IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ZYMOGENETICS, INC., a Washington Corporation,	)	
Plaintiff,	)	C. A. No: 06-500-SLR-MPT
v.	)	
BRISTOL-MYERS SQUIBB CO., a Delaware Corporation, and DOES 1 through 100,	)	
Defendants.	)	

DEFENDANT BRISTOL-MYERS SQUIBB COMPANY'S
MOTION FOR BIFURCATION OF DAMAGES AND
RENEWED MOTION FOR BIFURCATION OF WILLFUL INFRINGEMENT

Defendant Bristol-Myers Squibb Company ("Bristol") respectfully requests that the Court sever the issues of damages and willful infringement for separate trial after the resolution of liability, and stay discovery related to willful infringement pursuant to Federal Rule of Civil Procedure 42(b). In support of its request, Bristol states as follows:

I. Introduction

On October 15, 2007, Bristol submitted a letter memorandum to Magistrate Judge Thynge (D.I. 116) requesting bifurcation of the issue of willfulness (including discovery related thereto) and any potential enhanced damages stemming from willfulness. Magistrate Judge Thynge stated on November 8, 2007 during a teleconference with the parties that:

> I clearly don't believe that [bifurcating every case] was Seagate's intent but I do think that bifurcation is appropriate and I still think it's a discretionary matter for the court, particularly the trial judge.

(November 8, 2007 Transcript, D.I. 134, at 27).[1] Pursuant to that statement, and in view of the fact that to this case has been reassigned and trial date set, Bristol seeks to bifurcate the issues of damages and willfulness from the issue of liability.

Bifurcation of willfulness is appropriate because a decision to waive the attorney-client privilege should be made only when absolutely necessary, and therefore should be made after a decision on the merits concerning infringement is rendered. Such an approach is consistent with the Federal Circuit's new willfulness test set forth in *In re Seagate ("Seagate")*. *In re Seagate Tech., LLC*, 497 F.3d 1360 (Fed. Cir. 2007) (*en banc*).

Bifurcation of damages is particularly appropriate here because this case involves two patents concerning complicated biotechnology, multiple non-infringement and invalidity issues and complex damages issues. Absent bifurcation of willfulness and damages, there is a substantial risk of juror confusion. Moreover, as will be shown at trial, Bristol's Orencia® product does not infringe any of the claims of the patents-in-suit and the patents-in-suit will be shown to be invalid, and, therefore, there is a strong likelihood that a trial on damages will not be necessary.

Conducting a trial including both the issues of damages and willfulness will reduce judicial economy, require the parties to incur substantial unnecessary costs, increase the risk of prejudice to Bristol and risk juror confusion. Further, bifurcation of these issues will not prejudice ZymoGenetics.

Moreover, the availability of an interlocutory appeal further supports bifurcation because liability issues will be immediately dealt with on appeal and potentially moot any willfulness or damages issue. Under 28 U.S.C. § 1292(c)(2), a party receiving an adverse

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[1] Magistrate Judge Thynge stated that she was "not inclined at [that] stage, and where this case [was], to necessarily bifurcate willfulness because [she was] not going to be the judge

judgment that is "final except for an accounting" of a damage award may appeal to the Federal Circuit, at which time, the district court – if it so chooses – may stay further proceedings. The availability of immediate appellate review of infringement and validity determinations and related determinations, such as Markman, has been used by courts in deciding whether to bifurcate. *See, e.g., Eaton Corp. v. Auburn Gear Inc.*, 8 U.S.P.Q.2d 1373, 1374 (N.D. Ind. 1988); *Lemelson v. Apple Computer, Inc.*, 28 U.S.P.Q.2d 1412, 1423 (D. Nev. 1993).

The availability of an interlocutory appeal is even more compelling where the Markman and obviousness decisions are reviewed *de novo* by the Federal Circuit. Therefore, it is most efficient to wait for a final ruling on liability from the Federal Circuit before investing the time and resources necessary to try damages and willfulness.

For the reasons set forth in this Motion, Bristol respectfully requests that the Court sever the issues of damages and willful infringement for separate trial after the resolution of liability, and stay discovery related to willful infringement pursuant to Federal Rule of Civil Procedure 42(b).

II. APPLICABLE LAW

Bifurcation is governed by Federal Rule of Civil Procedure 42(b), which provides as follows:

> For convenience, to avoid prejudice, or to expedite and economize, the court may order a separate trial of one or more separate issues, claims, crossclaims, counterclaims, or third-party claims. When ordering a separate trial, the court must preserve any federal right to a jury trial.

(con't.)
trying this case." (November 8, 2007 Transcript, D.I. 134, at 23).

Fed. R. Civ. P. 42(b). "Courts when exercising their broad discretion to bifurcate issues for trial under Rule 42(b), should consider whether bifurcation will avoid prejudice, conserve judicial resources, and enhance juror comprehension of the issues presented in the case." *Ciena Corp. v. Corvis Corp.*, 210 F.R.D. 519, 520 (D. Del. 2002) (citation omitted). Here, each of the factors favors bifurcation.

In deciding a motion to bifurcate, "a district court has broad discretion in separating issues and claims for trial as part of its wide discretion in trial management." *Id.* (internal quotations and citation omitted). Bifurcation is particularly well-suited for complex patent cases, and as this Court recently recognized, "[i]n patent cases, bifurcation can be used to simplify the issues and to 'maintain manageability of the volume and complexity of the evidence presented to a jury.'" *Crown Packaging Tech., Inc. v. Rexam Beverage Can Co.*, 498 F. Supp. 2d 734, 736 (D. Del. 2007) (citation omitted); *see also Ciena*, 210 F.R.D. at 521 ("In the context of patent cases, 'experienced judges use bifurcation and trifurcation . . . to simplify the issues in patent cases . . . .'") (quoting Thomas L. Creel & Robert P. Taylor, *Bifurcation, Trifurcation, Opinions of Counsel, Privilege and Prejudice*, 424 PLI/Pat 823, 826 (1995)). Accordingly, "bifurcation of complex patent trials has become common." *Id.* at 521; *see also, e.g., Creo Prods. Inc. v. Presstek, Inc.*, 166 F. Supp. 2d 944, 948 (D. Del. 2001) (nothing that "the court bifurcated the trial into separate liability and damage phases"), *aff'd*, 305 F.3d 1337 (Fed. Cir. 2002) (noting that "the court bifurcated the trial into separate liability and damage phases"); *Purdue Pharma, L.P. v. F.H. Faulding & Co.*, 48 F. Supp. 2d 420, 423 (D. Del. 1999), *aff'd*, 230 F.3d 1320 (Fed. Cir. 2000).

A. Willfulness

In 1983, the Federal Circuit established a standard for evaluating willful infringement which placed an affirmative duty on potential infringers to exercise due care in determining whether or not activities are infringing, and to seek advice of counsel before initiating

potentially infringing activities. *Underwater Devices, Inc. v. Morrison-Knudsen Co.*, 717 F.2d 1380, 1389-90 (Fed. Cir. 1983), *overruled by In re Seagate*, 497 F.3d at 1371. Until the Federal Circuit *Knorr-Bremse* decision in 2004, failure to rely on or produce an opinion of counsel allowed the fact-finders to draw negative inferences against accused infringers.[2] *Id.* at 1370-71. In light of the affirmative duty, accused infringers commonly asserted an advice of counsel defense. *Id.* at 1369.

Seagate not only did away with the affirmative duty, it created a threshold test that should be met prior to delving into the subjective mind of the accused infringer. *Id.* at 1370-72. That is, *Seagate* created a prerequisite that should serve as a hurdle to a patentee's access to an accused infringer's attorney-client privileged material:

> . . . to establish willful infringement, a patentee must show by clear and convincing evidence that the infringer acted despite an objectively high likelihood that its actions constituted infringement of a valid patent. The state of mind of the accused infringer is not relevant to this objective inquiry. ***If this threshold objective standard is satisfied***, the patentee must also demonstrate that this objectively-defined risk (determined by the record developed in the infringement proceeding) was either known or so obvious that it should have been known to the accused infringer.

Id. at 1371 (emphasis added) (citations omitted).

This new two-part willfulness test must be proven by clear and convincing evidence. *Id.* Advice of counsel is not relevant to the first part of the test, the threshold objective element. The second part of the test, the subjective element, requires patentees to prove that the objectively-defined risk "was either known or so obvious that it should have been known to the

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[2] The *Knorr-Bremse* decision concluded that this negative inference "imposed 'inappropriate burdens on the attorney-client relationship.'" *Id.* at 1370 (citing *Knorr-Bremse Systeme Fuer Nutzfahzeuge GmbH v. Dana Corp.*, 383 F.3d 1337 (Fed. Cir. 2004) (*en banc*).

accused infringer." *Id.* It is during the analysis of the subjective element that advice of counsel becomes relevant.

Because advice of counsel is only relevant to the subjective element, it is only ***after*** the patentee meets the threshold objective element that an accused infringer should be required to elect whether to rely on advice of counsel, thereby waiving some degree of attorney-client privilege.[3] This is consistent with the concurring opinion authored by Judge Gajarsa and joined by Judge Newman. Judge Gajarsa gave his own interpretation of the two-part willfulness test, which he believed was consistent with the majority opinion. *Id.* at 1384. Judge Gajarsa stated:

> If Convolve is unable to show [the objective element], Seagate cannot be found to have willfully infringed, regardless of any evidence of its subjective beliefs. . . . Thus, Seagate's subjective beliefs may become relevant only if Convolve successfully makes this showing of objective unreasonableness. . . . ***Because no finding of objective unreasonableness has yet been made in this case, issues of attorney-client privilege and work product may not even need to be confronted.***

Id. (emphasis added). Therefore, bifurcation of willfulness is consistent with *Seagate*.

B. Damages

The wisdom of delaying the inquiry into complex damages issues until liability is resolved is reflected in 28 U.S.C. § 1292(c), which expressly provides for the finality of decisions in patent cases prior to an accounting. Damages issues are often bifurcated to conserve judicial resources and expedite the resolution of a litigation. "A preliminary finding on the question of liability may well make unnecessary the damages inquiry, and thus result in substantial saving of time of the Court and counsel and reduction of expense to the parties." *Smith v. Alyeska Pipeline Serv Co.*, 538 F. Supp. 977, 983 (D. Del. 1982) (internal quotations and citation omitted), *aff'd*,

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[3] As the first part of the willfulness test is an objective analysis, it is reasonable to assume that the claims should be construed properly prior to performing the analysis.

758 F.2d 668 (Fed. Cir. 1984). Without bifurcation, however, "the parties, as well as the Court, would inevitably be required to invest valuable time and effort to litigate potentially unnecessary issues if damages discovery and trial were to go forward now. In codifying a provision in the Federal Rules permitting bifurcation, Congress attempted to obviate the need for such potentially fruitless endeavors." *Princeton Biochemicals, Inc v. Beckman Instruments, Inc.*, 180 F.R.D. 254, 259 (D.N.J. 1997) (citation omitted).

Additionally, this Court has recently indicated that bifurcating damages in patent cases can create certain efficiencies. (*See, e.g.*, *Quinstreet, Inc. v. Parallel Networks, Inc.*, Civ. No. 06-495 (SLR) (March 17, 2008 Transcript at 28-29) (Ex. 1); *Callaway Golf Company v. Acushnet Company*, Civ. No. 06-91 (SLR) (November 30, 2007 Memorandum Order at 2) (Ex. 2)). Magistrate Judge Thynge also recognized that the Court in several cases in Delaware was bifurcating willfulness and damages for efficiency and judicial economy:

> I also recognize that all three judges, but, in particular, Judge Robinson and Judge Farnan, have been bifurcating more cases. And I recently did what I call a semi-bifurcation because the discovery had been essentially completed and I bifurcated out willfulness and damages from being presented to the jury in the go-around on liability.

(November 8, 2007 Transcript, D.I. 134, at 21-22). Bristol believes that bifurcation of damages would similarly be appropriate in the present case.

III. ARGUMENT

A. A Finding of Willfulness Under the Facts of the Present Case Would Be Extremely Remote

In the present case, the possibility of a finding of willfulness is extremely remote, which is a factor that weighs in favor of bifurcation. As the Federal Circuit stated in *Seagate*, a substantial question about invalidity is likely sufficient to avoid a charge of willfulness based on post-filing conduct (*i.e.*, the conduct of an accused infringer after the filing of a complaint). *In re*

Seagate, 497 F.3d at 1374. The same should hold true to avoid a charge of willfulness based on prelitigation conduct. Here, ZymoGenetics should not be permitted to deny that there was a substantial question concerning invalidity during much of the relevant prelitigation time period, as ZymoGenetics made representations to the United States Patent and Trademark Office ("USPTO") that there were such substantial questions of patentability.

In March of 2004, ZymoGenetics told the USPTO in Requests for Reexamination that there were "substantial questions of patentability" with respect to both of the patents involved in this litigation.[4] Until August 29, 2006 -- after ZymoGenetics filed the present lawsuit -- the '725 patent was involved in a reexamination proceeding that was granted pursuant to ZymoGenetics' patentability representations. The '026 patent was involved in a similar reexamination proceeding until July 4, 2006 -- about a month before the present lawsuit was filed. As stated in *In re Seagate*:

> "[A] willfulness claim asserted in the original complaint must necessarily be grounded exclusively in the accused infringer's pre-filing conduct. By contrast, when an accused infringer's post-filing conduct is reckless, a patentee can move for a preliminary injunction, which generally provides an adequate remedy for combating post-filing willful infringement."
> *In re Seagate*, 497 F.3d at 1374.

It would seem extremely unlikely that willfulness could be found based on prelitigation conduct -- especially in light of the fact that claims of both patents were modified

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[4] Regarding Unites States Patent No. 5,843,725 ("the '725 patent"), ZymoGenetics stated "[t]he disclosures of the following seven U.S. patents and articles raise a substantial question of patentability for each of the 49 claims of the '725 patent under 35 U.S.C. §102(b), §102(g) and/or §103(a) . . . ." (Ex. 3 at ZG001666). Similarly, regarding the Unites States Patent No. 6,018,026 ("the '026 patent"), ZymoGenetics stated "[t]he disclosures of the following seven U.S. patents and articles raise a substantial question of patentability for each of the 29 claims of the '026 patent under 35 U.S.C. §102(b), §102(g) and/or §103(a) . . . ." (Ex. 4 at ZG000754).

during reexamination -- as the relevant prelitigation time period was about a month. With respect to willfulness based on post-filing conduct, a patentee who does not move for a preliminary injunction should not be allowed to accrue enhanced damages based solely on the accused infringer's post-filing conduct. *Id.* This lawsuit was filed almost two years ago, and ZymoGenetics elected not to seek a preliminary injunction.

B. A Finding of Liability is Extremely Remote and Therefore The Issue of Damages Should be Bifurcated to Conserve Resources

As noted above, bifurcation of damages will conserve judicial resources and expedite the resolution of this litigation. If the jury finds no infringement or finds the patents invalid, there will be no need for a damages trial. Indeed, this Court has noted that it is often more efficient to bifurcate damages from liability issues. *Quinstreet, Inc. v Parallel Networks, Inc.*, Civ. No. 06-495 (SLR) (March 17, 2008 Transcript at 28-29) (Ex. 1). Since the liability issues and Markman decision will likely be appealed and reviewed on a *de novo* basis by the Federal Circuit, it is more efficient to wait for an appellate ruling prior to investing the time and resources necessary to try the damages and willfulness issues of the case.

Furthermore, even if the jury were to find Bristol liable for patent infringement, which Bristol believes unlikely, there is still the distinct possibility that a trial on damages and willfulness would not be necessary. A "separate trial of the issue of liability may present counsel the opportunity to obtain a final settlement of that issue or appeal without having reached the often time-consuming and difficult damages question." *Smith*, 538 F. Supp. at 983 (internal quotations and citation omitted).

Finally, "[t]he trial of the damages question in [a patent infringement] suit is often difficult and expensive, while being easily severed from the trial of the questions of validity and infringement of the patent." *Id.*; *see also Novopharm Ltd. v. Torpharm, Inc.*, 181 F.R.D. 308, 310

(E.D.N.C. 1998) ("Patent cases are often uniquely amenable to bifurcation because of the complex nature of the damages determination . . . "). Bifurcation of damages in this case will not prejudice ZymoGenetics and will conserve judicial resources and expedite the resolution of this litigation.

C. Bristol Will Likely Be Prejudiced Without Bifurcation of Willfulness and Damages

Bifurcation will not prejudice ZymoGenetics in any way because any harm associated with delay in recovering any potential damages award "could be remedied at the damages phase." *Industrias Metalicas Marva, Inc. v. Lausell*, 172 F.R.D. 1, 9 (D.P.R. 1997). However, if a single trial is held in which the issues of damages and willfulness are tried, there is a high likelihood of prejudice to Bristol.

For example, a single trial could very well lead to juror confusion that would be prejudicial to Bristol. If Bristol is required to put on its evidence of what would have been a reasonable royalty, to counter the evidence adduced by ZymoGenetics, the jury may erroneously view that as an admission of liability by Bristol.

Further, evidence in the willfulness and damages phase of the litigation would extend the trial of the case to produce and require the jury to hear evidence and instructions that will be mooted by a verdict of non-infringement or invalidity, and would potentially include divulgence of highly confidential and sensitive commercial information not necessary to any liability issue.

IV. CONCLUSION

For the foregoing reasons, Bristol respectfully requests the Court grant this motion to sever the issues of damages and willful infringement for separate trial after the resolution of liability, and to stay discovery related to willful infringement.

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UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on May 9, 2008, I electronically filed the foregoing document with the Clerk of Court using CM/ECF and caused the same to be served on the plaintiff at the address and in the manner indicated below:

BY HAND DELIVERY AND E-MAIL

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EXHIBIT 1

IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

- - -

QUINSTREET, INC.	:	CIVIL ACTION
Plaintiff	:	
v.	:	
PARALLEL NETWORKS, INC.,	:	
Defendant	:	NO. 06-495 (SLR)

- - -

Wilmington, Delaware
Monday, March 17, 2008
11:35 o'clock, a.m.

- - -

BEFORE: HONORABLE SUE L. ROBINSON, U.S.D.C.J.

- - -

APPEARANCES:

RICHARDS, LAYTON & FINGER
BY: KELLY FARNAN, ESQ.

-and-

Valerie J. Gunning
Official Court Reporter

APPEARANCES (Continued):

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-and-

JENNER & BLOCK
BY: DAVID R. BENNETT, ESQ.,
PAUL MARGOLIS, ESQ.,
EMILY C. JOHNSON, ESQ. (via telephone) and
BENJAMIN J. BRADFORD, ESQ. (via telephone)
(Chicago, Illinois)

Counsel for Defendant
Parallel Networks, LLC

relevant documents?

MR. MARGOLIS: Yes, your Honor.

THE COURT: And if I determined to bring in an IT, two or three witnesses, whoever QuinStreet identified, to testify here in Court about what platforms are used and how they're used and how we get to that information, it seems to me as though that you all are not communicating very well. And since, clearly, on the one hand, you complain when you only get 400,000 documents instead of a million documents, and then you complain when you get 400,000 documents, but you can't really figure out what's going on because there is too much information and it's hard to get through to what's in the documents.

So no matter what happens, there are always complaints.

So this is what I would suggest with respect to infringement, and that is that we bring in two or three people. We basically have an evidentiary hearing and we determine how best to identify relevant documents. And if, at the end of the day, we can't figure out how to do it, then the case goes away, basically.

Now, that's only part of the problem. It seems to me as well that if we're talking about -- I mean, I don't know what -- 400,000 pages of e-mails, I don't know what relevance they have. If we are talking about damages, I'm

happy to set damages aside. I never try damages anymore because they usually go away once the Federal Circuit finally resolves the issues. So set aside damages.

Now, the other issues in the case -- well, I don't know what other issues you have in the case. You're the one complaining about the discovery.

Are there any other issues in the case for which you have requested documents and feel as though you either have not gotten them or you can't determine whether you've gotten them because of the way the documents have been produced?

MR. MARGOLIS: I guess I would answer your question this way. We received -- I think Mr Doyle referenced that they had produced, I don't know -- he said 320,000 pages of tiffs. I think it's about 220,000 pages. About half of that are documents that I think they would say are related to invalidity. Of the first hundred thousand pages, almost the first hundred thousand pages, with the exception of about 15 or 20,000 pages of notebooks and unaudited financial statements. The rest of that are prior art, treatises, things from other people. So they've had no problem in taking the things that are related to their affirmative case and tiffing them.

The last group -- those first hundred thousand pages, those were about the only documents we received

EXHIBIT 2

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

CALLAWAY GOLF COMPANY,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Civ. No. 06-91-SLR
	)	
ACUSHNET COMPANY,	)	
	)	
Defendant.	)	

MEMORANDUM ORDER

At Wilmington this 30th day of November, 2007, having reviewed all the papers submitted in connection with the evidentiary issues raised at the pretrial hearing;

IT IS ORDERED that:

1. **Test golf balls.**[1] Evidence relating to Acushnet's test golf balls may be admitted, but only under the following specific circumstances. Dr. Statz may testify consistent with his expert report vis-a-vis the prior art and motivation to combine. He may not testify about the test golf balls. Only if Callaway, through its cross examination, raises an issue of fact that implicates the test golf balls[2] may such balls become the subject of testimony. More specifically, with permission and following Dr. Statz's testimony, Acushnet may present its fact witnesses to testify about the testing procedures. If a proper foundation is laid in this regard, Dr. Statz may retake the stand

[1]These balls may **not** be referred to as "prior art" balls or "hybrid" balls.

[2]At the conclusion of Dr. Statz's testimony, Acushnet may make its proffer as to the relevance of the test golf balls.

to relate how and why he relied on these results for his opinion of invalidity.

2. **Professional golfers.** I conclude that Callaway timely identified both Greg Norman and Phil Mickelson as witnesses. I also conclude, however, that the kind of testimony I had envisioned[3] their giving is more appropriately the subject of expert testimony. Therefore, none of the identified professional golfers may testify generally as to the characteristics of the patented golf balls (as discerned through personal play) or the golf ball market. Nevertheless, I understand that Mr. Mickelson has some personal experiences with Acushnet that may, or may not, be relevant[4] to the issues at bar. Therefore, I will entertain a proffer at the end of Acushnet's case in chief as to Mr. Mickelson's expected rebuttal testimony to determine, at that point, whether he is an appropriate fact witness (i.e., he has personal knowledge of relevant facts).

3. **Willfulness.** Upon further reflection, I have concluded that the issue of willfulness shall be bifurcated, to be tried with the issue of damages.

4. **Injunctive relief.** The entry of injunctive relief, if implicated by the verdict, shall be resolved through the course of post-trial briefing.

United States District Judge

[3]See e.g., D.I. 217, ex. 18.

[4]See, e.g., D.I. 355.

EXHIBIT 3

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Of:	Andrzej Z. Sledziewski et al.	Atty. Docket No.: 985.011USX
Patent No.	5,843,725	
Issued:	December 1, 1998	
Title:	METHODS OF PRODUCING SECRETED RECEPTOR ANALOGS AND BIOLOGICALLY ACTIVE DIMERIZED POLYPEPTIDE FUSIONS	

REQUEST FOR REEXAMINATION UNDER 35 U.S.C. §302 AND 37 C.F.R. §1.510

MS EX PARTE REEXAM
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

In accord with 37 C.F.R. §1.510, the Patent Owner, ZymoGenetics, Inc. (hereinafter ZymoGenetics), requests reexamination of all claims of U.S. Patent No. 5,843,725 (hereinafter the '725 patent, attached as Exhibit A). This request is filed within the period of enforceability of the '725 patent and is accompanied by the fee set forth in 37 C.F.R. §1.20(c). The '725 patent contains sequence listings which are on file in computer-readable form in the official file for U.S. Patent No. 5,843,725.

ZymoGenetics is also filing a reexamination request for related U.S. Patent No. 6,018,026.

I. STATEMENT UNDER 37 C.F.R. §1.510(b)(1)

The disclosures of the following seven U.S. patents and articles raise a substantial question of patentability for each of the 49 claims of the '725 patent under 35 U.S.C. §102(b), §102(e), §102(g) and/or §103(a), because there is a substantial likelihood that a reasonable Examiner would consider the patents and articles important in deciding whether or not these claims are patentable (M.P.E.P. §2242):

U.S. Patent No. 5,336,603 (" '603 Capon");

U.S. Patent No. 5,565,335 (" '335 Capon");

U.S. Patent No. 6,004,781 (" '781 Seed");

Gascoigne et al., *Proc. Natl. Acad. Sci. USA* 84:2936-2940, 1987 ("Gascoigne");

Traunecker et al., *Nature* 331:84-86, 1988 ("Traunecker");

Ellis et al., *Proc. Natl. Acad. Sci. USA* 83:8137-8141, 1986 ("Ellis");

Riedel et al., *Science*, 236:197-200, (April 1987) ("Riedel").

Notwithstanding this Statement, Zymogenetics believes that each and every claim of the '725 patent is distinguishable over these cited U.S. patents and articles.

II. SUMMARY AND IDENTIFICATION UNDER 37 C.F.R. §1.510 (b)(2)

The claims of the '725 patent are directed to methods for producing a secreted dimerized polypeptide fusion (claims 1-20), a secreted receptor analog (claims 21-27), a secreted PDGF receptor analog (claim 28) or a secreted multimerized polypeptide fusion (claims 29-49). The methods involve introducing into a eukaryotic host cell one or more DNA constructs encoding the polypeptide chains of the "polypeptide fusion" or "receptor analog", growing the host cell and isolating the dimerized or multimerized polypeptide fusion or receptor analog. In addition to encoding the polypeptide chains, the DNA constructs also include a transcriptional promoter and a secretory signal sequence. Each chain of the "dimerized or multimerized polypeptide fusion" comprises a "non-immunoglobulin polypeptide" requiring "dimerization" or "multimerization" for "biological activity" joined to a "dimerizing or multimerizing protein heterologous to said non-immunoglobulin polypeptide". Examples of methods for producing such fusions include methods for producing a ligand binding polypeptide, as the non-immunoglobulin polypeptide, fused to an immunoglobulin constant domain polypeptide as the dimerizing protein, and methods for producing a PDGF receptor analog wherein the non-immunoglobulin polypeptide is a PDGF receptor sequence of SEQ ID No. 36 joined to an immunoglobulin heavy chain constant region. The fusion is useful in assay, diagnostic and pharmaceutical treatment applications.

The claims of the '725 patent are provided in the attached copy of the '725 patent. The independent claims can be summarized as follows. These summaries are for illustration purposes only and are not to be regarded as statements about the terms of these claims. The claim terms are completely and fully set forth in the '725 patent.

A. CLAIM 1 OF THE '725 PATENT

Claim 1 is directed to a method for producing a secreted, active dimerized polypeptide fusion. The method includes introducing a DNA construct encoding a dimerizing polypeptide

fusion into a host cell, growing the cell and isolating the dimerized polypeptide fusion. The DNA construct includes, in part, a DNA sequence encoding a polypeptide chain comprising a non-immunoglobulin polypeptide joined to a dimerizing protein heterologous to the non-immunoglobulin polypeptide.

B. CLAIM 9 OF THE '725 PATENT

Claim 9 is directed to a method similar to that of claim 1 except that the DNA construct is a first DNA construct that encodes an immunoglobulin light chain constant region as the dimerizing protein, and a second DNA construct is also introduced into the host cell, which comprises in part a second DNA sequence encoding an immunoglobulin heavy chain constant region domain selected from a certain group and optionally encoding an immunoglobulin hinge or variable region.

C. CLAIM 15 OF THE '725 PATENT

Claim 15 is directed to a method similar to that of claim 9 except that the first DNA construct encodes an immunoglobulin heavy chain constant region domain as the dimerizing protein, and the second DNA construct includes in part a second DNA sequence encoding an immunoglobulin light chain constant region and optionally encoding an immunoglobulin variable region.

D. CLAIM 21 OF THE '725 PATENT

Claim 21 is directed to a method for producing a secreted receptor analog. The method includes the steps of introducing into a eukaryotic host cell a DNA construct encoding the receptor analog, growing the host cell and isolating the receptor analog from the host cell. The DNA construct comprises, in part, a DNA sequence encoding the receptor analog, which is a ligand-binding domain of a receptor requiring dimerization for biological activity joined to a dimerizing protein heterologous to the ligand-binding domain, and optionally an immunoglobulin hinge or variable region joined to the dimerizing protein.

E. CLAIM 28 OF THE '725 PATENT

Claim 28 is directed to a method for producing a PDGF receptor analog. The method is related to that of claim 15 except that the first DNA sequence encodes a PDGF receptor sequence as the non-immunoglobulin polypeptide, the second DNA sequence further encodes a second PDGF receptor sequence, and the host cell is a rodent myeloma cell.

F. CLAIM 29 OF THE '725 PATENT

Claim 29 is directed to a method for producing a secreted active multimerized polypeptide fusion. The method includes the steps of introducing into a eukaryotic host cell a DNA construct encoding the multimerized polypeptide fusion, growing the host cell to allow secretion of the peptide fusion, and isolating the polypeptide fusion. The DNA construct comprises, in part, a DNA sequence encoding a non-immunoglobulin polypeptide requiring multimerization for biological activity joined to a multimerizing protein selected from a group consisting of an immunoglobulin heavy chain or light chain constant region, and optionally encoding an immunoglobulin hinge or variable region joined to the multimerizing protein.

G. CLAIM 37 OF THE '725 PATENT

Claim 37 is directed to a method for producing a secreted active heteromultimeric polypeptide fusion. The method includes the steps of introducing into a eukaryotic host cell first and second DNA constructs each encoding a polypeptide fusion, growing the host cell to allow secretion of the polypeptide fusions and isolating the heteromultimeric polypeptide fusion. The first DNA construct includes, in part, a first DNA sequence encoding a first polypeptide fusion comprising a first non-immunoglobulin polypeptide joined to a first multimerizing protein selected from an immunoglobulin heavy or light chain constant region optionally including an immunoglobulin hinge or variable region. The second DNA construct includes, in part, a second DNA sequence encoding a second polypeptide fusion comprising a second non-immunoglobulin polypeptide joined to a second multimerizing protein selected from an immunoglobulin heavy or light chain constant region optionally including an immunoglobulin hinge or variable region.

III. DETAILED EXPLANATION UNDER 37 C.F.R. §1.510(b)(2)

ZymoGenetics provides the following detailed explanation of the pertinency and manner of applying the foregoing U.S. patents and articles to each claim of the '725 patent.

A. SUMMARY OF U.S. PATENTS AND ARTICLES

'603 Capon can be alleged to disclose a method for producing an "immunoadheson" that can be, for example, a fusion protein of the gp120 ligand binding region of the CD4 receptor joined to the constant region of an immunoglobulin. The fusion protein, a nucleic acid encoding the fusion protein, and host cells transformed with the nucleic acid are also allegedly disclosed. Production of multiple immunoadheson polypeptides from a host cell is also allegedly disclosed.

'335 Capon issued out of an application that was filed as a continuation of the application that issued as '603 Capon. Thus, the specifications are believed to be identical.

'781 Seed can be alleged to disclose a method for producing a fusion protein composed of a fragment of CD4 joined to an immunoglobulin light or heavy chain. The CD4 fragment replaces the variable region of the immunoglobulin chain and binds to the envelope protein gp120 of HIV. The fusion protein, a nucleic acid encoding the fusion protein, and host cells transformed with the nucleic acid can also be alleged to be disclosed.

Gascoigne et al. can be alleged to disclose a method for producing a chimeric protein composed of the variable domains of a T-cell receptor joined to the constant region of an immunoglobulin.

Traunecker et al. can be alleged to disclose a method for producing a chimeric protein composed of the extracellular domains of CD4 joined to the constant region of an immunoglobulin light chain.

Ellis et al. can be alleged to disclose a method for producing a hybrid receptor composed of the extracellular domain of the human insulin receptor joined to the transmembrane and cytoplasmic domains of the bacterial aspartate chemoreceptor.

Riedel et al. can be alleged to disclose a method for producing a chimeric receptor composed of the extracellular and transmembrane domains of human epidermal growth factor (EGF) receptor joined to the cytoplasmic domain of avian *erb*B oncogene product

B. MANNER OF APPLYING THE U.S. PATENTS AND ARTICLES TO THE '725 PATENT CLAIMS

Each of the '603 Capon, '335 Capon and '705 Seed U.S. patents and the Traunecker and Gascoigne articles allegedly disclose methods for producing fusion proteins composed of a ligand binding domain of a receptor joined to heterologous protein domains such as a constant region of an immunoglobulin. These patents and articles allegedly disclose the corresponding fusion protein products as well. Ellis allegedly discloses a method for producing a fusion protein composed of an insulin-binding domain of an insulin receptor joined to an intracellular domain of another receptor. Riedel allegedly discloses a method for producing a chimeric receptor of an EGF binding domain of an EGF receptor joined to an intracellular domain of another protein.

A reasonable Examiner allegedly would find that these U.S. patents and articles disclose features of the claimed methods of the '725 patent. These U.S. patents and articles may be seen to show methods for producing fusion protein chains allegedly similar to those of the '725 patent, namely those composed of ligand binding domains of receptors joined to heterologous protein domains such as the constant regions of immunoglobulins or intracellular domains other than immunoglobulin domains in the case of Ellis and Riedel. The methods for production allegedly include introduction of the appropriate DNA construct into host cells including prokaryotic and eukaryotic cells, and expression of the desired fusion protein. All of the references allegedly disclose such methods.

In particular, the '335 and '603 Capon patents allegedly provide examples of recombinant methods to make fusion proteins having adheson or ligand binding domains joined to immunoglobulin fusion partners. The ligand binding domains allegedly include those of CD1, CD2, CD4, CD8 and CD28 as well as the ligand binding domains of such receptors as the IgE receptor, the PDGF receptor, the CSF-1 receptor and the like. Their immunoglobulin fusion partners allegedly include the light and heavy chain constant and/or variable regions of such immunoglobulins as IgG, IgA, IgE, IgD and IgM. Production of several different fusion proteins by a single host cell are also allegedly described by these patents.

In particular, the '781 Seed patent allegedly discloses a similar fusion protein and a recombinant method to make it. The Seed fusion protein allegedly is an immunoglobulin of the IgM or IgG class having its variable region replaced by the ligand binding domain of CD4, the immune cell surface protein that binds to the envelope protein gp120 of the HIV virus. Similarly, Ellis and Riedel allegedly disclose methods for producing fusion proteins having intracellular domains other than immunoglobulin domains.

When the particulars of these disclosures are compared with the methods and fusion proteins recited by each of the 49 claims of the '725 patent, significant similarities are allegedly apparent. Each of the '725 patent claims recites, with either generic or specific language, a method for production of a fusion protein wherein a host cell is transformed with one or more DNA constructs encoding the fusion protein having a non-immunoglobulin polypeptide (such as a ligand binding domain) and a polypeptide domain heterologous to the non-immunoglobulin polypeptide such as a constant region domain of an immunoglobulin heavy or light chain. This kind of fusion protein and the recombinant method to produce it allegedly echo the fusion proteins, DNA constructs and methods for production disclosed by Capon, Seed, Traunecker, Gascoigne, Ellis and Riedel. For example, the '725 patent exemplifies a PDGF receptor polypeptide (SEQ ID No's 1 and 2) joined to the constant region of an immunoglobulin. The '335 and '603 Capon patents allegedly name this receptor as an example of an adheson joined to an immunoglobulin light or heavy chain constant region.

Consequently, the disclosures of these U.S. patents and articles raise a substantial question of patentability for each claim of the '725 patent. There is a substantial likelihood that a reasonable Examiner would consider these U.S. patents and articles important in deciding whether or not these claims are patentable. A reasonable Examiner would consider this question of patentability and appropriately apply the patent statutes 35 U.S.C. §§102(b), 102(e), 102(g) and/or 103(a) based upon the relevant filing and publication dates of these U.S. patents and articles under consideration. A reasonable Examiner would also investigate the entitlement of such U.S. patents to the filing dates pursuant to the statements of pendancy given in the Cross-References to Related U.S. Application Data provided in the U.S. patents, and would investigate the mailing dates of the articles under consideration.

IV. CONCLUSION

In view of the above information, ZymoGenetics respectfully requests issuance of an order for the reexamination of the claims of the '725 patent under 35 U.S.C. §304 and 37 C.F.R. §1.525. Notwithstanding the question of patentability that has been raised, ZymoGenetics believes that each and every claim of the '725 patent is distinguishable over the above-cited U.S. patents and articles, and that upon reexamination of the '725 patent, a certificate of patentability will be issued.

Respectfully submitted,

ZymoGenetics, Inc.,

By its Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
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(612) 373-6939

Date: March 16, 2004

By _____
A. James Nelson
Reg. No. 28,650

"Express Mail" mailing label number: EV 299 686 640 US
Date of Deposit: March 16, 2004
This paper or fee is being deposited on the date indicated above with the United States Postal Service pursuant to 37 CFR 1.10, and is addressed to the Commissioner for Patents, Mail Stop Patent Application, P.O. Box 1450, Alexandria, VA 22313-1450.

EXHIBIT 4

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Of:	Andrzej Z. Sledziewiski et al.	Atty. Docket No.: 985.012USX
Patent No.	6,018,026	
Issued:	January 25, 2000	
Title:	BIOLOGICALLY ACTIVE DIMERIZED AND MULTIMERIZED POLYPEPTIDE FUSIONS	

REQUEST FOR REEXAMINATION UNDER 35 U.S.C. §302 AND 37 C.F.R. §1.510

MS EX PARTE REEXAM
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-14150

In accord with 37 CFR §1.510, the Patent Owner, ZymoGenetics, Inc. (hereinafter "ZymoGenetics"), requests reexamination of all claims of U.S. Patent No. 6,018,026 (hereinafter the '026 Patent, attached as Exhibit A). This request is filed within the period of enforceability of the '026 patent and is accompanied by the fee set forth in 37 CFR §1.20(c). The '026 patent contains sequence listings which are on file in computer-readable form in the official file for U.S. Patent No. 6,018,026.

ZymoGenetics is also filing a reexamination request for related U.S. Patent No. 5,843,725.

I. STATEMENT UNDER 37 CFR §1.510(b)(1)

The disclosures of the following seven U.S. Patents and articles raise a substantial question of patentability for each of the 29 claims of the '026 patent under 35 U.S.C. §102(b), §102(e), §102(g) and/or §103(a) because there is a substantial likelihood that a reasonable Examiner would consider these U.S. patents and articles important in deciding whether or not these claims are patentable (M.P.E.P. §2242):

U.S. Patent No. 5,336,603 (" '603 Capon");

U.S. Patent No. 5,565,335 (" '335 Capon");

U.S. Patent No. 6,004,781 (" '781 Seed");

Gascoigne et al., *Proc. Natl. Acad. Sci. USA* 84:2936-2940, 1987 ("Gascoigne");

Traunecker et al., *Nature* 331:84-86, 1988 ("Traunecker");

Ellis et al., *Proc. Natl. Acad. Sci. USA* 83:8137-8141, 1986 ("Ellis");

Riedel et al., *Science*, 236:197-200, (April 1987) ("Riedel").

Not withstanding the Statement, Zymogenetics believes that each and every claim of the '026 patent is distinguishable from these cited U.S. patent and articles.

II. SUMMARY AND IDENTIFICATION UNDER 37 C.F.R. §1.510 (b)(2)

The claims of the '026 patent concern a dimerized (claims 1-8) or multimerized (claims 9-29) polypeptide fusion. Each chain of the dimerized or multimerized fusion contains two joined peptide fragments. One fragment is a "non-immunoglobulin polypeptide" such as a non-immunoglobulin polypeptide requiring dimerization or multimerization for biological activity and the other is a "dimerizing or multimerizing protein heterologous to said non-immunoglobulin polypeptide". Some claims specify that the dimerizing or multimerizing protein is a constant region of an immunoglobulin. An example of the non-immunoglobulin polypeptide is a ligand-binding domain of a cellular receptor such as a platelet-derived growth factor receptor. An example of the dimerizing protein is the constant region of a heavy chain of an immunoglobulin. The fusion is useful in assay, diagnostic, and pharmaceutical treatment applications.

The claims of the '026 patent are provided in the attached copy of the '026 patent. The independent claims can be summarized as follows. These summaries are for illustration purposes only and are not to be regarded as statements about the terms of these claims. The claim terms are completely and fully set forth in the '026 patent.

A. CLAIM 1 OF THE '026 PATENT

Claim 1 is directed to a biologically active dimerized polypeptide fusion. The fusion contains first and second chains. Each of the chains is constructed of a non-immunoglobulin polypeptide joined to a heterologous dimerizing protein. In particular, claim 1 recites a biologically active, dimerized polypeptide fusion comprising first and second polypeptide chains. Each of the polypeptide chains comprises a non-immunoglobulin polypeptide requiring dimerization for biological activity joined to a dimerizing protein heterologous to the non-immunoglobulin polypeptide.

B. CLAIM 9 OF THE '026 PATENT

Claim 9 is directed to a multimerized polypeptide fusion comprising a non-immunoglobulin polypeptide requiring multimerization for bioactivity, joined to an immunoglobulin light chain constant region, and an immunoglobulin heavy chain constant region selected from a certain specific group.

C. CLAIM 16 OF THE '026 PATENT

Claim 16 is directed to a heteromultimeric polypeptide fusion comprising first and second fusions wherein each comprises a non-immunoglobulin polypeptide joined to a multimerizing protein, wherein the multimerizing proteins are capable of associating to form a multimer.

III. DETAILED EXPLANATION UNDER 37 CFR §1.510(b)(2)

ZymoGenetics provides the following detailed explanation of the pertinency and manner of applying the foregoing U.S. patents and articles to the claims of the '026 patent.

A. SUMMARY OF U.S. PATENTS AND ARTICLES

'603 Capon can be alleged to disclose an "immunoadheson" that can be, for example, a fusion protein of the gp120 ligand binding region of the CD4 receptor joined to the constant region of an immunoglobulin. A nucleic acid encoding the fusion protein, host cells transformed with the nucleic acid and methods for treatment using the fusion protein can also be alleged to be disclosed.

'335 Capon issued out of an application that was filed as a continuation of the application that issued as '603 Capon. Thus, the specifications are identical.

'781 Seed can be alleged to disclose a single chain fusion protein composed of a fragment of CD4 joined to an immunoglobulin light or heavy chain. The CD4 fragment replaces the variable region of the immunoglobulin chain and binds to the envelope protein gp120 of HIV. A nucleic acid encoding the fusion protein, host cells transformed with the nucleic acid and methods for treatment using the fusion protein can also be alleged to be disclosed.

Gascoigne et al. can be alleged to disclose a chimeric immunoglobulin protein composed of a T-cell receptor variable domain joined to the constant region of an immunoglobulin.

Traunecker et al. can be alleged to disclose a chimeric immunoglobulin protein composed

of the extracellular domains of CD4 joined to the constant region of an immunoglobulin light chain.

Ellis et al. can be alleged to disclose a hybrid receptor protein composed of the extracellular domain of the human insulin receptor joined to the transmembrane and cytoplasmic domains of the bacterial aspartate chemoreceptor.

Riedel et al. can be alleged to disclose a chimeric receptor composed of the extracellular and transmembrane domains of human epidermal growth factor (EGF) receptor joined to the cytoplasmic domain of avian *erb*B oncogene product.

B. MANNER OF APPLYING THE U.S. PATENTS AND ARTICLES TO THE '026 PATENT CLAIMS

Each of the '603 Capon, '335 Capon and '705 Seed U.S. patents and the Traunecker and Gascoigne articles allegedly disclose fusion proteins composed of a ligand binding domain of a receptor joined to heterologous protein domains such as a constant region of an immunoglobulin. These patents and articles allegedly disclose the corresponding recombinant methods for producing these fusion proteins as well. Ellis allegedly discloses a method for producing a fusion protein composed of an insulin-binding domain of an insulin receptor joined to an intracellular domain of another receptor. Riedel allegedly discloses a method for producing a chimeric receptor of an EGF binding domain of an EGF receptor joined to an intracellular domain of another protein.

A reasonable Examiner allegedly would find that these U.S. patents and articles disclose features of the claimed polypeptide fusions of the '026 patent. These U.S. patents and articles may be seen to show fusion protein chains allegedly similar to those of the '026 patent, namely those composed of ligand binding domains of receptors joined to heterologous protein domains such as the constant regions of immunoglobulins or intracellular domains other than immunoglobulin domains in the case of Ellis and Riedel.

In particular, the '335 and '603 Capon patents allegedly provide examples of fusion proteins having adheson or ligand binding domains joined to immunoglobulin fusion partners. The ligand binding domains include those of CD1, CD2, CD4, CD8 and CD28 as well as the ligand binding domains of such receptors as the IgE receptor, the PDGF receptor, the CSF-1 receptor and the like. Their immunoglobulin fusion partners allegedly include the light and heavy chain constant regions or combined variable-constant regions of such immunoglobulins as IgG, IgA, IgE, IgD and IgM.

In particular, the '781 Seed patent allegedly discloses a similar fusion protein and a recombinant method to make it. The Seed fusion protein allegedly is an immunoglobulin of the IgM or IgG class having its variable region replaced by the ligand binding domain of CD4, the immune cell surface protein that binds to the envelope protein gp120 of the HIV virus.

Ellis and Riedel allegedly disclose fusion proteins having intracellular domains other than immunoglobulin domains.

When the particulars of these disclosures are compared with the fusion proteins recited by each of the 29 claims of the '026 patent, significant similarities are allegedly apparent. Each of the '026 patent claims recites, with either generic or specific language, a fusion protein having a non-immunoglobulin polypeptide (such as a ligand binding domain) and a polypeptide domain heterologous to the non-immunoglobulin polypeptide (such as a constant region domain of an immunoglobulin). This kind of fusion protein allegedly echoes the fusion proteins disclosed by Capon, Seed, Traunecker, Gascoigne, Ellis and Riedel. For example, the '026 patent exemplifies a PDGF receptor domain (SEQ ID No's 1 and 2) joined to the constant region of an immunoglobulin. Similarly, the '335 and '603 Capon patents allegedly name this same receptor as an example of an adheson joined to an immunoglobulin light or heavy chain constant region.

Consequently, the disclosures of these U.S. patents and articles raise a substantial question of patentability for each claim of the '026 patent. There is a substantial likelihood that a reasonable Examiner would consider these U.S. patents and articles important in deciding whether or not these claims are patentable. A reasonable Examiner would consider this question of patentability and appropriately apply the patent statutes 35 U.S.C. §§102(b), 102(e), 102(g) and/or 103(a) based upon the relevant filing and publication dates of these U.S. patents and articles under consideration. A reasonable Examiner would also investigate the entitlement of such U.S. patents to the filing dates pursuant to the statements of pendancy given in the Cross-References to Related U.S. Application Data provided in the U.S. patents, and would investigate the mailing dates of the articles under consideration.

IV. CONCLUSION

In view of the above information, ZymoGenetics respectfully requests issuance of an order for the reexamination of the claims of the '026 patent under 35 U.S.C. §304 and 37 CFR §1.525. Notwithstanding the question of patentability that has been raised, ZymoGenetics believes that upon re-examination of the '026 patent, a certificate of patentability will be issued.

Respectfully submitted,

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