

United States Court of Appeals for the Federal Circuit

02-1280, -1281

BRISTOL-MYERS SQUIBB COMPANY,

Plaintiff-Appellee,

V.

RHONE-POULENC RORER, INC., RHONE-POULENC RORER, S.A.,
And CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE,

Defendants-Appellants.

RHONE-POULENC RORER, INC. and RHONE-POULENC RORER, S.A.,

Plaintiffs/Counterclaim Defendants-Appellants,

and

CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE,

Counterclaim Defendant-Appellant,

V.

BRISTOL-MYERS SQUIBB COMPANY,

Defendant/Counterclaimant-Appellee.

Robert L. Baechtold, Fitzpatrick, Cella, Harper & Scinto, of New York, New York, argued for plaintiff-appellee. With him on the brief were Thomas H. Beck, Dominick A. Conde, William E. Solander, and Sandy Choi.

Donald R. Dunner, Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., of Washington, DC, argued for defendants-appellants. With him on the brief was Doris Johnson Hines. Of counsel on the brief was Ross J. Oehler, Aventis Pharmaceuticals Inc., of Bridgewater, New Jersey.

Appealed from: United States District Court for the Southern District of New York

Senior Judge Robert P. Patterson, Jr.

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CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE,

Counterclaim Defendant-Appellant,

v.

BRISTOL-MYERS SQUIBB COMPANY,

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DECIDED: April 15, 2003

Before CLEVINGER, SCHALL, and PROST, Circuit Judges.

PROST, Circuit Judge.

Rhone-Poulenc Rorer Inc., Rhone-Poulenc Rorer, S.A., and Centre National De La Recherche Scientifique (collectively "RPR") appeal from the judgments of the United States District Court for the Southern District of New York: (1) holding that RPR obtained United States Patent No. 4,924,011 ("the '011 patent") and United States Patent RE 34,277 ("the '277 patent") by inequitable conduct and, thus, that its '277 patent is unenforceable; and (2) denying RPR's motion for summary judgment of infringement of claim 14 of the '277 patent under 35 U.S.C. § 271(f)(1) and (2). Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., Nos. 95-CV-8833, 96-CV-2346, 98-CV-356, 2002 WL 59429 (S.D.N.Y. Jan. 16, 2002), 2001 WL 1263299 (S.D.N.Y. Oct. 19, 2001). Because the district court's holding that RPR committed inequitable conduct is not an abuse of discretion, we affirm.

I

The patents at issue claim a semi-synthesis of taxol, a cancer chemotherapeutic agent. The inventors' method involves modifying 10-deacetylbaccatin III ("10-DAB") with an acetyl group and adding a (2R, 3S) 3-phenylisoserine side chain ("the side chain") through an esterification reaction. Several hydroxyl groups, located on both the 10-DAB and side chain molecules, readily react to form other unwanted products. To overcome this problem, the inventors devised a method of utilizing "protecting groups" to prevent particular hydroxyl groups on the 10-DAB core and side chain molecules from reacting in side reactions and thereby preventing the formation of taxol. First, starting with 10-DAB, a hydroxy-protecting group is introduced at the C-7 hydroxyl position on the 10-DAB molecule to form the C-7 protected intermediate. Second, an acetyl group replaces the hydrogen atom that is bonded to the oxygen atom at the C-10 position on the 10-DAB molecule, forming protected Baccatin III. Third, the side chain is protected by a hydroxy-protecting group at its C-2' position and then esterified (or coupled) with the protected Baccatin III at its C-13 position. Lastly, the hydroxy-protecting groups at the C-7 position of the Baccatin III core and the C-2' position of the side chain are deprotected (removed) to form taxol.[1] Of particular significance in this appeal is that the subject patents stemmed from a scientific article, written by the named inventors of the patents, entitled "A Highly Efficient, Practical Approach to Natural Taxol," which was eventually published in the Journal of the American Chemical Society ("the JACS article").[2]

On approximately November 3, 1987, the inventors submitted a draft of what became the published JACS article to Jacques Pilard, a patent agent in the employ of RPR in France. The draft JACS article, written in English, stated that the conversion of 10-DAB to taxol "could be successfully achieved only with specific protecting groups and under unique reaction conditions."[3] (emphasis added). It also explained the limitations of several protecting groups as follows:

- "A methoxymethyl ["MOM"] protecting group at C-2' could not be removed following esterification" (footnote 16 of the JACS article).
- "The trimethylsilyl ["TMS"] group could also be selectively introduced at C-7, but it proved unstable to the subsequent esterification conditions" (footnote 13 of the JACS article).
- "The tert-butyldimethylsilyl ["TBDMS"] group could not be cleanly introduced" at C-7 (footnote 13 of the JACS article).

On approximately November 17, 1987, Mr. Pilard recommended to one of the inventors that the draft publication should or could be the subject of a patent application. In a letter sent to Mr. Pilard dated January 29, 1988, P.E. Simon of RPR's Grants and Licenses Department suggested that a patent application covering the inventors' semi-synthesis of taxol be filed in consideration of an exclusive license to RPR. On or about March 7, 1988, two of the inventors provided Mr. Pilard their resumes and an invention disclosure, entitled "Modes Operatoires," which described their semi-synthesis of taxol in detail. Consistent with the draft JACS article, the Modes Operatoires also explained the limitations of several protecting groups. Specifically, it stated the following:

- The regioselective protection of the hydroxyl at C-7 of 10-DAB was also obtained with TMS. "However, this [TMS] group proved too fragile in the esterifying reaction with the protected side chain."

- “The protecting reaction does not go forward with the [TBDM] chloride.” (English translation of French original)

Moreover, the Modes Operatoires stated the hydroxyl function of the side chain was protected with a wide variety of protective groups, such as the MOM group, but it did not state that MOM could be removed.

On March 10, 1988, Mr. Pilard began drafting a French patent application for the semi-synthesis of taxol. In claim 1 of the draft patent application, Mr. Pilard claimed the process as one “in which R2 is a hydroxy-protecting group . . . [and] in which R3 is a hydroxy-protecting group,” without specifying any limitation as to the hydroxy-protecting groups that could be used in the process. In claim 2 of the draft application, Mr. Pilard claimed the process according to claim 1 “in which R2 is chosen from [MOM and other compounds] . . . and R3 is chosen from trialkylsilyl groups in which each alkyl portion contains one to three carbon atoms.”^[4] (The '011 patent application is an English translation of the French application.) Not only did Mr. Pilard specify that MOM and TMS were permissible hydroxy-protecting groups in claim 2, but he also stated in the specification of the draft patent application that “R2 denotes, more especially, a [MOM and other compounds] . . . radical” and that “[p]referably, R3 is a [TMS] . . . radical.”

On approximately March 18, 1988, Mr. Pilard sent his draft of the French patent application to two of the inventors asking them to carefully review it and add all the complements and modifications they deemed necessary. They made no substantive changes to either the specification or the claims. Mr. Pilard filed the French patent application on April 6, 1988. The Journal of the American Chemical Society received the draft article on April 20, 1988, and it was published on August 17, 1988.

In March 1989, Mr. Pilard sent a copy of the French application and a search report dated November 24, 1988, generated by the French National Institute of Industrial Property, to J.A. Kemp & Company for translation into English and forwarding to Mr. Ellsworth H. Mosher, RPR's United States patent attorney. The search report did not list the JACS article and Mr. Pilard did not send a copy of the JACS article, the Modes Operatoires, or any of the inventors' test results to J.A. Kemp & Company or Mr. Mosher.

On April 3, 1989, Mr. Mosher filed the '011 patent application with the United States Patent and Trademark Office (“PTO”). The filed patent application, except for the abstract, is an English translation of the French patent application previously prepared and filed by Mr. Pilard. Mr. Mosher, who never received a copy of the JACS article from Mr. Pilard, did not disclose it to the PTO.

At some point during the prosecution of the '011 patent, the Examiner assigned to the '011 patent application asked the PTO Scientific Library to perform a computer search of chemical abstracts using the chemical structure of claim 1 as the subject matter to be searched. The generated search report listed the JACS article as “Answer 1 of 11” and identified, among other attributes, its year of publication, 1988. The search report also listed another article, authored by two of the inventors of the '011 patent and published in 1987, as “Answer 5 of 11.” The Examiner listed the 1987 article on a “Notice of

References Cited" (Form PTO-892). However, the Examiner did not place his initials next to either of the listed articles on the search report. He placed the search report in the file history. On May 8, 1990, the PTO issued the '011 patent.

On approximately January 31, 1991, Mr. Pilard wrote to the European patent office and withdrew the claims previously drawn in the counterpart European patent application. He replaced those claims with a single claim (similar to claims 2-7 of the '011 patent) for the inventors' semi-synthesis process.

On June 11, 1991, Mr. Pilard sent Mr. Frederick F. Calvetti, a United States patent attorney in a different law firm than the one employing Mr. Mosher, a letter by fax and post about filing a reissue patent application with additional claims directed to the disclosed but unclaimed intermediates of formulas IV and V of the '011 patent.^[5] Mr. Pilard's letter attached a copy of the '011 patent and the JACS article with footnote 16 circled, although it is unclear who circled the footnote. On June 13, 1991, Mr. Calvetti replied to Mr. Pilard's letter stating that the JACS article would not affect the grant of the original '011 patent because the journal publication was filed less than one year prior to the filing of the '011 patent application in compliance with 35 U.S.C. § 119, and that a reissue patent application could be filed.^[6]

On approximately June 24, 1991, Mr. Calvetti wrote Mr. Pilard's supervisor at RPR stating that the intermediate of formula V was likely patentable, but expressed reservations about the patentability of the intermediate of formula IV because it was derived from modifying a naturally occurring compound, which "may not be considered nonobvious." Mr. Pilard's response to Mr. Calvetti attached a document that discussed the reasons he believed the intermediates were patentable and included a draft of the proposed additional claims. The relevant portion of Mr. Pilard's letter stated:

The protecting group at C-7 has to be stable under the acetylating conditions and to the subsequent esterifying conditions. Furthermore, the elimination of the protecting groups has to be made under conditions which do not conduct to an epimerisation at the C-13 or at the C-2': . . . Even if protecting groups are known, it is difficult to select an appropriate protecting group without undue experimentation.

On November 1, 1991, Mr. Calvetti filed the '277 reissue patent application. In addition to all the claims in the '011 patent, the reissue application claimed three intermediates in the prior patent. Mr. Calvetti did not disclose the JACS article to the PTO upon filing the reissue application. During prosecution of the reissue application, the Examiner assigned to review the '277 patent application, the same Examiner who had reviewed the '011 patent application, requested a computer search of the newly claimed intermediates. That search result identified the JACS article. Mr. Calvetti, however, did not disclose the JACS article to the PTO during any of his interactions or communications with the agency at this point in time.

On approximately July 17, 1992, Mr. Pilard sent a letter to Mr. Calvetti identifying prior art and references published between the filing dates of the original patent application and the reissue patent applications. With regard to the latter category, Mr. Pilard identified seven documents, including the JACS article, and stated "[a]ccording to our evaluation, these references are irrelevant." On October 20, 1992, Mr. Calvetti interviewed with the Examiner regarding the reissue application. On or around December 14, 1992, Mr. Calvetti filed a response to an Official Action by the Examiner, but did not submit the JACS article to the PTO.

By letter dated December 15, 1992, Mr. Calvetti filed an information disclosure statement with the PTO citing and providing a copy of the JACS article, pursuant to Mr. Pilard's instructions. A receipt stamp of the PTO on the information disclosure statement bears the date January 14, 1993. In February 1993, subsequent to indicating that the reissue application would be allowed, the Examiner reviewed the information disclosure statement that listed the JACS article as a reference. On June 8, 1993, the PTO issued the '277 patent.

In October 1995, Bristol filed suit against RPR in the United States District Court for the Southern District of New York seeking a declaratory judgment that it does not infringe the '277 reissue patent and that the patent is invalid and unenforceable. RPR subsequently filed suit against Bristol in the United States District Court for the District of Delaware asserting infringement. The suit was transferred and consolidated with Bristol's New York case. In March 2001, the district court held a two-day evidentiary hearing on claim construction and interpretation of the JACS article. [71] The court issued an opinion finding by clear and convincing evidence that the inventors failed to provide material information by not providing the PTO with the JACS article during the prosecution of the '011 patent and that the Examiner did not review the article prior to issuing the '011 patent. Thereafter, in November 2001, the court held a four-day bench trial on the issue of RPR's intent. The court found by clear and convincing evidence that RPR procured the '011 and '277 patents by inequitable conduct by intentionally withholding material information from the PTO with intent to mislead and, therefore, held that the '277 patent is unenforceable. The court also denied RPR's motion for summary judgment on infringement under 35 U.S.C. § 271(f)(1) and (2), and subsequently declared the case exceptional and awarded Bristol costs and reasonable attorney fees to be determined by the court.

RPR filed a timely appeal and we have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

II

It is well settled that patent applicants are required to prosecute patent applications "with candor, good faith, and honesty." Molins PLC v. Textron, Inc., 48 F.3d 1172, 1178, 33 USPQ2d 1823, 1826 (Fed. Cir. 1995). A breach of this duty can take several forms: "affirmative misrepresentation of a material fact, failure to disclose material information, or submission of false material information." Id. Further, a breach of this duty, when coupled with an intent to deceive or mislead the PTO, constitutes inequitable conduct, which, when proven, renders the patent unenforceable. Id. at 1178, 33 USPQ2d at 1827.

To establish RPR's inequitable conduct, Bristol must show by "clear and convincing evidence" that RPR failed to disclose material information with an intent to mislead the PTO. Kingsdown Med. Consultants, Ltd. v. Hollister, Inc., 863 F.2d 867, 872, 9 USPQ2d 1384, 1389 (Fed. Cir. 1988); FMC Corp. v. Manitowoc Co., 835 F.2d 1411, 1415, 5 USPQ2d 1112, 1115 (Fed. Cir. 1987). Once the materiality of the information and RPR's intent to mislead have been established, the court must "weigh them to determine whether the equities warrant a conclusion that inequitable conduct occurred." Molins,

48 F.3d at 1178, 33 USPQ2d at 1827. Moreover, when balanced against high materiality, the showing of intent can be proportionally less. Brasseler, U.S.A I., L.P. v. Stryker Sales Corp., 267 F.3d 1370, 1381, 60 USPQ2d 1482, 1488 (Fed. Cir. 2001). Both materiality and intent to mislead are questions of fact reviewed for clear error. GFI, Inc. v. Franklin Corp., 265 F.3d 1268, 1273, 60 USPQ2d 1141, 1143 (Fed. Cir. 2001). We review the ultimate determination of inequitable conduct under an abuse of discretion standard. Molins, 48 F.3d at 1178, 33 USPQ2d at 1827.

On appeal, RPR challenges the district court's findings as to both materiality and intent to mislead.

A

We first review the district court's materiality finding. "Materiality is not limited to prior art but embraces any information that a reasonable examiner would be substantially likely to consider important in deciding whether to allow an application to issue as a patent." GFI, 265 F.3d at 1274, 60 USPQ2d at 1143-44 (emphasis in original). The district court found by clear and convincing evidence that the inventors failed to provide material information by not providing the JACS article to the PTO during the prosecution of the '011 patent and that the Examiner did not review the article prior to issuing the '011 patent.

We conclude that the district court's finding that the JACS article was material to the prosecution of the '011 patent from the standpoint of a reasonable patent examiner is not clearly erroneous considering the examiner's obligation to review the application for enablement under 35 U.S.C. § 112. The legal question of enablement involves an assessment of whether a patent disclosure would have enabled one of ordinary skill in the art at the time the application was filed to make and use the claimed invention without undue experimentation. Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). The patents specifically recommend using the TMS and MOM hydroxy-protecting groups in the esterification process, but the JACS article, from which the '011 patent application stemmed, reports that the TMS group was unstable in the esterification process and that the MOM group could not be removed after esterification. Moreover, the evidence supports the district court's finding that a reasonable patent examiner reviewing the subject patent application would have expected the use of TMS and MOM groups to yield more than trace amounts of taxol, but that a review of the JACS article would have raised doubts that the use of TMS and MOM would produce taxol in more than trace amounts. The '011 patent application emphasizes the importance of taxol and states, "[t]his process may be used to produce taxol in good yield." However, the JACS article declares limitations with regard to the use of TMS and MOM in producing taxol from 10-DAB. Footnote 13 of the JACS article, which relates the difficulties associated with using TMS, was consistent with testimony at the hearing that TMS historically was known not to be very useful. In addition, Bristol's expert, Dr. Elias J. Corey, testified that a person of ordinary skill in the art would understand footnote 16 of the article to mean that the inventors

had unsuccessfully examined MOM as a possible protecting group. Moreover, one of the inventors testified that using MOM would result in something between a very bad yield and zero. No expert witness testified that a person of ordinary skill in the art would see the TMS or MOM failures reported in the article as related to just one experiment or that such a person would know that TMS or MOM could be made to work under other experimental conditions. In addition, there was no testimony by any of the inventors suggesting how further experimentation with TMS or MOM could be carried out or how a person of ordinary skill in the art would know what to do to make these protecting groups work efficiently. Under the circumstances, a reasonable Examiner would have wanted to know whether the unsuccessful use of MOM and TMS discussed in the JACS article affected the ability of a person of ordinary skill in the art to practice the invention, which specifically taught the use of MOM and TMS, without undue experimentation. Therefore, the district court did not clearly err in concluding that the limiting statements in the JACS article with regard to the unsuccessful use of TMS and MOM in producing taxol would have raised an important issue in a reasonable examiner's mind as to whether the inventors had broadened the patent beyond that legally permissible based on the examiner's review of the application for enablement.

In affirming the district court's decision, we reject the four arguments raised by RPR on appeal challenging the finding of materiality. RPR essentially asks this court to substitute its view of the evidence and credibility of the witnesses for the district court's careful and thorough fact finding. We cannot provide such relief because our task as a reviewing court is not to make factual determinations in the first instance, but to review the district court's factual findings for clear error. Brasseler, 267 F.3d at 1379, 60 USPQ2d at 1487. RPR first argues that the Examiner must have determined the JACS article was immaterial because he "likely considered" the article during the '011 patent prosecution and still allowed the patent.^[8] According to RPR, applying the statutorily mandated presumption of patent validity assumes that the Examiner performed his job properly or regularly and leads to the conclusion that the Examiner must have read all the references on the search report requested by him. See Am. Hoist & Derrick Co. v. Sowa & Sons, Inc., 725 F.2d 1350, 1359, 220 USPQ 763, 770 (Fed. Cir. 1984) (noting that imposition of presumption of validity standard is related to presumption that PTO does its job properly). The Examiner did not initial any of the items on the search report, which listed the JACS article as "Answer 1 of 11," but the Examiner listed "Answer 5 of 11" from the report on a form PTO-892. RPR contends that the lack of the examiner's initials on the '011 computer search report is consistent with his "regular" practice and does not rebut the presumption of validity/regularity or the logical conclusion that the Examiner in fact considered every listing on the search report, including the JACS article, to determine what to list on the form PTO-892.

We uphold the district court's finding that the Examiner did not review the JACS article during the '011 patent prosecution because the MPEP and the record evidence belie RPR's insistence that the lack of the Examiner's initials next to the listing of the article on the search report supports a finding that he reviewed the article. The MPEP § 717.05 (5th ed. Rev. 6 Oct. 1987) states that an examiner "should indicate which publications [on a search printout] were reviewed by initialing and dating the copy of the printout in the left margin adjacent to each reviewed publication." Thus, had the Examiner been

performing his duties “regularly,” he would have initialed and dated “Answer 5 of 11” on the search report and the JACS article if he read it. Those are not the facts presented. Rather, the file history does not contain a copy of the JACS article and the Examiner did not initial and date the listing of the article on the search report, a copy of which he placed in the file history.^[9] Moreover, the district court did not find convincing or credible the opinion of RPR’s expert that the Examiner had reviewed the article despite the provisions of the MPEP because he had the discretion to initial and date listings on the search report. See Refac Int’l, Ltd. v. Lotus Dev. Corp., 81 F.3d 1576, 1582, 38 USPQ2d 1665, 1670 (Fed. Cir. 1996) (stating that the district court is best suited to make credibility determinations and we accord such determinations deference). The lack of any objective evidence that the Examiner reviewed the article in connection with his review of the ’011 patent application supports the court’s finding that the JACS article was not before the PTO in its review of the ’011 patent application. See Rohm & Haas Co. v. Crystal Chem. Co., 722 F.2d 1556, 1572-73, 220 USPQ 289, 302 (Fed. Cir. 1983) (concluding that a presumption that an examiner was able to find, with his expertise and adequate time, the critical data when he was presented with a “mountain of largely irrelevant data” ignores the real world conditions under which examiners work).

RPR next argues that materiality is lacking because it is undisputed that the Examiner considered the JACS article during the ’277 reissue prosecution, but did not reject any claims because of it. In support of its argument, RPR notes this court’s statement in an opinion on RPR’s petition for a writ of mandamus in an earlier phase of this case that “it is by no means clear that Bristol-Myers will ultimately prevail in making a showing of fraud sufficient to render the patents unenforceable. . . . To be sure, the fact that the JACS article was disclosed to the examiner in the reissue prosecution but did not lead the examiner to reject the application is relevant evidence favoring RPR with regard to the issue of materiality.” In re Rhone-Poulenc Rorer, Inc., 178 F.3d 1309 (Fed. Cir. 1998) (Table).

We conclude, however, that the district court did not clearly err in finding that the JACS article was material notwithstanding the Examiner’s decision to issue the ’277 reissue patent after RPR disclosed the JACS article to the PTO. First, RPR’s reliance on this court’s previous mandamus order is misplaced because the court was not deciding the issue of materiality favorably to RPR on the limited record then before it. Indeed, this court also recognized that the district court had made explicit findings adverse to RPR on the issues of materiality and this court was not persuaded that those findings were clearly wrong. Id. Second, although the examiner’s allowance of the reissue patent after considering the JACS article is probative evidence, that does not end the materiality inquiry. Molins, 48 F.3d at 1179, 33 USPQ2d at 1827 (stating that “the result of a PTO proceeding that assesses patentability in light of information not originally disclosed can be of strong probative value in determining whether the undisclosed information was material”). This court has articulated the materiality criterion as follows:

[T]he standard to be applied in determining whether a reference is “material” is not whether the particular examiner of the application at issue considered the reference to be important; rather, it is that of a “reasonable examiner.” Nor is a reference immaterial simply because the claims are eventually deemed by an examiner to be patentable thereover.

Id., 33 USPQ2d at 1828 (citation omitted); PerSeptive Biosystems, Inc. v. Pharmacia Biotech, Inc., 225 F.3d 1315, 1322, 56 USPQ2d 1001, 1006 (Fed. Cir. 2000) (stating that a patent may be valid and yet be rendered unenforceable due to inequitable conduct). Indeed, in Molins, the court affirmed a finding of inequitable conduct, notwithstanding that the withheld reference was later cited in a reexamination and the claims were allowed to issue.

We recognize that [the withheld references] were cited eventually to the PTO and that the examiner initialed them and passed the reexamination application to issue thereafter. However, the references were not cited when they should have been.

48 F.3d at 1182, 33 USPQ2d at 1830.

RPR further contends that the record contains other evidence that weighs against a finding of materiality. Specifically, RPR relies on Mr. Pilard's characterization of the article in 1992 as "irrelevant," and Mr. Calvetti's statement in 1991 that the article did not "affect" the patent. RPR further argues that the inventors understood that TMS and MOM would work in their claimed process and were justified in describing TMS and MOM as preferred. RPR contends that the JACS article reports results under "specially developed reaction conditions," which are not required by the patent claims, and further notes that the article's footnotes do not state that TMS and MOM would never work. According to RPR, the inventors understood, and a person of ordinary skill in the art reviewing the subject patent would have understood, that under conditions other than those in the JACS article, TMS and MOM would work. In support, RPR notes that in a footnote of the district court's opinion the court stated, "[t]he inventors may have had a basis to think that MOM could be used to produce taxol" and that an inventor testified that TMS and "TES" (with which successful results were reported in the JACS article) are very similar molecules.

Having considered the evidence relied upon by RPR to support its argument that the JACS article is immaterial, we conclude that the district court did not clearly err in finding that the JACS article was material for three reasons. First, the district court did not find Mr. Pilard's 1992 statement, that the article is "irrelevant," persuasive or credible. Rather, the district court found that given Mr. Pilard's extensive chemical engineering background, he would have known that a person of ordinary skill in the art would read the statements in the JACS article either to apply to TMS and MOM at any yield or, at the very least, to be unclear. Specifically, the district court could not reconcile Mr. Pilard's knowledge that "the protecting group at C-7 has to be stable . . . to the subsequent esterifying conditions" with his position that the statement in the JACS article, TMS "proved unstable to the subsequent esterification conditions," was not adverse. Likewise, the district court was unable to reconcile Mr. Pilard's statement that "the elimination of the protecting groups has to be made under conditions which do not conduct to an epimerisation at the . . . C-2" with his position that the statement, "[a MOM] protecting group at the C-2' could not be removed following esterification," was not adverse. Also, Mr. Calvetti's assessment of the article was

limited to whether or not he thought the JACS article was prior art.

Second, it is the explicit statements in the JACS article that made the article material to the prosecution of the subject patents, not the information that could have been included in the article. In the same footnote referred to by RPR above, the district court stated that although one of the inventors successfully deprotected MOM, albeit in poor yield, from deacetyl taxol, the inventors did not claim the results in the article. Rather, the article stated that the authors were unsuccessful at using TMS or MOM to yield taxol in anything other than poor yield. Indeed, as discussed above, no expert testified that a person of ordinary skill in the art would see the TMS or MOM failures in the article as related to just one experiment or that such a person would know how to make TMS or MOM work as protecting groups under other experimental conditions.

Third, materiality is determined from the viewpoint of a reasonable patent examiner, Molins, 48 F.3d at 1179, 33 USPQ2d at 1828, and not the subjective beliefs of the patentee. To the extent that the opinion of the inventors as to how a reasonable examiner would have viewed the article sheds light on materiality, the district court did not find the testimony persuasive because it was “the self-serving testimony of an interested witness” and was supported by neither objective evidence nor by the testimony of any independent expert. See Refac Int’l. Ltd., 81 F.3d at 1582, 38 USPQ2d at 1670. The court instead found persuasive what the inventors explicitly stated in the article as compared to what was claimed in the subject patent and stated in the specification.

Lastly, RPR argues that the district court’s holding on inequitable conduct is contradictory to its holding denying Bristol’s motion for summary judgment for lack of enablement pursuant to 35 U.S.C. § 112. Specifically, RPR contends that the district court’s finding that the JACS article is material to enablement because a person of ordinary skill in the art would read the article to mean that TMS and MOM were unsuitable to produce taxol is directly contradicted by the declaration of Bristol’s expert, Dr. Corey, that the use of TMS and MOM was known and obvious.

We conclude, however, that the district court’s holding on inequitable conduct is not contradictory to its holding on enablement. The issue of whether a reference would be considered important by a reasonable examiner in determining whether a patent application is allowable, including whether the invention is enabled, is a separate issue from whether the invention is actually enabled. Dr. Corey testified that based on the explicit statements made by the inventors in the article, a person of ordinary skill in the art in 1998 reading the article, specifically footnotes 13 and 16, would have concluded that TMS and MOM were unsuitable or unsatisfactory protecting groups to use in the described process for producing taxol. That testimony illuminates how such a person would interpret the JACS article, but does not expound upon whether the subject invention is in fact enabled. The district court denied Bristol’s summary judgment motion for lack of enablement because it failed to show by clear and convincing evidence that a person of ordinary skill in the art would be required to engage in

undue experimentation to practice the full scope of the claimed invention. In so doing, it relied partly on Dr. Corey's declaration that certain claims in the '277 patent were obvious. As the district court later explained, it rejected Bristol's counsel's argument that Dr. Corey's affidavit should be construed more narrowly in view of his earlier testimony in the trial proceedings because Bristol was relying on counsel's argument rather than providing an affidavit from Dr. Corey to that effect. Thus, to the extent an inconsistency existed, it was with regard to Bristol's position that the '277 patent was obvious and its position that the '277 patent was not enabled, not in the district court's holdings on materiality and enablement.

In sum, we conclude that the district court did not clearly err in finding that the JACS article was material to the prosecution of the '011 patent. We next review the district court's intent finding.

B

Intent to mislead does not require direct evidence, and is typically inferred from the facts. GFI, 265 F.3d at 1274, 60 USPQ2d at 1144; Brasseler, 267 F.3d at 1375-76, 60 USPQ2d at 1484 (stating that intent may be inferred when a patent applicant knew, or should have known, that withheld information could be material to the PTO's consideration of the patent application); Merck & Co. v. Danbury Pharmacal, Inc., 873 F.2d 1418, 1422, 10 USPQ2d 1682, 1686 (Fed. Cir. 1989) (stating that intent is most often proven by a showing of acts the natural consequences of which are presumably intended by the actor). Further, where withheld information is material and the patentee knew or should have know of that materiality, he or she can expect to have great difficulty in establishing subjective good faith sufficient to overcome an inference of intent to mislead. Akron Polymer Container Corp. v. Exxel Container, Inc., 148 F.3d 1380, 1384, 47 USPQ2d 1533, 1536 (Fed. Cir. 1998); GFI, Inc., 265 F.3d at 1275, 60 USPQ2d at 1144-45.

The district court found by clear and convincing evidence that: (1) Mr. Pilard intentionally drew the '011 patent more broadly than warranted by the information he possessed; (2) he was aware of the JACS article at the time he drafted the patent application and at the time he provided Mr. Mosher materials for filing the '011 patent; (3) he was aware of the PTO duty of disclosure; and (4) his attempted justifications for not disclosing the JACS article were insufficient grounds for not supplying it to the PTO Examiner and were not credible.^[10] These findings led the court to conclude that Mr. Pilard intentionally withheld the JACS article from Mr. Mosher and the PTO with an intent to mislead the Examiner and that this inequitable conduct was not cured during the prosecution of the '277 reissue application.

We conclude that the district court's finding that Mr. Pilard intentionally withheld the JACS article in an attempt to mislead the PTO in connection with the prosecution of the '011 patent is not clearly erroneous. The evidence established that Mr. Pilard prepared the French patent application based on the invention disclosure, Modes Operatoires, provided by the inventors, which included the information in footnotes 13 and 16. The evidence also established that he read the draft JACS article and had it in his possession at the time he drafted the application. Although these two documents explicitly asserted

the limitations of using TMS as a C-7/R3 protecting group and MOM as a C-2'/R2 protecting group, the patent application did not disclose these limitations. [111] None of the inventors testified that they recalled any communication with Mr. Pilard informing him that R2 and R3 could be defined as any hydroxy-protecting group, that R2 was preferably MOM, or that R3 was preferably TMS. Moreover, at his deposition, Mr. Pilard could not recall any support whatsoever for having claimed in the application that TMS or MOM could be used to produce taxol or for stating that they were the preferred protecting groups. Mr. Pilard was responsible on behalf of RPR for providing Mr. Mosher all information relevant to the filing of the '011 patent application, and there is no dispute that he understood the PTO duty of disclosure. Yet, despite being aware of the information in the JACS article from which the '011 patent application stemmed, he did not provide Mr. Mosher, RPR's U.S. patent attorney, a copy of the JACS article. He provided Mr. Mosher only with a copy of the French patent application that he had filed and a copy of the French search report generated by the National Institute of Industrial Research, which did not list the JACS article. In a case such as this, where Mr. Pilard was intimately familiar with the article because the inventors with whom he worked wrote it, he approved the article for publication, and the article was in his possession while he was drafting the French patent application, the determination that Mr. Pilard knew of the significance of the JACS article in combination with the finding that he knew of the duty to disclose is sufficient to establish intent.

In affirming the district court's decision, we reject the four arguments raised by RPR on appeal challenging the finding of intent to deceive. In making these arguments, RPR again asks us to substitute our view of the evidence and credibility of the witnesses for that of the district court's finding of intent to deceive. RPR first argues that contemporaneous documents establish that those prosecuting the patents were acting in good faith, which is inconsistent with an intent to mislead. In support of its good faith argument, RPR notes that Mr. Pilard approved publication of the JACS article in a widely circulated journal without requesting that the inventors omit or somehow qualify the footnotes. RPR also relies on the fact that Mr. Pilard forwarded the article to Mr. Calvetti and that in response to Mr. Pilard's instructions, Mr. Calvetti disclosed the article to the PTO.

We conclude, however, that the district court did not clearly err in finding an intent to deceive after considering the evidence relied upon by RPR to support its good faith argument. In our view, RPR's argument misses the mark because RPR's duty of disclosure was to the PTO and publishing the article did not amount to RPR disclosing the article to the PTO. The article's appearance on a computer search report requested by the Examiner during the prosecution of the '011 patent was not the result of an affirmative action taken by RPR to disclose the article to the PTO. Furthermore, the issue is RPR's intent during the prosecution of the original application. Thus, RPR's disclosure during reissue is irrelevant to the inquiry of whether RPR acquired the '011 patent by engaging in inequitable conduct.

RPR next argues that those prosecuting the '011 patent believed the JACS article was immaterial. According to RPR, Mr. Pilard's assessment in 1992 that the JACS article was "irrelevant" is contemporaneous evidence that he did not believe the JACS article was material negating a finding of intent to mislead. We conclude, however, that the district court did not clearly err in rejecting RPR's argument that intent to mislead the PTO was lacking on this ground. Mr. Pilard's

assessment occurred after the issuance of the '011 patent and, thus, does not shed light on Mr. Pilard's intent with regard to the prosecution of the '011 patent application. In addition, as discussed above, the district court did not find this evidence persuasive or credible.

RPR further argues that the evidence establishes that the inventors had a reasonable basis to think that TMS and MOM could work without undue experimentation to produce taxol at the time the application was filed, which demonstrates a lack of intent to mislead. RPR also makes a similar argument that the inventors' approval of the application undercuts a finding of intent to deceive because by doing so the inventors communicated their beliefs that TMS and MOM would work in their process to Mr. Pilard.

We conclude, however, that the district court did not clearly err in finding an intent to deceive after considering the evidence of the inventors' purported beliefs for three reasons. First, even assuming the inventors fostered a belief that TMS and MOM would work in the patented process, the JACS article drafted by the inventors did not assert such a belief or explain its foundation.^[12] Second, it is RPR's intent with regard to not disclosing the article to the PTO that is relevant, not whether the inventors' beliefs supported a finding of enablement. See *FMC Corp.*, 835 F.2d at 1415, 5 USPQ2d at 1115. Third, none of the inventors could recall any communication with Mr. Pilard informing him that R2 and R3 could be defined as any hydroxy-protecting group, that R2 was preferably MOM, or that R3 was preferably TMS.

Lastly, RPR argues that the January 29, 1988, letter from Mr. Simon to Mr. Pilard urging him to seek a broad patent did not provide Mr. Pilard with any improper motive because it was not improper for RPR to seek broad patent rights. RPR's argument misses the mark because the district court did not find that RPR's motivation to seek a broad patent rights was an "improper" motive. Rather, the district court found that seeking broad patents was a motive held by Mr. Pilard and more importantly concluded that Mr. Pilard drew the patent application more broadly than warranted in light of the limiting statements in the JACS article and the Modes Operatoires and having done so had a reason to not submit these documents to the PTO. These findings are not clearly erroneous.

We have considered RPR's remaining arguments challenging the district court's findings with regard to intent to deceive, as well as materiality, and conclude that they lack merit as well. Therefore, we agree with the district court that Mr. Pilard failed to disclose the JACS article with intent to mislead the patent office in connection with the prosecution of the '011 and '277 patents.

CONCLUSION

In sum, we conclude that the district court did not abuse its discretion in determining that the inventors' conduct, in its entirety, warrants holding the '277 patent unenforceable. Therefore, we affirm the district court's final judgment concluding that RPR obtained the '011 and '277 patents by inequitable conduct and holding the '277 patent unenforceable. Because the '277 patent is unenforceable, we decline to address RPR's arguments that the district court erred in denying its motions for summary judgment of infringement of claim 14 of the '277 patent under 35 U.S.C. § 271(f)(1) and (2).

AFFIRMED.

^[11] The patents at issue refer to the hydroxy-protecting group at C-2' of the side chain as R2 and the hydroxy-protecting group at C-7 of 10-DAB as R3.

^[12] Four of the six authors of the JACS article were named inventors on the '011 patent application. Aside from the difference in the listed authors of the draft and published JACS articles, the substance of the draft and the published JACS articles is the same.

[3] The published version of the JACS article changed “under unique reaction conditions” to “under specially developed reaction conditions, as described below.”

[4] TMS is a trialkylsilyl in which each alkyl portion contains one carbon atom and, thus, comes within claim 2’s definition of R3. The alkyl portion of TBDMS contains four carbon atoms and therefore does not fall within claim 2’s definition of R3.

[5] Formula IV is protected Baccatin III and formula V is protected taxol.

[6] Section 119 states that “no patent shall be granted on any application for patent for an invention which had been patented or described in a printed publication in any country more than one year before the date of the actual filing of the application in this country.”

[7] The district court referred several matters to a Special Master, including the “interpretation of the JACS article” relating to materiality of the JACS article. The Special Master filed a Report and Recommendation with his findings, which the district court fully adopted.

[8] RPR also argues that the district court erred as a matter of law when it stated that the presumption of validity did not apply when considering the materiality of the JACS article. This argument, however, mischaracterizes the district court’s ruling. The district court framed the materiality issue as whether a reasonable patent examiner reviewing the ’011 patent application and file history prior to issuing the ’011 patent would consider the JACS article material. However, the presumption of patent validity is applicable only to issued patents. See 35 U.S.C. § 282. Thus, the district court correctly stated that the Special Master, who had to place himself in the position of a reasonable patent examiner reviewing the pending ’011 patent application and file history, did not err by failing to utilize a presumption of patent validity. The district court also stated that presuming PTO regularity in light of the fact that the file history of the ’011 patent is out of compliance with the directive of the Manual of Patent Examining Procedures (“MPEP”) is unwarranted. We read this to mean that the presumption of PTO regularity was rebutted by the facts in this case.

[9] MPEP § 717.05 also states that “[t]he search printout should be placed in the application file.”

[10] Mr. Pilard did not appear at the hearing on intent, and thus, the district court had to rely on the portions of his videotaped depositions submitted by the parties and a transcript of his depositions to assess his credibility. The district court found Mr. Pilard to be lacking in credibility because in light of the fact that he had been prepared for three days prior to his initial deposition, his responses at that deposition were less than candid. We accord the district court’s credibility determination substantial deference. Refac Int’l. Ltd., 81 F.3d at 1582.

[11] Specifically, the draft JACS article stated that only “specific protecting groups” and “unique reactions conditions” were successful in producing taxol, that TMS was “unstable” during the esterification process, that MOM could not be removed following esterification, and that TBDMS “could not be clearly introduced.” The invention disclosure stated that TMS was “too fragile,” but did not say that MOM could be removed following esterification, and that a reaction with TBDMS “does not go forward.”

[12] Because we assume the credibility of the inventors’ beliefs, we do not address the district court’s finding that the inventors could not have provided Mr. Pilard with any reasonable scientific basis for believing that that the patented process could work with any hydroxy-protecting group or that the testimony on this subject was not credible.