F.3d 1374, 1378 (Fed. Cir. 1998). Accordingly, Lilly's motion for JMOL on anticipation must be denied. In addition, the "great weight of the evidence" does not support Lilly on anticipation, so Lilly's Rule 59 motion on that ground is denied as well.

VI. Indefiniteness

Lilly next asserts that the evidence at trial establishes that claim 1 of the '124 patent is invalid for indefiniteness. Prior to trial, Lilly argued that the Court's construction of claim 1 as requiring the "inhibitor of phosphodiesterase (PDE) V" to be at least 20 times more selective for PDE5 than for PDE1 through PDE4 rendered claim 1 indefinite. The Court treated the question of indefiniteness as a legal issue related to claim construction and rejected Lilly's indefiniteness argument. Dkt. No. 234, at 28-47; Dkt. No. 294, at 5-8.

Pointing to the trial testimony of its expert, Dr. Joseph A. Beavo, Lilly contends that the Court must revisit its pretrial ruling on indefiniteness. Contrary to Lilly's submission, however, nothing in Dr. Beavo's testimony affects the Court's determination that the "inhibitor of phosphodiesterase (PDE) V" limitation, as construed, does not render claim 1 of the '124 patent fatally indefinite.

[14] Prior to trial, Lilly represented that it was prepared to introduce evidence that the Cheung publication could be found in other libraries. See Dkt. No. 200, at 13. No such evidence was offered at trial, however.

To begin with, there is nothing "indefinite" about a requirement that a particular inhibitor be 20 times more selective for one PDE than for another. The '124 patent describes the potency of a PDE inhibitor by reference to its "IC_{50} value," which is the concentration of the PDE inhibitor necessary to inhibit 50 percent of the PDE enzyme's hydrolysis of the target substrate molecules (cAMP or cGMP). '124 patent, col. 8, ll. 5-9. The specification of the '124 patent asserts that there are "known methods" for determining whether a compound is a PDE5 inhibitor, such as those described in two cited articles from 1989 and 1990. In addition, the patent provides, as an example, a description of the procedure used to determining the level of enzyme activity by a method known as the peak fractionation method; that description is based on a 1995 paper by Michael C. Truss et al. Id., col. 7, line 38, through col. 8, line 16; see also Dkt. No. 343, Trial Tr. at 664-65.

It does not matter whether it was difficult, using the testing protocols that were described in the patent (and that were available as of the patent's priority date), to determine exactly the levels of activity of a particular compound vis-à-vis different PDEs. The "20 times" requirement is clear on its face. For that reason, even though Dr. Beavo was critical of the testing protocols described in the patent, Dkt. No. 343, Trial Tr. at 671-91, nothing in Dr. Beavo's testimony suggests that the "20 times" requirement is indefinite. In particular, he does not suggest that there is no way to determine whether a particular compound is 20 times as selective for one PDE than for another or that available testing methods are so unreliable that the claim 1 of the '124 patent "fail[s] to inform, with reasonable certainly, those skilled in the art about the scope of the invention." Nautilus, Inc. v. Biosig Instruments, Inc., 134 S. Ct. 2120, 2124 (2014). Thus, even if the patent had contained no description of any particular testing protocol, the "20 times" requirement would not have been invalid for indefiniteness.

Beyond that, while Dr. Beavo was critical of the protocol described in the Truss article, which discussed the use of the peak fractionation method to determine the presence of PDEs in a pig's bladder, he did not suggest that the fractionation method itself could not be used to obtain reliable data regarding the relative effectiveness of PDE5 inhibitors. Rather, he was critical of the particular application of that method in the three articles cited in the patent. His quarrel with the Truss article was that the methodology used did not adequately separate PDE5 from other PDEs, and his quarrel with the other two articles was that they did not test for PDE5, but instead tested for other PDEs. See Dkt. No. 343, Trial Tr. at 691. On cross-examination, Dr. Beavo acknowledged that the peak fractionation method had been used to identify the presence of PDE5 in tissues other than a pig's bladder. Id., Trial Tr. at 700-03. Whatever the validity of Dr. Beavo's criticism of the testing protocol used in the Truss paper and in the other two cited articles, Dr. Beavo's testimony does not undermine the use of peak fractionation as a method of determining the presence of PDE5, and thus as a means of determining the IC_{50} values of various PDE5 inhibitors.

The peak fractionation testing methodology disclosed in the three articles cited in the '124 patent may have produced different results depending on "experimental conditions," as testified by Dr. Beavo. Dr. Beavo's testimony, however, did not establish that the fractionation method described in the articles was so unreliable as to provide no guidance in determining the selectivity of particular compounds for various PDEs. To the contrary, Dr. Bell testified that the methods for testing potency and selectivity referred to in the '124 patent "are very common and are commonly used throughout the industry." Dkt. No. 344, Trial Tr. at 1284. He added that the fractionation method described in the articles cited in the '124 patent "was the standard method that was being used particularly in industry at the time" of the patent. Id., Trial Tr. at 1284-85.

For that reason as well, the Court rejects Lilly's argument that Dr. Beavo's testimony established that the requirement that the PDE5 inhibitor claimed in the '124 patent had to be at least 20 times as selective for PDE5 than for PDE1 through PDE4 rendered the claims invalid for indefiniteness.

VII. Claim Constructions

In the next portion of its brief, Lilly casts the widest possible net, asserting, without specificity, that it is entitled to JMOL "based on the claim constructions given by the Court to the jury, including those constructions given over Lilly's objections." Dkt. No. 375, at 51. In addition, Lilly asserts, without supporting argument, that the Court's constructions of the terms "prophylaxis," "a person in need thereof," "effective amount," and "inhibitor of phosphodiesterase (PDE) V" were all erroneous. Id. at 52. Because Lilly has made no new arguments in its JMOL motion with respect to its assertions based on claim construction, the Court will not rehearse at length each of the claim construction rulings made earlier in the case.

As for the last of the claim constructions that Lilly contests, "inhibitor of phosphodiesterase V," the Court addressed Lilly's argument at length in an order filed on March 3, 2017. Dkt. No. 234, at 3-12. That discussion will not be repeated here. As for the claim terms "a person in need thereof" and "effective amount," the Court notes that Lilly offered no competing constructions for the terms; rather, Lilly simply argued that those terms were indefinite. See Dkt. No. 106, at 18, 22. As for the construction of the term "prophylaxis," Lilly has no ground for arguing that the Court's construction was erroneous, inasmuch as the Court essentially adopted Lilly's proposed construction of that term, and Lilly agreed to the Court's construction. Compare Dkt. No. 115, at 5-6 (Court stating at the claim construction hearing that "Defendants have suggested that 'prophylaxis' should be construed to mean 'prevention of a

disease or a process that can lead to disease.' . . . [I]f it comes to giving a jury an instruction, I think it would be very helpful to have a definition of 'prophylaxis.' So I would be inclined to give such a definition, and that seems to me as good a definition as any.") with Dkt. No. 346, Trial Tr. at 1412 (instructing the jury that "[t]he term 'prophylaxis' means 'prevention of the progression or development of the disease.'"); see also Dkt. No. 115, at 16 (Lilly's counsel arguing at the claim construction hearing that the term "prophylaxis has to include prevention," and agreeing that prevention was "clear enough" in the Court's construction of "prophylaxis"). A party "cannot be allowed to create a new claim construction dispute following the close of the jury trial," Broadcom Corp. v. Qualcomm Inc., 543 F.3d 683, 694 (Fed. Cir. 2017), particularly when the party challenges a construction that the party itself endorsed.

VIII. New Trial

In addition to arguing generally that it is entitled to a new trial on each of the grounds asserted in its JMOL motion (including some as to which the sole logical consequence of Lilly's prevailing would be the entry of judgment in Lilly's favor, not a new trial), Lilly makes a separate argument for a new trial on four different grounds.

A. The Jury Instruction on Enablement

Claim 1 of the '124 patent recites, in part, a "method for prophylaxis or treatment of benign prostatic hyperplasia." At the charge conference, Lilly requested an instruction that the '124 specification must enable a person of ordinary skill in the art to practice both the "treatment" and "prophylaxis" of BPH, and that it would not be sufficient for the patent to enable treatment alone. Dkt. No. 325, at 5-6. The Court declined to give such an instruction. Dkt. No. 346, Trial Tr. at 1396. Both at that time and in a later written order, see Dkt. No. 359, at 7-10, the Court explained that it denied the requested instruction on three grounds: (1) that the

evidence at trial focused almost entirely on treatment; (2) that treatment and prophylaxis, as those terms were used in the patent, were largely overlapping; and (3) that a specific instruction requiring enablement of both treatment and prophylaxis could be confusing to the jury.

First, as the Court noted in its order addressing Lilly's requested instruction, there was very little discussion of the issue of prophylaxis during the course of the trial; the focus of the evidence, including the evidence supporting Lilly's invalidity defense, was on treatment. To the extent that prophylaxis was discussed at all, it was discussed in the context of treatment (such as testimony from Lilly's expert that prophylaxis included preventing a patient's BPH symptoms from becoming worse).

In support of its proposed instruction, Lilly points out in its brief, Dkt. No. 375, at 53, that Dr. Roehrborn testified that a person of ordinary skill in the art would not be able to determine the amount of a PDE5 inhibitor that would be required for the effective treatment of BPH. Dkt. No. 342, Trial Tr. at 545. Dr. Roehrborn was then asked, "Did the ['124] patent provide any information that you can determine or a person of ordinary skill in the art can regarding the effective amount that would be given to have prophylaxis of BPH?" He responded, "No it does not." Id. In response to another question, Dr. Roehrborn stated: "So, prophylaxis, meaning to prevent either the disease or prevent it from getting worse, would be probably the toughest assignment because it's so variable, would take such a long time to study it, and it would take a lot of people to study it." Id., Trial Tr. at 528.

Lilly points to no other evidence beyond those two conclusory statements regarding the enablement or written description issues as they pertain to prophylaxis. Instead, throughout the trial, including in other portions of Dr. Roehrborn's testimony, prophylaxis and treatment were treated together as a single process. See Dkt. No. 342, Trial Tr. at 546-47 (Dr. Roehrborn: "And

when it comes to looking at the issue of prevention or progression, it is even more complicated because it is highly unpredictable of a thousand men, how many of them will progress and how many will the symptoms get worse. . . . So, if you want to show an effect on preventing or progression, it would take a long, long time."); id., Trial Tr. at 547 (Dr. Roehrborn: "it is very difficult to define an effective amount given that the claim involves prevention, prophylaxis, and treatment").

Second, and relatedly, the terms "treatment" and "prophylaxis," as used in the '124 patent, do not describe distinct processes. In its initial claim construction order in this case, the Court acknowledged that, as UroPep's expert explained, there was "no clear distinction [drawn] between prophylaxis and treatment for BPH." Dkt. No. 131, at 9. The Court stated that "a course of medication designed to deal with the condition could be regarded as either prophylaxis or treatment, depending on the physician's judgment as to whether the patient has BPH or merely has risk factors for BPH or has at least one of the symptoms of BPH." Id. The Court noted that the uncertainty as to whether therapy should be considered treatment or prophylaxis might create a categorical difficulty, but "because the patent claims at issue in this case cover both prophylaxis and treatment, the overlapping nature of the two terms is not problematical." Id. at 9-10.

Similarly, Dr. Roehrborn defined prophylaxis as "meaning to prevent either the disease or prevent it from getting worse." Dkt. No. 342, Trial Tr. at 527; see also id., Trial Tr. at 546-47 (referring to "prevention or progression"). Given that the terms "prophylaxis" and "treatment" are largely overlapping and that Lilly made no effort at trial to suggest that they required significantly different analysis under the written description or enablement requirements, there was no need to instruct the jury that it needed to conduct a separate invalidity analysis for each

term. Any such instruction would simply have been confusing to the jury in light of the manner in which the case was tried.

Finally, the instruction that Lilly sought was directed to the principle that section 112, paragraph 1, requires that the specification enable the full scope of the claim, not just a single embodiment or group of embodiments. See Liebel-Flarsheim, 481 F.3d 1378-79. The Court in fact gave such an instruction, directing the jury that "[t]o be valid, a patent must contain a description of the manner of making and using the invention that would enable a persons of skill in the art to make and use the full scope of the invention without undue experimentation. Lilly contends that claim 1 of the '124 patent is invalid because the patent does not contain a sufficiently full and clear description of how to make and use the full scope of the invention. In order to invalidate the '124 patent for lack of enablement, Lilly must prove by clear and convincing evidence that the '124 patent would not have enabled such a person to make or use the full scope of the invention." Dkt. No. 346, Trial Tr. 1428; see also id., Trial Tr. 1429.[15] The principle to which Lilly's proposed instruction was directed was thus already incorporated in the Court's charge, although not with the specificity that Lilly requested. Thus, nothing barred Lilly from making a specific argument to the jury as to non-enablement of prophylaxis in its closing argument, but Lilly chose not to do so.

The Court therefore denies the motion for a new trial based on the failure to instruct as to the separate enablement of prophylaxis.

[15] At Lilly's request, the Court gave a similar instruction with regard to the written description requirement: "The written description requirement is satisfied if a person of ordinary skill reading the patent would have recognized that it describes the full scope of the invention that is claimed in the patent and that the inventor actually possessed the full scope of the invention as of the filing date of the patent." Dkt. No. 346, Trial Tr. at 1426; see also id., Trial Tr. at 1427; Dkt. No. 344, Trial Tr. at 1365 (Lilly's counsel argued that, as to written description, "whenever we talk about the invention, we need to talk about the full scope of the invention.").

B. The Court's Failure to Instruct on Laws of Nature

Lilly contends that the Court should have instructed the jury that laws of nature are not patentable. The Court declined to give such an instruction because Lilly did not challenge the '124 patent on grounds of unpatentability under 35 U.S.C. § 101. Lilly concedes that it did not raise a section 101 challenge to the patent, but it contends that it was entitled to such an instruction anyway, and that the failure to give that instruction was prejudicial error.

Prior to trial, Lilly submitted a proposed instruction that a person who discovered that fires require oxygen would not be entitled to a patent on the process of making a fire by lighting a flame in the presence of oxygen. Dkt. No. 250-2, at 19-20; Dkt. No. 317-1, at 14. That instruction, however, was part of Lilly's requested instruction on anticipation; it related to the role of inherency in the law of anticipation, not to the principle that a natural phenomenon cannot be patented.[16] The Court declined to include the "fire and oxygen" example in its instruction on anticipation. In its proposed instructions, Lilly did not request an instruction on a section 101 defense or to the effect that laws of nature are not patentable.

During the charge conference at trial, Lilly requested that the Court instruct the jury that "the simple discovery that PDE5 is in the prostate or that PDE5 plays a functional role in the prostate is not . . . part of the analysis for this claim." Dkt. No. 353, Trial Tr. at 1361. In a brief filed in support of its request that the Court give such an instruction, Lilly asked the Court to instruct the jury that "the discovery of a phenomenon of nature cannot be the basis for patent protection." See Dkt. No. 325, at 4. As legal authority in support of that request, Lilly cited 35 U.S.C. § 101 and two cases applying section 101, Association for Molecular Pathology v.

[16] Lilly's proposed instruction was taken directly from an opinion dealing with the law of inherent anticipation, EMI Grp. N. Am., Inc. v. Cypress Semiconductor Corp., 268 F.3d 1342, 1351 (Fed. Cir. 2001). The Court is unaware of that language ever having been used outside of that context.

Myriad Genetics, Inc., 133 S. Ct. 2107 (2013), and Mayo Collaborative Services v. Prometheus Laboratories, Inc., 566 U.S. 66 (2012). The Court declined to give that instruction, noting that Lilly had not raised section 101 as a defense in this case. Dkt. No. 346, Trial Tr. at 1397.

For the Court to in effect introduce a section 101 defense into the case for the first time at the instruction stage would have been entirely unwarranted. Lilly did not plead section 101 as a defense in its answer, and nothing in the pretrial proceedings or the presentation of the case to the jury laid the basis for a section 101 defense. An instruction essentially directed to such a defense would have been confusing to the jury and unfairly prejudicial to UroPep.

Moreover, the instruction requested by Lilly in its brief on the jury instructions following the charge conference, Dkt. No. 353, would have been misleading. While it is true that a patent cannot be obtained on a natural law or phenomenon, it would be incorrect to instruct the jury that "the discovery of a phenomenon of nature cannot be the basis for patent protection," as Lilly requested. The discovery of a natural law or a phenomenon of nature can indeed serve as the "basis" for patent protection, as long as the phenomenon of nature is applied to achieve a useful result. As the Supreme Court has explained, "a process is not unpatentable simply because it contains a law of nature or a mathematical algorithm. It is now commonplace that an *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection." Diamond v. Diehr, 450 U.S. 175, 187 (1981) (quoting Parker v. Flook, 437 U.S. 584, 590 (1978)).

The language proposed by Lilly at the charge conference would have been even worse. Lilly requested that the Court instruct the jury that "the simple discovery that PDE5 is in the prostate or that PDE5 plays a functional role in the prostate is not part of the analysis for this claim." Dkt. No. 344 Trial Tr. at 1361. Such an instruction would have been clearly wrong. It

is perfectly legitimate for the discovery of the functional role of PDE5 to be "part of the analysis" of patentability, particularly when that discovery is applied to the administration of a PDE5 inhibitor in an effective amount to treat BPH—a prostatic disease. Diehr and other section 101 cases stand for the proposition that, in addition to reciting a law of nature, a patent must apply that law of nature to a problem in a way that reflects that the inventor has "invent[ed] or discover[ed]" a "new and useful process." 35 U.S.C. § 101; see Mayo Collaborative Servs. v. Prometheus Labs. Inc., 566 U.S. at 72 ; Bilski v. Kappos, 561 U.S. 593, 611 (2010). Lilly did not propose an instruction that would have made clear to the jury the distinction drawn by the Supreme Court in Diehr, so it would have been legal error for the Court to instruct the jury in the manner Lilly suggested. Accordingly, it was not legal error for the Court to decline to instruct the jury in accordance with Lilly's proposed language on the subject of the unpatentability of laws of nature. [17]

C. The Exclusion of the Bunnage References

Prior to trial, UroPep moved to strike a reference that Lilly had proposed to use in support of its invalidity defense. UroPep's motion was based on its contention that the reference had not been timely disclosed. Dkt. No. 253. The reference consisted of two applications filed on behalf of Pfizer Inc. by Mark Edward Bunnage—a Patent Cooperation Treaty application, WO 98/49166 ("the Bunnage PCT Application"), Dkt. No. 253-2, and an earlier application filed in the United Kingdom, to which the PCT application claims partial priority ("the Bunnage UK Application"), Dkt. No. 256-1.

Lilly disclosed the Bunnage PCT Application to UroPep early in the proceedings, listing it as "additional relevant art" in Lilly's initial invalidity contentions, without further elaboration.

[17] The Court also addressed Lilly's section 101 argument in detail in a post-trial memorandum opinion. Dkt. No. 359, at 13-14.

Dkt. No. 256-3, at 1. Lilly did not disclose the earlier Bunnage UK Application at that time; the Bunnage UK Application was not disclosed until the time of Dr. Bell's deposition in January 2017, long after the date had passed for disclosing prior art references in the defendant's invalidity contentions.

Lilly served amended invalidity contentions a month before trial indicating that Lilly planned to use the Bunnage reference as invalidating prior art at trial. Dkt. No. 253-1. UroPep then moved to strike that reference on the ground that it was an untimely disclosure of invalidating prior art. In response, Dkt. No. 256, Lilly withdrew the designation of the Bunnage PCT Application as prior art and argued instead that the two Bunnage applications should be admissible to show "simultaneous invention," a secondary consideration that bears on the issue of obviousness. See Geo M. Martin Co. v. Alliance Mach. Sys. Int'l LLC, 618 F.3d 1294, 1305 (Fed. Cir. 2010); Ecolochem, Inc. v. S. Cal. Edison Co., 227 F.3d 1361, 1379 (Fed. Cir. 2000).[18]

The Court ruled that the failure to disclose the Bunnage UK Application in Lilly's invalidity contentions and the disclosure of the simultaneous invention theory, in violation of the Court's Discovery Order, barred the affirmative use of those applications at trial. The Court stated, however, that Lilly would be permitted "to make use of that evidence for impeachment to the extent UroPep opens the door by offering contrary testimony." Dkt. No. 293, at 8-9.

1. Lilly begins by reiterating its contention that the Bunnage applications should have been admissible as affirmative evidence. As the Court noted in its initial order striking the use of the Bunnage applications as affirmative evidence, Lilly did not disclose the Bunnage UK

[18] Lilly withdrew the applications as prior art after UroPep pointed out that, as a legal matter, neither Bunnage application qualified as prior art to the '124 patent. The Bunnage PCT Application was filed in November 1998, long after the July 9, 1997, priority date of the '124 patent. Although the Bunnage UK Application was filed in April 1997, it was an unpublished foreign application and therefore did not qualify as prior art under 35 U.S.C. § 102(e).

Application at any point before January 2017, long after the invalidity contentions had been served and after the parties' expert reports had been exchanged. Lilly did not disclose its intention to use either application to prove "simultaneous invention" until March 31, 2017, only about two weeks before the trial.

There is no plausible ground for arguing that the Bunnage UK Application should have been admitted, as its disclosure was long out of time. Admitting it into evidence would have been plainly prejudicial to UroPep, which would have been denied the opportunity to have its experts consider and comment on the reference. As for the Bunnage PCT Application, although it was listed in a lengthy collection of "additional prior art" in Lilly's initial invalidity contentions, it was not discussed in any of Lilly's expert's reports, and the "simultaneous invention" theory of admissibility for that application was not disclosed until shortly before trial. As the Court noted in its order on the motion to strike the Bunnage applications, Dkt. No. 293, at 7-8, the Court's Discovery Order required Lilly to disclose the legal theories and factual bases for its claims and defenses. But prior to March 31, 2017, Lilly made no mention of the "simultaneous invention" component of its obviousness defense or the proposed role of the Bunnage applications as supporting a simultaneous invention theory.

Even if the Bunnage PCT Application had not been excludable because of Lilly's failure to satisfy its obligations under the Discovery Order, Lilly would not have been allowed to offer expert testimony regarding that document (or the theory of simultaneous invention), as Lilly does not point to any place where any of its experts discussed the document (or that theory) in their reports. It is therefore unclear to the Court how Lilly would have been able to offer the Bunnage PCT Application and the simultaneous invention theory at trial. Accordingly, the Court adheres

to its ruling on UroPep's motion to strike and holds that it was not error to exclude both Bunnage applications from Lilly's affirmative case.

2. The second issue that Lilly raises in the portion of its JMOL brief directed to the Bunnage applications relates to the Court's refusal to permit Lilly to use the applications during the cross-examination of Dr. Bell. Analysis of Lilly's argument on that issue requires a detailed recitation of the pertinent portions of Dr. Bell's deposition and the corresponding events at trial.

During Dr. Bell's deposition, Lilly asked Dr. Bell if he knew whether Pfizer, Dr. Bell's employer, had ever identified BPH as a target for a PDE5 inhibitor. Dkt. No. 256-2, at 65. Dr. Bell responded that it had. Asked if he knew when that had occurred, Dr. Bell referred to a patent application. When Lilly showed him the Bunnage PCT Application, Dkt. No. 253-2, which was filed in 1998, he recognized that as an application filed by Pfizer scientists. Lilly then pointed to the earliest priority date listed on that application, which was April 25, 1997. Dr. Bell agreed that the April 25, 1997, date was before the filing date of the '124 patent. Dkt. No. 256-2, at 66-67. Lilly then directed Dr. Bell's attention to a passage in the Bunnage PCT Application that recites various therapeutic uses for certain selective PDE5 inhibitors, including the treatment of BPH. Id. at 68. Finally, Lilly asked Dr. Bell the following questions:

> **Q.** So Pfizer scientists, at least by April of 1997, had identified PDEV inhibitors as useful to treat BPH?
>
> **A.** Since—I don't know. There are subsequent priority dates and a filing date. I don't know from this whether that initial filing included BPH.
>
> **Q.** We're going to educate you, sir.

Id. at 68-69.

Lilly then showed Dr. Bell the earlier Bunnage UK Application, Dkt. No. 256-1, and directed his attention to the page that listed the priority date for that application as April 25, 1997. Lilly then asked, "And that corresponds to the earliest priority date on [the later Bunnage

PCT Application], doesn't it?" Dr. Bell responded, "I would presume so, since you—never having looked at the initial documents, that looks sensible to me." Dkt. No. 256-2, at 69. Lilly then pointed out the reference to BPH in the UK Application and asked, "So, at least as of April 1997, Pfizer scientists had found that selective and potent PDE V inhibitors would be useful to treat BPH, and put it in a patent application, right?" Dr. Bell responded, "Yes, they believed it would be." Id. at 70.

On direct examination at trial, UroPep asked Dr. Bell if other PDE5 inhibitors, such as sildenafil, could be used to treat BPH, and Dr. Bell responded that they could. Dkt. No. 342, Trial Tr. at 320-21. UroPep did not ask Dr. Bell if he knew whether Pfizer had ever considered patenting sildenafil. On cross-examination, Lilly asked the following question: "And are you aware that Pfizer scientists themselves have discovered the use and filed a patent claim on the use of sildenafil to treat BPH before 1997, the filing date of the UroPep patent?" Id., Trial Tr. at 343. UroPep objected on the ground that the question violated the Court's previous order excluding the Bunnage applications except for impeachment purposes in the event that UroPep opened the door to impeachment with those applications.

The Court permitted Lilly to ask Dr. Bell how he knew that sildenafil can be used to treat BPH, but directed Lilly not to question Dr. Bell about the Bunnage applications. Dkt. No. 342, Trial Tr. at 346-48. When Lilly asked Dr. Bell how he knew that sildenafil can be used to treat BPH, Dr. Bell answered that he knew it from reading a 2014 paper on the subject. Id., Trial Tr. at 348. Lilly then asked Dr. Bell if he recalled "when Pfizer scientists first began looking at sildenafil to treat BPH," to which Dr. Bell responded, "I don't know the exact answer. I think—I believe it would have been after they filed the initial submission to the FDA in 1997, in September 1997." Id., Trial Tr. at 349. Lilly then asked, "Do you have any information that

Pfizer scientists were looking at using sildenafil to treat BPH before September of 1997?" Dr. Bell replied, "I do not." Id., Trial Tr. at 349-50.

At that point, Lilly sought to impeach Dr. Bell with his deposition testimony. Lilly represented (incorrectly) that "[h]is testimony in his deposition is he recalled the date. And I can refresh his recollection." Dkt. No. 342, Trial Tr. at 350.[19] UroPep objected on the ground that Dr. Bell's trial testimony did not contradict his deposition testimony. UroPep argued that Dr. Bell's testimony at the deposition was not based on his independent knowledge, but merely consisted of his reading from the Bunnage applications that Lilly provided to him. Id., Trial Tr. at 350-51. Lilly then asserted (again, incorrectly) that Dr. Bell remembered the April 1997 date in his deposition "after I refreshed his recollection."[20] Id., Trial Tr. at 351. Lilly argued that it was entitled to use the Bunnage applications to "re-refresh" Dr. Bell's recollection and to impeach him regarding his response to the question about his knowledge as to when Pfizer began looking at sildenafil to treat BPH. Id. Regarding the deposition, the Court asked Lilly's counsel, "What is said that suggests this is refreshment of recollection as opposed to simply recitation of something that is on the document?" Id., Trial Tr. at 353. Lilly's counsel replied, "He said he

[19] Dr. Bell did not testify in his deposition that he recalled the priority date of the Bunnage UK Application. Dr. Bell learned that date only because Lilly's counsel put the Bunnage applications before him and decided to "educate" him by pointing the date out to him. Dkt. No. 256-2, at 69. Thus, use of the Bunnage applications did not refresh Dr. Bell's recollection at the deposition and would not have refreshed his independent recollection at trial; at most, the Bunnage applications would have refreshed his recollection of Lilly's having pointed out the April 1997 date to him at his deposition.

[20] As noted, Dr. Bell's recollection was not refreshed as to that date at his deposition; he was simply directed to the date and accepted it as true. See Dkt. No. 256-2, at 69 ("Q. And this is identified as a priority document. If you go to the third page of Exhibit 5, do you see the stamp April 25, 1997 with the number 0708406.5? A. I do. Q. And that corresponds to the earliest priority date on Exhibit 4, doesn't it? A. I would presume so, since you – never having looked at the initial documents, that looks sensible to me.").

didn't know, and I handed him a document, and then he learned." Id. The court then had the following exchange with Lilly's counsel:

> **The Court:** Well, that's different from saying it refreshes his recollection. If you handed me a copy of your graduation – college graduation diploma and said, "Do you know when I graduated from college," I would look at it, and I would say, "Well, you know, 1984" or whatever. That wouldn't refresh my recollection.
>
> **[Lilly's counsel]:** Well, that's what I would like permission to do now is refresh his recollection with the documents that refreshed his recollection in the –
>
> **The Court:** Well, if it didn't refresh his recollection and all he did is recite what is on the documents, then that gets into just introducing the documents with no valid reason other than to get the documents in because we are not refreshing recollection. And that's not inconsistent with his testimony in the deposition.

Id., Trial Tr. at 354. The Court then ruled that there had been no showing that Dr. Bell "has an independent recollection that's been refreshed by the showing of the document." Id., Trial Tr. at 355.

Lilly argues that it was entitled to question Dr. Bell about the Bunnage applications either to refresh his recollection or to impeach him. Both theories are flawed, however.

As for refreshing Dr. Bell's recollection, it appears that Dr. Bell may have seen the Bunnage PCT Application in the course of his work on this case. See Dkt. No. 256-2, at 66; Dkt. No. 342, Trial Tr. at 356-57. But there is no indication that he had seen, or knew of, the earlier Bunnage UK Application, or that he was aware of the reference to the April 1997 priority date listed in the Bunnage PCT Application. Lilly's counsel simply pointed that date out to him at Dr. Bell's deposition. That does not constitute refreshing recollection. At trial, likewise, the use of the Bunnage applications would not have refreshed Dr. Bell's independent recollection as to the April 25, 1997 priority date. Simply showing Dr. Bell the April 25, 1997, date did not have the effect of "refreshing" his recollection; Lilly sought to use the Bunnage applications not to refresh Dr. Bell's independent recollection of the April 25, 1997, priority date, but to elicit the fact that he had agreed that the 1997 date was found in the Bunnage applications after having

been shown the date during his deposition. That use of the Bunnage applications would have been a distortion of the refreshing recollection procedure set forth in Rule 612 of the Federal Rules of Evidence.

It is well established that Rule 612 allows a writing to be used to refresh a witness's recollection only if the writing actually refreshes the witness's memory. See United States v. Carey, 589 F.3d 187, 190 (5th Cir. 2009); Thompson v. United States, 342 F.2d 137, 139-40 (5th Cir. 1965). The document must be used for purposes of refreshing, "and not for purposes of putting words in the mouth of the witness." Esperti v. United States, 406 F.2d 148,150 (5th Cir. 1969). The court "has the discretion to withhold any writing from a witness where the judge believes that the document will be the source of direct testimony rather than the key to refreshing the witness's independent recollection." United States v. Weller, 238 F.3d 1215, 1221 (10th Cir. 2001).

The policies underlying Rule 612 require that a court guard against the risk that a witness will testify from "false memory" by simply repeating the contents of the writing he has been shown. See 4 Marc S. Brodin et al., Weinstein's Federal Evidence § 612.02[2] (2d ed. 2017) ("Rule 612 is intended to curb the false memory that might occur when a witness who purports to testify based on a refreshed recollection merely parrots the contents of the writing."); 28 Charles Alan Wright & Victor S. Gold, Federal Practice & Procedure § 6184, at 511-12 (2d ed. 2012) (same); United States v. Faulkner, 538 F.2d 724, 727 (6th Cir. 1976) ("[C]aution must be exercised to insure that the document is not used to put words into the mouth of the witness."). In this case, it is evident to the Court that the Bunnage applications were not being used to refresh Dr. Bell's independent recollection, but to attempt to get the priority date of April 25, 1997, before the jury by having Dr. Bell recite that date that had been shown to him at his

deposition. The use of the Rule 612 procedure for that purpose would violate Rule 103(d) of the Federal Rules of Evidence, which provides that, "[t]o the extent practicable, the court must conduct a jury trial so that inadmissible evidence is not suggested to the jury by any means." See Rush v. Ill. Cent. R.R. Co., 399 F.3d 705, 717 (6th Cir. 2005) ("[T]he trial court may abuse its discretion when otherwise inadmissible evidence is introduced to the jury through the guise of refreshing a witness's recollection.").

As for impeachment, a similar problem is presented. At Dr. Bell's deposition, Lilly showed Dr. Bell the priority dates listed in the Bunnage PCT Application and showed him the Bunnage UK Application, which he had not seen before. As Lilly stated during the deposition, it showed the Bunnage applications to Dr. Bell in order to "educate" him as to their contents. Lilly then got Dr. Bell to agree that the priority date of April 25, 1997 was listed on those documents. At trial, Lilly asked Dr. Bell a question that was designed either to elicit an answer regarding the contents of the Bunnage applications, based on what Lilly showed him at the deposition, or to lead to Lilly's use of the applications for impeachment if he did not testify at trial that as of April 1997, Pfizer scientists had found that PDE5 inhibitors "would be useful to treat BPH and put it in a patent application." Dkt. No. 342, Trial Tr. at 354.

When Dr. Bell testified that he believed Pfizer scientists began looking at sildenafil to treat BPH in September of 1997, Lilly sought to impeach him by questioning him about the contents of the Bunnage applications. That is an improper use of impeachment, as it would enable a party to avoid limitations on the use of a document by permitting the party to question a witness about the document at a deposition and then either exploit his newly obtained knowledge of the document at trial or impeach him if he did not testify at trial consistently with the contents of the document.

Courts have frequently warned against the improper use of impeachment evidence, advising, for example, that it is improper to use evidence for impeachment that is inadmissible as substantive evidence when the purpose of its use is not to impeach the witness but to put inadmissible evidence before the jury. See United States v. Gomez-Gallardo, 915 F.2d 553, 555 (9th Cir. 1990) ("[T]he government must not knowingly elicit testimony from a witness in order to impeach him with otherwise inadmissible evidence."); United States v. Hogan, 763 F.2d 697, 702 (5th Cir. 1985); United States v. Webster, 734 F.2d 1191, 1192 (7th Cir. 1984); United States v. Miller, 664 F.2d 94, 97 (5th Cir. 1981); United States v. DeLillo, 620 F.2d 939, 946 (2d Cir. 1980); United States v. Pantone, 609 F.2d 675, 683 (3d Cir. 1979); United States v. Morlang, 531 F.2d 183, 190 (4th Cir. 1975) ("impeachment by prior inconsistent statement may not be permitted where employed as a mere subterfuge to get before the jury evidence not otherwise admissible"). Impeachment is not a mechanism for getting substantive evidence before the jury that is not otherwise admissible; as one court put it, "the maximum legitimate effect of the impeaching testimony can never be more than the cancellation of the adverse answer by which the party is surprised." United States v. Crouch, 731 F.2d 621, 623 (9th Cir. 1984).

That principle applies here. Lilly cannot be permitted to get the contents of an otherwise inadmissible document before the jury by showing the document to a witness at his deposition and then using it for impeachment purposes if the witness testifies at trial in a manner that is arguably inconsistent with the text of the document the witness was shown in his deposition.

The impeachment of Dr. Bell would have been improper for a second reason as well: the lack of a conflict between Dr. Bell's testimony in his deposition and his testimony at trial. Lilly's argument is based on a single statement in the two Bunnage applications that "the

compounds [certain PDE5 inhibitors] are of value in the treatment of male erectile dysfunction (MED) and female sexual dysfunction (FSD), but clearly will be useful also for treating other medical conditions for which a potent and selective cGMP PDE5 inhibitor is indicated. Such conditions include [a list of various maladies, including BPH]." Dkt. Nos. 253-2 and 256-1. At trial, Dr. Bell was asked, "Today, do you recall when Pfizer scientists first began looking at sildenafil to treat BPH?" to which he answered, "I believe it would have been after they filed the initial submission to the FDA in 1997, in September 1997." Dkt. No. 342, Trial Tr. at 349. He was also asked, "Do you have any information that Pfizer scientists were looking at using sildenafil to treat BPH before September of 1997," to which he answered, "I do not." Id., Trial Tr. at 349-50.

Because the questions referred to when Pfizer scientists began "looking at using sildenafil to treat BPH," Dr. Bell's answers were not inconsistent with his deposition testimony in which he acknowledged that the Bunnage applications had recognized that PDE5 inhibitors could be of value in the treatment of a variety of medical conditions. It would have been reasonable for Dr. Bell to interpret the question about when Pfizer began "looking at using sildenafil" to treat a particular condition as entailing a more active interest in treating BPH than merely recognizing the possibility that sildenafil could be effective against that disease. Thus, the evidence Lilly sought to use for impeachment would not have contradicted Dr. Bell's testimony.

Finally, whatever limited value the Bunnage applications would have had in impeaching Dr. Bell's credibility would have been swamped by the unfair prejudice to UroPep from the use of those materials at trial. Lilly acknowledged that the Bunnage applications were not prior art, but the introduction of the contents of those materials at trial would have carried a substantial risk that the jury would conclude that the '124 patent was invalid because it was predated by the

Bunnage UK Application. It is by no means clear that a limiting instruction would have cured the prejudicial effect of allowing the Bunnage applications into the case in that manner. To be sure, if UroPep had opened the door to the use of those applications for impeachment purposes, it would have had to live with the risk that a limiting jury instruction would not have been effective. But UroPep did not open that door.

In sum, Lilly's invocation of the rules governing impeachment and refreshing recollection is not suited to the facts of this case, where Lilly attempted to create the basis for the admission of otherwise inadmissible evidence and then attempted to get the evidence in through cross-examination. This is not a case of UroPep's having opened the door, but rather a case of Lilly having encountered a wall, kicked a hole in the wall, and then insisted on the right to walk through it.

The Court discerns no error in the disposition of the issues at trial relating to the Bunnage applications.

D. Allowing Cross-examination of Dr. Rotella Regarding His Patent

At trial, UroPep cross-examined Lilly's expert, Dr. Rotella, regarding a patent on which Dr. Rotella was a named inventor. The cross-examination was designed to challenge Dr. Rotella's opinions on the infirmities of the '124 patent by showing similarities between the '124 patent and Dr. Rotella's patent. Lilly contends that the cross-examination of Dr. Rotella regarding his patent was improper and was sufficiently prejudicial to require the grant of a new trial.

At the outset of the trial, the parties agreed that Lilly would not raise a "scope" objection to the cross-examination of Dr. Rotella with respect to matters on which he was examined at his deposition and with respect to any opinions he had given in the case. Dkt. No. 342, Trial Tr. at

265-66; see also Dkt. No. 343, Trial Tr. at 785-86. In his expert report, Dr. Rotella offered opinions on a number of subjects, including obviousness, and he was questioned about those opinions during his deposition. Accordingly, under the parties' agreement, Dr. Rotella was subject to cross-examination on the issue of obviousness, even though his trial testimony was limited to the issues of written description and enablement, and did not include an expert opinion on obviousness.

Dr. Rotella's patent, U.S. Patent No. 6,087,368 ("the '368 patent") is entitled "Quinazolinone Inhibitors of cGMP Phosphodiesterase." It claims priority to a provisional application filed on June 8, 1998. The '368 patent discloses "[n]ovel quinazolinone compounds, methods of using such compounds in the treatment of cGMP-associated conditions such as erectile dysfunction, and pharmaceutical compositions containing such compounds." Dr. Rotella is one of five named inventors on the '368 patent. Dkt. No. 252-1, at 2.

UroPep did not seek to have the '368 patent admitted into evidence, and it was not admitted. Instead, UroPep used it to cross-examine Dr. Rotella with regard to his opinions as to the invalidity of UroPep's '124 patent. Lilly counters that UroPep should not have been permitted to use the '368 patent in that manner because nothing in the patent is inconsistent with or contradicts Dr. Rotella's testimony.

The Court disagrees. First, the '368 patent, with a priority date of 1998, lists a large number and variety of conditions that are amenable to treatment with PDE5 inhibitors, but it does not list BPH among those conditions. Dkt. No. 252-1 ('368 patent, col. 16, line 66, through col. 17, line 15). The point of UroPep's questioning was that it is reasonable to infer from the omission of any reference to BPH in the Rotella patent that as of 1998, the inventors of the '368 patent, including Dr. Rotella, did not regard BPH as a potential treatment target of PDE5

inhibitors. For that reason, the omission of any reference to BPH in the ’368 patent arguably contradicts Dr. Rotella’s conclusion in his expert report that it would have been obvious to persons of skill in the art to use PDE5 inhibitors to treat BPH in 1997. As for written description and enablement, Dr. Rotella based his invalidity opinions in part on the absence of quantitative clinical data in the ’124 patent. See Dkt. No. 177-8, at 74; Dkt. No. 252-7, at 147. But, as Dr. Rotella acknowledged on cross-examination at trial, the ’368 patent also does not disclose quantitative clinical data. See Dkt. No. 343, Trial Tr. at 844-47. The absence of such data arguably contradicts Dr. Rotella’s opinion that clinical data is required in this setting for persons of skill in the art to describe what the invention is (written description) and show them how to make and use it (enablement).

With regard to obviousness, Lilly argues that the list of targeted conditions in the ’368 patent did not purport to be exhaustive, and that the patent’s failure to mention BPH as a target disease for PDE5 inhibitors was therefore insignificant. With regard to written description and enablement, Lilly contends that the ’368 patent is otherwise distinguishable from the ’124 patent; for example, the ’368 patent contains a much more detailed disclosure and narrower claims than the ’124 patent. While it is arguable that the differences between the ’124 and ’368 patents provide at least a possible answer to UroPep’s assertions of inconsistency between the ’368 patent and Dr. Rotella’s invalidity opinions, that point was properly left to Lilly to make through redirect examination and argument to the jury.

Lilly further contends that any infirmities or omissions in Dr. Rotella’s ’368 patent are irrelevant, because the ’124 patent has to stand on its own merits, without regard to whether the ’368 patent is valid. While it is true that the validity of the ’124 patent does not turn on whether the’368 patent is valid, that was not the point of UroPep’s cross-examination. Rather, it was

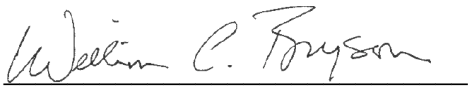
proper for UroPep to point out the similarities between the two patents, as the jury might reasonably have concluded that the parallels between Dr. Rotella's patent and the '124 patent bore on the credibility of Dr. Rotella's critique of the '124 patent.

Finally, Lilly suggests that it did not have enough time in the course of the five-day trial "to teach the jurors the needed principles of advanced medicinal chemistry or patent law to understand the defects in UroPep's facile arguments," Dkt. No. 375, at 60, and that the cross-examination of Dr. Rotella raised complex issues that Lilly did not have an opportunity to address in the time allotted. Prior to trial, however, the parties agreed that the trial could be conducted in five days. Dkt. No. 251, at 18. Lilly sought 14 hours of trial time during that five-day period, but the Court advised the parties that it would be difficult to fit 14 hours of testimony from each side into a five-day trial. The Court then offered to give each side 12 hours to present its case, and neither party objected that it could not reasonably present its case in that period. See Dkt. No. 320, at 289. Lilly had the opportunity, on Dr. Rotella's redirect examination, to correct any misapprehensions it felt may have been created by the cross-examination, and it took full advantage of that opportunity. The Court sees no merit in Lilly's late-blooming claim that it did not have sufficient time to respond to the issues raised by UroPep's cross-examination of Dr. Rotella. In fact, the Court notes that Lilly was able to fit into its case four affirmative defenses, lengthy testimony on damages, and background on Lilly's development of Cialis. Lilly's claim that it did not have enough time rings hollow. Lilly is not entitled to a new trial on that ground.

For the foregoing reasons, Lilly's motion for judgment as a matter of law and a new trial is denied. The Clerk is directed to close the case.

IT IS SO ORDERED.

SIGNED this 25th day of August, 2017.



WILLIAM C. BRYSON
UNITED STATES CIRCUIT JUDGE