UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

PROMETHEUS LABORATORIES, INC.,

Plaintiff,

v.

MAYO COLLABORATIVE SERVICES dba MAYO MEDICAL LABORATORIES and MAY CLINIC ROCHESTER,

Defendants.

AND RELATED COUNTER-CLAIM.

Civil No. 04cv1200 JAH (RBB)

ORDER:

1. **GRANTING DEFENDANTS' MOTION FOR SUMMARY JUDGMENT OF PATENT INVALIDITY PURSUANT TO 35 U.S.C. § 101 [Doc. No. 502];**
2. **DENYING AS MOOT PLAINTIFF'S MOTION FOR SUMMARY JUDGMENT OF NO PATENT EXHAUSTION [Doc. No. 494];**
3. **DENYING AS MOOT PLAINTIFF'S MOTION FOR SUMMARY JUDGMENT OF DECLARATORY INFRINGEMENT OF PATENT NOS. 6,355,623 AND 6,680,302 [Doc. No. 439];**
4. **DENYING AS MOOT PLAINTIFF'S MOTION TO STRIKE DECLARATION OF DR. BRUCE BOSTROM [Doc. No. 549]**

INTRODUCTION

Now before the Court are three motions for summary judgment filed by the parties, and a motion to strike the declaration of Dr. Bruce Bostrom filed by Plaintiff. The motions have each been fully briefed and oral argument has been entertained. After careful consideration of the pleadings and relevant exhibits presented by the parties, the oral argument presented at the hearing, and for the reasons set forth below, this Court **GRANTS** Defendants' motion for

summary judgment of patent invalidity thereby invalidating the patents-in-suit as violative of 35 U.S.C. § 101. Accordingly, Plaintiff's motions for summary judgment of no patent exhaustion and for declaratory judgment of infringement are **DENIED as moot**, and will not be addressed herein. Plaintiff's motion to strike the declaration of Dr. Bruce Bostrom is also **DENIED as moot**.

BACKGROUND

A. Factual Background

Plaintiff, Prometheus Laboratories ("Plaintiff" or "Prometheus"), is the exclusive licensee of two patents: U.S. Patent Nos. 6,355,623 ("the '623 patent") and 6,680,302 ("the '302 patent") (collectively "the patents-in-suit"). The patents-in-suit involve measurements of the level of certain metabolites in the blood of patients taking thiopurine drugs, including the anti-Crohn's disease drug azathioprine ("AZA"), for treatment of either gastrointestinal autoimmune diseases or non-gastrointestinal autoimmune diseases. The patented test provides a means to measure the level of two metabolites: 6-thioguinine ("6-TG") and 6-methylmercaptopurine ("6-MMP"), which, according to the patent, indicates that an adjustment in drug dosage may be required at metabolite levels "greater than about 400" and "greater than about 7000," respectively, in order to avoid toxic side effects.

Defendants, Mayo Collaborative Services dba Mayo Medical Laboratories and Mayo Clinic Rochester (collectively "Defendants" or "Mayo") developed a test ("the accused test") to measure the same metabolites but using different levels, 450 6-TG and 5700 6-MMP. In June 2004, Defendants announced they intended to begin use of their accused test, offering it for sale to potential purchasers, but the announcement was later rescinded. The instant lawsuit followed.

B. Procedural History

Plaintiff filed its patent infringement complaint on June 15, 2004. On January 27, 2005, Defendants filed a motion for summary judgment seeking a declaration of non-infringement, which this Court denied on November 22, 2005. Doc. No. 227. Plaintiff filed a cross-motion for summary judgment, seeking a judicial declaration that Defendants' accused test literally

infringes Claim 7 of the '623 patent, which this Court granted in its November 22, 2005 order.[1] Defendants filed a motion seeking relief from the Court's November 22, 2005 order, which the Court denied. Doc. Nos. 230 and 260.

On December 13, 2005, this Court granted both parties' motions to amend their respective pleadings. Doc. No. 234. Plaintiff filed a first amended complaint ("FAC") on December 22, 2005. Doc. No. 236. Defendants filed an answer to the FAC, along with amended counterclaims, on January 13, 2006. Doc. No. 241. On April 14, 2006, the parties stipulated to the filing of a second amended complaint ("SAC"). Doc. No. 267.

Three separate motions for summary judgment followed. On January 9, 2007, Plaintiff filed a motion for summary judgment of no patent exhaustion. Doc. No. 494. Defendants filed an opposition to Plaintiff's motion on February 22, 2007. Doc. No. 519. Plaintiff filed a reply on March 1, 2007. Doc. No. 529.

Defendants filed a motion for summary judgment of patent invalidity under 35 U.S.C. § 101 on January 29, 2007.[2] Doc. No. 502. Plaintiff filed an opposition to Defendants' motion on February 28, 2007. Doc. No. 528. Defendants filed their reply on March 9, 2007. Doc. No. 542. Included in Defendants' reply brief was a declaration by Dr. Bruce Bostrom. Plaintiff subsequently filed a motion to strike Dr. Bostrom's declaration. Doc. No. 549. Defendants filed an opposition to Plaintiff's motion and Plaintiff filed a reply. Doc. Nos. 566 and 568.

On March 8, 2007, Plaintiff filed a motion for summary judgment of declaratory judgment of infringement. Doc. No. 539. Defendants filed an opposition to Plaintiff's motion on April 12, 2007. Doc. No. 561. Plaintiff filed a reply on April 19, 2007. Doc. No. 565.

The Court rescheduled the motion hearing on the first summary judgment motions so

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[1] In its November 22, 2005 order, this Court construed the following terms contained in the patents-in-suit: (1) "greater than about 400" was construed to mean "any level above 340 to 460"; and "indicates a need" was construed to mean "a warning that an adjustment in dosage may be required." Doc. No. 227 at 18.

[2] Defendants also filed, on January 25, 2007, a motion to strike Plaintiff's jury demand. Doc. No. 501. Because Plaintiff did not oppose the motion, the Court subsequently granted the motion and struck the jury demand. Doc. No. 546.

that all motions (including the motion to strike the declaration of Bruce Bostrom) could be heard on the same day, May10, 2007, and set a briefing schedule for the remaining pleadings. On May 10, 2007, after all the motions were fully briefed, this Court heard oral argument from the parties and took all four motions under submission.

On October 1, 2007, while the motions were still under submission, the parties filed a joint application requesting permission to submit additional briefing on two recently decided Federal Circuit cases: In re Comiskey, 499 F.3d 1365 (Fed. Cir. 2007), and In re Nuijten, 500 F.3d 1346 (Fed. Cir. 2007). Doc. No. 584. The Court granted the request, and on October 26, 2007, Defendants submitted a brief regarding Comiskey and Nuijten. Doc. No. 586. Plaintiff submitted its own brief on November 9, 2007. Doc. No. 588. Defendants then requested, and were granted, leave to file a reply brief, which they filed on November 19, 2007. Doc. No. 590, Exhibit A. Plaintiff then submitted a sur-reply brief on November 30, 2007. Doc. No. 593.

DISCUSSION

Defendants have moved for summary judgment on the grounds that the patents-in-suit are invalid because they impermissibly claim unpatentable subject matter under 35 U.S.C. § 101. Specifically, Defendants contend that the patents impermissibly claim natural phenomena – the correlations between thiopurine drug metabolite levels on the one hand and therapeutic efficacy and toxicity on the other – and the claims "wholly pre-empt" use of the natural phenomena. See Doc. No. 502 at 11-12.

A. Legal Standards

1. Summary Judgment

Summary judgment is appropriate under Rule 56(c) of the Federal Rules of Civil Procedure where the moving party demonstrates the absence of a genuine issue of material fact and entitlement to judgment as a matter of law. Fed. R. Civ. P. 56(c); Celotex Corp. v. Catrett, 477 U.S. 317, 322 (1986). A fact is material when, under the governing substantive law, it could affect the outcome of the case. See Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248 (1986); Freeman v. Arpaio, 125 F.3d 732, 735 (9th Cir. 1997). A dispute about a material fact

is genuine if "the evidence is such that a reasonable jury could return a verdict for the nonmoving party." Anderson, 477 U.S. at 248.

A party seeking summary judgment always bears the initial burden of establishing the absence of a genuine issue of material fact. See Celotex, 477 U.S. at 323. The moving party may satisfy this burden in two ways: (1) by presenting evidence that negates an essential element of the nonmoving party's case or (2) by demonstrating that the nonmoving party failed to make a showing sufficient to establish an element essential to that party's case on which that party will bear the burden of proof at trial. Id. at 322-23. "Disputes over irrelevant or unnecessary facts will not preclude a grant of summary judgment." T.W. Elec. Serv., Inc. v. Pacific Elec. Contractors Ass'n, 809 F.2d 626, 630 (9th Cir. 1987). "The district court may limit its review to the documents submitted for purpose of summary judgment and those parts of the record specifically referenced therein." Carmen v. San Francisco Unified Sch. Dist., 237 F.3d 1026, 1030 (9th Cir. 2001). Therefore, the court is not obligated "to scour the record in search of a genuine issue of triable fact." Keenan v. Allen, 91 F.3d 1275, 1279 (9th Cir. 1996) (citing Richards v. Combined Ins. Co., 55 F.3d 247, 251 (7th Cir. 1995)). If the moving party fails to discharge this initial burden, summary judgment must be denied and the court need not consider the nonmoving party's evidence. See Adickes v. S.H. Kress & Co., 398 U.S. 144, 159-60 (1970).

If the moving party meets the initial burden, the nonmoving party cannot defeat summary judgment merely by demonstrating "that there is some metaphysical doubt as to the material facts." Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp., 475 U.S. 574, 586 (1986); see also Anderson, 477 U.S. at 252 ("The mere existence of a scintilla of evidence in support of the nonmoving party's position is not sufficient."). Rather, the nonmoving party must "go beyond the pleadings and by her own affidavits, or by the depositions, answers to interrogatories, and admissions on file, designate specific facts showing that there is a genuine issue for trial." Celotex, 477 U.S. at 324 (quoting Fed. R. Civ. P. 56(e)) (internal quotations omitted).

When ruling on summary judgment, the court may not make credibility determinations, and inferences to be drawn from the facts must be viewed in the light most favorable to the

party opposing the motion. Masson v. New Yorker Magazine, 501 U.S. 496 (1991); see also Anderson, 477 U.S. at 249, Matsushita, 475 U.S. at 587.

2. Section 101

Defendants move for summary judgment for patent invalidity under 35 U.S.C. § 101. Section 101 provides that:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.[3]

35 U.S.C. § 101.

The Supreme Court has construed section 101 broadly, observing that Congress intended statutory subject matter to include "anything under the sun that is made by man." Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980). However, it is well settled that there are qualifications to the apparent sweep of this statement. In Chakrabarty, the Supreme Court explained that:

> [A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E = mc^2$; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of . . . nature, free to all men and reserved exclusively to none.'

447 U.S. at 309 (quoting Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948)). Accordingly, the Supreme Court has specifically excluded from patentable subject matter: "laws of nature, natural phenomena, and abstract ideas." Diamond v. Diehr, 450 U.S. 175, 185 (1981). As the Court explained, "[p]henomena of nature, though just discovered, mental processes and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." Gottschalk v. Benson, 409 U.S. 63, 67 (1972).

In assessing patentability under section 101 in the context of method patents, the Supreme Court has explained that a method patent is not invalid "simply because it contains a law of nature or a mathematical algorithm." Parker v. Flook, 437 U.S. 584, 590 (1978). But, if the claim "recites" a law of nature or a mathematical algorithm, the court must analyze

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[3]The word "process" is defined in 35 U.S.C. § 100(b): "The term 'process' means process, art, or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material."

whether the claim is seeking patent protection for the phenomenon "in the abstract" or whether the claim implements a natural phenomenon "in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect." Diehr, 450 U.S. at 191. Thus, where the claim "wholly pre-empts" all uses of the natural phenomenon or abstract idea such that the "practical effect is a patent on the [phenomenon] itself" the claim is invalid under section 101. Benson, 409 U.S. at 71-72; see also Diehr, 450 U.S. at 187.

It is also important to note that "[p]atentability does not depend on which form the claim takes." Nuijten, 500 F.3d at 1362. As the Supreme Court has repeatedly explained, an "unpatentable principle" will not transform into a "patentable process" simply by adding conventional method steps. Flook, 437 U.S. at 588-90; see also Diehr, 450 U.S. at 191-92. If such were the case, "the determination of patentable subject matter [would] depend simply on the draftman's art." Id. at 593.

Whether a patent claim is invalid for failure to comply with section 101 is a question of law appropriate for summary judgment. AT&T Corp. v. Excel Comm. Inc., 172 F.3d 1352, 1355 (Fed. Cir. 1999). When conducting the section 101 analysis, the claims must be examined "as a whole." Diehr, 450 U.S. at 188. The Supreme Court has specifically cautioned that it is "inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis." Id. at 188. Moreover, it is improper to consider the "novelty" of an element or step in a process claim. Id. at 188-89. Instead, novelty is a separate requirement set forth in 35 U.S.C. § 102.

Finally, Defendants who are challenging the validity of the claims of the patents-in-suit must show that the claims at issue are invalid by clear and convincing evidence. Minnesota Mining and Mfg. Co. v. Chemque Inc., 303 F.3d 1294, 1301 (Fed. Cir. 2002). Thus, Defendants must show by clear and convincing evidence that the claims at issue (1) recite a "natural phenomenon," and (2) "wholly pre-empt" use of said phenomenon.

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B. Analysis

Defendants contend that (1) the patents-in-suit claim the "correlation between the recited metabolite levels and therapeutic efficacy and/or toxicity" which is an unpatentable "natural, observable phenomenon"; and (2) the patents impermissibly preempt use of the correlation. Doc. No. 502 at 11, 13.

1. Recitation of Unpatentable Natural Phenomena

The first step in determining patentability under section 101 is to determine whether the claims "recite" a "natural phenomenon." See Diehr, 450 U.S. at 187; see also In re Meyer, 688 F.2d 789, 795 (C.C.P.A. 1982). For the reasons set forth below, this Court finds the patents-in-suit claim the correlations between certain thiopurine drug metabolite levels and therapeutic efficacy and toxicity, and said correlations are natural phenomena.

a. The Patents-in-Suit Recite the Correlations

Defendants assert that the patents-in-suit recite the correlation between thiopurine drug metabolite levels on the one hand and therapeutic efficacy and toxicity on the other. See Doc. No. 502 at 11-12. According to Defendants, the patents contain these correlations in the "wherein" clauses at the end of each claim. Though the "wherein" clauses are preceded by two steps – (1) "administering" a drug and (2) "determining" metabolite levels – Defendants argue that because both these steps have been performed in the prior art for decades, and each is a necessary step to making any use of metabolite levels, the claims cover the correlations themselves. Plaintiff counters that the claims at issue do not "recite" the correlations, rather the claims recite treatment methods which do not run afoul of section 101. See Doc. No. 528 at 1 n.1, 13.

Plaintiff has framed the patents-in-suit as treatment methods in that the claims purport to cover a "method for optimizing therapeutic efficacy" and/or "reducing toxicity" in patients taking AZA drugs for treatment of either gastrointestinal autoimmune diseases or non-gastrointestinal autoimmune diseases. For example, Claim 1 of the '302 patent states:

> 1. A method of optimizing therapeutic efficacy for treatment of an immune mediated gastrointestinal disorder, comprising:
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> (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
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> (b) determining the level of 6-thioguanine in said subject having said

> immune-mediated gastrointestinal disorder wherein the levels of 6-thioguanine less than about 230 pmol per 8x108 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and wherein the levels of 6-thioguanine greater than about 400 pmol per 8x108 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

In the summary judgment order filed November 22, 2005, this Court construed the "indicates a need" language found in the "wherein" clause to mean "when the identified metabolites reach the specified level, the doctor is warned or notified that a dosage adjustment may be required." Doc. No. 227 at 17. As construed, the claims have three steps: (1) administer the drug to a subject; (2) determine metabolite levels; and (3) be warned that an adjustment in dosage may be required.

However, the fact that the inventors have framed the claims as "treatment methods" does not make the claims patentable. Indeed, "one can reduce any process to a series of steps. The question is what those steps embody." Lab. Corp. of Am. Holdings v. Metabolite, Inc., 126 S.Ct. 2921 (2006) (Breyer, J., dissenting from dismissal of certiorari) (emphasis in original); see also In re Grams, 888 F.2d 835, 839 (Fed. Cir. 1989) (explaining that the critical question is: "What did applicants invent?") (quoting In re Abele, 684 F.2d 902, 907 (C.C.P.A. 1982)).

Here, a careful review of the claims of the patents-in-suit reveals that the steps embody only the correlations themselves. First, the "administering" and "determining" steps are merely necessary data-gathering steps for any use of the correlations. However, an "unpatentable principle" will not transform into a "patentable process" simply by adding conventional method steps. Flook, 437 U.S. at 588-90; accord Meyer, 688 F.2d at 794 ("[data-gathering] step[s] cannot make an otherwise nonstatutory claim statutory"). Thus, the Court must look to the third step to determine what the applicants claim to have invented. However, as construed, the final step – the "warning" step (i.e. the "wherein" clause) – is only a mental step. That is, the "warning" step does not require that dosage be adjusted, or any other action. Indeed, contrary to Plaintiff's assertion, the "warning step" does not require that the doctor (or any person) "provide" a warning. See Doc. No. 528 at 14. Rather, it is the metabolite levels themselves that "warn" the doctor that an adjustment in dosage may be required.

Thus, the claims include only two active steps: "administering" the drug and "determining" metabolite levels, which are merely data-gathering steps; plus the additional

mental step that the doctor be warned (by the metabolite levels) that an adjustment in dosage may be required. Therefore, the claims recite the correlations themselves. That is, what the inventors claim to have discovered is that particular concentrations of 6-TG and 6-MMP correlate with therapeutic efficacy and toxicity in patients taking AZA drugs.

b. The Correlations Are Natural Phenomena

Because the patents-in-suit claim the correlations, the Court must next determine whether the correlations are "natural phenomena." Defendants argue that the correlation between thiopurine drug metabolite levels and therapeutic efficacy and toxicity results from innate metabolic activity in the human body, and the correlations are therefore "natural phenomena." Doc. No. 542 at 5.[4] Plaintiff counters that the claimed correlations cannot be natural phenomena because the correlations would not have existed without the intervention of man-made drugs.[5] Doc. No. 528 at 8.

This Court finds that there can be little doubt that the claimed correlations are "natural phenomena." According to Plaintiff's own expert, Dr. Bloomfield, "the key therapeutic aspect

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[4]Doc. No. 542 is Defendants' reply in support of their motion for summary judgment of patent invalidity. Defendants submitted, in support of their reply brief, the declaration of Dr. Bruce Bostrom, which declaration Plaintiff separately moves to strike. See Doc. No. 549. Specifically, Plaintiff contends (1) Dr. Bostrom presents purely expert opinion but was not disclosed as an expert witness during discovery; (2) to the extent Dr. Bostrom's declaration is factual, Defendants also never disclosed him as a fact witness during discovery; and (3) Defendants should have presented the declaration with their moving papers and the late presentation is prejudicial to Plaintiff. Plaintiff argues that the declaration should be stricken for any of these reasons. See id. In the alternative, if the Court does not strike the declaration, Plaintiff requests it be permitted to file a sur-reply and attaches a proposed sur-reply to the motion as an exhibit. See id., Exh. A. Defendants filed an opposition to Plaintiff's motion to strike and Plaintiff filed a reply to Defendants' opposition. However, this Court has not considered Dr. Bostrom's declaration in deciding the instant motion and, therefore, Plaintiff's motion to strike is DENIED as moot.

[5] Plaintiff contends "Congress has not excluded treatment methods or discovered correlations occurring from a man-made drug from patent protection and, in fact, has rejected proposed legislation to make treatment methods unpatentable. Id. (citing Morgan Decl., Exh. 11 (1995 Cong. U.S. HR 1127 (104th Congr., 1st Sess.)). The bill proposed that "a patent may not be issued for any invention or discovery of a technique, method, or process for performing a surgical or medical procedure, administering a surgical or medical therapy, or making a medical diagnosis, except that if the technique, method, or process is performed by or as a necessary component of a machine, manufacture, or composition of matter or improvement thereof which is itself patentable subject matter, the patent on such machine, manufacture, or composition of matter may claim such technique, method, or process." 1995 Cong. HR 1127 (104th Congr., 1st Sess.). However, Defendants, in reply, urge the Court to ignore this irrelevant point because the failure to enact this legislation provides no support for the validity of the claims at bar. Doc. No. 542 at 14. This Court agrees with Defendants. The fact that Congress rejected legislation making treatment methods unpatentable is irrelevant, and not an appropriate basis for a determination of Congressional intent.

of such thiopurine drugs is that they are converted ***naturally*** by enzymes within the patient's body to form an agent that is therapeutically active." Doc. No. 542, Exh. R ¶ 15 (emphasis added). Moreover, Dr. Seidman, one of the patents' inventors, concedes that the inventors merely observed these natural correlations by studying a "database of patient's information" which included patients taking 6-MP drugs. See Doc. No. 502, McClenahan Decl., Exh. K at 103-105. Dr. Seidman further testified that he believes the correlation still exists in the current patient population. Thus, the inventors of the patents-in-suit did not "invent" the claimed correlation. Rather, 6-TG and 6-MMP are products of the natural metabolizing of thiopurine drugs, and the inventors merely observed the relationship between these naturally produced metabolites and therapeutic efficacy and toxicity.

The case law supports this conclusion. In Funk Bros., for example, an inventor discovered a previously unknown feature of certain types of bacteria – that they could, "by certain methods of selection and testing, be isolated and used in mixed cultures" without inhibiting the properties of one another. 333 U.S. at 130. The patents at issue in that case claimed an inoculant for crops comprising a combination of these bacteria. Id. at 128, n.1. The Supreme Court held the claims invalid. The Court explained that the inventor did not "create" the "state of inhibition or non-inhibition in bacteria." Id. at 130. Rather, "[t]heir qualities are the work of nature." Id.

The same is true in the present case. The inventors here did not "create" the correlation between thiopurine drug metabolite levels and therapeutic efficacy and toxicity. Instead, the correlation results from a natural body process, which as the inventors concede, was pre-existing in the patient population, and it exists in the patient population today. Thus, just as in Funk Bros., the claimed correlations are "the work of nature."

The facts of the present case are also similar to those of Lab. Corp.[6] The patent in Lab. Corp. claimed a method of measuring the level of an amino acid, called homocysteine, in the

[6]The Court takes note of Plaintiff's objections to the Lab Corp. opinion, namely that the opinion is not binding precedent and the dissent was issued on an incomplete record. And although at the time of the hearing on Defendants' motion this Court was not of the opinion that Lab. Corp. is directly relevant, after further review, this Court now finds that while Lab. Corp. does not hold precedential value, its reasoning is persuasive and relevant. A review of the case law in this area reveals that Lab Corp. is the case that is most factually similar to the present case. Thus, the Court would be remiss to ignore the case entirely.

blood, which correlated with a deficiency in two vitamins: cobalamin and folate. Lab. Corp., 126 S.Ct. at 2923-24. At the trial level, Lab. Corp. (the alleged infringers) did not argue invalidity under section 101, and instead based their invalidity arguments on other grounds. See Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings, 370 F.3d 1354 (Fed. Cir. 2004). The Federal Circuit, on appeal, rejected the invalidity arguments without addressing section 101. Id. The Supreme Court granted certiorari in order to determine whether the claim was invalid on the grounds that it improperly seeks to "claim a monopoly over a basic scientific relationship," Pet. for Cert. i, namely, the relationship between homocysteine and vitamin deficiency. Lab. Corp., 126 S.Ct. at 2922. However, the Court never reached the issue because the writ was subsequently dismissed as improvidently granted apparently because the issue was not raised below. Id.

Nonetheless, Justice Breyer (joined by Justices Stevens and Souter), dissented from the dismissal of certiorari, and presented a lengthy dissenting opinion explaining why the patent should be found invalid under section 101. See id. at 2922-29. Justice Breyer, after reviewing the relevant cases in the subject area, stated:

> Even were I to assume (purely for argument's sake) that [the claim] meets certain general definitions of process patentability, however, it still fails the one at issue here: the requirement that it not amount to a simple natural correlation, *i.e.*, a 'natural phenomenon' . . .
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> At most, respondents have simply described the natural law at issue in the abstract patent language of a 'process.' But they cannot avoid the fact that the process is no more than an instruction to read some numbers in light of medical knowledge. One might, of course, reduce the 'process' to a series of steps, *e.g.*, Step 1: gather data; Step 2: read a number; Step 3: compare the number with the norm; Step 4: act accordingly. But one can reduce *any* process to a series of steps. The question is what those steps embody. And here, aside from the unpatented test, they embody only the correlation between homocysteine and vitamin deficiency that the researchers uncovered. In my view, that correlation is an unpatentable 'natural phenomenon' and I can find nothing in [the claim] that adds anything more of significance.

Id. at 2928 (Breyer, J., dissenting from dismissal of certiorari) (internal citations omitted) (emphasis in original).

Although this Court notes that the dissent in Lab. Corp. does not have precedential value, the Court finds Justice Breyer's reasoning persuasive. Indeed, the claims in the patents-in-suit are clearly analogous to the claim in Lab. Corp. The claim at issue in Lab Corp. comprised two

steps: "[(1)] assaying a body fluid for an elevated level of total homocysteine; and [(2)] correlating an elevated level of total homocysteine in said body fluid with deficiency of cobalamin or folate." Id. at 2924. The "assaying" step in Lab Corp. is akin to the "administering" and "determining" steps in the claims of the patents-in-suit as both are necessary steps for any use of the correlations. Similarly, Lab Corp.'s "correlating" step is akin to the "wherein" clause in the present case as both recite the claimed correlation. Thus, the same reasoning that led Justice Breyer to conclude that the correlation between elevated homocysteine levels and deficiency of cobalamin or folate is a natural phenomenon supports the finding that the correlation between thiopurine drug metabolite levels and therapeutic efficacy and toxicity is a natural phenomenon.

Plaintiff argues, however, that the claimed correlations cannot be found to be natural phenomena because the correlations would not have existed without the intervention of man-made drugs. Plaintiff points out that thiopurine drugs are man-made drugs. Doc. No. 528 at 10. When these drugs are introduced into the body, they metabolize "to form an 'active metabolite' which then treats the patient's disease." Id. at 10-11. Thus, according to Plaintiff, because "the 6-TG and 6-MMP metabolites do not naturally exist in the body . . . [and would not exist] but for the administration of a man-made drug" the claimed correlations cannot be deemed "natural phenomena." Id. at 11. In support of this argument, Plaintiff cites to cases where courts have upheld as patentable claims involving the efficacy of man-made compositions, see e.g., Merck & Co. v. Teva Pharm., Inc., 347 F.3d 1367, 1369, 1372 (Fed. Cir. 2003), as well as claims involving portions of genes and proteins (which do not exist in nature). See e.g., Fiers v. Revel, 984 F.2d 1164, 1166, 1172 (Fed. Cir. 1993).

However, in the Court's view, the cases Plaintiff cites do not support the patentability of the claims because the claims in the present case, unlike the claims in the cases cited by Plaintiff, do not cover the man-made compositions themselves or use of man-made compositions to treat inflammatory bowel disease or autoimmune diseases. In Merck, for example, the claims covered a method for treating osteoporosis through the administration of a bisphosphonic acid, a man-made composition. 347 F.3d at 1369. The claims at issue in that case specifically covered use of the acid in the treatment method. Id. at 1369. This contrasts

with the present case where the claims cover the correlations themselves, rather than use of the man-made composition to treat the targeted disease, as this Court has already found. Because the patents-in-suit claim the correlations, the relevant inquiry is whether the correlations are "man-made," not whether a man-made drug was used to produce the correlation.[7]

Again, the present case is most similar to Funk Bros. In that case, the claimed combination of bacteria was "man-made." That is, the claimed strains of bacteria had to be manually isolated and mixed, and therefore would not exist in nature without human intervention. 333 U.S. at 130. Despite this human intervention, the claim was nonetheless unpatentable under section 101. Id. at 132. As such, per Funk Bros., claims do not gain patentability simply by including man-made compositions. Thus, the patents-in-suit do not gain patentability solely by virtue of the fact that man-made drugs are used in connection with the claimed correlation.

The recent Federal Circuit case, Nuijten, further supports this finding. Nuijten concerned a patent application which disclosed "a technique for reducing distortion induced by the introduction of 'watermarks' into signals." 500 F.3d at 1348. The court analyzed whether Nuijten's "signal claim" fell within any of the four statutory classes of patentable subject matter: process, machine, manufacture, or composition of matter. Id. at 1353. Ultimately, the court concluded that the claim was unpatentable because it did not fit within any of the statutory categories. Id. at 1357. In ruling that the claim was not a "manufacture" the court explained that the claimed signal was "man-made, in the sense of having been encoded, generated, and transmitted by artificial means," however "artificiality is insufficient by itself to render something a 'manufacture.'" Id. at 1356. Thus, the fact that the claimed signal was "man-made" did not automatically make the claim patentable. To the contrary, although the claimed signal was "man-made," it was still unpatentable.[8]

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[7]This same reasoning makes Fiers inapposite as well. Plaintiff cites to Fiers merely because it involved man-made compositions – purified DNA. Plaintiff argues that if claims to portions of genes and proteins (which do not exist in nature) are not "natural phenomenon" then the correlations cannot be "natural phenomenon" either. Doc. No. 528 at 11.

[8]Plaintiff's argument that Nuijten is "irrelevant to the present case" is to no avail. Doc. No. 588 at 25. Plaintiff would have the Court believe that the Nuijten holding "had nothing to do with whether or not the claimed subject matter was 'man-made.'" Id. This is incorrect. The Federal Circuit's finding that the claimed

In short, the correlation between particular 6-TG and 6-MMP metabolite levels and therapeutic efficacy and toxicity is not an "invention." Rather, 6-TG and 6-MMP are products of the natural metabolizing of thiopurine drugs, and the inventors merely discovered the relationship between these naturally produced metabolites and therapeutic efficacy and toxicity.

2. Preemption

Because the Court has determined that the claims of the patents-in-suit recite a natural phenomenon, the Court must next determine whether the claims "wholly pre-empt" use of the natural phenomenon such that the "practical effect is a patent on the [phenomenon] itself." Benson, 409 U.S. at 71-72; see also Diehr, 450 U.S. at 187. Defendants argue that because the "administering" and "determining" steps are necessary to using the correlations, Plaintiff's claims "wholly pre-empt" use of the correlations in violation of Supreme Court precedent, and are thus invalid under section 101. Doc. No. 502 at 13-14. In opposition, Plaintiff argues first, that the relevant tests is the alternative "transformation/results" test not the preemption test. See Doc. No. 528 at 7-8. Second, even if the Court applies the preemption test, the claims do not "wholly pre-empt" all uses of the correlations. This Court finds that (a) the preemption test is the relevant test and (b) Plaintiff's claims "wholly pre-empt" use of the correlations.

a. The Preemption Test

The case law is clear, if a claim that recites unpatentable subject mater "wholly pre-empts" all practical use of the unpatentable subject matter, the claim is invalid under section 101. Benson, 409 U.S. at 71-72; see also Diehr, 450 U.S. at 187. Benson involved an attempt to patent "a method of programming a general-purpose digital computer to convert signals from binary-coded decimal form into pure binary form." Id. at 65. The conversion was achieved through use of an algorithm, defined as "[a] procedure for solving a given type of mathematical problem." Id. at 67. The claims "were not limited to any particular art or technology, to any

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signal was "man-made" and yet not a "manufacture," was one of several reasons why the court ultimately determined that the claim was unpatentable. Thus, Nuijten confirms that claims do not gain patentability simply because they incorporate something that is "man-made." Finally, Plaintiff's argument that Nuijten is irrelevant because the present case recites "a process" is similarly unpersuasive. As the Court already found, although the patents-in-suit are framed as "method claims," they claim the correlations themselves.

particular apparatus or machinery, or to any particular end use." Id. at 64. The Supreme Court concluded that because the claimed process "has no substantial practical application except in connection with a digital computer" the patent "would wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself." Id. at 71-72. For this reason, the Court held the patent invalid. Benson is binding Supreme Court precedent, and the preemption test articulated therein is clearly applicable to the present case.

Moreover, contrary to Plaintiff's contention, Defendants need not meet the additional burden of showing that the claims do not "transform" an article or physical object to a different state or thing and/or do not produce a "useful, concrete and tangible result." Doc. No. 528 at 7-8 (citing AT&T, 172 F.3d at 1357-58). The case law in this area reveals that the additional showing urged by Plaintiff is not required. In Flook, for example, the Supreme Court did not even mention the alternative transformation/result standard, and instead focused on whether the claims "wholly pre-empt" all uses of the natural phenomenon. 437 U.S. at 589-90.[9] Also, although Comiskey mentions the "transformation" test, it does so in regards to process patents reciting algorithms or abstract concepts in claims directed to industrial processes. Such claims clearly differ from those in the present case. The Comiskey court specifically noted that "process claims not limited to claiming an abstract concept or algorithm (i.e., a mental process) **may not be subject to the same requirements**." 499 F.3d at 1377 n.12 (emphasis added).

As for the "useful, concrete and tangible result" standard, the Supreme Court has never applied that standard. See Lab. Corp., 126 S. Ct. at 2928 (pointing out that the Supreme Court has never held "that a process is patentable if it produces a 'useful, concrete, and tangible result' . . . and if taken literately, the statement would cover instances where this Court has held the contrary") (Breyer, J., dissenting). Furthermore, while the Federal Circuit has applied the standard, it has always done so in the context of computer-related inventions involving algorithms for data manipulation. See e.g., State Street Bank and Trust Co. v. Signature Fin. Group, Inc., 149 F.3d 1368 (Fed. Cir. 1998).

[9]During oral argument, Plaintiff argued that Flook was "overruled" by the Supreme Court in Diehr. See May 10, 2007 Hearing Transcript at 38:14-24. However, in Comiskey, the Federal Circuit repeatedly cited Flook and also explained the case. 499 F.3d at 1371, 1375, 1376, 1377-78. This confirms that Flook remains good law.

Thus, this Court finds that the claims at issue are not subject to either the transformation test or the "useful, concrete and tangible" result test.

b. The Claims "Wholly Pre-empt" the Use of the Correlation

Defendants argue that the claims "wholly pre-empt" use of the correlation because the only practical use of the correlation is in drug treatment for gastrointestinal autoimmune diseases and non-gastrointestinal autoimmune diseases, and anyone seeking to employ the correlation must conduct the only active steps recited in the claims – administer the drug and determine metabolite levels. Doc. No. 502 at 13-15. This Court agrees.

This Court has already found that the claims recite the correlations. Specifically, the Court has found that the "administering" and "determining" steps are merely necessary data-gathering steps for any use of the correlations, and the "warning" step is only a mental step whereby the metabolite levels warn the doctor that an adjustment in dosage may be required. Thus, the claims cover the correlations themselves. That is, what the inventors claim to have discovered is that particular concentrations of 6-TG and 6-MMP correlate with therapeutic efficacy and/or toxicity in patents taking AZA drugs. Because the claims cover the correlations themselves, it follows that the claims "wholly pre-empt" the correlations.

For the same reason, the Court rejects Plaintiff's argument that it may preclude others from using the correlations "in conjunction with all the other steps in their claimed process." Doc. No. 528 at 19 (citing Diehr, 450 U.S. at 187; Arrhythmia Research Tech., Inc. v. Corazoniz Corp., 958 F.2d 1053, 1059 (Fed. Cir. 1992)). Again, the only "other steps" recited in the claims are the "administering" and "determining" steps, which are necessary data-gathering steps. And, the inclusion of such steps cannot "transform an unpatentable principle into a patentable process." Diehr, 450 U.S. at 191-192.

The Court also finds Plaintiff's supposed examples of other permissible uses of the correlations unavailing. Doc. No. 528 at 19-20. First, the law does not require that every conceivable use be preempted to invalidate the claim. Rather, it is enough that the unpatentable subject matter recited in the claims has "no substantial practical application" outside the context of the claims. Benson, 409 U.S. at 71-72. In Benson, the Court found that the mathematical formula involved in that case had "no substantial practical application except

in connection with a digital computer." Id. Thus, a patent which claimed "a method of programming a general-purpose digital computer to convert signals from binary-coded decimal form into pure binary form" through the use of a mathematical formula would "wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself." Id. at 65, 71-72. The same is true in the present case. Because the correlations have "no substantial practical application" outside of the treatment for immune mediated gastrointestinal disorders and autoimmune diseases, it does not matter that uses outside of this context are not foreclosed.

Second, the alternate uses cited by Plaintiff as not being preempted do not change the fact that the "practical effect" of the patent would be a "patent on the [phenomenon] itself." Id. at 72. Plaintiff outlines six possible uses not foreclosed by the claimed methods: (1) use in research; (2) for diseases other than autoimmune or gastrointestinal diseases;[10] (3) use when results are given in units other than red blood cells; (4) building upon the correlations; (5) publishing articles in scientific journals concerning the correlations; and (6) testing and determining metabolite levels so long as no warning is given. Doc. No. 528 at 20. None of these uses, however, make the subject claims patentable. In Benson, the claimed algorithm could have been used in research and scientific journals could have published articles about it, however, the claim was still invalid. Also, as discussed above, there are no known practical uses other than treatment for autoimmune or gastrointestinal diseases. Thus, the fact that uses for other diseases are not foreclosed, if true, is of no consequence. Finally, that testing and determining metabolite levels is not preempted "so long as the doctors are not warned that doses may need to be adjusted" does not aid Plaintiff's argument because under this scenario the correlations would not be used at all. Thus, despite these supposed alternate uses, the claims "wholly pre-empt" use of the correlation such that the "practical effect is a patent on the

[10]The Court notes that Plaintiff's position taken here is inconsistent with the record in this case. Plaintiff has accused Defendants' researcher, Dr. Rokea el-Azhary, of infringement for conducting a study to determine whether there were different correlations for dermatologic diseases than for gastrointestinal diseases. Plaintiff's expert opined that this research amounted to infringement, and at oral argument, Plaintiff argued that its claims covered dermatologic diseases. See May 10, 2007 Hearing Transcript at 21:10-13.

[correlation] itself." Benson, 409 U.S. at 71-72.[11]

3. In re Comiskey Cannot Save Plaintiff's Claims

The recent Federal Circuit case In re Comiskey does not change the result. Plaintiff argues that even if the Court determines that the correlations are natural phenomena, Comiksey demonstrates that the inclusion of patentable subject matter (i.e. machines) in the claim makes the claims patentable under section 101. Doc. No. 593 at 1. The Court disagrees. First, this Court notes that Comiskey is not directly on point because the facts of that case are wholly dissimilar from the facts of the present case. Second, contrary to Plaintiff's argument, Comiskey does not hold that the inclusion of a machine in the claim automatically makes the claims patentable. Third, if the Court were to apply the Comiskey analysis to the present case, the claims of the patents-in-suit are still unpatentable under section 101.

Comiskey involved an application for a business method patent on a system of mandatory arbitration of disputes involving legal documents such as wills and contracts. 499 F.3d at 1368. Some of the claims contained multiple mental steps, but did not require the use of any technology, while other claims required the use of a computer or other device to perform the steps of the method. Id. at 1369, 1379. Indeed, the later claims recited the use of technology in the claims themselves: "wherein access to the mandatory arbitration is established through the Internet, intranet, World Wid Web, software applications, telephone, television, cable, video [or radio], magnetic, electronic communication, or other communication means." Id. at 1379. The Federal Circuit reviewed the claims for compliance with section 101, and held that the claims which did not require the use of a computer amounted to abstract mental processes that could not be patented under section 101. Id. at 1381. At the same time, however, the

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[11]Plaintiff seeks to bolster its claims by distinguishing Benson and instead relying on Chakrabarty and Arrhythmia. See Doc. No. 528 at 21. Plaintiff argues that Benson is inapplicable because the claim in that case was only to the mathematical algorithm and included no limitation to any art, technology, or use. Id. Instead, Plaintiff points to Chakrabarty and Arrhythmia as support for its argument that the claims do not wholly preempt use of the correlations. However, this Court has already held that the claims in this case, similar to the claims in Benson, are only to the correlations themselves. Moreover, Chakrabarty is distinguishable on its facts. The claims in that case were to a new, non-naturally occurring bacterium. Conversely, in the present case the inventors did not invent a new organism, rather, they merely discovered an unpatentable natural correlation. Arrhythmia is also inapposite. In that case the court applied the so-called Freeman-Walter-Abele test, which the Federal Circuit has since held "has little, if any, applicably to determining the presence of statutory subject matter." See Arrhythmia, 958 F.2d at 1059-60; State Street, 149 F.3d at 1374.

court held that the claims which required the use of a computer or other device claimed patentable subject matter under section 101 (though the claims were remanded so the Patent Office could determine whether the use of the technology would have been non-obvious under 35 U.S.C. § 103). Id. In reaching this decision, the court explained that "while the mere use of the machine to collect data necessary for application of the mental process may not make the claim patentable subject matter, these claims in combining the use of machines with a mental process, claim patentable subject matter." Id. at 1380 (citations omitted). Thus, the distinction between the patentable claims and the unpatentable claims was whether the claims were "tied to a particular apparatus." Id. at 1379.

Relying on Comiskey, Plaintiff argues that the patents-in-suit meet the requirements of section 101 because the claims "involve specific machines." Doc. No. 593 at 2. According to Plaintiff, the asserted claims of the patents-in-suit "inherently require" the use of "specific machines" to detect the levels of metabolites. Doc. No. 588 at 14. "These machines include a detector, a pump and an injector." Id. Moreover, Plaintiff asserts, "dependent claims 6, 14, 24, 30 and 53 of the '623 Patent expressly require the use of a machine capable of performing high pressure liquid chromatography (HPLC)." Id. Thus, according to Plaintiff, the claims are patentable.

However, even assuming *arguendo* that Comiskey is applicable, Plaintiff's reading of the case is too broad. Plaintiff would have the Court find that under Comiskey, any "involvement" of a machine or composition of matter in a method claim is enough to render the claims patentable under section 101. See id. at 1. However, prior case law suggests that this is not the rule. Instead, the Supreme Court has previously held claims unpatentable under section 101 even though they "involve" a machine or composition of matter. In Flook the Supreme Court held claims invalid under section 101 even though they involved the catalytic chemical conversion of hydrocarbons, which are compositions of matter. 437 U.S. at 596. Similarly, in Benson the patentees sought to claim "a method of programming a general-purpose digital computer to convert signals from binary-coded decimal form into pure binary form," and despite the clear involvement of a computer, the Court held the claims unpatentable under section 101. 409 U.S. at 65. The Federal Circuit has done the same. In Grams the court held

claims unpatentable under section 101 even though one step of the claim required the use of a machine. 888 F.2d at 836. In that case the claims covered a "method of diagnosing an abnormal condition in an individual." Id. The first, and only physical, step in the claim was "performing clinical tests on individuals to obtain data." Id. at 840. The clinical tests were "produced by a standard chemical analyzer that measures the levels of the chemical biological components," i.e. a machine. Nonetheless, the Federal Circuit held the claims unpatentable under section 101. The difference between those cases and Comiskey is that in Flook, Benson and Gram the use of the machine or composition of matter was merely incidental, while in Comiskey the machine was "tied to" the operation of the claim and in fact recited in the claim. Thus, the better reading of Comiskey is that claims which are "tied to a particular apparatus" may be invalid, while claims that involve machines in a merely incidental fashion are not foreclosed.

Applying Comiskey to the present case, the patents-in-suit would be invalid **if** the claims were "tied to a particular apparatus." However, this is not the case. Rather, the machines identified by Plaintiff are merely incidental to the claims just as in Flook, Benson and Grams. The present case is most similar to Grams as the "determining" step in the present case is analogous to the "performing" step in Grams. In both instances, the mere involvement of a machine in a data-gathering step cannot render the claim statutory. See Grams, 888 F.2d at 840. Moreover, the patents-in-suit are easily distinguishable from the claims at issue in Comiskey. In Comiskey, the use of technology was explicitly recited in the claims. See id. at 1379. However, the patents-in-suit do not even mention any machines, thus it would be disproportionate to conclude that the claims are "tied to a particular apparatus." It follows that even applying Comiskey, the claims of the patents-in-suit are invalid under section 101.

4. There Are No Genuine Issues of Material Fact Precluding Summary Judgment

In its final effort, Plaintiff argues that there are four underlying factual issues precluding summary judgment in Defendants' favor: (1) whether the claims at issue claim a "natural phenomenon"; (2) whether the claims at issue transform an article into a different state or thing; (3) whether the claims at issue produce a useful, concrete, and tangible result; and (4) whether the claims at issue "wholly preempt" all uses of the inventors' correlation. Doc. No.

528 at 27. However, these issues do not represent factual disputes, and instead concern interpretation of the claims and the proper application of section 101 to the facts of this case. These are clearly questions of law, and are thus appropriate for summary judgment. See AT&T Corp., 172 F.3d at 1355 (explaining that whether a patent claim is invalid under section 101 is a question of law appropriate for summary judgment).

5. Conclusion

Based on the foregoing, this Court finds that there is no genuine issue of material fact to be resolved as to whether the patents-in-suit are directed to statutory subject matter in compliance with 35 U.S.C. § 101. This Court finds by clear and convincing evidence that the patents-in-suit recite a natural phenomenon – the correlations between thiopurine drug metabolite levels and therapeutic efficacy and/or toxicity – and the claims "wholly pre-empt" use of said correlations. Therefore, the claims are invalid under section 101.

CONCLUSION AND ORDER

Accordingly, IT IS HEREBY ORDERED that Defendants' motion for summary judgment on patent invalidity pursuant to 35 U.S.C. § 101 is **GRANTED.**

IT IS FURTHER ORDERED that:

1. Plaintiff's motion for summary judgment of no patent exhaustion is **DENIED as moot**.
2. Plaintiff's motion for summary judgment for declaratory infringement of patent nos. 6,355,623 and 6,680,302 is **DENIED as moot**.
3. Plaintiff's motion to strike the declaration of Dr. Bruce Bostrom is **DENIED as moot.**

DATED: March 28, 2008

JOHN A. HOUSTON
United States District Judge