IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GLAXOSMITHKLINE LLC and SMITHKLINE BEECHAM (CORK) LIMITED, Plaintiffs, v. GLENMARK PHARMACEUTICALS INC., USA, Defendant.	)	Civil Action No. 14-877-LPS-CJB
GLAXOSMITHKLINE LLC and SMITHKLINE BEECHAM (CORK) LIMITED, Plaintiffs, v. TEVA PHARMACEUTICALS USA, INC., Defendant.	)	Civil Action No. 14-878-LPS-CJB

REPORT AND RECOMMENDATION

In these two related actions filed by Plaintiffs GlaxoSmithKline LLC and SmithKline Beecham (Cork) Limited (collectively, "GSK" or "Plaintiffs") against Defendant Glenmark Pharmaceuticals Inc., USA ("Glenmark") and Teva Pharmaceuticals USA, Inc. ("Teva") (collectively, "Defendants"), GSK alleges induced infringement of United States Patent No. RE40,000 (the "Asserted Patent" or the "'000 patent"). Presently before the Court is Defendants' motion for summary judgment of invalidity (the "Motion").[1] (Civil Action No. 14-877-LPS-

[1] The Court notes that the Motion is included in Defendants "Combined Motion for Summary Judgment and to Exclude Certain Expert Testimony" in which they, *inter alia*, move

CJB (hereinafter "*Glenmark* Action"), D.I. 214; Civil Action No. 14-878-LPS-CJB (hereinafter "*Teva* Action"), D.I. 248)[2] The Court recommends that Defendants' Motion be DENIED.

I. BACKGROUND

A. The Parties

GSK manufactures and sells the drug carvedilol under the trade name COREG®. (D.I. 60 at ¶¶ 8, 22) Plaintiff SmithKline Beecham (Cork) Limited is the owner, by assignment, of the '000 patent, which relates to methods of administering carvedilol; Plaintiff GlaxoSmithKline LLC is the patent's exclusive licensee. (*Id.* at ¶¶ 37-38; *see also* '000 Patent)

Defendants are engaged in the business of developing, manufacturing, and distributing generic versions of branded drug products throughout the United States. (*See, e.g.*, *Glenmark* Action, D.I. 61 at ¶ 47; *Teva* Action, D.I. 60 at ¶ 47; D.I. 105 at ¶ 47)

B. Discovery of Carvedilol as a Treatment for Congestive Heart Failure

Congestive heart failure (or "CHF"), which has been construed by the Court to mean "a condition that occurs as a result of impaired pumping capability of the heart and is associated with abnormal retention of water and sodium[,]" (D.I. 165 at 43), affects over 5 million people in the United States, (D.I. 298 (hereinafter, "McCann Decl. Vol. I"), ex. 2 at ¶ 23). Symptoms of CHF include dyspnea (breathlessness), poor exercise intolerance, fatigue and edema (swelling of the legs). (D.I. 253 (hereinafter, "Rosendorff Decl."), ex. A at ¶ 28; McCann Decl. Vol. I, ex. 2

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for summary judgment with respect to other issues in addition to invalidity. (*Teva* Action, D.I. 248, 249) This Report and Recommendation solely addresses Defendants' invalidity arguments. The Court's decisions with respect to the remaining aspects of Defendants' combined Motion will be forthcoming.

[2] For simplicity's sake, the Court will refer to the "D.I." number in the *Teva* Action, unless otherwise indicated.

at ¶ 24) Historically, approximately half of the people that developed CHF died within 5 years of diagnosis. (*See* '000 patent, col. 1:55-57;[3] McCann Decl. Vol. I, ex. 2 at ¶ 23) Before 1997, the only treatments approved by the United States Food and Drug Administration ("FDA") for heart failure were diuretics, certain angiotensin converting enzyme ("ACE") inhibitors and digoxin/digitalis. (McCann Decl. Vol. I, ex. 2 at ¶ 25) These drugs were used to treat the symptoms of heart failure. (*Id.*) Controlled clinical trials also demonstrated that ACE inhibitors reduced the risk of mortality from heart failure by about 20%. (*Id.*)

Carvedilol has been a known beta blocker since at least 1978. (U.S. Patent No. 4,503,067; *see also* McCann Decl. Vol. I, ex. 2 at ¶ 29) Beta blockers are compounds that prevent stimulation of the adrenergic receptors responsible for increased heart rate and contractility, and thus they can cause the heart to pump slower or with less force. (McCann Decl. Vol. I, ex. 2 at ¶ 27) Historically, beta blockers were contraindicated in the treatment of CHF because of the medical community's "widely-held concern" that this type of drug would further reduce the diseased and/or damaged heart's ability to pump blood through the body. (*Id.* at ¶¶ 27-28; *see also* D.I. 299 (hereinafter, "McCann Decl. Vol. II"), ex. 53 at 50, 55 (Glenmark's expert Sean C. Beinart, M.D. noting that when he was in medical school in the "mid-'90s" he was taught "capital letters, beta blockers are contraindicated [for CHF]"); '000 patent, col. 3:56-60) For example, guidelines published in 1993 regarding the treatment of high blood pressure indicated that beta blockers were "[r]elatively or [a]bsolutely [c]ontraindicated" in patients with cardiac failure. (McCann Decl. Vol. I, ex. 3 at Table 8; *see also* GSK's Anticipation and

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[3] The '000 patent appears on the dockets in these actions more than once, including as an exhibit to the Joint Claim Construction Chart. (D.I. 73, ex. B) Citation to the patent will simply be to the "'000 patent."

Obviousness Presentation, Slide PDX-104)

Nevertheless, dating back to the mid-1970s, groups were studying the effectiveness of beta blockers to treat patients with CHF. In 1975, a group of Swedish researchers hypothesized that beta blockers could "influence the progression of congestive cardiomyopathy and prolong life in these patients[,]" (D.I. 264 (hereinafter, "Riley Decl. Vol. I"), ex. 3 at 1034-35), and by 1979, they published their first clinical trial which "suggested that [beta blockers] prolong[] survival in patients with congestive cardiomyopathy[,]" (*id.*, ex. 4 at 1374-75; *cf.* ex. 5 at ¶ 269). A study published in 1994 by Japanese physicians noted that "[e]vidence for the effectiveness of long-term [beta blockers] in the treatment of heart failure has been increasingly accumulated" and concluded that the survival rate in patients with dilated cardiomyopathy was significantly improved by beta-blocker therapy. (*Id.*, ex. 6 at 355-58)

As to carvedilol, in particular, the prior art included studies showing that it improved hemodynamics and symptoms in patients with CHF. (*See, e.g.*, *id.*, ex. 5 at ¶¶ 245-47, 293, 302; Rosendorff Decl., ex. A at ¶¶ 147-52, 156-58) For instance, an abstract published in early 1993 described a study of carvedilol in 54 patients with CHF due to either idiopathic or ischemic dilated cardiomyopathy; the abstract concluded that "[c]arvedilol is well tolerated and improves both symptoms and cardiac function in [such patients]." (Riley Decl. Vol. I, ex. 7; *see also* Rosendorff Decl., ex. A at ¶ 156) That same year, a researcher from Australia, Dr. David T. Kelly, published an article that (1) described recent studies that "have demonstrated symptomatic improvement with carvedilol in patients with heart failure" and (2) summarized a planned "multicentre trial" (which was known as the "ANZ pilot study" and was conducted by another physician, Dr. Norman Sharpe) "to evaluate [the drug's] efficacy and safety" (hereinafter, the

"Kelly reference" or "Kelly"). (Riley Decl. Vol. I, ex. 8 (hereinafter, "Kelly");[4] *see also* D.I. 297 at 13, 17 n.12)

In the late 1980s, meanwhile, the named inventors of the '000 patent (Mary Ann Lukas-Laskey, Robert Ruffolo, Jr., and Neil Howard Shusterman of GSK's predecessor and Gisbert Sponer and Klaus Strein of Boehringer Mannheim Pharmaceuticals Corporation) were investigating the possible uses of carvedilol (then in development as a drug to treat hypertension) to treat different diseases. (McCann Decl. Vol. I, ex. 2 at ¶ 30; '000 patent, col. 3:15-36) They pursued promising research suggesting that carvedilol could be used to successfully treat CHF, receiving approval from the FDA to initiate a clinical trial in 1992. (McCann Decl. Vol. I, ex. 2 at ¶ 30) According to Dr. Ruffolo, the reaction from his colleagues was very negative, due to concerns that a beta blocker like carvedilol would actually hasten the death of those with CHF. (McCann Decl. Vol. II, ex. 81 at GSK00983250) One colleague told him that he was "'going to kill a lot of people with that drug[.]'" (*Id.*) GSK's Chief Executive Officer received a letter protesting the studies of carvedilol in CHF patients as resembling "'the studies done by the Nazi scientists in the death camps of World War II[.]'" (*Id.*; *see also* McCann Decl. Vol. I, ex. 4 at 86) In light of these concerns, GSK established a Data and Safety Monitoring Board ("DSMB") to monitor the trial and to stop it if carvedilol, in fact, was killing patients. (McCann Decl. Vol. I, ex. 4 at 87)

In February 1995, the DSMB did indeed terminate the clinical trial early, but based on the finding of a significant effect of carvedilol on *survival* in CHF patients. (*Id.*; *see also id.*, ex. 2 at

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[4] David T. Kelly, *Carvedilol in Heart Failure*, 82 Suppl. 3 Cardiology, 45-49 (1993).

¶ 33; *id.*, ex. 6; *id.*, ex. 7; *id.*, ex. 8 at 329-30) The trial revealed that patients treated with carvedilol had an approximately 65% lower risk of death than those given placebo. (*Id.*, ex. 11 at GSK00776812; *see also id.*, ex. 8 at 243-44; '000 patent, col. 3:60-64) In light of this data, the DSMB believed that it would be "'unethical'" to maintain a placebo arm of the study. (McCann Decl. Vol. I., ex. 6-7; *see also id.*, ex. 4 at 87) The results of the clinical trial were published in *The New England Journal of Medicine*. (*Id*, ex. 11)

In November 1995, GSK sought FDA approval of carvedilol to reduce the risk of mortality caused by heart failure. (*Id.*, ex. 13 at ¶ 34) The FDA initially rejected GSK's application, but after receiving additional confirmatory data and analysis, in May 1997, the FDA ultimately approved carvedilol as the first beta blocker for the treatment of CHF, as an adjunctive therapy. (*Id.* at ¶¶ 34-35; *see also* D.I. 297 at 5-6) The next month, GSK launched COREG. (McCann Decl. Vol. I, ex. 14 at ¶ 10)

By 2004, the FDA had approved COREG for three indications:

> **1.1 Heart Failure:** COREG® is indicated for the treatment of mild-to-severe chronic heart failure of ischemic or cardiomyopathic origin, usually in addition to diuretics, ACE inhibitors, and digitalis, to increase survival and, also, to reduce the risk of hospitalization. . .
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> **1.2 Left Ventricular Dysfunction Following Myocardial Infarction:** COREG is indicated to reduce cardiovascular mortality in clinically stable patients who have survived the acute phase of a myocardial infarction and have a left ventricular ejection fraction of ≤40% (with or without symptomatic heart failure). . .
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> **1.3 Hypertension:** COREG is indicated for the management of essential hypertension []. It can be used alone or in combination with other antihypertensive agents, especially thiazide-type diuretics[.]

(D.I. 60, ex. F at 1160) In 2006-2007 (and prior to the entry into the market of Defendants' generic carvedilol in September 2007), sales of COREG peaked at approximately $1.6 billion per year. (*See* McCann Decl. Vol. II, ex. 82 at GSK00983295; *see also* D.I. 297 at 6) And by 2007, treatment guidelines specifically recommended carvedilol for treatment of heart failure. (McCann Decl. Vol. I, ex. 13 at ¶ 50) Dr. Ruffolo and Dr. Lukas have received a number of awards for their work in developing the invention claimed in the '000 patent. (*Id.* at ¶¶ 381-83; McCann Decl. Vol. II, ex. 82)

C. '000 Patent

In June 1995, the inventors filed a patent application directed to a method of using carvedilol to decrease the risk of mortality caused by CHF; the patent issued in June 1998 as U.S. Patent No. 5,760,069 (the "'069 patent"), entitled "Method of Treatment for Decreasing Mortality Resulting from Congestive Heart Failure." (*See* '000 patent) The FDA published the '069 patent in the "Approved Drug Products with Therapeutic Equivalence Evaluations" publication (the "Orange Book") as covering COREG for use in decreasing mortality caused by CHF. (*See* McCann Decl. Vol. I, ex. 15)

In November 2003, GSK requested a reissue of the '069 patent, and on January 8, 2008, that patent reissued as the '000 patent. ('000 patent) In February 2008, GSK replaced the '069 patent in the Orange Book with the '000 patent, and it identified "Decreasing Mortality Caused By Congestive Heart Failure" as the method of use covered by the '000 patent that should be included as the "use code" in that publication. (McCann Decl. Vol. I, ex. 16 at GSK00592204, GSK00592217)

The '000 patent contains 9 method claims directed to methods of decreasing mortality

caused by CHF in a patient in need thereof by administering carvedilol in a manner recited in the claims. ('000 patent) GSK asserts all but claim 5 against Defendants in these actions. (D.I. 249 at 3) Claim 1 is the only independent claim of the '000 patent, and it reads:

> **1.** A method of decreasing mortality caused by congestive heart failure in a patient in need thereof which comprises administering a therapeutically acceptable amount of carvedilol in conjunction with one or more other therapeutic agents, said agents being selected from the group consisting of an angiotensin converting enzyme inhibitor (ACE), a diuretic, and digoxin,
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> > *wherein the administering comprises administering to said patient daily maintenance dosages for a maintenance period to decrease a risk of mortality caused by congestive heart failure, and said maintenance period is greater than six months.*

('000 patent, col. 8:30-40 (emphasis in original)) The italicized portion of the claim is the portion that was added during the reissue proceeding.

The limitations "decreasing mortality caused by congestive heart failure" and "to decrease a risk of mortality caused by congestive heart failure" will be referred to herein as the "decreasing mortality limitations." The Court has construed the decreasing mortality limitations as claim limitations that mean "'attempt[ing] to reduce the probability that a patient will die as a result of congestive heart failure.'" (D.I. 165 at 43-44; *see also* D.I. 290 at 6-7)

D. Procedural History

On July 3, 2014, GSK commenced these actions. (*Glenmark* Action, D.I. 1; *Teva* Action, D.I. 1) GSK alleges that Defendants induce infringement of the '000 patent by making, offering to sell, selling, importing, and otherwise promoting and distributing generic carvedilol tablets. (*Glenmark* Action, D.I. 59, 175; *Teva* Action, D.I. 60, 211) On October 16, 2014, Chief Judge

Leonard P. Stark referred these cases to the Court to hear and resolve all pretrial matters, up to and including the resolution of case-dispositive motions. (*Glenmark* Action, D.I. 16; *Teva* Action, D.I. 18) After a *Markman* hearing, (*Glenmark* Action, D.I. 118; *Teva* Action, D.I. 147), the Court issued a Report and Recommendation on claim construction on June 3, 2016, (*Glenmark* Action, D.I. 133; *Teva* Action, D.I. 165). Chief Judge Stark overruled objections to that Report and Recommendation on February 17, 2017 as to all but one term ("maintenance dosages"). (*Glenmark* Action, D.I. 251; *Teva* Action, D.I. 290)

Briefing on the instant Motion was completed on March 3, 2017, (D.I. 313), and the Court held oral argument on the Motion (and various other summary judgment and *Daubert* motions filed in the case) on March 24, 2017, (D.I. 335 (hereinafter, "Tr.")). A 5-day trial is set to begin in the *Teva* Action on June 12, 2017. (D.I. 38, 329)

II. STANDARD OF REVIEW

A. Summary Judgment

A grant of summary judgment is appropriate where "the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). The moving party bears the burden of demonstrating the absence of a genuine issue of material fact. *See Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 585-86 & n.10 (1986). If the moving party meets this burden, the nonmovant must then "come forward with specific facts showing that there is a *genuine issue for trial*." *Id.* at 587 (emphasis in original) (internal quotation marks and citation omitted). If the nonmoving party fails to make a sufficient showing on an essential element of its case with respect to which it has the burden of proof, the moving party is entitled to judgment as a matter of law. *Celotex Corp. v.*

Catrett, 477 U.S. 317, 322-23 (1986). During this process, the Court will "draw all reasonable inferences in favor of the nonmoving party, and it may not make credibility determinations or weigh the evidence." *Reeves v. Sanderson Plumbing Prods., Inc.*, 530 U.S. 133, 150 (2000).

However, in order to defeat a motion for summary judgment, the nonmoving party must "do more than simply show that there is some metaphysical doubt as to the material facts." *Matsushita*, 475 U.S. at 586; *see also Podobnik v. U.S. Postal Serv.*, 409 F.3d 584, 594 (3d Cir. 2005) (party opposing summary judgment "must present more than just bare assertions, conclusory allegations or suspicions to show the existence of a genuine issue") (internal quotation marks and citation omitted). The "mere existence of *some* alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment; the requirement is that there be no *genuine* issue of *material* fact." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247-48 (1986) (emphasis in original). Disputes over facts that could alter the outcome are "material," and a factual dispute is genuine only where "the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Id.* at 248. "If the evidence is merely colorable, . . . or is not significantly probative, . . . summary judgment may be granted." *Id.* at 249-50 (internal citations omitted). A party asserting that a fact cannot be—or, alternatively, is—genuinely disputed must support the assertion either by citing to "particular parts of materials in the record, including depositions, documents, electronically stored information, affidavits or declarations, stipulations (including those made for purposes of the motion only), admissions, interrogatory answers, or other materials"; or by "showing that the materials cited do not establish the absence or presence of a genuine dispute, or that an adverse party cannot produce admissible evidence to support the fact." Fed. R. Civ. P. 56(c)(1)(A) &

(B).

B. Invalidity

A patent granted by the United States Patent and Trademark Office (the "PTO") is presumed to be valid. 35 U.S.C. § 282(a); *Microsoft Corp. v. i4i Ltd. P'ship*, 131 S. Ct. 2238, 2245-46 (2011). The rationale underlying this presumption of validity is that "the PTO, in its expertise, has approved the claim[.]" *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 426 (2007). The burden of proving invalidity rests with the patent challenger at all times, who, when disputed questions of fact arise, must establish a patent's invalidity by clear and convincing evidence in order to prevail. *Microsoft Corp.*, 131 S. Ct. at 2245-49; *see also id.* at 2253 (Breyer, J., concurring). Clear and convincing evidence places within the mind of the fact finder "an abiding conviction that the truth of [the] factual contentions are highly probable." *Procter & Gamble Co. v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009) (quoting *Colorado v. New Mexico*, 467 U.S. 310, 316 (1984)). When a defendant attempts to rely on prior art that was before the patent examiner during prosecution in challenging the validity of a patent, its burden is "especially difficult[.]" *Glaxo Grp Ltd. v. Apotex, Inc.*, 376 F.3d 1339, 1348 (Fed. Cir. 2004) (citation omitted).

C. Anticipation

A claim is anticipated under 35 U.S.C. § 102(a) or (b) if:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or
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> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for

patent in the United States . . . .

35 U.S.C. § 102.[5] A patent claim is anticipated if each and every limitation is found, either expressly or inherently, in a single prior art reference. *In re Gleave*, 560 F.3d 1331, 1334 (Fed. Cir. 2009) (citing *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 471 F.3d 1369, 1375 (Fed. Cir. 2006)); *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1321-22 (Fed. Cir. 2003). This test mirrors, to some extent, the test for infringement, and "it is axiomatic that that which would literally infringe if later anticipates if earlier." *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1378 (Fed. Cir. 2001). In order to anticipate, however, a reference must enable one of skill in the art to make and use the invention without undue experimentation, *In re Gleave*, 560 F.3d at 1334 (citing *Impax Labs., Inc. v. Aventis Pharms. Inc.*, 545 F.3d 1312, 1314 (Fed. Cir. 2008)), and must also "show all of the limitations of the claims arranged or combined in the same way as recited in the claims[,]" *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1370 (Fed. Cir. 2008).

Anticipation is a question of fact. *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343 (Fed. Cir. 2005). If there are no genuine disputes underlying the anticipation inquiry, then the issue is ripe for judgment as a matter of law. *Id.*

III. DISCUSSION

With this Motion, Defendants move for summary judgment on the ground that the

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[5] The Court will rely upon the version of 35 U.S.C. § 102 in effect prior to passage of the Leahy-Smith America Invents Act ("AIA"); this prior version of Section 102 applies to all patents with an effective filing date of on or before March 16, 2013, including the asserted patent in this action. *See Solvay S.A. v. Honeywell Int'l Inc.*, 742 F.3d 998, 1000 n.1 (Fed. Cir. 2014) (noting that the "AIA amendments apply only to applications and patents with an effective filing date of March 16, 2013, or later").

asserted claims of the '000 patent (i.e., all claims except for claim 5) are invalid because: (1) claims 1-3 and 6-9 are anticipated by Kelly; and (2) claims 4, 6 and 7 are obvious based on Kelly in combination with other references. (D.I. 249 at 3) Below, the Court will address the arguments as to anticipation.[6]

The Kelly reference—which is cited as prior art in the "Other Publications" section of the '000 patent, ('000 patent at 2)—was published in *Cardiology* in 1993 by Dr. Kelly, an Australian physician, (*see* Kelly). In the article, Dr. Kelly explains that recent evidence suggested that sustained treatment with beta blockers had been shown to improve symptoms in patients with heart failure. (*Id.* at TCAR0011939) Dr. Kelly then discusses two small studies involving carvedilol in particular. These studies suggested that the drug improved symptoms and hemodynamics of heart failure (such as exercise tolerance, ejection fraction and pulmonary arterial wedge pressure). (*Id.* at TCAR0011941) Dr. Kelly next describes the planned, but "not yet started[,]" "multicentre trial" in Australasia involving 450 patients with ischaemic heart failure (i.e., heart failure after a heart attack). (*Id.*) That trial was designed to evaluate the efficacy and safety of administering carvedilol to these patients and to study the effect of the drug on the symptoms and hemodynamics of heart failure. (*Id.* at TCAR0011939, TCAR0011941)

Defendants argue that in this description of the planned trial, Kelly expressly discloses the administration of carvedilol in CHF patients at the same dose, on the same schedule, with the

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[6] Because the Court ultimately concludes that there is a genuine issue of material fact with respect to whether Kelly anticipates claims 1-3 and 6-9, the Court need not address Defendants' assertion that claims 4, 6 and 7 are obvious based on Kelly in view of other references. That is, for the same reason as there is a genuine issue of material fact as to whether Kelly anticipates the claimed invention, a genuine issue of fact exists as to whether Kelly, in combination with other references, renders the claimed invention obvious.

same concomitant drugs and over the same time period as is disclosed in claims 1-3 and 6-7 of the '000 patent. With respect to the decreasing mortality limitations, Defendants do not dispute (for purposes of this Motion) that the prior art did *not* disclose the mortality benefit associated with administering carvedilol to CHF patients. (D.I. 249 at 7 n.5; Tr. at 50) But they assert that with regard to the decreasing mortality limitations, GSK has simply claimed the inherent result of following the method of treatment set out in Kelly. Thus, they argue, the '000 patent runs afoul of well-settled law that "[a] claim to the alleged discovery of a new result for an old method, even if an actual discovery, is not patentable" and that "Kelly [inherently] anticipates the claims in suit." (D.I. 249 at 4)

For its part, GSK responds that summary judgment of invalidity is not appropriate. It argues this is so because, at a minimum (1) there are material disputes of fact as to whether Kelly describes the same method of treatment as claimed in the '000 patent; (2) the decreasing mortality limitations constituted a "new use" of carvedilol that is therefore patentable over Kelly; and (3) Kelly does not enable the claims of the '000 patent. (D.I. 297 at 1-2, 12-20)

The Court will first examine whether there are material disputes of fact regarding whether Kelly expressly discloses the same treatment protocol as that claimed in the '000 patent. The Court will then turn to the parties' dispute as to whether Kelly inherently discloses the decreasing mortality limitations. Lastly, the Court will address whether there are material disputes of fact regarding whether Kelly is nonenabling.

A. Whether Kelly Expressly Discloses the Claimed Treatment Method

With regard to whether Kelly expressly discloses the same method of treatment as claimed in the '000 patent, the Court begins by focusing on independent claim 1. Again, that

claim requires that carvedilol be administered:

> (1) to CHF patients;
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> (2) in a "therapeutically acceptable amount" (with the specification explaining that the "preferred course" of treatment is to start a patient on a dosage regimen of 3.125 mg twice daily for two weeks and increasing to a "maintenance dose" of 25 mg twice per day);
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> (3) in conjunction with an ACE inhibitor, diuretic or digoxin; and
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> (4) in daily maintenance dosages for a maintenance period that is greater than six months.

('000 patent, cols. 5:27-39, 8:30-40)

GSK argues, *inter alia*, that a reasonable jury could find that Kelly does not "'clear[ly] and unambiguous[ly]'" disclose "administering maintenance dosages of carvedilol . . . for a maintenance period greater than six months." (D.I. 297 at 18) (quoting *Cheese Sys., Inc. v. Tetra Pak Cheese & Powder Sys., Inc.*, 725 F.3d 1341, 1352 (Fed. Cir. 2013)); *see also* (GSK's Anticipation and Obviousness Presentation, Slides PDX-129-31).

Turning back to Kelly, the reference summarizes the planned trial involving 450 patients with CHF in a paragraph as follows:

> The study will look to see if beta blockade has the same type of effect in ischaemia as it does in cardiomyopathy.[7] The use of . . . ACE[] inhibitors is not essential but is encouraged. This will be the first *long-term study* utilising beta blockade in ischaemic cardiomyopathy. Patients will be randomly assigned to treatment with carvedilol or placebo in a two-group parallel-designed study, and data on exercise capacity, left-ventricular function and size will be compared to baseline and after *6 and 18 months of follow-up*.

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[7] Earlier in the article, Kelly explains that the use of beta blockers in patients with cardiomyopathic heart failure had shown an improvement in cardiac output, ventricular function and general patient well-being. (Kelly at TCAR0011940)

> Patients will be given a test dose of 6.25 mg of carvedilol and then if satisfactory will be titrated to a maximal dose over a period of 2-3 weeks. The first dose of carvedilol is 3.125 mg. Patients will initially take 3.125 mg twice daily for 7 days, in the second week 6.25 mg, then 12.5 mg and the following week 25 mg twice daily, which will be the maximal dose used.

(Kelly at TCAR0011941 (emphasis added)) A few paragraphs later, after a discussion of another planned study with carvedilol in patients with congestive cardiomyopathy stabilized on ACE inhibitors, Kelly notes that "[i]n 1991 it is difficult to ethically promulgate a trial in chronic heart failure without concomitant use of ACE inhibitors[.]" (*Id.* at TCAR0011942)

Although it is a close question, viewing the evidence in the light most favorable to GSK, the Court finds that a genuine issue of material fact exists as to whether Kelly discloses administering carvedilol for a maintenance period that is greater than six months. Defendants argue that Kelly discloses this limitation, in that Kelly describes how carvedilol "will be given in a 'long-term study' for 6 to 18 months[,]" (D.I. 249 at 6), with certain data being compared to baseline (i.e., at the start of the study) and "'after 6 to 18 months of follow-up[,]'" (Defendants' Invalidity Presentation, Slide 12 (quoting Kelly at TCAR0011941)). However, as GSK notes, Kelly never expressly states that the patient is to actually receive carvedilol for all of that time.

Indeed, as GSK's counsel pointed out during oral argument, (Tr. at 90-91), Kelly discusses the administration of carvedilol to patients at three instances in the reference. In the first instance, describing a small previous study, Kelly explains that the effects of carvedilol in 17 patients with chronic heart failure were examined, with testing and blood pressure measured "before and after 8 weeks of carvedilol[.]" (Kelly at TCAR0011941) In the second instance, Kelly describes how carvedilol and another beta blocker were compared in a study of 16 patients,

with both drugs improving ejection fraction and heart rate "after 4-6 months of therapy[.]" (*Id.*) In those two instances, then, Kelly made it clear how long the patients actually received the drug. In the third instance, however—the discussion of the planned trial at issue here—Kelly does not "expressly" say for how long a period of time patients would receive carvedilol. (Tr. at 90) Instead, Kelly states that patients would be assigned to treatment with carvedilol or placebo and that certain data would be compared "to baseline" and "after 6 and 18 months *of follow-up.*" (Kelly at TCAR0011941 (emphasis added))

During a deposition, GSK's expert, Peter A. McCullough, M.D., was questioned by Teva's counsel regarding the nature of Kelly's disclosure on this subject: that is, as to whether Kelly discloses administration of daily maintenance dosages of carvedilol for a maintenance period greater than six months. Dr. McCullough opined that a person of ordinary skill in the art would not "read [] that into" the Kelly reference, and that "the dose exposure of how many months the patients will physically take carvedilol in the trial is not disclosed in Kelly." (McCann Decl. Vol. I, ex. 48 at 200-01)[8] Although Defendants retort that Dr. McCullough's "hyper-literal approach" to Kelly amounts to a "conclusory assertion[]" that Kelly did not disclose the limitation, (D.I. 313 at 6), Dr. McCullough does provide further fact-based explanation in support of his opinion. He explained that Kelly "doesn't state that [administration

[8] In its briefing, GSK points to four paragraphs of Dr. McCullough's expert report and to several pages of his deposition as supporting its position that Kelly does not disclose "administering maintenance dosages of carvedilol [for a maintenance period] greater than six months." (D.I. 297 at 18 (citing McCann Decl. Vol. I, ex. 48 at 193-202, 207-208; *id.*, ex. 13 at ¶¶ 204-07)) But as Defendants point out, no cited portion of the *expert report* actually supports this particular argument. (*See* D.I. 313 at 6) Instead, these four paragraphs are devoted to GSK's argument that because Kelly does not disclose the decreasing mortality limitations, it cannot anticipate the claimed method. (*See* McCann Decl. Vol. I, ex. 13 at ¶¶ 204-07) Therefore, the Court does not consider them here.

of the maximum dose of carvedilol] will be carried on for a period of time or not[,]" and that because Kelly instead simply states that the certain data regarding "left ventricular function and size [are to] be compared to baseline and after 6 and 18 months, the person of skill in the art *wouldn't know how long carvedilol would be continued* and when these assessments would be done *and if the investigators were looking for a residual effect after stopping the drug* and for what period of time." (McCann Decl. Vol. I, ex. 48 at 199-200 (emphasis added); *see also* Tr. at 91-92 (GSK's counsel asserting, in line with Dr. McCullough's comments, that if a patient is being administered carvedilol in a study to "make him feel better[,]" then the intent of the study could be to give the patient the drug, stop administration when they feel better and then "follow-up" to "see how [the patient is] doing in 6 months and 18 months[,]" or it could mean that the study administers carvedilol "continually" during the 18 month period—"but the point is that you don't know. . . . when you're treating symptoms versus treating mortality, it can make a difference in how long you might [administer] the drug")) Dr. McCullough further noted that typical clinical trial protocols are "hundreds of pages long" and "very detailed[,]" providing full descriptions "of the dosing of a medication[,] specifically for how long it's given[.]" (McCann Decl. Vol. I, ex. 48 at 201-02) Kelly is no such protocol, according to Dr. McCullough, since it does not state "the dose exposure of how many months the patients will physically take carvedilol in the trial[.]" (*Id.* at 201)

In order to resolve this disputed issue, the factfinder will need to make credibility determinations and weigh the evidence relied upon by the competing experts. (*See* Tr. at 92 (GSK's counsel noting that whether Dr. McCullough's view of the disclosure in Kelly is "hyper-literal" is a jury question in light of the summary judgment standard); *see also* GSK's

Anticipation and Obviousness Presentation, Slide PDX-132) At the summary judgment stage, however, making such credibility determinations or weighing the evidence is exactly what the Court may *not* do. *Marino v. Indus. Crating Co.*, 358 F.3d 241, 247 (3d Cir. 2004).[9] And so, for these reasons, the Court concludes that the record, taken in the light most favorable to GSK, could support a finding that there is not clear and convincing evidence that Kelly discloses every limitation of the claimed method of treatment.[10]

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[9] It is also true that there are plenty of reasons why a juror might ultimately end up agreeing with Defendants as to what Kelly discloses in this respect. For one thing, the "teaching in the prior [art] reference need not be *ipsissimis verbis*" in order to be anticipatory. *Structural Rubber Prods. Co. v. Park Rubber Co.*, 749 F.2d 707, 716 (Fed. Cir. 1984). And a juror might well conclude, after hearing from the experts, that a person of skill in the art would understand Kelly's reference to a "long-term study" to be disclosing the intended continuous administration of the drug for 6-18 months (especially in light of Kelly's disclosure of prior studies that involved therapy lasting for up to six months). Moreover, the very first sentence of Kelly notes that "*[s]ustained* oral treatment with beta blockers has been shown to improve symptoms in patients with chronic heart failure." (Kelly at TCAR0011939) "Sustained," of course, usually means something that continues for an extended period of time or without interruption. But it is the jury who should consider the weight of such arguments.

[10] To the extent that GSK suggests in its brief that Kelly does not disclose the administration of carvedilol with ACE inhibitors, (*see* D.I. 297 at 18), the Court does not agree that there is a genuine issue of material fact with respect to this limitation. Although GSK is correct that the paragraph describing the planned study in Kelly notes that the use of ACE inhibitors "is not essential but is encouraged," (Kelly at TCAR0011941), the very next page of the reference states that "in 1991 it is difficult to ethically promulgate a trial in chronic heart failure without concomitant use of ACE inhibitors[,]" (*id.* at TCAR0011942). And while Dr. McCullough opined that Kelly did not disclose the *proportion* of patients that would and would not receive ACE inhibitors along with carvedilol, he acknowledged that "it may be difficult ethically, as pointed out [in Kelly], to do a trial where no patients are on ACE inhibitors because, as [that sentence in Kelly] implies, ACE inhibitors were thought to be a base therapy that was indicated in patients with [CHF]." (McCann Decl. Vol. I, ex. 48 at 194-96; *see also* D.I. 313 at 7 (Defendants noting that "Dr. McCullough did not testify that Kelly did not teach the use of ACE inhibitors in combination with carvedilol; he simply refused to offer an opinion on the proportion of subjects in the [] trial [discussed in Kelly] that were on an ACE inhibitor")) GSK did not further press this argument during oral argument. (*See, e.g.*, GSK's Anticipation and Obviousness Presentation, Slides PDX 127-32)

That conclusion compels a recommendation that Defendants' Motion be denied. Nevertheless, the Court will next proceed to address the parties' dispute relating to whether Kelly inherently discloses the decreasing mortality limitations.

B. Inherent Anticipation

1. Legal Principles of Inherent Anticipation

It is well-settled that a prior art reference may anticipate a patent claim when the claim limitations not expressly found in that reference are nonetheless inherent in it. *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349 (Fed. Cir. 2002). "In general, a limitation or the entire invention is inherent and in the public domain if it is the natural result flowing from the explicit disclosure of the prior art." *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1377 (Fed. Cir. 2005) (internal quotation marks and citations omitted); *see also Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 970 (Fed. Cir. 2001). "In some cases, the inherent property corresponds to a claimed new benefit or characteristic of an invention otherwise in the prior art[,]" and in such circumstances, "the new realization alone does not render the old invention patentable." *Perricone*, 432 F.3d at 1377; *see also Bristol-Myers Squibb*, 246 F.3d at 1376 ("Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent.").[11] When a prior art method is at issue, the inherent anticipation

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[11] In *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801 (Fed. Cir. 2002), the United States Court of Appeals for the Federal Circuit provided a helpful hypothetical to illustrate that method claims reciting the same steps of a known method in order to obtain a different, newly-discovered benefit are not patentable:

> Inventor A invents a shoe polish for shining shoes . . . . Inventor A receives a patent having composition claims for shoe polish. Indeed, the preamble of these hypothetical claims recites "a composition for polishing shoes." . . . Inventor B could not [later]

doctrine "examines the natural and inherent results in that method without regard to the full recognition of those benefits or characteristics within the art field at the time of the prior art disclosure." *Perricone*, 432 F.3d at 1378; *see also Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) ("[I]nherent anticipation does not require that a person of ordinary skill in the art at the time would have recognized the inherent disclosure."); *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1366 (Fed. Cir. 1999) ("Where . . . the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results.").

To show inherent anticipation, the patent challenger must demonstrate that the claim limitation said to be inherent in the prior art is "necessarily present in the prior art, not merely probably or possibly present." *Akamai Techs., Inc. v. Cable & Wireless Internet Servs., Inc.*, 344 F.3d 1186, 1192 (Fed. Cir. 2003); *see also MEHL/Biophile*, 192 F.3d at 1365 (noting that inherent anticipation "may not be established by probabilities or possibilities") (citation omitted). The "mere fact that a certain thing *may* result from a given set of circumstances is not sufficient"

> secure claims on the method of using the composition for shining shoes because the use is not a "new use" of the composition but, rather, the same use shining shoes. . . . Suppose Inventor B discovers that the polish also repels water when rubbed onto shoes. Inventor B could not likely claim a method of using the polish to repel water on shoes because repelling water is inherent in the normal use of the polish to shine shoes. . . . In other words, Inventor B has not invented a "new" use by rubbing polish on shoes to repel water. Upon discovering, however, that the polish composition grows hair when rubbed on bare human skin, Inventor B can likely obtain method claims directed to the new use of the composition to grow hair.

289 F.3d at 809-10.

but if the "disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function" then "the disclosure should be regarded as sufficient [to anticipate]." *MEHL/Biophile*, 192 F.3d at 1365 (citation omitted) (emphasis in original). "Whether a claim limitation is inherent in a prior art reference is a factual issue on which evidence may be introduced." *Rapoport v. Dement*, 254 F.3d 1053, 1057 (Fed. Cir. 2001).

2. Whether Kelly Inherently Anticipates the Decreasing Mortality Limitations

GSK makes a number of arguments as to why Kelly does not inherently anticipate the decreasing mortality limitations. The Court will take them up in turn.

a. Whether the Decreasing Mortality Limitations Constitute an "Inherent Result" or a "New Use"

The primary dispute with respect to the decreasing mortality limitations (assuming *arguendo* that Kelly discloses all of the physical steps of the claimed treatment protocol) is whether these limitations constitute a *new use* of a known process, which may be patentable, or instead constitute a *newly discovered result* of a known process, which is not patentable under the doctrine of inherent anticipation. (D.I. 249 at 6-11; D.I. 297 at 13-18); *see also Bristol-Myers Squibb*, 246 F.3d at 1376 ("new uses of known processes may be patentable") (citing 35 U.S.C. § 100(b)). GSK asserts that "[r]eduction in mortality was not a newly discovered benefit; it was a new use"; it claims this is underscored by the Court's construction of the decreasing mortality limitations as requiring administration of the claimed drugs with the intent to "attempt to reduce the probability that a patient will die" from CHF. (D.I. 165 at 44; *see also* D.I. 297 at 2; *id.* at 16-17 ("Thus, the issue is not, as Defendants imply, whether the claimed combination of drugs, if

administered as maintenance dosages for more than six months, would inherently reduce mortality, but whether Kelly inherently discloses the requisite intent.")) Defendants respond that GSK's position attempts to "rewrit[e] the law of inherent anticipation" and that it "fails as a matter of law." (D.I. 313 at 2, 5; *see also id.* at 1 ("GSK's argument is based on a clearly erroneous reading of the case law of inherent anticipation.")) And because Kelly "discloses giving the *same* combination of drugs to the *same* class of patients in the *same* dosages for the *same* duration to treat the *same* condition[,]" Defendants contend that a reduction in the risk of mortality is an (unpatentable) inherent result of following that treatment protocol. (*Id.* at 1, 2 (emphasis in original))

This dispute presents a difficult legal issue.[12] But for the reasons set out below, the Court is persuaded that Defendants' view is in line with precedent from the United States Court of Appeals for the Federal Circuit regarding the inherent anticipation doctrine.

As an initial matter, the parties' dispute raises the question of *how* courts determine whether a limitation is directed to a new use of a known process, or is instead merely a newly discovered, yet inherent result of a known process. According to Defendants, "[t]o determine whether a use is 'new,' courts compare the actual steps of the patent with the method in the prior art reference" and they assess whether there is a "'manipulative difference'" in the steps of the methods. (D.I. 313 at 3-4 (citations omitted); *see also* Defendants' Invalidity Presentation, Slide 15; Tr. at 58-60) If so, the patent claims a "new use" that is patentable; if not, the patent wrongly claims a new result from an old use. (Defendants' Invalidity Presentation, Slide 15) For its part,

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[12] *See, e.g.*, *In re Montgomery*, 677 F.3d 1375, 1383 (Fed. Cir. 2012) (Lourie, J., dissenting) ("Inherency is a very tricky concept in patent law.").

GSK asserts that even if "the method [in the prior art] were the same [as in the asserted patent], if the use is different and not present in the prior art, then it's patentable." (Tr. at 85; *see also id.* at 103 (GSK's counsel arguing that the issue in disputes like these is whether the purpose disclosed in the patent is in the prior art—if it is not, than that is a "new use even if the method was the same"))

A look at the caselaw demonstrates that courts struggling with this issue articulate a legal test mirroring that set out by Defendants. For example, in *Bristol-Myers Squibb Co. v. Boehringer Ingelheim Corp.*, 86 F. Supp. 2d 433 (D.N.J. 2000), *aff'd in relevant part*, 246 F.3d 1368 (Fed. Cir. 2001), the claims at issue were directed to parenteral administration of 135-175 mg/m^2 of taxol to patients suffering from taxol-sensitive tumors over about three hours, while premedicating the patient to reduce or eliminate hypersensitivity reactions. 86 F. Supp. 2d at 440. The Court held that these claims were anticipated by a reference ("Kris"), that described treating patients suffering from the same types of tumors by administering the same drug to those patients, in the same dose, for the same duration, and that also suggested that further studies were needed to assess the safety of premedicating such patients. *Id.* at 440-42. Although the patent claims at issue also recited "stated goals of reducing toxicity levels and tumor regression" that were not mentioned in Kris, *id.* at 442, the Court explained that Kris still anticipated, whether such phrases were construed as claim limitations or were regarded as non-limiting statements of purpose. The Court reached this conclusion in light of precedent teaching that where a method has already been "disclosed to the public"—that is, "where the prior art discloses the steps of a process and" the patentee "did not manipulate or otherwise alter the basic application . . . disclosed in the prior art[,]"—he cannot patent as a new invention "unexpected or unappreciated

results from" that method. *Id.* at 442-43 (internal quotation marks and citation omitted).[13] In other words, the Court found that even if reducing toxicity was a claim limitation, such results were the necessary consequence of practicing the method steps set out in Kris and were thus inherently contained in Kris. On appeal, the Federal Circuit affirmed this decision, explaining that the claimed process was "not directed to a new use; it is the same use, and it consists of the same steps as described by Kris." *Bristol-Myers Squibb*, 246 F.3d at 1376.

The Federal Circuit again applied this test in *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368 (Fed. Cir. 2005). In *Perricone*, the prior art patent ("Pereira") disclosed topical application of a cosmetic composition to skin and hair. 432 F.3d at 1376. The patents at issue (the "Perricone patents") claimed methods of treating or preventing sunburns, and methods of treating skin damage or disorders (i.e., to help achieve particular skin benefits) by topical application of a particular compound. *Id.* at 1371, 1378. The Federal Circuit explained that if Pereira "discloses *the very same methods*, then the particular benefits [claimed in the Perricone patents] must naturally flow from those methods even if not recognized as benefits at the time of Pereira's disclosure." *Id.* at 1378 (emphasis added). Thus, Pereira would anticipate if its disclosure of topical application was the same application step as claimed in the Perricone patents, even though Pereira "does not disclose any benefit directed to skin sunburn, or any of the other specific skin disorders, as claimed by [the Perricone patents]." *Id.* at 1376, 1378.

With respect to claims in the Perricone patent directed to *treating* sunburn, which specifically required application of the composition to skin sunburn, the Court held that Pereira

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[13] Notably, certain claims of the patent at issue were directed to the treatment of ovarian cancer, a type of cancer not referenced in Kris. *Bristol-Myers Squibb*, 86 F. Supp. 2d at 440. Those claims were not found to be anticipated by Kris. *See id.* at 442.

did not anticipate because it "did not disclose topical application *to skin sunburn*[.]" *Id.* at 1378-79 (emphasis in original). The Perricone patent, then, recited a "new method" in this regard, and therefore a "new *use* of the composition disclosed by Pereira, i.e., the treatment of skin sunburn." *Id.* (emphasis added). Meanwhile, the Court found that Pereira anticipated the remainder of the claims of the Perricone patents that merely required application of the composition to (1) exposed skin surfaces to prevent sunburn or (2) to skin to treat damaged or aging skin. *Id.* at 1379-80. The Court explained that Pereira discloses the very same composition and teaches *the same topical application*, and that using "the same composition claimed by Dr. Perricone in the same manner claimed by Dr. Perricone naturally results in the same claimed skin benefits." *Id.*[14]

As noted above, GSK has a contrary view. That is, according to GSK, even if the

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[14] Following this precedent, district courts have applied this test (i.e., asking whether the allegedly new method requires a different physical step in practicing the method than that disclosed in the prior art) in assessing whether a patentee's asserted new use of a known method is indeed new. *See, e.g.*, *Aventis Pharms., Inc. v. Barr Labs., Inc.*, 411 F. Supp. 2d 490, 523 (D.N.J. 2006) (noting that "in comparing the process of the invention with that in the prior art, the [*Bristol-Myers Squibb*] [C]ourt looked for an identity of physical steps" and "[a]pplying this approach to the present case, the new method and the old method have an identity of physical steps" and "the fact that the [] process [in the asserted patent] is associated with a new intended result [administration of a drug while avoiding certain cardiac events] does not render it patentably new"); *Wedeco UV Techs., Inc. v. Calgon Carbon Corp.*, Civil Action No. 01-924 (JAG), 2006 WL 1867201, at *14 (D.N.J. June 30, 2006) (recognizing that in *Bristol-Myers Squibb*, in comparing the process of the invention with that in the prior art to determine whether the invention claimed a patentably new use, the Court "looked for an identity of physical steps" and applying this approach to the facts before it to determine that "the new method and the old method have an identity of physical steps" and therefore the new method was "associated with a new intended result [that] does not render [it] patentably new"); *cf. Innovatit Seafood Sys. LLC v. Comm'r for Patents*, 573 F. Supp. 2d 96, 98 (D.D.C. 2008) (concluding that "the application of [an] old process [subjecting shellfish to high pressure] to [a] new purpose [pasteurizing the shellfish], *without any meaningful change in the procedure*, is [not] patentable over" a prior art reference that taught the same process for a different purpose, shucking shellfish) (emphasis added).

physical steps of the method in the prior art and the physical steps of the method in the claimed invention are exactly the same, and the only thing that is different is the intended purpose for the steps, that is patentable. (*See, e.g.*, Tr. at 85, 87-88) GSK hinges this position on *Rapoport v. Dement*, 254 F.3d 1053 (Fed. Cir. 2001). (*Id.* at 73 (GSK's counsel explaining that "I think everything that I'm going to say is designed around the case *Rapoport*"); D.I. 297 at 13 (GSK calling *Rapoport* "the key case on point")) In doing so, however, GSK overlooks some key, distinguishing facts in *Rapoport*.

Rapoport involved an interference, and the disputed count (in the "Dement Application") disclosed a method of treating sleep apnea by administering a therapeutically effective amount of buspirone to a patient in need of such treatment. *Rapoport*, 254 F.3d at 1055-56. It was known that patients suffering from sleep apnea often exhibited various secondary symptoms due to lack of sleep, including anxiety. *Id.* at 1055. Rapoport argued that the Dement Application was anticipated by a prior art reference (the "FPR Publication") that focused on the administration of buspirone to treat anxiety. *Id.* at 1058, 1060-61. The FPR Publication mentioned the possibility of administering buspirone to patients suffering from sleep apnea, but "for the purpose of treating *anxiety* in such patients, not for the purpose of treating the sleep apnea disorder itself." *Id.* at 1061 (emphasis added). Rapoport argued that "[a]s long as one administers buspirone to a patient with sleep apnea in a therapeutically effective amount," certain claims of the Dement Application at issue were anticipated by the FPR Publication. *Id.*

The Federal Circuit rejected Rapoport's argument, explaining that his anticipation theory deemed irrelevant "the reasons for administering buspirone to the patient" and "the time of administration[.]" *Id.* In other words, the Court did not find the Dement Application anticipated

because the uses of buspirone at issue in Dement and in the FPR Publication were *different*—they involved treating *two different conditions*—sleep apnea and anxiety—and, accordingly, *the dosing schedule of buspirone was different* for each of those conditions. To that end, the *Rapoport* Court explained that the Dement Application stated that a dose of about 10-60 mg of the drug would usually occur "at the hour of sleep[,]"—a timing consistent with "treatment of the underlying sleep apnea disorder, which by definition manifests itself during sleep[.]" *Id.* at 1060; *see also id.* at 1062. Meanwhile, the FPR Publication discussed administering buspirone to some patients (who were *not* reported to be suffering from sleep apnea) in a single dose of 10 mg at an unspecified time, and to other patients in doses of 10 mg three times a day, never specifying that administration of the drug was to be at bedtime. *Id.* at 1061-63. In view of these facts, the Court rejected Rapoport's argument that the proposed dosing regimen set out in the FPR Publication would necessarily result in a therapeutically effective amount of buspirone for the purpose of treating sleep apnea and, accordingly, declined to find that the FPR Publication inherently anticipated the Dement Application. *Id.*[15]

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[15] Other courts evaluating inherent anticipation arguments with respect to method of treatment claims have similarly found that an invention is directed to a new (and thus patentable) use where there is a manipulative difference in the new method, as compared to the method disclosed in the prior art reference (such as treatment of different patient populations). *See, e.g.*, *In re '318 Patent Infringement Litig.*, 578 F. Supp. 2d 711, 726-27 (D. Del. 2008) (rejecting the defendants' argument that the asserted patent, directed to methods of treating a subset of progressive dementias with galanthamine, was anticipated by a prior art reference that discussed treating patients suffering from arrested dementia (a different type of dementia than progressive dementia) with galanthamine, explaining that even though "the two types of dementias have common symptoms[,] . . . the conditions differ [and therefore the prior art reference's] disclosure of the use of galanthamine for one condition does not necessarily equate to a disclosure of the use of galanthamine to treat the other"); *Glaxo Grp. Ltd. v. Teva Pharms. USA, Inc.*, No. C.A.02-219 GMS, 2004 WL 1875017, at *18-20 (D. Del. Aug. 20, 2004) (rejecting the argument that a patent directed to the treatment of migraine headache pain with ondansetron inherently anticipated the asserted patents directed to the treatment of nausea and vomiting with ondansetron, explaining

Rapoport, then, simply underscores that the above-articulated test, which looks at whether the methods disclosed in the prior art and asserted patent teach the same physical steps, is the correct one to apply here. There was no inherent anticipation in *Rapoport* because the invention and the prior art disclosed two different uses of buspirone. The invention disclosed a use for treating sleep apnea, by taking the drug in a particular dose at night. But the prior art disclosed another use for treating anxiety—a condition that could be caused by sleep apnea, but that need not include the same patient population as those suffering from sleep apnea—by taking different doses of the drug at unspecified times. (*See* Tr. at 96-97; D.I. 313 at 4 (Defendants explaining that in *Rapoport*, "the claim limitation resulted in a manipulative difference in the use of the drug compared to the prior art—the treatment of two *different* patient populations[;] . . . [w]hile some patients who had anxiety had it because of sleep apnea, the Court found treatment of anxiety differed from the way one would treat sleep apnea itself")); *see also Perricone*, 432 F.3d at 1386 (Bryson, J., dissenting) (pointing out that *Rapoport* involved a prior art method that was directed at a different objective from that of the claimed invention, wherein "the prior art was a method for treating anxiety by administering a certain dosage of a particular drug three times a day, while the invention was a method for treating sleep apnea by administering a larger dosage of the same drug at the time of sleep"). And so *Rapoport* cannot stand for the proposition that if the physical steps of the treatment method are exactly the same and the patient populations are identical—and the only difference is that the invention at issue states that the administration

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that while nausea and vomiting were symptoms of migraine, "not every migraine patient will experience either of these two symptoms in any given migraine attack" and therefore "the administration of ondansetron to treat migraine is not directed at the same purpose as administration of the drug to patients in need of nausea and emesis relief").

will be for a *different purpose* than that focused upon in the prior art—this will constitute a new, patentable use. Indeed, GSK has not cited to a case that does stand for such a proposition.

Turning then to the facts here, and assuming *arguendo* that Kelly discloses the administration of carvedilol with ACE inhibitors in daily maintenance dosages for a maintenance period greater than six months, then there would be no manipulative difference in the methods disclosed in Kelly and those disclosed in the '000 patent. Both Kelly and the '000 patent require administration of carvedilol to the same patient population—patients with CHF. (D.I. 313 at 2; Tr. at 66, 98) And so, as Defendants explain, "GSK [] discovered another benefit of the use of carvedilol to treat CHF—that in addition to symptomatic improvement and increased quality of life, carvedilol also increases the chances the patient lives longer. But that is not a new use of carvedilol. Indeed, the desire or intent to 'decrease mortality' does not and cannot impact how carvedilol is used in CHF patients." (D.I. 249 at 7) In other words, if there are no actual differences in the treatment protocol when one is treating the symptoms of CHF versus when one is attempting to decrease a CHF patient's risk of mortality, then practicing the treatment protocol described in Kelly (assuming that to amount to the same method disclosed in the '000 patent) will *necessarily (or inherently) result* in "decreas[ing] [] the risk of mortality" in CHF patients. (*Id.* at 9; *see also* Riley Decl. Vol. I, ex. 10 at 236 (Dr. McCullough acknowledging in his deposition that "it's impossible for a physician to prescribe carvedilol in a patient with heart failure without having this treatment effect of reducing the probability that a patient will die of heart failure"); Tr. at 56 ("[I]f you follow the protocol that is in Kelly, you will reduce mortality associated with CHF")); *see also, e.g.*, *Cubist Pharms., Inc. v. Hospira, Inc.*, 75 F. Supp. 3d 641, 660 (D. Del. 2014) (finding that following the steps of the suggestion for future study disclosed in the prior art

reference would "have the physiological effect of minimizing skeletal muscle toxicity" which was the claim limitation that was not expressly disclosed in the reference, and concluding that, since "minimizing skeletal muscle toxicity was a necessary accompaniment to the other disclosed claimed limitations [it was] therefore [] inherently disclosed" by the prior art reference).[16]

In view of these facts, the Court does not agree with GSK that the facts of this case are "on point" with those in *Rapoport*. (Tr. at 74) Again, *Rapoport* involved the use of a drug to treat two *different conditions*, anxiety and sleep apnea; though anxiety might be a *symptom* of sleep apnea in a particular case, it was still a *separate*, *distinct condition* that was treated *differently* than sleep apnea.[17] This case might be similar to *Rapoport* if, for example, the evidence demonstrated that (1) some CHF patients would develop hypertension due to certain

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[16] During oral argument, GSK's counsel asserted that "treating symptoms is not the same thing as treating mortality[,]" (Tr. at 82-83), and pointed for support to a portion of Dr. McCullough's report in which Dr. McCullough explains that "[s]everal studies published prior to the claimed invention clearly demonstrated that drugs designed to improve *symptoms, functional status, hemodynamics, cardiac function, or other intermediate measures* of heart failure either *had no effect on mortality* or *increased mortality*[,]" (GSK's Anticipation and Obviousness Presentation, Slide PDX-120) (citing McCann Decl. Vol. I, ex. 13 at ¶ 193) (certain emphasis omitted, certain emphasis in original)). But none of these studies cited by Dr. McCullough involved carvedilol, and so none are persuasive in this context. (McCann Decl. Vol. I, ex. 13 at ¶¶ 194-201)

[17] It is true that, as GSK points out, (D.I. 297 at 13-14), the *Rapoport* Court at times utilizes language suggesting that the "intent" or "purpose" for which the method is administered matters in the inherent anticipation analysis. *See, e.g.*, *Rapoport*, 254 F.3d at 1061 (noting that the FPR Publication did not disclose the administration of buspirone "with the intent to cure [sleep apnea]" and though it did mention the possibility of administering buspirone to patients suffering from sleep apnea, that was for the "purpose of treating anxiety in such patients, not for the purpose of treating the sleep apnea disorder itself"). However, as explained above, the purpose or intent for administering buspirone *did* matter in *Rapoport*, because it resulted in a *manipulative difference* in the method disclosed in the prior art versus the method disclosed in the application (since there were two different patient populations at issue—patients needing treatment for sleep apnea and patients needing treatment for anxiety).

symptoms of CHF, and (2) there was a prior art reference discussing the administration of carvedilol to patients with hypertension, and a later patent disclosing a method of administering carvedilol to CHF patients to treat CHF. There would then be a manipulative difference in the methods—administering the drug to two different patient populations—and therefore the later patent might claim a patentable new use of carvedilol. But those are not the facts here. Kelly discloses treating CHF patients with carvedilol to determine whether it improved certain symptoms/hemodynamics. The '000 patent, for its part, does not disclose treating a different *symptom* of CHF, but instead discloses achieving a particular *result*—decreasing the CHF patient's risk of mortality—after giving the drug to the same patient population at issue in Kelly (those who suffer from CHF).[18] And this, the Federal Circuit has said, is not patentable; "[w]hile [the inventors] may have recognized something about [the administration of carvedilol in CHF patients] that was not known before, [the inventor's] claims do not describe a new method."

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[18] Indeed, even the way inventor Dr. Lukas described the genesis of the invention seems to underscore that the '000 patent claims a *result* of treating CHF patients. (*See, e.g.*, D.I. 73, ex. E at 17 at ¶¶ 62-64 (Affidavit of Dr. Lukas explaining that GSK designed a study to determine the effect of carvedilol on clinical endpoints and exercise tolerance, which demonstrated "the surprising result of a 65% decrease in the risk of mortality"—a "very powerful, beneficial effect of carvedilol for treatment of patients with CHF"); *see also* McCann Decl. Vol. I, ex. 8 at 79-80 (inventor Dr. Shusterman explaining that the clinical trials of CHF patients "were not actually designed to look at survival" but that that was the "surprise finding of the [] trials"); D.I. 73, ex. O at GSK00009589 ("Applicants, for the first time, demonstrated through the clinical data presented in the instant application that an agent considered useful for treating CHF, i.e., carvedilol, *not only relieved the symptoms of [CHF], but also reduced the risk of mortality in CHF patients by about 67%*" (emphasis added))) Of course, if the treatment protocol used in the trials that became limitations of the '000 patent claims were unknown in the prior art, the patent would claim a patentable new use of a new method. But if the treatment protocol for treating CHF patients was already taught in the prior art, this evidence further suggests that decreasing mortality of CHF patients is not a new use distinct from treating their CHF, but instead is a benefit that "must naturally flow from" practicing that very same method disclosed in the prior art. *See Perricone*, 432 F.3d at 1378.

Cruciferous, 301 F.3d at 1352.[19]

Defendants point out that GSK's logic appears to contradict the basis of the inherent anticipation doctrine. That is, Defendants note that by GSK's logic, it could have written claims directed to methods of giving carvedilol to CHF patients with the intent to treat left ventricular dysfunction and to treat exercise capacity, and then each time it determined a new symptom/hemodynamic in the CHF patient that the drug helped with, GSK could have written another claim (because those claims would amount to new "uses," even though the drug is administered to exactly the same patient population via exactly the same dosing regime). (Tr. at 99)

The Court agrees with Defendants that such claiming falls outside the realm of patentability in light of the inherent anticipation doctrine. The Court has struggled with this result, because it appears a harsh one, in light of GSK's allegations as to how the inventors here pushed forward, despite great skepticism and resistance, to discover carvedilol's extremely beneficial effect of reducing mortality, something that was simply not known at the time Kelly

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[19] *See also, e.g.*, *In re Montgomery*, 677 F.3d at 1377, 1381 (finding that, even if claims directed to the administration of ramipril for the treatment or prevention of stroke included an efficacy requirement, a prior art reference, HOPE would inherently anticipate the claims at issue, as it disclosed a protocol for the administration of ramipril to stroke-prone patients, and "administering ramipril to stroke-prone patients inevitably treats or prevents stroke"); *Application of May*, 574 F.2d 1082, 1090 (C.C.P.A. 1978) ("Both appellants and May describe methods for effecting analgesia. While appellants have discovered a hitherto unknown property, to wit, nonaddictiveness, of the species disclosed by May, such discovery does not constitute a new use."); *Sepracor Inc. v. Dey, L.P.*, 657 F. Supp. 2d 478, 485-86 (D. Del. 2009) (explaining that to the extent that defendants could establish at trial that the prior art disclosed the use of optically pure R(-) albuterol for the treatment of asthma in humans, the claims at issue (directed to a method of treating asthma in an individual with albuterol while reducing side effects associated with chronic administration of racemic albuterol, by the administration of optically pure R(-) albuterol) "would be directed not to a new use, but merely an added benefit [reducing side effects] of an old use").

was published. (D.I. 297 at 1); *cf. In re Montgomery*, 677 F.3d 1375, 1383 (Fed. Cir. 2012) (Lourie, J., dissenting) (noting that while the "salutary goal" of the doctrine of inherency is to "prevent subject matter that is effectively in the public's possession from being retrieved by a patent and withdrawn from the public domain[,]" the doctrine's "downside is withholding patent protection from that which the public knew nothing about until a later inventor found it"). And the Court recognizes that this area of the law is not easily traversed.[20] Nevertheless, the Court feels compelled to reach this result here. It is convinced that the outcome flows from the content of the inherent anticipation doctrine itself, which does not include an exception for the later discovery of life-saving inherent results of a known method, and not due to the wrongful application of that precedent.

b. Prosecution History

GSK also argues that Defendants' inherent anticipation argument should fail because the PTO "confronted and rejected essentially the same inherency argument that Defendants advance here." (D.I. 297 at 17) As GSK describes it, the PTO initially rejected GSK's claims in view of prior art that disclosed the use of carvedilol to improve the quality of life or symptoms of heart failure, explaining that decreasing mortality resulting from heart failure is "inherent" in the prior art. (*Id.* (citing McCann Decl. Vol. I, ex. 49 at GSK00000077; Ex. 50 at GSK00009485)) GSK reports that it responded that, *inter alia*, "there is a recognized distinction between (a) treating

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[20] For example, it could be said that the result of the application of the inherent anticipation doctrine here is in some conflict with the maxim that "that which would literally infringe if later anticipates if earlier[,]" *Bristol-Myers Squibb*, 246 F.3d at 1378, in light of the fact that the Court has earlier construed the decreasing mortality limitation as a claim limitation, relying in significant part on the rationale expressed in *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003), (D.I. 165 at 8-22).

quality of life or symptoms of [CHF] and (b) treating [CHF] mortality[,]" and that the PTO later recognized that these differences amounted to different uses of carvedilol, leading to the issuance of the patent. (*Id.* (citing McCann Decl. Vol. I, ex. 49 at GSK00000109-16, GSK00000165))

In the Court's view, however, the PTO did not confront an identical inherency argument. The PTO's rejection did not rely on Kelly, but instead on, *inter alia*, a prior art patent directed to the use of carvedilol for indications other than CHF. (McCann Decl. Vol. I, ex. 49 at GSK00000077) That patent, United States Patent No. 5,308,862 ("Ohlstein"), issued on May 3, 1994, and is directed to a method of treatment using carvedilol to "prevent restenosis following percutaneous transluminal coronary angioplasty [] and prevent development of atherosclerosis." (*See* Ohlstein at Abstract) The specification makes a passing reference to CHF—it explains that carvedilol is "useful in the treatment of . . . hypertension and having utility in angina and . . . CHF" due to its beta blocking properties. (*Id.*, col. 4:12-26) Otherwise, the patent is "very different" than Kelly—it is primarily about "using [c]arvedilol to treat other indications" and does not say a thing about the proper dosages or dosing schedule with respect to CHF. (Tr. at 50-51)

A close look at the prosecution history also reveals that, in order to overcome the rejection based on Ohlstein, the applicants did not exactly argue that treating CHF and decreasing the CHF patient's risk of mortality are two very different things. Rather, the applicants asserted that the claims should issue over Ohlstein because that reference discussed "[t]he treatment of symptoms [of CHF], *such as high blood pressure*"—"Ohlstein can only be understood, in the context of one skilled in the art in 1995, as referring to *hypertension treatment* (*i.e.*, symptomatic treatment) in the presence of CHF." (McCann Decl. Vol. I, ex. 49 at GSK00000111-113

(emphasis added)) The applicants then cited to *Rapoport* as an analogous case. And that citation makes sense in the context of their argument. *Rapoport* distinguishes treating sleep apnea from treating anxiety, which can be caused by sleep apnea *but which is a separate condition.* And as to Ohlstein, applicants argued that treating CHF patients to decrease mortality was different than treating *hypertension* in CHF patients, which can be caused by CHF but which is a separate condition that also exists in persons who do not have CHF. Kelly, meanwhile, is not about treating a separate condition than CHF—it is about treating CHF.

c. Whether "Intent" Rescues the Claims from Being Inherently Anticipated

In another attempt to avoid the inherent anticipation doctrine, GSK asserts that because the Court construed the decreasing morality limitations as claim limitations that require "administering the claim[ed] drugs *with the intent* to attempt to reduce the probability that a patient will die from heart failure," the proper way to assess the inherent anticipation question is to ask whether Kelly discloses the requisite *intent.* (D.I. 297 at 16-17 (certain emphasis omitted, emphasis in original)) Kelly would easily fail such an inquiry, as there is no dispute that Kelly's disclosed planned study intended to foster a different outcome in patients—to make patients feel better and to improve heart function metrics. (*Id.* at 17)

But the Court is not persuaded that simply adding an "intent" limitation to the claim successfully avoids the doctrine of inherent anticipation. As previously noted, GSK has not pointed the Court to any case in which there was no manipulative difference between the physical steps of the methods disclosed in the invention and the prior art, and yet because the claimed

invention included an "intent" requirement, the claim was not inherently anticipated.[21] If this were permissible, it would seem to conflict with the Federal Circuit's instruction that inherent anticipation does not require that a person of ordinary skill in the art at the time would have recognized the inherent disclosure. (D.I. 249 at 9 (citing *Schering Corp.*, 339 F.3d at 1377)); *see also Cruciferous*, 301 F.3d at 1349 ("Inherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art.") (internal quotation marks and citations omitted). The Court agrees with Defendants that there does not seem to be a difference between claims that require prerequisite *knowledge* of an inherent result, which the Federal Circuit has repeatedly said is not sufficient to make a claim patentable, and claims that require prerequisite *intent* of achieving a particular result. (D.I. 313 at 5) The Court also agrees with Defendants that were an intent limitation enough to claim around inherent anticipation, that would essentially eviscerate the doctrine. (D.I. 313 at 5; *see also* Tr. at 94-95 (Defendants' counsel asserting that "a finding [] of no inherent anticipation based on the intent element will completely destroy the doctrine of inherent anticipation because everybody will simply add those elements when they write claims, or they will go back and do re-issues and re-exams or they will add them in [*inter partes* review proceedings]"))

d. Conclusion

For these reasons, assuming *arguendo* that Kelly discloses all of the physical steps of the

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[21] The Court notes that in *Perricone*, the Federal Circuit agreed with the district court's construction of the preambles in the Perricone Patents (reciting the purposes of the methods as achieving particular skin benefits) as limiting; nonetheless, the Court found inherent anticipation of such claims where the prior art reference disclosed the "application step" of the claims. *Perricone*, 432 F.3d at 1371, 1378 & n.*; *see also* (D.I. 313 at 2-3).

claimed treatment protocol (and further assuming *arguendo* that Kelly is enabling, an issue that the Court has found to be in genuine dispute below), the Court concludes that Kelly inherently anticipates the decreasing mortality limitations.

C. Whether Kelly is Enabled

Lastly, the Court addresses whether Plaintiffs have articulated a genuine dispute of material fact as to whether Kelly is enabled. GSK asserts Kelly does not enable claims 1-3 and 6-9 of the '000 patent, and that it therefore cannot be an anticipatory reference. (D.I. 297 at 19-20; Tr. at 92-93)

As noted above, in order to anticipate, a reference must, *inter alia*, enable a person of skill in the art to practice or carry out the method at issue without undue experimentation, *In re Gleave*, 560 F.3d at 1334-35, thus placing the allegedly disclosed matter in the possession of the public, *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1345 (Fed. Cir. 2008); *Akzo N.V. v. U.S. Int'l Trade Comm'n*, 808 F.2d 1471, 1479 (Fed. Cir. 1986). The inquiry as to whether "undue experimentation" is required is "'not a single, simple factual determination, but rather . . . a conclusion reached by weighing many factual considerations.'" *Martek Bioscis. Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1378 (Fed. Cir. 2009) (quoting *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)). Determining what level of experimentation qualifies as "'undue,' so as to render a disclosure non-enabling, is made from the viewpoint of persons experienced in the field of the invention." *Elan Pharms., Inc. v. Mayo Found. for Med. Educ. & Research*, 346 F.3d 1051, 1055 (Fed. Cir. 2003). The Federal Circuit has provided several factors that may be utilized in determining whether a disclosure would require undue experimentation (the "*Wands* factors"): (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 claims. *In re Wands*, 858 F.2d at 737.[22] "Whether a prior art reference is enabling is a question of law based upon underlying factual findings." *SmithKline Beecham Corp.*, 403 F.3d at 1342-43 (citation omitted). Thus, if there is a genuine dispute of fact as to whether a prior art reference is nonenabling, summary judgment may not be granted. *Cf. SRI Int'l, Inc. v. Internet Sec. Sys., Inc.*, 511 F.3d 1186, 1194 (Fed. Cir. 2008).

GSK sets out three arguments as to why Kelly does not enable the invention of the '000 patent. For the reasons explained below, the Court is not persuaded that the first two establish a genuine dispute of fact as to whether Kelly is nonenabling. But the third argument does establish such a dispute of fact.

First, GSK argues that Kelly does not enable the invention of the '000 patent since it does not address *decreasing mortality in CHF patients*. In GSK's view, enablement of the invention claimed in the '000 patent requires evidence in the prior art reference that carvedilol can actually reduce the probability that a patient will die from CHF; accordingly, GSK asserts, a person of skill in the art beginning with Kelly would need to conduct a large, multi-center trial showing a risk in the reduction of heart failure mortality. (McCann Decl. Vol. I, ex. 13 at ¶¶ 213-15; D.I. 297 at 20) According to GSK, then, Kelly does not enable the claimed invention because it contains no working examples or case descriptions demonstrating that carvedilol could in fact be

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[22] A court need not consider every one of the *Wands* factors in its analysis to find a disclosure enabling. *See Streck, Inc. v. Research & Diagnostic Sys., Inc.*, 665 F.3d 1269, 1288 (Fed. Cir. 2012).

used to reduce the risk of mortality due to CHF. (McCann Decl. Vol. I, ex. 13 at ¶ 214; D.I. 297 at 20)[23]

Assuming *arguendo* here that Kelly discloses all of the physical steps of the treatment protocol set out in the '000 patent, the Court agrees with Defendants that this particular argument by GSK does not suffice to overcome the presumption of enablement. The Federal Circuit has explained that "the fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention." *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1321 (Fed. Cir. 2004). And so GSK's argument that Kelly is not enabling because it does not contain evidence that the treatment protocol *reduces mortality caused by CHF* seems to miss the point of inherent anticipation, which "does not require a person of ordinary skill in the art to recognize the inherent disclosure in the prior art at the time the prior art is created."

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[23] GSK had first asserted that denial of Defendants' Motion is warranted because Defendants' experts offered no opinion on whether Kelly enabled the claims. (D.I. 297 at 19-20) It is not as simple as that, however, in light of the presumption of enablement. As our Court has explained, for Section 102 purposes, a district court should presume that a prior art printed publication is enabled. *Lambda Optical Sols. LLC v. Alcatel Lucent USA Inc.*, Civil Action No. 10-487-RGA, 2015 WL 5734427, at *1 (D. Del. Sept. 30, 2015); *see also Lambda Optical Solutions, LLC v. Alcatel-Lucent USA Inc.*, Civil Action No. 10-487-RGA-CJB, 2015 WL 12806435, at *4 (D. Del. July 24, 2015) (citing cases). Ultimately, it is the patentee who bears the ultimate "burden of proving the nonenablement of [here, the prior art publication] before the district court." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1355 (Fed. Cir. 2003). The patentee's burden is to overcome the presumption of enablement by a preponderance of the evidence. *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1307 (Fed. Cir. 2006) ("On remand, the district court found that Amgen had met its burden of proving by a preponderance of the evidence that the Sugimoto patent was not enabled."); *Cubist Pharms.*, 75 F. Supp. 3d at 661 ("The patentee, however, bears the burden of overcoming the presumption of prior art enablement by a preponderance of the evidence.") (citing *Amgen*, 314 F.3d at 1355-56). Thus, a defendant's failure to offer expert testimony with respect to enablement of a prior art reference is not an automatic reason to deny a motion for summary judgment of anticipation.

SmithKline Beecham Corp., 403 F.3d at 1343; *see also, e.g.*, *Only the First, Ltd. v. Seiko Epson Corp.*, 822 F. Supp. 2d 767, 788 (N.D. Ill. 2011) ("Again, for a reference to be enabled [for purposes of inherent anticipation], 'contemporaneous recognition of the [] necessary features or results' is not required.") (quoting *Toro Co.*, 355 F.3d at 1321).

Second, GSK points out that Defendants' expert opined that claim 1 of the '000 patent is not enabled pursuant to 35 U.S.C. § 112 ("Section 112") because the specification fails to disclose adequate supporting clinical trial data, (D.I. 297 at 20 n.14; *see also* McCann Decl. Vol. I, ex. 13 at ¶ 214 & n.205 (citing McCann Decl. Vol. II, ex. 55 at ¶ 79)), and argues that this opinion is inconsistent with Defendants' position that Kelly is an enabling disclosure, (Tr. at 92-93). But this argument overlooks that the standard for enablement of a prior art reference for purposes of anticipation is lower than the enablement standard under Section 112. *See, e.g.*, *Novo Nordisk Pharms., Inc. v. Bio-Tech. Gen. Corp.*, 424 F.3d 1347, 1355 (Fed. Cir. 2005).

In the case of an invention teaching a process, to be enabling under Section 112, the specification must adequately disclose to the person of skill in the art how to carry out the claimed invention without undue experimentation, *see In re '318 Patent Infringement Litig.*, 583 F.3d 1317, 1323 (Fed. Cir. 2009), *and* the specification must also "disclose as a matter of fact a practical utility for the invention," *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1323 (Fed. Cir. 2006) (internal quotation marks and citation omitted). In other words, unless the evidence demonstrates that the person of skill in the art would accept without question statements regarding the effects of the claimed drug products, an applicant must present evidence to demonstrate that the claimed products do indeed have those effects. *Id.*; *see also, e.g.*, *In re '318 Patent Infringement Litig.*, 583 F.3d at 1323-24 (finding that the patent specification

regarding the use of galantamine to treat Alzheimer's disease failed to satisfy the enablement requirement of Section 112 because the application did not establish utility, as "the specification, even read in the light of the knowledge of those skilled in the art, does no more than state a hypothesis and propose testing to determine the accuracy of that hypothesis").

On the other hand, with respect to enablement of a method under Section 102, the Federal Circuit has explained that while one must show that a person of ordinary skill would know how to "practice or to carry out" the method in light of the reference, the prior art reference need not "demonstrate the invention's *utility*." *In re Gleave*, 560 F.3d at 1335 (emphasis in original); *see also AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1055 (Fed. Cir. 2010) ("[U]nlike enablement under [Section] 112, a reference need not . . . demonstrate utility or efficacy to be enabling in the context of [Section] 102."). For example, in the context of a claimed method for treating a disease, "a prior art reference need not disclose 'proof of efficacy' to anticipate the claim." *In re Gleave*, 560 F.3d at 1335.

In light of the fact that the enablement standards are not identical for Section 102 and Section 112, GSK's argument that Defendants' enablement positions are inconsistent does not help it. Thus, while the Kelly reference would not have to show that carvedilol actually decreases mortality in CHF patients to be enabling, the '000 patent specification would have to disclose evidence to demonstrate that the invention does indeed have that effect.[24] *See, e.g., id.* at 1334 (explaining that as long as the reference discloses all of the claim limitations explicitly or inherently and enables the subject matter that falls within the scope of the claims, the reference

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[24] As the issue of Section 112 enablement is not presently before the Court, the Court takes no position on that issue at this time.

anticipates—"no 'actual creation or reduction to practice' is required'" and "[t]his is so despite the fact that the description provided in the anticipating reference might not otherwise entitle its author to a patent") (citation omitted).

Third, GSK asserts that Kelly does not enable a person of ordinary skill in the art to practice the claims without undue experimentation because Kelly is too theoretical, in that it "created substantial uncertainty regarding the administration of beta blockers to heart failure patients." (D.I. 297 at 20 (citing McCann Decl. Vol. I, ex. 13 at ¶ 191)) As explained above, a prior art reference relied upon in an inherent anticipation defense must *itself* be "sufficiently described and enabled[.]" *Toro Co.*, 355 F.3d at 1321. This enablement requirement ensures that the public was sufficiently in "possession of the desired subject matter." *Elan Pharms.*, 346 F.3d at 1055.

While the parties have not pointed the Court to much caselaw that discusses the enablement requirement in similar circumstances, the Federal Circuit has provided some guidance in *In re Montgomery*, 677 F.3d 1375 (Fed. Cir. 2012). In that case, the majority found a prior art reference ("HOPE") to inherently anticipate and enable claims directed to the administration of inhibitors of the renin-angiotensin system (including ramipril) for the treatment or prevention of stroke. 677 F.3d at 1382-83. HOPE described the design of a large, simple randomized trial involving over 9,000 patients at high risk for cardiovascular events such as stroke, who would receive ramipril and vitamin E in the prevention of, *inter alia*, stroke. *Id.* at 1378. The study had begun, with all patients having been randomized and receiving ramipril or a placebo for at least one month, but had not been completed. *Id.* The majority ultimately rejected the patent applicant's argument that "HOPE was merely a proposal for future research that was

not enabled[.]" *Id.* at 1379. In arriving at this conclusion, the majority did make clear that while anticipation "requires only an enabling disclosure, not actual creation or reduction to practice," in its view, a prior art disclosure of a proposal for testing that amounts to an "invitation to investigate" or an "abstract theory" would not be sufficiently enabling. *Id.* at 1382 (internal quotation marks and citations omitted).[25] And the majority then provided an example of what would qualify as a non-enabling, mere invitation to investigate: i.e., "a document that recited administration of all known compounds for treatment of all known diseases, with no evidence that any of these treatments would be effective, would not inherently anticipate all method-of-treatment claims involving those compounds and diseases." *Id.* at 1382 n.13.

On the one hand, the disclosure in Kelly can be seen as being more concrete than the exemplary "invitation to investigate" set out by the *Montgomery* Court, in that the planned multicentre trial in Kelly was focused on the use of particular drugs (carvedilol, along with "encouraged" use of ACE inhibitors), in particular dosage levels (from 3.125 mg up to 25 mgs, taken twice daily), to treat particular symptoms (increase levels of cardiac output and ventricular function, and exercise capacity) of patients who have a particular condition (CHF, caused by ischaemic heart disease). (Kelly at TCAR0011941) And while the Federal Circuit does not

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[25] The decision in *In re Montgomery* was not unanimous. Judge Lourie dissented, explaining that in his view, "[i]n the unpredictable arts, rarely if ever will an untested proposal necessitating further study and optimization meet the stringent inevitably requirement of inherent anticipation" as "a mere description of a process that, *if it* had been carried out, *might* yield a particular *undisclosed* result is not an inherent anticipation of that result." 677 F.3d at 1384-85 (emphasis in original); *see also id.* at 1385 ("The results of a proposed study . . . are neither predictable nor inevitable."). Thus, Judge Lourie opined that the planned study described in HOPE did not inherently anticipate the pending claims, since "[t]he HOPE reference is only a description of what has not been carried out; whether or not, if carried out, it would inherently accomplish the claimed result is not before us, for HOPE is only a plan." *Id.* at 1385.

require "evidence that [a treatment method described in the prior art] would be 'effective[,]" *Impax Labs., Inc.*, 468 F.3d at 1383, Kelly does discuss some evidence suggesting that the treatment to be provided in the planned trial may be effective—evidence of other recent studies that had demonstrated that administration of carvedilol caused symptomatic improvement in these areas in patients with heart failure, (Kelly at TCAR0011939-41). *Cf. Cubist Pharms.*, 75 F. Supp. 3d at 659-61 (concluding post-trial that the "brief disclosure" in the prior art reference that noted that based on certain of the drug's characteristics, dosages in a particular range "'are predicted to be effective'" was an enabling reference that inherently disclosed "minimizing skeletal muscle toxicity" where that disclosure "identified *the exact* dosage amounts and interval claimed by the [asserted] patent") (emphasis in original).

Yet on the other hand, the disclosure in Kelly regards a planned but not yet started trial, and so in that sense, can be seen as more "abstract" than was the HOPE disclosure. (*See* D.I. 297 at 13 n.8) As for HOPE, the majority *Montgomery* Court explained that the protocol described therein was "far from an abstract theory"—instead it was "an advanced stage of testing designed to secure regulatory approval" that was to "obtain data for submission to regulatory agencies on the effect of ramipril on cardiovascular diseases including stroke based on substantial evidence that ramipril improved cardiovascular health, including by treating stroke risk factors such as hypertension." 677 F.3d at 1382. In contrast, the disclosure in Kelly of the planned multicentre trial was certainly not at that kind of "advanced stage," as it had not yet started. (D.I. 297 at 13) To that end, Dr. McCullough opines in his report that "at best, Kelly 1993 discloses a theoretical attempt to determine whether the disclosed treatment will improve the symptoms of ischemic heart failure patients." (McCann Decl. Vol. I, ex. 13 at ¶ 191) That is, "Kelly 1993 proposes a

yet to be conducted clinical trial designed to determine *if* carvedilol has an effect on exercise capacity, left ventricular function, and left ventricular size in patients with ischemic heart disease as their cause of heart failure." (*Id.* at ¶ 185 (emphasis in original)) Kelly's brief disclosure "does not disclose [] which of the various available study methods would be used to assess the effects of carvedilol on exercise capacity, left ventricular function, and left ventricular size" and it "does not provide any details of the trial . . . since the methods of the trial had not been published and the study had not yet begun." (*Id.* at ¶ 186)

In the Court's view, Dr. McCullough's opinion that Kelly is too theoretical, together with the disclosure of Kelly itself and the guidance in *In re Montgomery*, suffices to create a genuine issue of fact as to whether Kelly is nonenabling. There is a fact question as to whether Kelly's disclosure of a planned (but not initiated) trial was sufficiently concrete to truly put the content of that study in the possession of the public.

C. Conclusion

In sum, while it is a close question, construing the evidence in the light most favorable to GSK, the Court concludes that there is a genuine dispute of material fact as to whether Kelly discloses administering maintenance dosages for a maintenance period greater than six months. Therefore, Defendants have not established as a matter of law that Kelly anticipates the claims of the '000 patent, and the Court recommends that Defendants' Motion be denied on this ground.

Additionally, the Court concludes that GSK's arguments regarding the decreased mortality limitations are based on an incorrect reading of the law of anticipation.

Lastly, the Court finds a material factual dispute as to whether Kelly is enabled.

IV. CONCLUSION

For the reasons set forth above, the Court recommends that Defendants' Motion for Summary Judgment of Invalidity be DENIED, in the manner described herein.

This Report and Recommendation is filed pursuant to 28 U.S.C. § 636(b)(1)(B), Fed. R. Civ. P. 72(b)(1) and D. Del. LR 72.1. The parties may serve and file specific written objections by no later than **May 12, 2017**; responses are due by no later than **May 22, 2017.** The failure of a party to object to legal conclusions may result in the loss of the right to de novo review in the district court. *See Sincavage v. Barnhart*, 171 F. App'x 924, 925 n.1 (3d Cir. 2006); *Henderson v. Carlson*, 812 F.2d 874, 878-79 (3d Cir. 1987).

The parties are directed to the Court's Standing Order for Objections Filed Under Fed. R. Civ. P. 72, dated October 9, 2013, a copy of which is available on the District Court's website, located at http://www.ded.uscourts.gov.

Because this Report and Recommendation may contain confidential information, it has been released under seal, pending review by the parties to allow them to submit a single, jointly proposed, redacted version (if necessary) of the Report and Recommendation. Any such redacted version shall be submitted no later than **May 9, 2017** for review by the Court, along with a clear, factually detailed explanation as to why disclosure of any proposed redacted material would "work a clearly defined and serious injury to the party seeking closure." *Pansy v. Borough of Stroudsburg*, 23 F.3d 772, 786 (3d Cir. 1994) (internal quotation marks and citation omitted). The Court will subsequently issue a publicly-available version of its Report and Recommendation.

Dated: May 2, 2017

Christopher J. Burke
UNITED STATES MAGISTRATE JUDGE