IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ZYMOGENETICS, INC., a Washington Corporation,	)	
Plaintiff,	)	Civil Action No: 06-500-SLR-MPT
v.	)	
BRISTOL-MYERS SQUIBB CO., a Delaware Corporation, and DOES 1 through 100,	)	**REDACTED PUBLIC VERSION**
Defendants	)	

BRISTOL-MYERS SQUIBB COMPANY'S ANSWERING BRIEF OPPOSING ZYMOGENETICS, INC.'S MOTION FOR SUMMARY JUDGMENT OF VALIDITY OF PATENTS-IN-SUIT WITH RESPECT TO THE CAPON PATENTS AND THE SEED PATENT

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Dated: August 18, 2008

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Pursuant to the Court's Order dated August 4, 2008, Bristol-Myers Squibb Company ("Bristol") submits this answering brief in opposition to ZymoGenetics, Inc.'s ("ZymoGenetics'") Motion for Summary Judgment of Validity of Patents-in-Suit with Respect to the Capon Patents and the Seed Patent [1] (D.I. 239). Bristol previously submitted a Response to ZymoGenetics Statement of Material Facts concerning ZymoGenetics' summary judgment motion of validity which included a declaration of Dr. Jeffrey V. Ravetch, M.D., Ph.D. (*see* D.I. 207 and 208).

INTRODUCTION

Faced with several patents (*i.e.*, the Capon and Seed Patents)[2] that it cannot dispute disclose the same alleged invention claimed in the patents-in-suit[3], all of which were filed before ZymoGenetics' priority date, ZymoGenetics must lose on validity unless it is able to show that it made the invention at an earlier date. In an attempt to do so, ZymoGenetics argues that it conceived the alleged inventions "no later than" January 4-5, 1988 (several weeks before the Seed Patent priority date) and was diligent in reducing that conception to practice "prior to" September 28, 1988 (the priority date for the Capon Patents).

For the alleged conception, ZymoGenetics relies on a laboratory notebook entry [redacted] Those admissions confirm that whatever is recorded on that notebook page is insufficient to satisfy the requirements for

[redacted]

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[1] Bristol notes that ZymoGenetics' motion for summary judgment is neither case dispositive nor disposes of all of Bristol's claims concerning validity of the patents-in-suit.

[2] The Capon Patents describe fusing PDGF-R to an immunoglobulin – ZymoGenetics' purported preferred embodiment.

[3] The patents-in-suit are U.S. Patent Nos. 5,843,725 and 6,018,026.

conception Further, elements of the alleged inventions are not present in the laboratory notebook entry – and this is a further fatal flaw in ZymoGenetics' conception argument.

Next, ZymoGenetics' "evidence" concerning reduction to practice fails to prove any resulting fusion proteins were "dimers" or that any resulting fusion proteins were "biologically active", both of which are required. As such, ZymoGenetics has failed to prove that it reduced the alleged inventions to practice

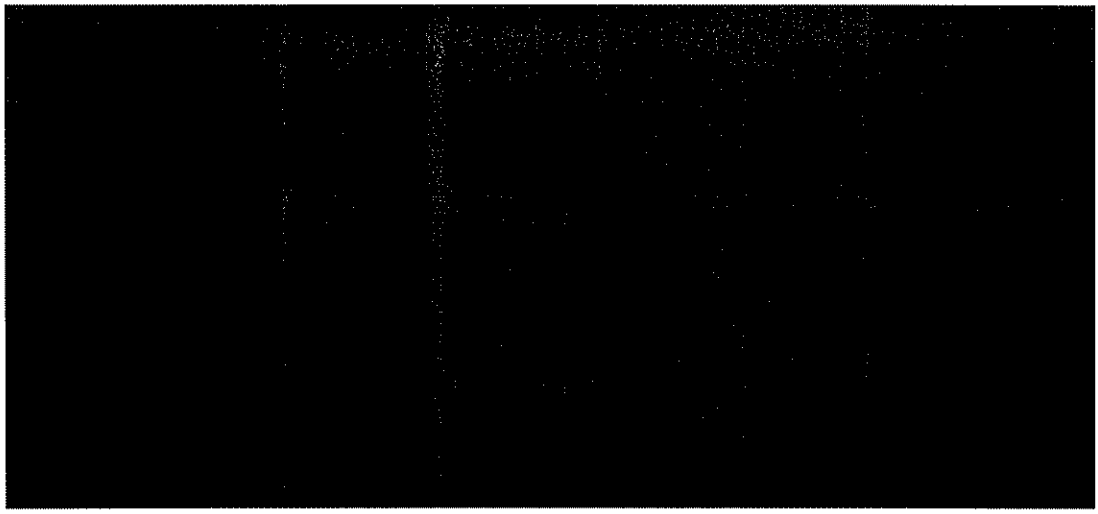
Finally, ZymoGenetics' arguments concerning "diligence" in reducing the alleged inventions to practice are also legally insufficient, as there are unexplained gaps spanning months between the alleged conception date and purported reduction to practice

BACKGROUND

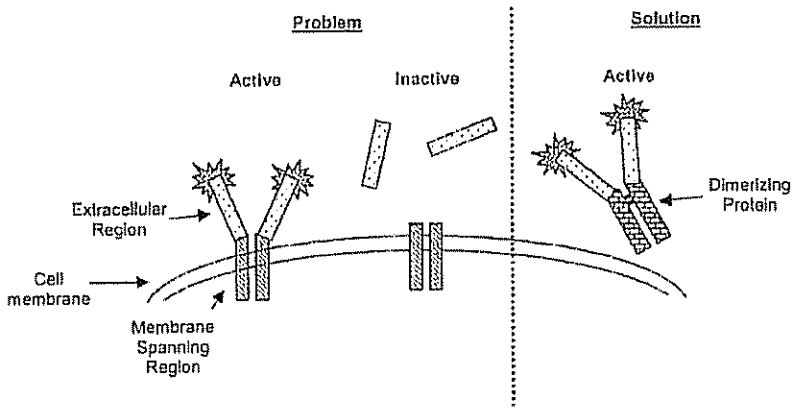
I. Understanding of Technical Terms

In an effort to minimize duplication, Bristol respectfully points to the "Technical Background" section of Bristol's Opening Claim Construction Brief for a brief discussion of the technical terms used herein. (D.I. 179 at 3-9).

II. ZymoGenetics' Characterization of its Invention



[redacted] The problem and solution are depicted in the following figure



ZymoGenetics based the patents-in-suit on the solution to this problem reflected in the foregoing figure Therefore, in order to show its solution worked (*i e*, was reduced to practice), ZymoGenetics needs to show it made fusion protein dimers that were biologically active

III. The Claims at Issue

ZymoGenetics is asserting Claims 1-4, 7 and 30 of U S Patent No 6,018,026 ("the '026 Patent") against Bristol (Declaration of John W Kirkland In Support of Bristol-Myers Squibb Company's Motion for Summary Judgment of Noninfringement) (D I 174, Exh 3 at 6, 7) ; (*Id*, Exh 4 at 8-10). There is one independent claim (Claim 1). Claim 1 is excerpted below, with changes made during reexamination of the '026 Patent in italics

> 1. A biologically active, dimerized polypeptide fusion, comprising:
>
> first and second polypeptide chains, wherein each of said polypeptide chains comprises a non-immunoglobulin polypeptide requiring dimerization for biological activity joined to a dimerizing

> protein heterologous to said non-immunoglobulin polypeptide, *wherein the dimerizing protein is selected from the group consisting of yeast invertase, at least a portion of an immunoglobulin light chain comprising at least an immunoglobulin light chain constant region domain, and at least a portion of an immunoglobulin heavy chain comprising at least an immunoglobulin heavy chain constant region domain*.

(*Id.*, Exh 1 at ZG 000003) [5]

ZymoGenetics is asserting Claims 1-3, 5, 6, 21, 22, 24, 25, 50 and 51 of U S Patent No. 5,843,725 ("the '725 Patent") against Bristol (*Id*, Exh 3 at 6); (*Id*, Exh 4 at 4-8) The only independent claims asserted are Claims 1 and 21 '725 Patent Claims 1 and 21 are excerpted below The portions in italics reflect changes made during reexamination of the '725 Patent

> 1. A method for producing a secreted active dimerized polypeptide fusion, comprising:
> introducing into a eukaryotic host cell a DNA construct comprising a transcriptional promoter operatively linked to a secretory signal sequence followed downstream by and in proper reading frame with a DNA sequence encoding a non-immunoglobulin polypeptide requiring dimerization for biological activity joined to a dimerizing protein heterologous to said non-immunoglobulin polypeptide;
> growing said host cell in an appropriate growth medium under physiological conditions to allow the secretion of a dimerized polypeptide fusion encoded by said DNA sequence; and
>
> isolating said dimerized polypeptide fusion from said host cell, *wherein the dimerizing protein is selected from the group consisting of yeast invertase, at least a portion of an immunoglobulin light chain comprising at least an immunoglobulin light chain constant region domain and at least a*

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[5] Claim 2 (which depends on Claim 1) limits the resulting fusion to a homodimer Claim 3 (which depends on Claim 1) limits the dimerizing protein of one of the chains to an immunoglobulin heavy chain constant region Claim 4 (which depends on Claim 3) requires the immunoglobulin heavy chain be joined to an immunoglobulin hinge region Claim 7 (which depends on Claim 1) limits the dimerizing protein to one of several heavy chain constant region domains of an immunoglobulin Claim 30 (which depends on Claim 1) limits the dimerizing protein to an immunoglobulin heavy chain comprising an immunoglobulin heavy chain constant region domain joined to an immunoglobulin heavy chain hinge region

portion of an immunoglobulin heavy chain comprising at least an immunoglobulin heavy chain constant region domain

(*Id.*, Exh. 2 at ZG 000844).[6]

21. A method for producing a secreted receptor analog, comprising:

introducing into a eukaryotic host cell a DNA construct comprising a transcriptional promoter operatively linked to at least one secretory signal sequence followed downstream by and in proper reading frame with a DNA sequence encoding a ligand-binding domain of a receptor requiring dimerization for biological activity joined to a dimerizing protein heterologous to said ligand-binding domain, and optionally an immunoglobulin hinge or variable region *joined* to said dimerizing protein;

growing said host cell in an appropriate growth medium under physiological conditions to allow the secretion of a receptor analog encoded by said DNA sequence; and isolating said receptor analog from said host cell,
wherein the dimerizing protein is selected from the group consisting of yeast invertase, at least a portion of an immunoglobulin light chain comprising at least an immunoglobulin light chain constant region domain, and at least a portion of an immunoglobulin heavy chain comprising at least an immunoglobulin heavy chain constant region domain

(*Id.*)[7]

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[6] Claim 2 (which depends on Claim 1) limits the resulting fusion to a homodimer. Claim 3 (which depends on Claim 1) limits the dimerizing protein to one of several heavy chain constant region domains. Claim 5 (which depends on Claim 1) limits the dimerizing protein to an immunoglobulin heavy chain constant region. Claim 6 (which depends on Claim 5) requires the immunoglobulin heavy chain be joined to an immunoglobulin hinge region. Claim 50 (which depends on Claim 1) limits the dimerizing protein to an immunoglobulin heavy chain comprising an immunoglobulin heavy chain constant region domain joined to an immunoglobulin heavy chain hinge region.

[7] Claim 22 (which depends on Claim 21) limits the dimerizing protein to one of several heavy chain constant region domains of an immunoglobulin. Claim 24 (which depends on Claim 21) limits the dimerizing protein to an immunoglobulin heavy chain constant region. Claim 25 (which depends on Claim 24) requires the immunoglobulin heavy chain constant region be joined to an immunoglobulin hinge region. Claim 51 (which depends on Claim 21) limits the dimerizing protein to an immunoglobulin heavy chain comprising an immunoglobulin heavy chain constant region where an immunoglobulin hinge region is joined to the dimerizing protein.

IV. Claim Construction

ZymoGenetics presumably construed the claims terms according to its own proposed constructions. As such, Bristol has addressed conception and reduction to practice in the context of ZymoGenetics' proposed constructions, with the exception of "biologically active" and "active" for which ZymoGenetics never provided a construction. For the claims containing these terms (Claim 1 of the '026 Patent and Claim 1 of the '725 Patent and all claims depending thereon), the construction applied by Bristol in this brief was "exhibits one or more biological activities of its native counterpart." (*See* D.I. 179 at 17-19). And as pointed out in Bristol's opening claim construction brief, Claim 21 and all claims which depend thereon must be "active" in that they require the method produce a fusion protein that binds ligand. (*Id.* at 17, fn 9).

ZymoGenetics does not address all of the elements of the claims or the claim terms in the context of arguments it made during claim construction. The likely reason for this avoidance is because it would expose its inconsistent positions in how, on the one hand, it construes the claims in arguing for its own alleged acts constituting invention, while, on the other hand, arguing that Bristol infringes.



[redacted] ZymoGenetics has since recanted that position and now argues that binding is not a biological activity, because it needs to do that in an attempt to support its infringement argument [10] [redacted]

Redacted

V. **The Seed and Capon Patents**

U.S. Patent No. 6,004,781 (the "Seed Patent") is entitled "Nucleic Acid Encoding Ig-CD4 Fusion Proteins" and describes, *inter alia*, fusing a molecule called CD4 to an immunoglobulin. U.S. Patent Nos. 5,336,603; 5,565,335; 6,117,655; and 6,710,169 (the "Capon Patents") describe immunoglobulin fusion proteins with various objectives including "increasing the affinity" of the protein for its binding partner.

[redacted]

Redacted

[10] This, of course, is because ZymoGenetics cannot contend in good faith that CTLA4 "requires dimerization for biological activity" if binding is a biological activity.

As conceded by ZymoGenetics, the priority date of the Seed Patent is January 22, 1988 and the priority date of the Capon Patents is September 28, 1988 (Memorandum of Points and Authorities In Support of Plaintiff ZymoGenetics, Inc.'s Motion for Summary Judgment of Validity of Patents-In-Suit with Respect to the Capon Patents and Seed Patent) (D.I 161 at 3-4) ZymoGenetics' motion does not contest the fact that these references disclose subject matter that falls within the asserted claims of the patents-in-suit and are therefore anticipatory, unless ZymoGenetics can establish an earlier date of invention.

ARGUMENT

I. Summary of the Law

A. Summary Judgment

Summary judgment should only be granted if ZymoGenetics can show that there is no genuine issue of material fact and that it is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(c) A fact is material if it is one that "might affect the outcome of the suit under the governing law . . . " *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986). A dispute regarding a material fact is "genuine" so as to warrant the denial of summary judgment "if the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Id.*

There is no dispute that the Capon and Seed Patents pre-date ZymoGenetics' priority date. And ZymoGenetics has not argued in its brief that the Seed and Capon Patents do not anticipate (indeed, it would be hard to imagine such an argument, because the Capon Patent describes PDGF-R immunoglobulin fusions – ZymoGenetics' purported preferred embodiment) Under such circumstances, ZymoGenetics has the burden to proffer evidence showing the alleged inventions took place before the Seed and Capon priority dates. *See Mahurkar v. C.R.*

Bard, Inc., 79 F.3d 1572, 1576-77 (Fed. Cir. 1996). ZymoGenetics has not proffered such evidence.

B. Prior Invention

As ZymoGenetics' brief indicates, in order to be entitled to a date of invention prior to the Seed and Capon patents, it must adduce evidence of a complete conception and it must connect the alleged conception with a reduction to practice by reasonable diligence so that they are substantially one continuous act. (Memorandum of Points and Authorities In Support of Plaintiff ZymoGenetics, Inc.'s Motion for Summary Judgment of Validity of Patents-In-Suit with Respect to the Capon Patents and the Seed Patent) (D.I. 161 at 5, citing *Mahurkar*).

1. The Legal Requirements of Conception, Generally

Conception requires the "formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice." *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1376 (Fed. Cir. 1986). The inventor must have an idea that is completely formed with enough details so that a person of ordinary skill could understand the invention, and only ordinary skill would be needed to make the invention. *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1228 (Fed. Cir. 1994). A conception is not complete if it does not encompass all claim limitations. *See Singh v. Brake*, 317 F.3d 1334, 1340 (Fed. Cir. 2002). An idea that is simply a "hope" or a research plan is not a conception because it must be a "specific, settled idea, a particular solution to the problem at hand." *Burroughs Wellcome*, 40 F.3d at 1228; *see also Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993) (merely identifying a plan to accomplish an intended result without defining any means to do so "is an attempt to preempt the future before it has arrived.") If the inventor must experiment to finalize his idea, then conception is not complete until the working invention is actually made. *Burroughs Wellcome*, 40 F.3d at 1229.

2. When Conception Cannot Occur until an Invention is Reduced to Practice

In technical areas where there is uncertainty as to whether or not an idea will yield the intended result, it is not possible to form a complete conception until the invention is actually reduced to practice. *Id.* ("A conception is not complete if the subsequent course of experimentation, especially experimental failures, reveals uncertainty that so undermines the specificity of the inventor's idea that it is not yet a definite and permanent reflection of the complete invention as it will be used in practice.") When conception cannot be completed prior to reduction to practice, it is sometimes referred to as simultaneous conception and reduction to practice.[11] *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991)(holding that simultaneous conception and reduction to practice occurs when "an inventor is unable to establish a conception until he has reduced the invention to practice through a successful experiment.").

3. Reduction to Practice

Reduction to practice is the second essential step of invention. *Hybritech*, 802 F.2d at 1376. Actual reduction to practice is complete only if and when an embodiment of the invention meeting every claim limitation is produced and is shown to work for its intended purpose. *See id.*

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[11] Simultaneous conception and reduction to practice is focused on whether the invention, once produced, will possess all of the claimed characteristics. *Hitzeman v. Rutter*, 243 F.3d 1345, 1358 (Fed. Cir. 2001).

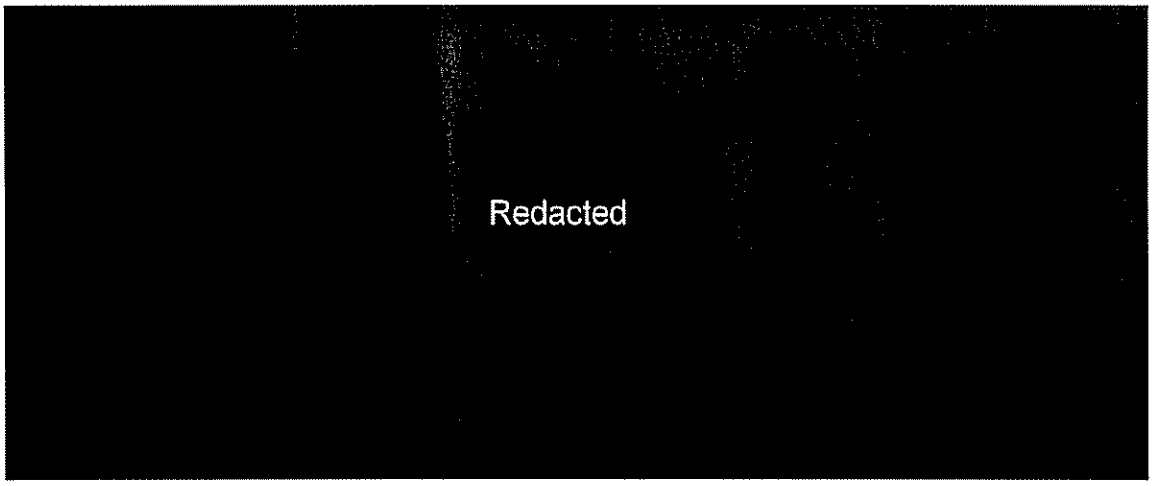
II. ZymoGenetics has Failed to Produce Evidence it Conceived of the Alleged Inventions Before the Seed and Capon Patents

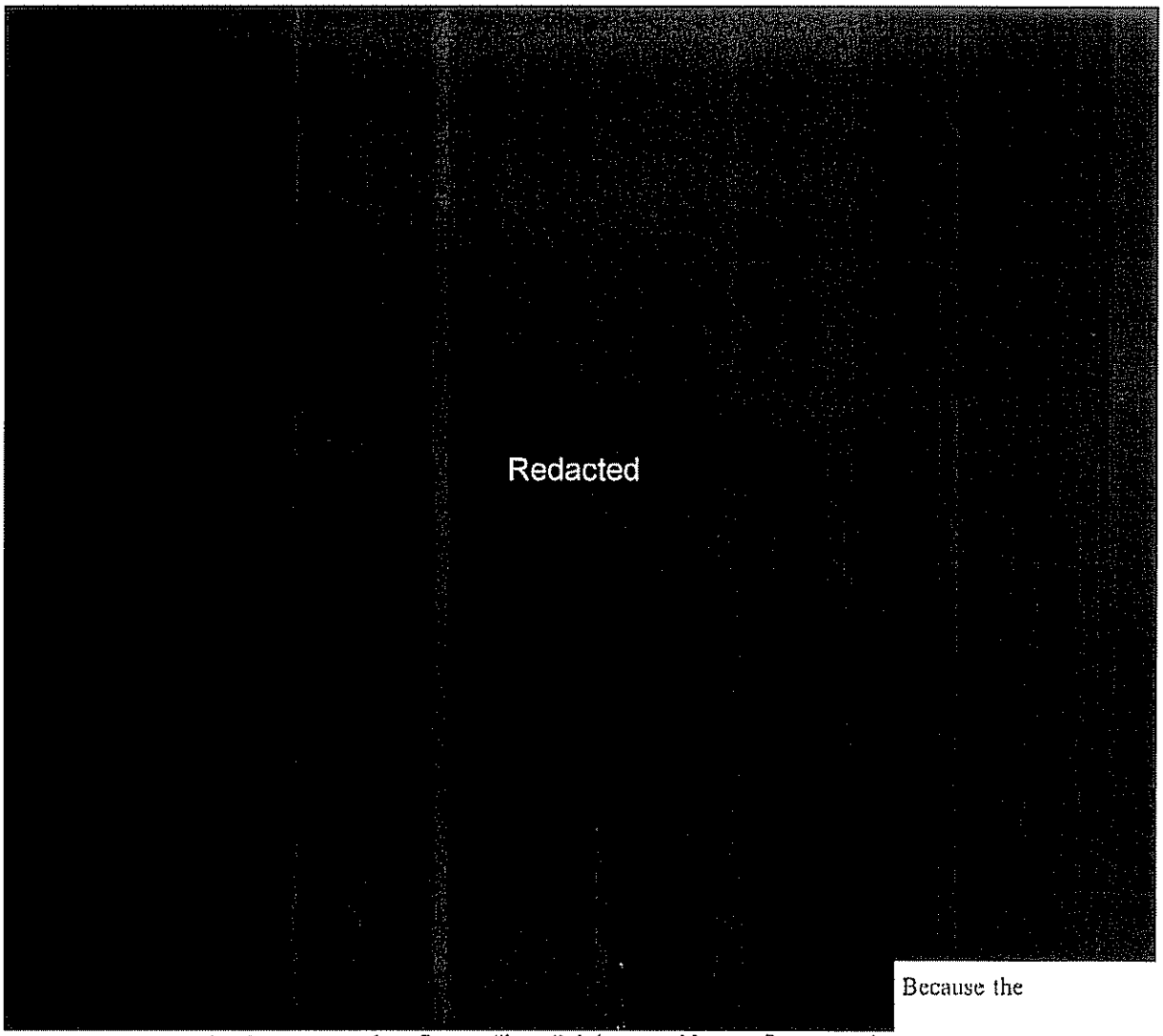
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Further, for the alleged inventions at issue, conception could not have been completed until they were actually reduced to practice

A. [redacted] A "hope" is not sufficient to satisfy the legal requirements of a conception. *Burroughs Wellcome*, 40 F 3d at 1228

The words of the laboratory notebook entry clearly show that it was no more than a hope and a research plan that was riddled with uncertainty:



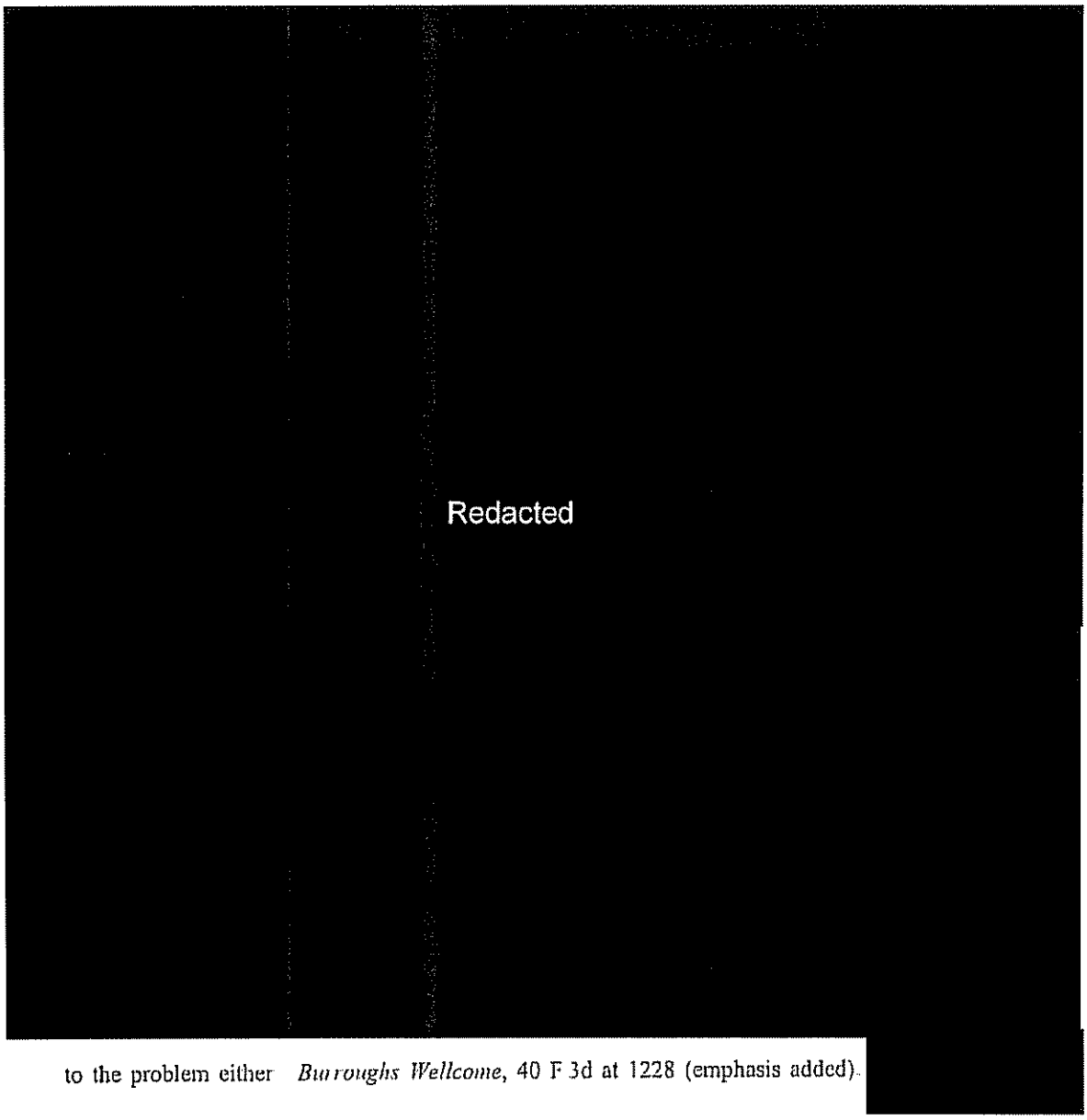


Because the laboratory notebook entry merely reflects a "hope", it is not evidence of a conception.

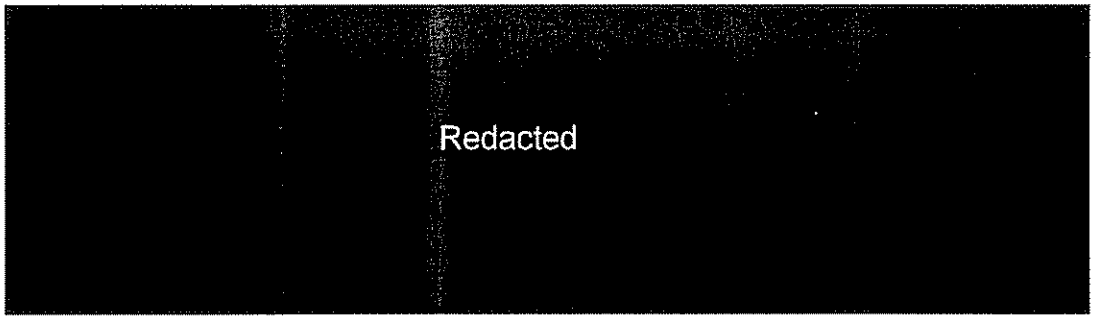
B. [redacted]

A conception must be a "specific, settled idea, a particular solution to the *problem* at hand." *Burroughs Wellcome*, 40 F 3d at 1228 (emphasis added) Yet, as of January 4-5, 1988,

the named inventors did not even know what the problem was The laboratory notebook entry states:



to the problem either *Burroughs Wellcome*, 40 F 3d at 1228 (emphasis added).



Because there was no "specific, settled idea, a particular solution to the problem at hand", the January 4-5, 1988 laboratory notebook entry is not evidence of a conception.

C. 

If the inventor must experiment to finalize his idea, then conception is not complete until the working invention is actually made *Burroughs Wellcome*, 40 F.3d at 1229. And, if undue experimentation is required to reduce the invention to practice there is no conception *See Alpert v Slatin*, 305 F 2d 891, 894 (C C P.A. 1962)(holding no conception until the actual reduction to practice due to the extensive research carried out after the alleged conception); *Amgen*, 927 F 2d at 1206-07 (holding that conception could not occur until an actual reduction to practice where a method to make the claimed amino acid sequence was uncertain and persons of skill in the art had failed to make the claimed amino acid sequence using that method)

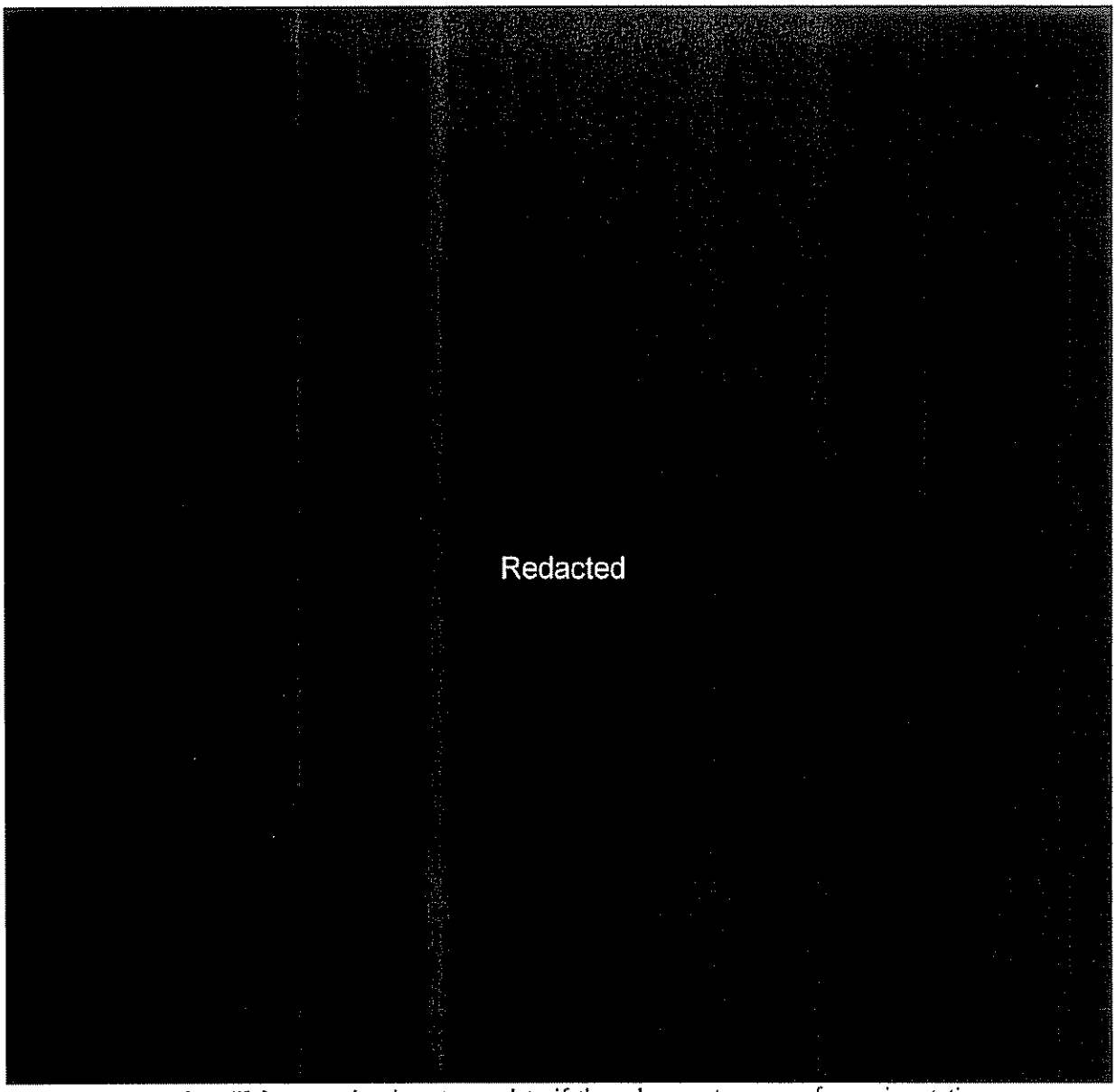


It is undisputed that further experimentation was required before determining whether the suggestions would work. [redacted]

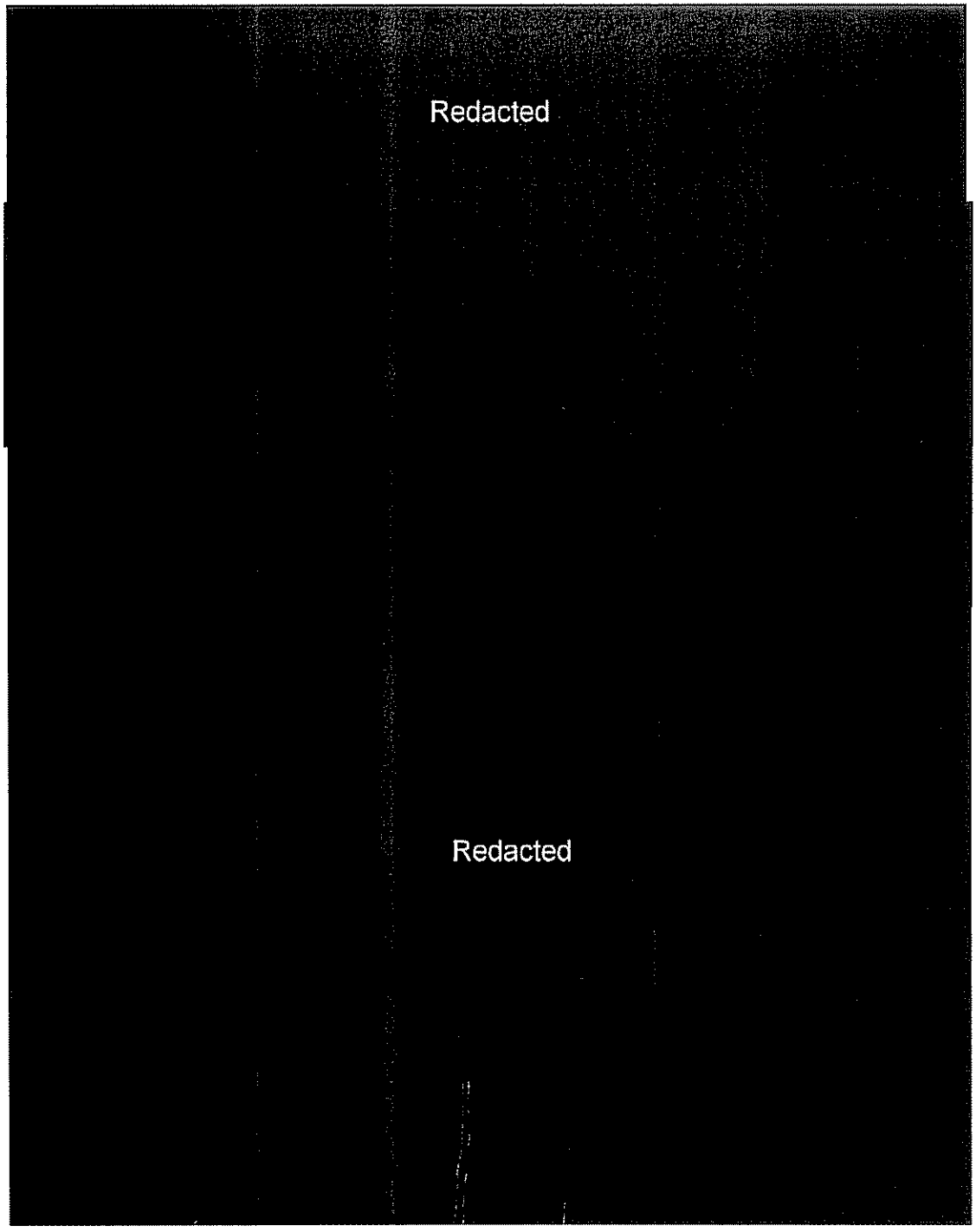
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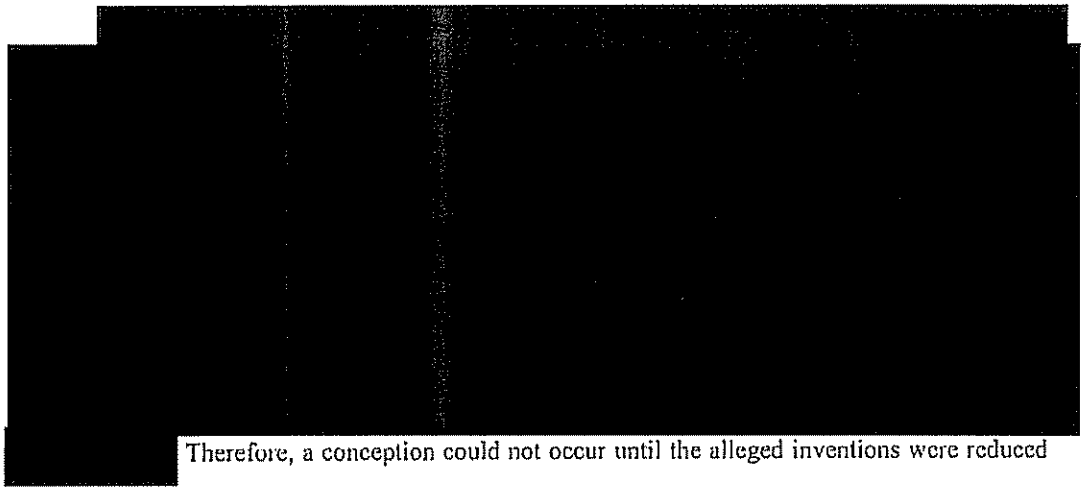
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Further, "[a] conception is not complete if the subsequent course of experimentation, *especially experimental failures*, reveals uncertainty that so undermines the specificity of the inventor's idea that it is not yet a definite and permanent reflection of the complete invention as it will be used in practice." *Burroughs Wellcome Co.*, 40 F.3d at 1229 (emphasis added) Redacted


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(D.I. 163, Ex 1 at 182:10-183:11)(objection omitted)(emphasis added) This testimony does not state or suggest that the alleged invention (*i e*, a dimeric biologically active fusion protein) could be accomplished without undue experimentation. In fact, it suggests otherwise Due to the uncertainty, a conception could not have occurred until an embodiment was reduced to practice



Therefore, a conception could not occur until the alleged inventions were reduced to practice

D. The January 4-5, 1988 Laboratory Notebook Page did not Encompass all of the Claim Limitations

A conception is not complete if it does not encompass all claim limitations. *See Singh*, 317 F.3d at 1340; *see also Izumi Products Co v Koninklijke Philips Electronics N V*, 315 F Supp. 2d 589, 607 (D Del 2004)(holding plaintiffs failed to prove prior conception since their evidence did not contain the idea of all limitations of the claim)

In establishing conception, ZymoGenetics must "show possession of every feature recited in the count, and that every limitation of the count must have been known to the inventor at the time of the alleged conception" *See Hitzeman*, 243 F.3d at 1354

ZymoGenetics does not address most of the limitations of the asserted claims For example, nowhere does it address: "eukaryotic host cells," "transcriptional promoters,"

"secretory signal sequences," etc. (Claim 21 of the '725 Patent) (D.I. 174, Exh. 2 at ZG 000844). And all asserted claims require either a non-immunoglobulin polypeptide or ligand-binding domain of a receptor "requiring dimerization for biological activity." (*Id.*, Exh. 1 at ZG 000003; *Id.*, Exh. 2 at ZG 000844). Yet, there is no discussion of a polypeptide or a receptor "requiring dimerization for biological activity" in the laboratory notebook entry. At best, there was speculation that dimerizing might affect the affinity of PDGF-R for PDGF. (D.I. 163, Ex. 1 at 182:10-183:1; 183:12-17). Because ZymoGenetics has failed to address all the claim limitations, and because each of the claim limitations is not present in the purported conception document, ZymoGenetics has failed to provide evidence of a conception.

Further, while ZymoGenetics cites to its expert, this evidence is merely opinion, not fact, and is insufficient to create an indisputable fact [redacted]. Therefore, ZymoGenetics has failed to set forth evidence of a conception.

III. ZymoGenetics has Failed to set Forth Evidence that it ever Reduced the Alleged Inventions to Practice

ZymoGenetics asserts the alleged inventions were reduced to practice before September 28, 1988. In order for its allegation to prevail, it must set forth evidence that an embodiment of the invention *meeting every claim limitation* was produced and *works for its intended purpose* prior to this date. *See Hybritech*, 802 F.2d at 1376. Again, ZymoGenetics ignores the vast majority of the claim limitations. For this reason alone ZymoGenetics' allegation that it reduced

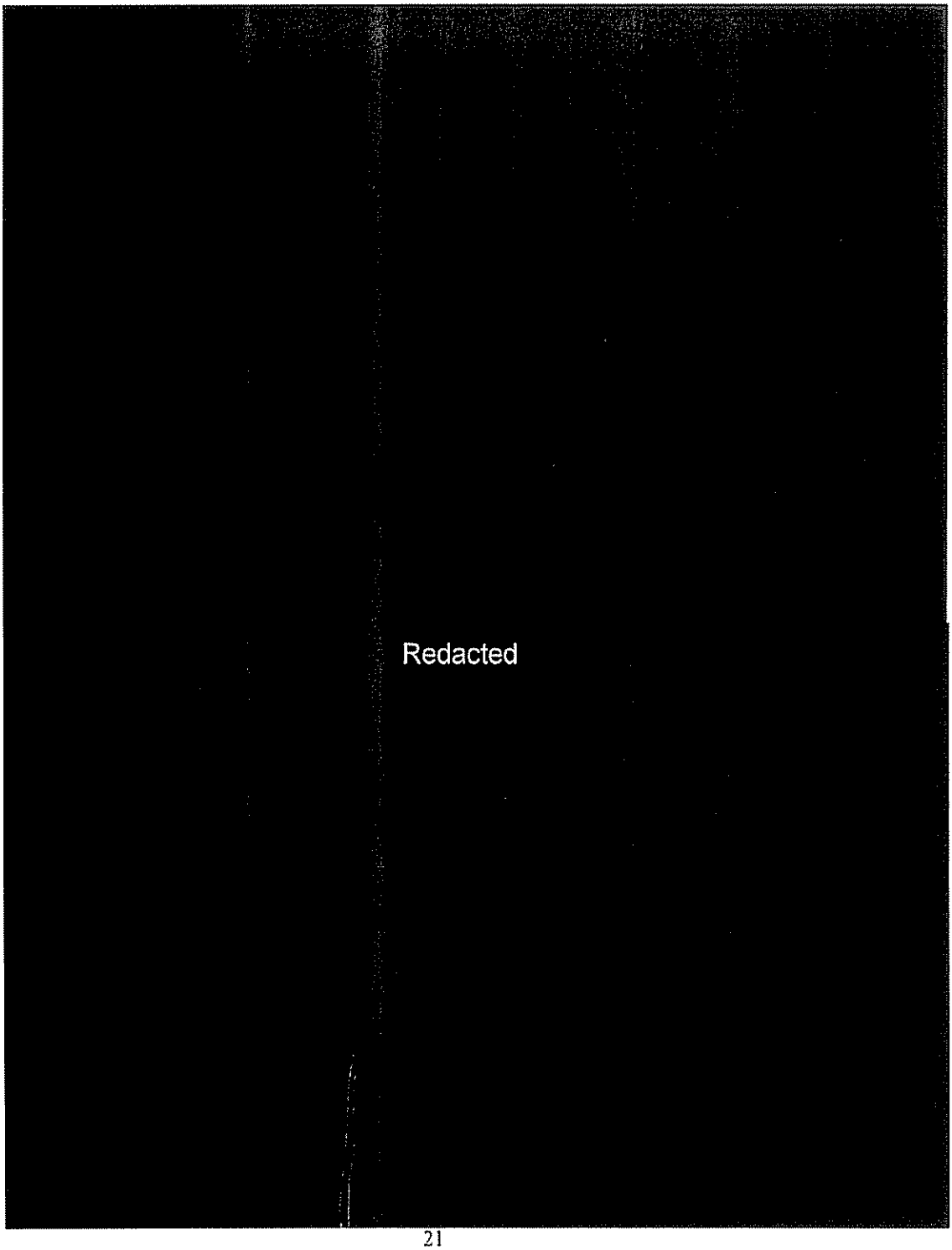
the alleged inventions to practice should fail In particular, ZymoGenetics has not set forth evidence of at least the following:

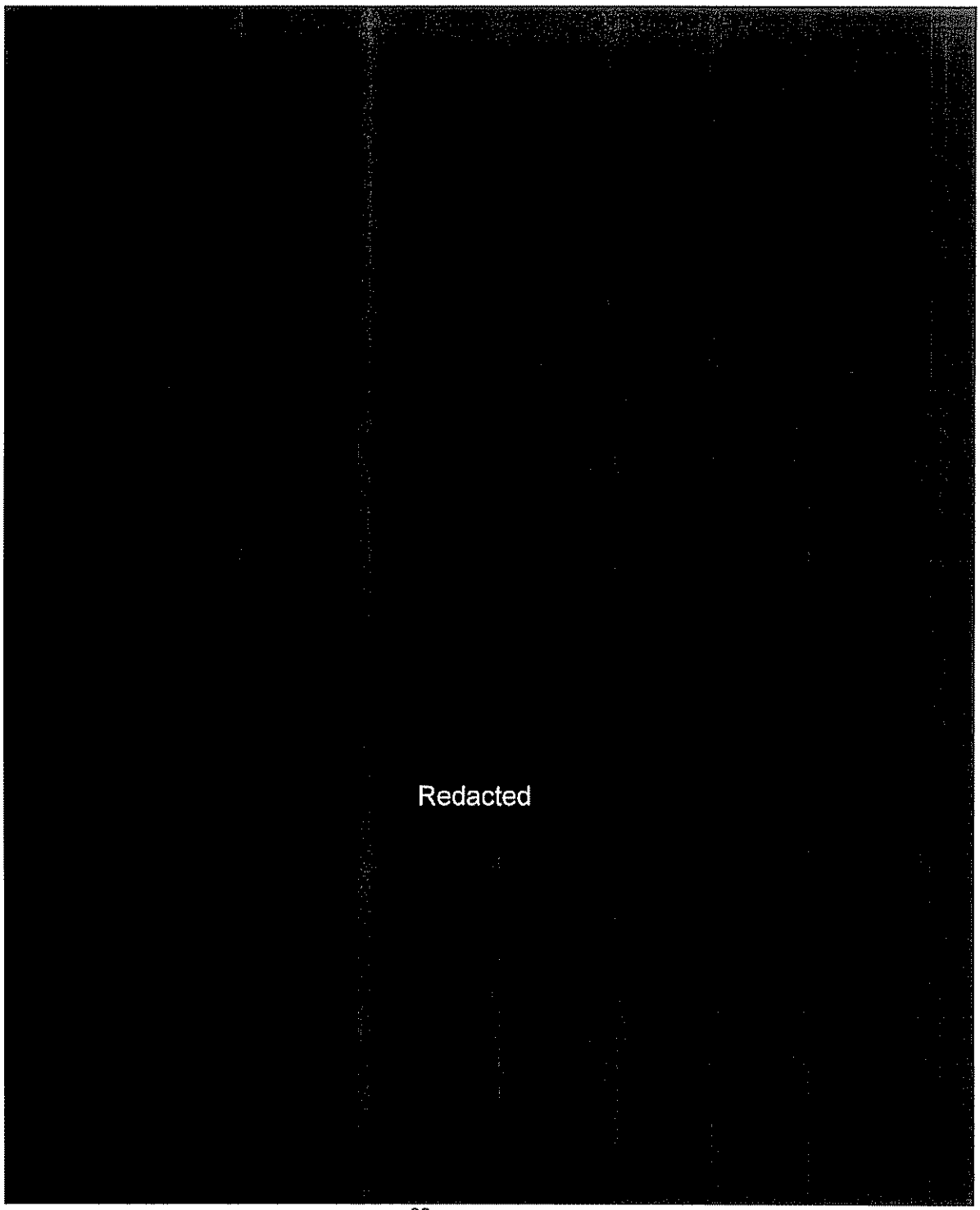
- That its purported "dimerizing proteins" were in fact associating to form dimers
- That its resulting fusion proteins were biologically active.

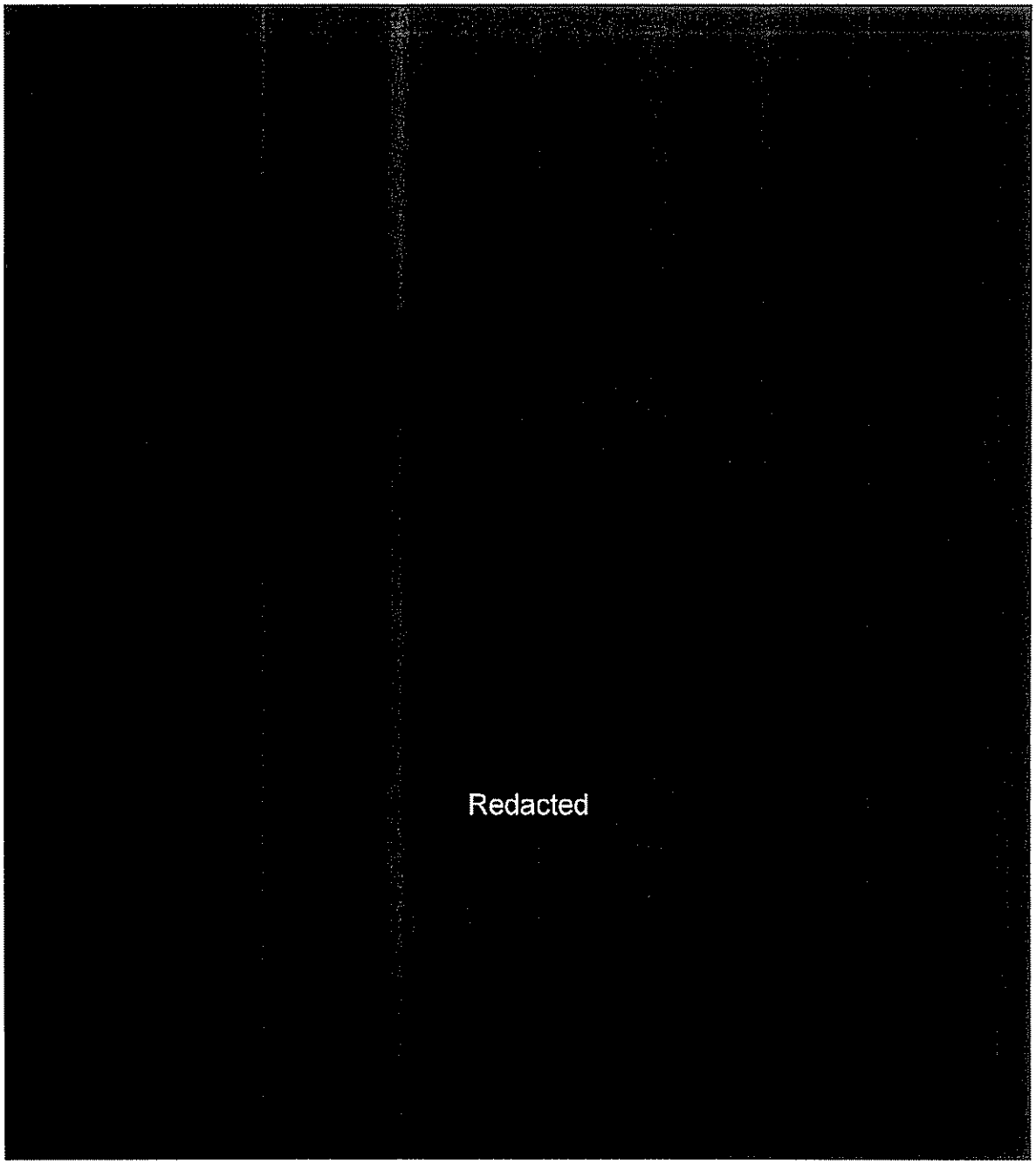
A. ZymoGenetics has not Set Forth Evidence that it Made Dimers

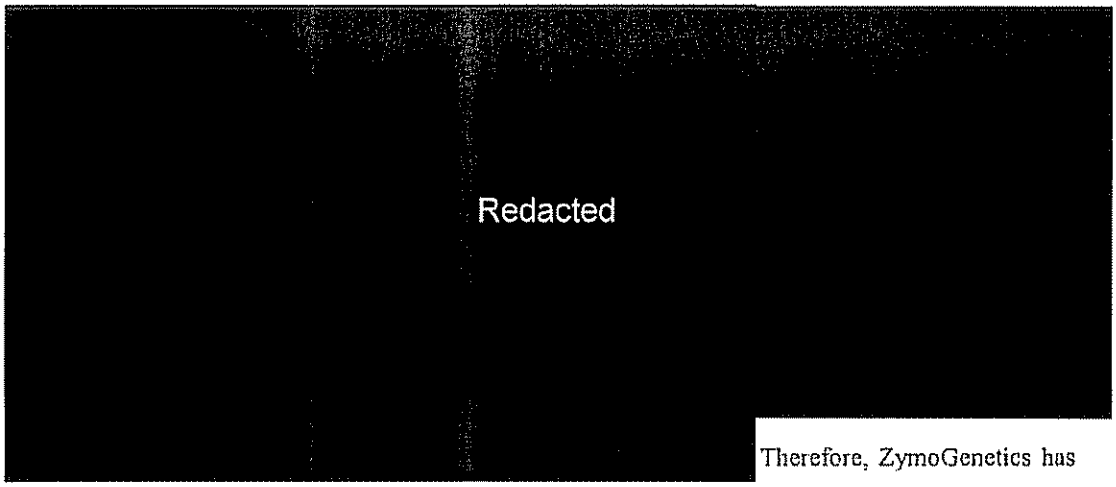
Not surprisingly, ZymoGenetics does not directly address dimerization of the fusion protein in its brief Rather, it relies on the "opinion" of its expert, Dr Purdue

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Therefore, ZymoGenetics has failed to show any evidence that it reduced its alleged inventions to practice – because despite the fact that every asserted claim contains the limitation "dimerizing protein", it never showed any purported dimerizing proteins were in fact associating to form dimers.[16]

The Federal Circuit has held that direct evidence that an inventor prepared a fusion protein having the claimed structure is necessary. For example, in *Schendel v. Curtis*,[17] Schendel attempted to argue an earlier invention date (by way of prior reduction to practice) than the Curtis application. *Schendel v. Curtis*, 83 F.3d 1399, 1400-02 (Fed. Cir. 1996). The claims at

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[15] 

[16] ZymoGenetics' proposed construction of "dimerizing protein" is "A polypeptide chain having affinity for a second polypeptide chain, such that the two chains associate under physiological conditions to form a dimer. The second polypeptide chain may be the same or a different chain." (Plaintiff ZymoGenetics, Inc.'s Opening Claim Construction Brief at 11) (D.I. 156). Therefore, ZymoGenetics must prove, at a minimum, that its purported dimerizing protein was actually functioning as a dimerizing protein.

[17] While the *Schendel v. Curtis* appeal was based on an interference proceeding, it is relevant to reduction to practice of fusion proteins and the uncertainty related thereto.

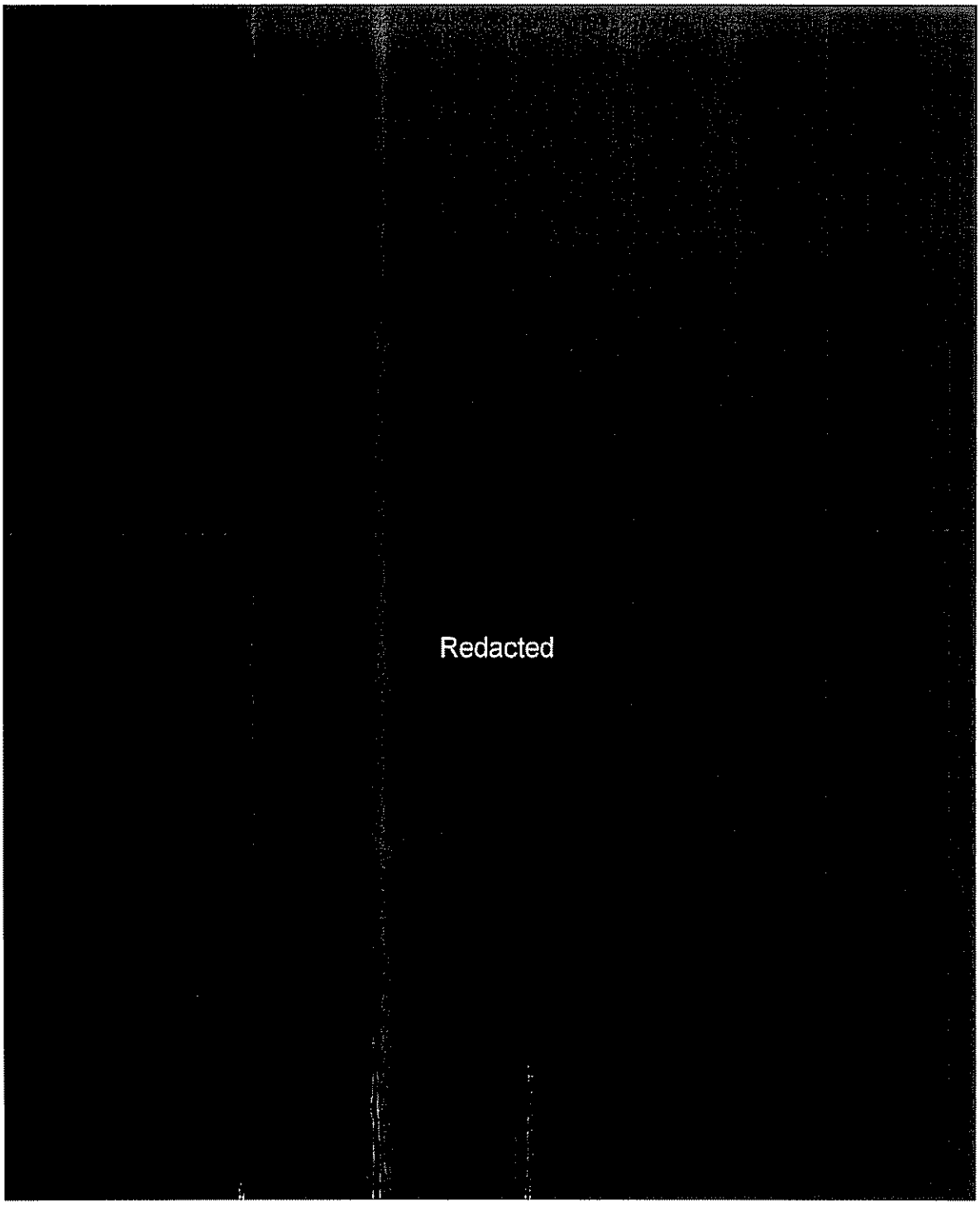
issue were the manufacture of a fusion protein composed of "IL-3" joined to "G-CSF." *Id.* at 1401, fn5. The Federal Circuit concluded that Schendel did not provide direct evidence that he had prepared a fusion protein having the structure required by the count. *Id.* at 1402-03. While Schendel had stated he constructed a plasmid and lab notebooks suggested obtaining primers, "he provided no data showing what he obtained was the purported fusion protein." *Id.* at 1403. The record was "devoid of any explanation linking the biological activity data to the composition or structure of the purported fusion protein." *Id.* Like Schendel, the present record is devoid of any evidence that what ZymoGenetics made was a fusion protein that was a dimer and was biologically active.

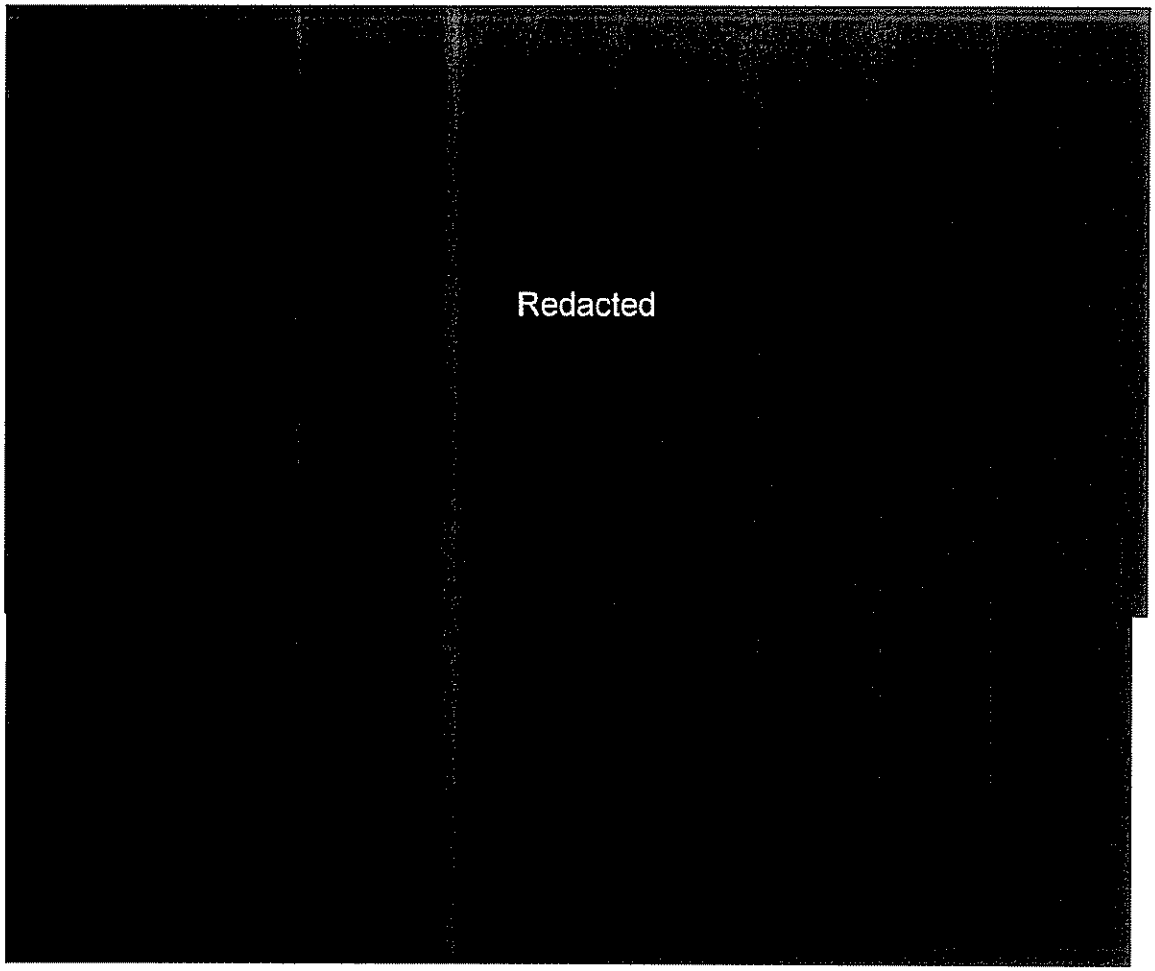
B. ZymoGenetics has not Set Forth Evidence that it Made a "Biologically Active" Fusion Protein

ZymoGenetics' goal was to make a dimerized biologically active fusion protein. (*See* generally D.I. 123); (*See also* Preambles to Asserted Claims of the Patents-In-Suit) (D.I. 174, Exh. 1 at ZG 000003; Exh. 2 at ZG 000844). But under ZymoGenetics' improper assertion that binding is not a biological activity, it cannot assert that it ever made a "biologically active" fusion protein – because the experiments it cites to are binding experiments. In an attempt to sweep this glaring inconsistency under the rug, it states that ZymoGenetics' scientists made a "functional" fusion protein rather than one that was "biologically active". (*See, e.g.*, D.I. 161 at 11-12) (D.I. 165 at ¶¶ 10-12).[18] But the goal was not a "functional" protein, the goal was a "biologically active" fusion protein.

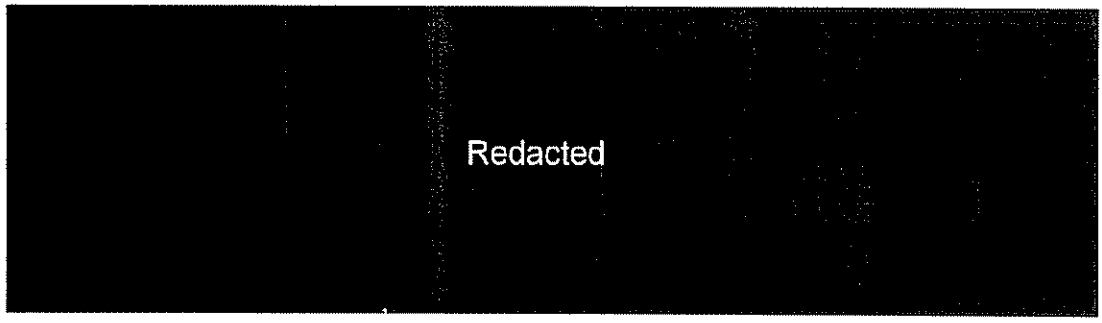
Even analyzed under the correct interpretation that binding is a biological activity, ZymoGenetics' arguments would fail [redacted]

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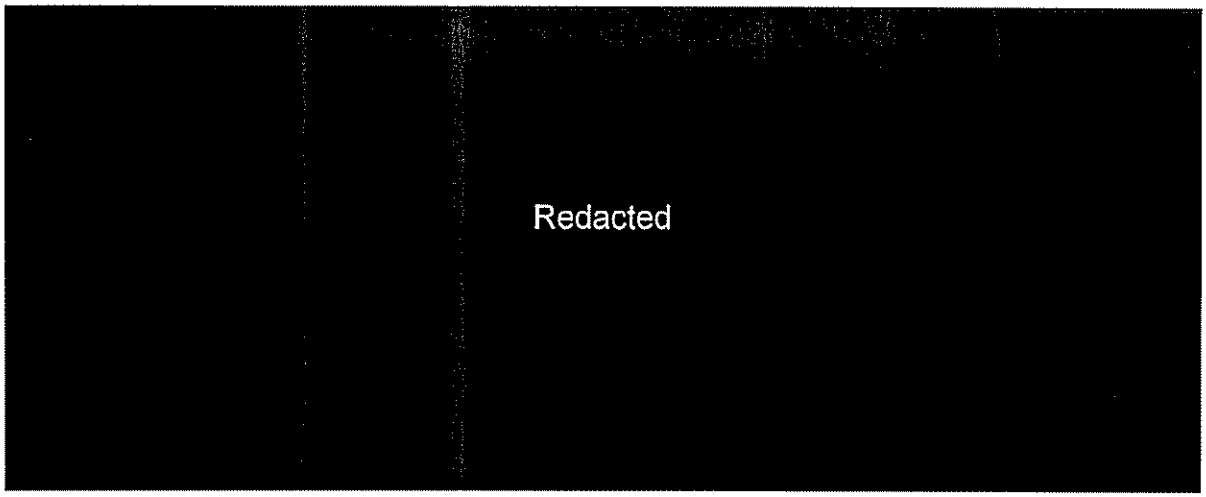
ZymoGenetics has failed to set forth evidence of a reduction to practice



IV. ZymoGenetics has Failed to set forth Evidence of Diligence

Even if ZymoGenetics' alleged inventions were conceived on January 4-5, 1988 (which they were not) and it set forth evidence it actually reduced the alleged invention to practice (which it did not), ZymoGenetics has failed to set forth evidence of diligence between its purported conception and alleged reduction to practice. ZymoGenetics does not allege any actual reduction to practice prior to the January 22, 1988 priority date of the Seed Patent. To avoid the invalidating effect of Seed, ZymoGenetics must show a prior conception coupled with a continuous and reasonable diligence starting before January 22, 1988 and continuing without interruption up to a reduction to practice. *See Griffith v. Kanamaru*, 816 F.2d 624, 625-26 (Fed Cir. 1987). In other words, as ZymoGenetics' brief states, it must "connect the conception with its reduction to practice . . . so that they are substantially one continuous act." (D.I. 161 at 5)

ZymoGenetics sets forth its arguments concerning diligence on pages 9-11 of its brief. Out of the 200+ days between the alleged conception (January 4-5, 1988) and the purported first possible reduction to practice (September 1, 1988), ZymoGenetics cites to documents that indicate the scientists worked on the project for 7 days during this time period – March 22, 1988; April 18-22, 1988; and June 30, 1988.



Redacted Therefore, there is an unexplained gap between January 4-5, 1988 and March 22, 1988. More than 70 days passed before ZymoGenetics' alleges any work commenced – *and the priority date of the Seed Patent (i.e., January 22, 1988) falls squarely in the midst of this time period*. *See In re Mulder*, 716 F.2d 1542, 1545 (Fed. Cir. 1983) (holding applicant failed to show reasonable diligence where applicant presented no evidence of diligence during a two-day period prior to the critical date).

The next event relied on by ZymoGenetics comes nearly a month later -- April 18-22, 1988. Redacted ZymoGenetics' analysis of diligence in its brief stops there.[21] ZymoGenetics provides no explanation of the unexplained gaps in time and therefore it has failed to set forth evidence concerning diligence. *See Litchfield v. Eigen*, 535 F.2d 72, 76-77 (CCPA 1976)(J. Rich)(holding inventors failed to establish diligence when they provided no explanation for inactivity in testing compound).[22]

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[21] While not addressing these in its arguments concerning diligence, ZymoGenetics also identifies September 1 and 12-19, 1988 as dates when activities occurred, but does not rely on these in its arguments concerning diligence.

[22] In the case law cited by ZymoGenetics, the inventors showed continuous activity during the critical period. *Monsanto Co. v. Mycogen Plant Science, Inc.*, 261 F.3d 1356, 1368-70 (Fed. Cir. 2001) (cited by ZymoGenetics); *Brown v. Barbacid*, 436 F.3d 1376, 1380-82 (Fed. Cir. 2006) (inventors produced laboratory notebooks that showed continuous daily activity) (cited by ZymoGenetics). In contrast, ZymoGenetics has cited to several discrete events over a 9 month time period and unsubstantiated general allegations of diligence. *See American Standard, Inc. v. Pfizer, Inc.*, 722 F. Supp. 86, 122 (D. Del. 1989)("general assertions of diligence without corroboration are insufficient . . . "); *Chen v. Bouchard*, 347 F.3d 1299, 1311-12 (Fed. Cir. 2003) (failing to find reasonable diligence when the junior party cited no evidence of who performed what activities during the critical period).

evidence of diligence – there must be outside corroboration *See Gould v. Schawlow*, 353 F 2d, 908, 919-920 (C C.P.A 1966); *see also Loral Fairchild Corp v Victor Co of Japan, Ltd*, 931 F. Supp. 1014, 1030 (E D N.Y 1996)(Circuit Judge Rader sitting by designation) ("[a]n inventor must provide specific details on activity during the critical period. General testimony that the inventor worked continuously and diligently will not suffice")

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Because ZymoGenetics has failed to provide evidence of continuous activity or specific details on activity during the critical period, its summary judgment motion should fail.

V. ZymoGenetics' Attempt to Exclude Dr. Ravetch's Opinions

ZymoGenetics claims that the testimony of Bristol's expert, Dr. Ravetch, is "legally insufficient . . . because he erroneously assumes that the inventors must have the complete 'operative' invention in order for there to be conception." (D I 161 at 8). The standard applied by Dr. Ravetch in his expert report is precisely the standard that must be applied when determining conception -- *i e*, a "the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice." *Burroughs Wellcome*, 40 F 3d at 1228 (citation omitted)

ZymoGenetics also claims that Dr. Ravetch's opinions are "legally inadequate" and rehashes its Daubert motion by claiming that Dr Ravetch does not provide a "basis" for his opinions In lieu of an expansive discussion on this issue, Bristol submits that Dr Ravetch's opinions are legally adequate and respectfully invites the Court to review Bristol's Answering Brief to ZymoGenetics' Motion to Exclude Bristol's experts testimony (D I 212). However, it should be pointed our that ZymoGenetics' conduct made it unreasonable for Dr Ravetch to address conception and reduction to practice in a detailed fashion in his opening expert report

Relying on Fed. R. Civ. P. 33(d), ZymoGenetics identified more than 5,000 laboratory notebook pages in response to Bristol's interrogatory concerning conception and reduction to practice. (Plaintiff ZymoGenetics' Fifth Supplemental Response to Bristol-Myers Squibb Company's First Set of Interrogatories: No. 4) (V.A.B. Exh. 4 at 5-6). Magistrate Thynge considered the number of pages to be overly burdensome and ordered ZymoGenetics to cull down this number (D.I. 109 at 43-44). While ZymoGenetics reduced the number of pages, there were still more than 1,000 laboratory notebook pages identified at the time that Dr. Ravetch authored his expert report. (V.A.B. Exh. 4 at 6-7). It was not until Dr. Purdue's rebuttal expert report that the number of laboratory notebook pages relied upon for conception and reduction to practice was reduced to less than 30 pages. And, as Dr. Ravetch had not yet had an opportunity to address Dr. Purdue's opinions (as these were set forth in Dr. Purdue's rebuttal report), Dr. Ravetch filed a declaration to address them. (D.I. 208).

CONCLUSION

For the foregoing reasons, ZymoGenetics' motion for summary judgment should be denied.

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FOR THE DISTRICT OF DELAWARE

CERTIFICATE OF SERVICE

I hereby certify that on August 18, 2008, I electronically filed the foregoing document with the Clerk of the Court using CM/ECF which will send notification of such filing to the following and which has also been served as noted:

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I hereby certify that on August 18, 2008, the foregoing document was sent to the following non-registered participants in the manner indicted:

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FOR THE DISTRICT OF DELAWARE

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