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The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 276

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

RONALD A. HITZEMAN, ARTHUR D. LEVINSON
and DANIEL G. YANSURA

Junior Party,¹

v.

WILLIAM J. RUTTER, PABLO D.T. VALENZUELA,
BENJAMIN D. HALL and GUSTAV AMMERER

Senior Party²

Patent Interference No. 102,416

FINAL HEARING: January 20, 1999

Before SOFOCLEOUS, DOWNEY and ELLIS, ***Administrative Patent Judges.***

ELLIS, ***Administrative Patent Judge.***

Interference No. 102,416

FINAL DECISION

This is an interference between HITZEMAN et al. and RUTTER et al. Rutter is senior party by virtue of Application 06/289,915, filed August 4, 1981.

As a preliminary matter, we point out that the subject matter of the present proceeding, Interference 102,416, is related to Interference 102,989, and many of the issues raised on appeal are the same. Consequently, the parties presented arguments for both interferences at the final hearing on January 20, 1999. Thus, concurrent with the present decision, this merits panel is also rendering a decision in Interference 102,989. However, we are not consolidating the interferences. The issues raised in each interference have been considered only on the basis of the evidence provided therein.

I. Background

Hepatitis B virus (a.k.a. serum hepatitis) is a major world-wide health problem which causes, *inter alia*, severe liver damage and death. It has been reported, prior to the filing of the present applications, that the plasma of humans infected with the virus show three major particulate structures containing the

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280, 815-819 (1979), see p. 815, col. 1, para. 2].

The subject matter at issue is directed to a DNA expression vector which comprises a promoter capable of expression in a yeast host cell, a DNA sequence which encodes the hepatitis B virus surface antigen (hereinafter HBsAg), and translational start and stop signals; wherein said vector must be capable of directing the expression of an HBsAg particle having a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles.³ Since the particles consist essentially of the surface antigen, they are said to be useful as a vaccine against hepatitis B viral infection.

Count 1, the sole count at issue, reads as follows:

Count 1

A DNA expression vector capable of replication and phenotypic selection in [a] yeast host strain comprising a promoter compatible with a yeast host strain and a DNA sequence encoding hepatitis B surface antigen, said sequence being positioned together with translational start and stop signals in said vector under control of said promoter such that in a transformant yeast strain it is expressed to produce hepatitis B surface antigen in particle form having a sedimentation rate which is virtually identical to that of authentic 22 nm hepatitis surface antigen particles;

or

a method of producing hepatitis B surface antigen in particle form suitable for use in conferring immunogenicity to hepatitis B virus in a susceptible human which

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comprises:

- (a) providing a DNA transfer vector capable of replication and phenotypic selection in yeast host strains,
- (b) providing a DNA fragment comprising a promoter compatible with a yeast host strain,
- (c) providing a DNA fragment encoding hepatitis B surface antigen,
- (d) assembling the fragments of steps (a), (b), and (c) together with translational start and stop signals for the fragment of steps (c) to form a replicable expression vector so that said sequence of step (c) is under control of said promoter,
- (e) transforming a yeast strain with the vector of step (d),
- (f) allowing the yeast transformant to grow under fermentation conditions until said hepatitis B surface antigen is produced therein, and
- (g) recovering said hepatitis B surface antigen in particle form having a sedimentation rate which is virtually identical to that of authentic 22 nm hepatitis surface antigen particles.

The claims of the parties which correspond to Count 1 are:

Hitzeman et al.: Claims 1 through 11.

Rutter et al. : Claims 6 through 14 and 20 through 34.

Both parties filed briefs and were represented by counsel at Final Hearing.

No issue of interference-in-fact or separate patentability of the claims is raised.

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- (1) Whether the ability of the expression vector to produce HBsAg in particle form having a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles is a limitation of the count.
- (2) Whether Hitzeman et al. have established an earlier date of conception.
- (3) If Hitzeman et al. were the first to conceive, were Hitzeman et al. diligent to an actual reduction to practice?⁵

In addition, the following opposed motions were filed:

- (4) Motion to strike the rebuttal testimony of Hitzeman et al. witnesses Drs. Dreesman and Peterson from the record, filed by the party Rutter et al. (Paper No. 230).
- (5) If party Rutter's motion to strike is denied, a motion to admit the surrebuttal testimony of their witnesses Drs. Robinson, Holland and Schekman, filed by Rutter et al. (Paper No. 230).
- (6) Motion to strike Rutter Exhibit RS-7 offered into evidence by junior party Hitzeman from the record, filed by Rutter et al. (Paper No. 231).

⁴(...continued)

II.
Decision on Motions

Motion (4)

The Rutter et al. motion to strike the rebuttal testimony of Hitzeman et al. witnesses Drs. Dreesman and Peterson from the record (Paper No. 230) is **granted** for the reasons set forth therein. This merits panel agrees with Rutter et al. that the ability of the expression vector to “inherently” express HBsAg in the form of particles having a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles, is part of Hitzeman et al.'s case-in-chief. Accordingly, the rebuttal testimony is improper and will be stricken from the record.

Motion (5)

This motion is dismissed as moot inasmuch as it is contingent on the denying of Rutter et al.'s motion (4), **supra**, which was granted.

Motion (6)

This motion is also dismissed as moot since it is indirectly contingent on the granting of Rutter et al.'s motion (5), **supra**, which was dismissed. That is, Rutter's Exhibit RS-7 was offered into testimony during the cross examination of Dr. Schekman as part of the surrebuttal testimony for Rutter et al. Since the surrebuttal testimony of

III.
The Count

Conception requires that “a party ***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.***” [Emphases added.] ***Coleman v. Dines***, 754 F.2d 353, 359, 224 USPQ 857, 862 (Fed. Cir. 1985). However, before we can determine whether a party has demonstrated conception of an invention within the scope of the count, we must first determine what are the limitations of the count.

Here, the parties agree that establishing conception requires, at a minimum, a showing by Hitzeman et al., that they envisioned as their invention, a chemical compound comprising a DNA expression vector capable of replication and phenotypic selection in a yeast host cell comprising a promoter compatible with a yeast host strain, a DNA sequence encoding hepatitis B surface antigen, and translational start and stop signals in operative linkage. At issue is whether establishing conception of an invention within the scope of the count requires that Hitzeman et al. demonstrate that they envisioned that expression of the DNA sequence would result in the production of HBsAg particles, wherein said particles have a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles. Thus, we must determine whether

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expression vector “produce HBsAg in particle form having a sedimentation rate which is virtually identical to that of authentic 22 nm hepatitis surface antigen particles” is an inherent property of the DNA construct set forth in the count. Hitzeman Brief, p. 57, last sentence. According to Hitzeman et al.,

Nothing is added to the definition of the structure by this recitation of the count. The formation of particles is a naturally occurring consequence of the expression of the vector of the Count in yeast. Particle formation is not the result of manipulation of the content of the DNA, i.e., particle formation require [sic, requires] no human DNA manipulation for it to occur. Brief, p. 58, para. 1.

Thus, as we understand it, Hitzeman et al.’s position is that particle formation is an inherent characteristic of the yeast host cell which is transformed with the DNA expression vector and, therefore, it is not necessary for them to provide evidence of the conception of said particles or their sedimentation rate.⁶ Hitzeman Brief, pp. 57-61. We find that this argument fails on several accounts.

First, Hitzeman et al. have not provided any evidence to support the position that the formation in yeast of HBsAg particles having a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles is an inherent characteristic of an expression vector comprising, *inter alia*, a yeast-compatible promoter and a DNA

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sequence encoding HBsAg. We point out that statements in the brief cannot take the place of evidence in the record. ***Meitzner v. Mindick***, 549 F.2d 775, 782, 193 USPQ 17, 22 (CCPA), ***cert. denied***, 434 U.S. 854 (1977).

Second, Hitzeman et al. have not cited any case law to support the “inherency” theory they propose. To the contrary, as discussed above, the court has held that conception requires that “every limitation of the count must have been known to the inventor” on the alleged date. ***Coleman v. Dines, supra***. Thus, it reasonably follows, that in order to establish conception of an invention within the scope of the count, Hitzeman et al. must show that they envisioned an invention having all the limitations set forth therein.

Third, the count is not directed to any DNA vector comprising the DNA sequence encoding HBsAg, but only to those vectors wherein expression of said DNA sequence results in the production of HBsAg particles, such that said particles have a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles. Thus, the DNA vector of the count is distinguished from vectors comprising the identical components but which (i) do not direct the expression of HBsAg in any

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expression vector having five elements as follows:

(1) a DNA expression vector capable of replication and phenotypic selection in a yeast host cell; which comprises:

(2) a promoter compatible with a yeast host strain;

(3) a DNA sequence encoding HBsAg which is operably linked to said promoter;

(4) translational start and stop signals which are directly and operably linked to said DNA sequence; and

(5) wherein the expression of said DNA sequence results in the production of HBsAg in particle form wherein said particles have a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles.

Our finding that element (5), above, is a limitation, which the parties must have envisioned in order to establish conception of an invention within the scope of the count, is further evident from the *ex parte* prosecution of the applications involved, and the motions filed, in this interference proceeding.

A. Ex parte prosecution

It is well settled that the insertion of a limitation into a claim to overcome the examiner's rejection "is strong, if not conclusive, evidence of materiality." *Cf. Parks v. Fine*, 773 F.2d 1577, 1579, 227 USPQ 432, 434 (Fed. Cir. 1985). In turning to the

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originally presented in Hitzeman Application 06/298,236, filed August 31, 1981, and Application 06/599,387, filed April 12, 1984, were directed to a DNA expression vector capable of expressing HBsAg in particle form.⁷ After Hitzeman et al. amended the claims to recite the expression of HBsAg in particle form "having a sedimentation rate which is virtually identical to that of authentic 22 nm hepatitis surface antigen particles," in the preliminary amendment filed in continuation Application 07/042,604, filed April 22, 1987, the examiner indicated that the claims were allowable over the applied prior art. Paper No. 13, filed April 27, 1987, pp. 1-2; PTO Office action, p. 4, mailed October 8, 1987 in Paper No. 15; HX "Rutter Exhibit 32," pp. 1-2. That this amendment to the claims was necessary to overcome the examiner's rejection is confirmed by the testimony of Mr. Hensley, counsel for Hitzeman et al. Mr. Hensley testified that the

⁷ Claim 1, as originally filed, in Hitzeman Applications 06/298,236 and 06/599,387, reads as follows:

1. A DNA expression vector capable of replication and phenotypic selection in yeast host strain comprising a promoter compatible with a yeast host strain and a DNA sequence encoding hepatitis B surface antigen, said sequence being positioned together with translational start

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amendment to the claims was made in order to have the claims allowed.⁸

Contrary to Hitzeman et al.'s arguments on pp. 58-59 of the main Brief, we find that the prosecution of the Rutter et al. applications involved in the present interference proceeding⁹ follows basically the same line of reasoning. The originally-filed claims were directed to a DNA vector comprising a yeast promoter and a DNA segment encoding HBsAg.¹⁰ Only after Rutter et al. copied claims from Hitzeman U.S. Patent

⁸ The testimony of Mr. Hensley reads as follows:

Q. In looking at Exhibit 30, can you identify how you have responded to that continued rejection in Exhibit 29?

A. The claims were amended to recite particle size. That was my response.

Q. And that amendment is made in Exhibit 30?

A. Yes.

Q. And the amendment was made in order to have the claims allowed?

A. The Office action led me to believe that they would be, upon that amendment; yes.

⁹ We direct attention to the Rutter et al. applications: Application 06/289,915, filed August 4, 1981; Application 06/402,330, filed July 27, 1982; and Application

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4,803,164¹¹ which contained the limitation that the yeast promoter, when expressed, produced “hepatitis B antigen in particle form having a sedimentation rate which is virtually identical to that of authentic 22 nm hepatitis surface antigen particles,” was the subject matter of the Rutter application deemed patentable by the examiner. This amendment to the claims also laid the foundation for the present interference proceeding.

Thus, the *ex parte* prosecution of both the Hitzeman et al. and Rutter et al. applications indicates that the claim limitations as to the particulate form and sedimentation rate of the yeast-derived HBsAg product set forth in the claims (and count 1) are the physical properties which distinguish the present invention from the applied prior art. That is, were it not for these properties the examiner would have maintained his rejection that the mere expression of a DNA sequence encoding HBsAg in transformed yeast host cells would have been obvious to one of ordinary skill in the art over the applied prior art which taught the expression of an HBsAg product (HBsAg monomers) in transformed *E. coli* host cells. Accordingly, from the *ex parte* prosecution, it is reasonable to conclude that the production of “hepatitis B surface antigen in particle form having a sedimentation rate which is virtually identical to that of

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B. Motions filed in the present interference proceeding

That the particle form and the sedimentation rate of the HBsAg product made in yeast are limitations of the count is also evinced by Hitzeman et al.'s actions in response to Rutter et al.'s motion to amend the count "to eliminate any reference to sedimentation rate and particle size." Preliminary Motion to Amend Count under 37 CFR § 1.633(c)(1), Paper No. 12, p. 2, submitted December 20, 1990. In the opposition to the motion, Hitzeman et al. argued that the limitation that the particles have a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles was necessary to distinguish Rutter et al.'s claimed invention over the prior art. We direct attention to the ***Hitzeman et al. Opposition to Rutter et al. Motion to Amend Count under 37 CFR § 1.633(c)(1)***, filed January 22, 1991, in Paper No. 26, see p. 5, para. 1 and the para. bridging pp. 5-6. The Examiner-in-Chief (hereinafter, Administrative Patent Judge or APJ) denied the motion to amend stating:

for the reasons stated in the Hitzeman opposition (Paper No. 26).
The EIC agrees with Hitzeman that the proposed count removes a

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particle is a limitation which was necessary in order to overcome the prior art applied in the examiner's rejection, Hitzeman et al. are now in a poor position to argue that it should not be a limitation which must have been envisioned in order to establish conception of an invention within the scope of the count.

In view of the foregoing, we find that the production of the 22 nm HBsAg particles in transformed yeast host cells is the crux of the invention described in the count. That is, it is the feature which distinguishes (i) the vector of the count from other recombinant vectors which comprise a DNA sequence encoding HBsAg, and (ii) the HBsAg product made by the vector of the count as opposed to the HBsAg monomers made using other vectors described in the prior art. Hitzeman et al. do not offer any case law which supports their position that the doctrine of inherency applies to conception. To the contrary, the court has held that for conception (and reduction to practice) there "must be **contemporaneous recognition and appreciation** of the invention represented by the counts." [Emphasis added.] **Breen v. Henshaw**, 472 F.2d 1398, 1401, 176 USPQ 519, 521 (CCPA 1973) (Conception of an invention cannot be established **nunc pro tunc**). Accordingly, we hold that in order to establish conception of an invention within the scope of the count, each party must demonstrate

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of every feature recited in the count).

IV. Conception

Conception is the touchstone of inventorship, the completion of the mental part of the invention. **Sewall v. Walters**, 21 F. 3d 411, 415, 30 USPQ2d 1356, 1359 (Fed. Cir. 1994). As set forth by the court in **Burroughs Wellcome Co. v. Barr Laboratories, Inc.**, 40 F.3d 1223, 1228, 32 USPQ2d 1915, 1919 (Fed. Cir. 1994):

Conception is complete only when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation. [Citations omitted.]

* * *

... the test for conception is whether the inventor had an idea that was definite and permanent enough that one skilled in the art could understand the invention; the inventor must prove conception by corroborating evidence, preferably by showing a contemporaneous disclosure. An idea is definite and permanent when the inventor has a specific, settled idea, a particular solution to the problem at hand, and not just a general goal or a research plan he hopes to pursue. **See Fiers v. Revel**, 984 F.2d 1164, 1169, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993); **Amgen, Inc. v. Chugai Pharmaceutical Co**, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1989) (no conception of chemical compound based solely on its biological activity). The conception analysis necessarily turns on the inventor's ability to describe his invention with particularity. Until he can do so, he cannot prove possession of the complete mental picture of the invention. These rules ensure that patent rights attach only when an idea is so far developed that the inventor can point to a definite, particular invention.

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(CCPA 1976); *Linkow v. Linkow*, 517 F.2d 1370, 1373, 186 USPQ 223, 225 (CCPA 1975); *Frilette v. Kimberlin*, 412 F.2d 1390, 1391, 162 USPQ 148, 149 (CCPA 1969), *cert. denied*, 396 U.S. 1002 (1970). See also 37 CFR § 1.657(1993).

Hitzeman et al. allege that they had complete conception of an invention within the scope of the count on February 3, 1981. Hitzeman Brief, p. 49. According to Hitzeman et al., “[t]he Count requires a DNA construct comprising (1) a yeast promoter, (2) a terminator of transcription, and (3) a DNA sequence encoding HBsAg and which is capable of expressing HBsAg in particle form in yeast.” *Id.*, p. 62. As such, Hitzeman et al. were the first to conceive of the invention of the count.¹² *Id.* Thus, Hitzeman et al. contend that “all of the DNA fragments required to construct the DNA of the count were known and available to the Genentech inventors as of February, 1981.” *Id.*, p. 63. As to the production, in yeast, of HBsAg particles having a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles, Hitzeman et al. present two arguments: (i) that the Hitzeman co-inventors “had a hope that particles would be produced” in yeast, and (ii) “[t]his recitation in the Count merely recites an inherent property of the DNA construct of the Count.” *Id.*, p. 57.

¹² We take issue with Hitzeman et al.’s characterization of the limitations required

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As evidence of conception of a definite and permanent idea of the complete and operative invention, Hitzeman et al. provide the testimony of Dr. Hitzeman (HR 996) and a page from one of his laboratory notebooks which is said to describe a planning session with Dr. David Goeddel (HX16, p. 51). The testimony of Mr. Hagie and Dr. Goeddel are offered as independent corroboration of this evidence. ***Price v. Symsek***, 988 F.2d 1187, 1196, 26 USPQ2d 1031, 1038 (Fed. Cir. 1993) (Inventor testimony offered to show conception, diligence or communication to another must be corroborated).

As evidence that Hitzeman et al. were in possession of all the DNA fragments required to construct the DNA of the count, Hitzeman et al. rely on work performed on various projects in which Dr. Hitzeman, Dr. Levinson and Mr. Yansura were engaged prior to February 3, 1981. This includes European patent application 060057 (HX21) and the corresponding U.S. application 06/237,913; the testimony of co-inventor, Mr. Yansura (HR1871-722; HR1939; HR1867-73; HX35, HX34); the "Fourth Quarter Scientific Progress Report, November 1, 1979- February 25, 1980," source undisclosed (HX8); and a 1980 publication of Dr. Hitzeman (HX26). This work is said to be corroborated by Mr. Hagie (HX6, 7, 10, 11, 18 and 27-28); Ms. Chen (HR1990-92,

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yeast, Hitzeman et al. rely on the testimony of co-inventor Dr. Hitzeman (HR1116-18; HR1113). Hitzeman et al. do not provide any independent corroboration of this testimony.

As to Hitzeman et al.'s position that the production of HBsAg particles is an inherent property of the DNA construct of the count, we direct attention to our discussion on pp.8-16, above. Briefly stated, as a positive limitation of the count, Hitzeman et al. have the burden of demonstrating that this limitation was known at the time of the alleged date of conception. ***Coleman v. Dines, supra.***

We do not find, based on the record before us, that Hitzeman et al. have sustained their burden of proving, by a preponderance of the evidence, that they conceived of an invention within the scope of the count on February 3, 1981. Our reasons follow.

Discussion

A. Dr. Hitzeman's testimony and laboratory notebook page

Dr. Hitzeman testified that on February 3, 1981, he had a meeting with Dr. Goeddel¹³ to discuss goals for the expression of other heterologous genes in yeast.¹⁴

¹³ Dr. Goeddel was Dr. Hitzeman's supervisor from September 1980 through

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Hitzeman Brief, p. 34; HR996. Dr. Hitzeman has provided a page from his laboratory notebook (HX16, p. 51) which is said to describe the February 3rd planning session with Dr. Goeddel. The notebook page reads as follows:

friday
guy
- Flasher's lab
? to el
ly to and
per yet
interior assays
n scale
- look
coli
guy (102)
178 (Holladay)
day
gal. opt.
cloned
To Page No.
Date 2/3/51

large range of expression
CD13 + 2µ plasmid
have a low 2 cur

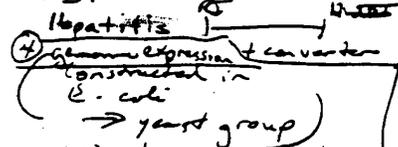
LIF — Dave Goodell

Friday 1:30-2 call Post doc Art Levenson

Lab tech

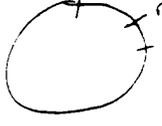
- | <u>Present spot</u> | <u>new system</u> |
|--|--|
| ① characterizes (protein LIFD)
- give Noel extract to see if behaves the same | ① Design P&K protein
② hook up with (protein with couple etc) |
| ② SOS at what level needed for paper with Ben Hall | ③ 2µ vector
④ recombinant plasmid |
| ③ use for FIF hepatitis | ⑤ LIF A do first screen in chemical trials |

ask about 20,000 FIF 16,000



ask his permission
④ requires genetic converter

① PT screen look for secreted



Xho → with Xho 20% go
Bac - kinase label

give Dave strains for coli. expression MDRK

According to Hitzeman et al., the notebook page shows “a proposed scheme for expressing HBsAg using both ADH (‘old system’)¹⁵ and PGK (‘new system’).”¹⁶ Brief, p. 62, para. 2. However, from a review of the referenced notebook page, we find that under the column entitled “present system,” Entry 3 reads “use for FIF... Hepatitis;” whereas, Dr. Hitzeman testified that this means using the ADH-1 promoter to express

¹⁵ On p. 51 of HX 16 we find two columns labeled as “present system” and “new system.” We do not find a column entitled “old system.”

¹⁶ Dr. Hitzeman testified that:

A. “Present System” refers to the ADH-1 [alcohol dehydrogenase] promoter, we were just discussing what would be next [HR997, lines 17-19].

* * *

A. ...

And 3, use the present system for fiberglass [sic, fibroblast] interferon, hepatitis. And that’s the RI-Hind III fragment that we had on hand.

No. 4, I don’t remember what that refers to, except to ask his permission -- ask Ben for permission to do these various things.

Q. What do you mean by “these various things”?

A. Since we were collaborating, to ask him whether we could use the present system, what’s referred to as the present system above, to produce various things, like fiberglass [sic, fibroblast] interferon, hepatitis [HR998, lines 6-18].

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fibroblast interferon and hepatitis. HR997-998. We also find that Entry 4 is not understandable; whereas, Dr. Hitzeman testified that it refers to asking Dr. Ben Hall for permission to use the ADH-1 promoter to produce fibroblast interferon and hepatitis.¹⁷

Id. We do **not** find any mention of (i) a DNA expression vector having limitations (1)-(5), **supra**, (ii) hepatitis B **surface** antigen, (iii) HBsAg particles, or (iv) the production in yeast of HBsAg particles having a sedimentation rate which is virtually identical to that of the 22 nm HBsAg particle. Under the column entitled “new system,” we find under Entry 1, a reference to “sequence PGK promoter,” but we do not find any mention of (i) a DNA vector as set forth in limitations (1)-(4), **supra**, (ii) hepatitis, (iii) hepatitis B **surface** antigen, (iv) HBsAg particles, or (v) the production in yeast of HBsAg particles having a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles. The only protein listed under the “new system” is “LeIFD,”¹⁸ which Entry 5 states “do first . . . in clinical trials.” Thus, on its face, the laboratory notebook page does not show Dr. Hitzeman’s conception of an invention

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having the five limitations of the count. Nor do we find that the laboratory notebook page directly corresponds with Dr. Hitzeman's explanation of its contents.

Moreover, Dr. Hitzeman's testimony and documentation must be independently corroborated. **Hahn v. Wong**, 892 F.2d 1028, 1032, 13 USPQ2d 1313, 1317 (Fed. Cir. 1989); **Price v. Symsek**, 988 F.2d at 1193-94, 26 USPQ2d at 1036 (Conception cannot be established by the inventor's testimony alone; it must be corroborated). The "purpose of the requiring corroboration is to prevent fraud." **Berry v. Webb**, 412 F.2d 261, 167, 162 USPQ 170, 174 (CCPA 1969). An inventor's own notebook is not independent corroborative evidence. **Reese v. Hirst**, 661 F.2d 1222, 1233, 211 USPQ 936, 947 (CCPA 1981). Laboratory notebooks must be authenticated by a witness who can satisfactorily identify them, and explain their significance.¹⁹ 37 CFR § 1.671(f) requires a witness to explain the entries on the various pages of the notebooks/exhibits. This explanation enables the opposing party and this Board to determine whether the witness's testimony is supported by contemporaneous documentation or whether a party is relying on the witness's oral testimony. Thus, Hitzeman et al. must provide testimony of witnesses, other than the inventors, to explain the entries on the referenced laboratory notebook page and/or to confirm that Dr. Hitzeman had

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operative invention” to them on the critical date. ***Burroughs Wellcome Co. v. Barr Labs., Inc., supra.***

According to Hitzeman et al., (i) the testimony of Dr. Goeddel corroborates the meeting of February 3, 1981 during which Dr. Hitzeman discussed his plan to express the DNA sequence encoding HBsAg in yeast, and (ii) Dr. Hitzeman’s laboratory notebook page is corroborated by Mr. Hagie. Hitzeman Brief, p. 62, para. 2.

B. Non-inventor witness, Mr. Hagie

Hitzeman et al. argue that Mr. Hagie²⁰ corroborates the proposed scheme for expressing HBsAg using both the ADH and PGK promoters as set forth in Dr. Hitzeman’s laboratory notebook; however, they have not pointed to any particular sections of Mr. Hagie’s testimony for support. Brief, p. 62, para. 2. Instead, Hitzeman et al. have referred generally to the entire Hitzeman record, i.e., “(HR).” ***Id.*** We find such a sweeping reference to the record as a whole to be equivalent to no citation. The requirements for the parties’ briefs are clearly set forth in 37 CFR § 1.656(b) (1993). In particular, 37 CFR § 1.656(b)(4)(1993) requires the brief to contain:

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[a]n argument, which may be preceded by a summary, which shall contain the contentions of the party with respect to the issues to be decided, and the reasons therefor, **with citations to the cases, statutes, other authorities, and parts of the record relied on** [emphasis added].

The parties will not be relieved of their obligation to comply with these rules. The Board will not speculate as to the basis for the conclusions of fact and law made by a party in its brief where no adequate reference to the record or citation of authority is proffered. Nor will the Board search through the record to find facts which might support the position taken by a party in its brief. Rather, conclusions of fact and law made by a party without appropriate citation to the record or citation of authority will be taken as attorney argument. Compare **Ex parte McCullough**, 7 USPQ2d 1889, 1892 (Bd. Pat. App. & Inter. 1987); **Ex parte Meyer**, 6 USPQ2d 1966, 1968-69 (Bd. Pat. App. & Inter. 1988); **In re Mehta**, 347 F.2d 859, 863-64, 146 USPQ 284, 286 (CCPA 1965). Argument of counsel cannot take the place of objective evidence. **Meitzner v. Mindick, supra**.

As to Mr. Hagie's alleged witnessing²¹ of the laboratory notebook page on February 3, 1981, we point out that the mere signing of a notebook page, without an

²¹ The photocopy of HX16, p. 51, provided by Hitzeman et al. is not a complete

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accompanying explanation as to the meaning of the notations on said page, is of limited probative value. This is particularly true in the case before us since Dr. Hitzeman's notebook page is cryptic in nature and is not self-explanatory. The box on laboratory notebook page which purportedly bears Mr. Hagie's signature is merely labeled "witnessed and understood by me." We direct attention to 37 CFR § 1.671(f)(1993) which states that "the significance of documentary and other exhibits identified by a witness in an affidavit or during oral deposition shall be discussed with particularity by a witness." Mr. Hagie has not provided any such discussion.²² Thus, Mr. Hagie's witnessing of the notebook page alone, without any testimony that Dr. Hitzeman communicated the subject matter of the count to him, establishes only that the

²² Mr. Hagie testified (HR379, lines 11-23) as follows:

Q. On what date did you sign Page 51, Mr. Hagie?

A. February 3, 1981.

Q. Was the yellow page that's taped to that page of the notebook on that page at the time you signed it?

A. Yes.

Q. Was the information that's on the yellow page on there when you signed Page 51?

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notebook page existed on February 3, 1981. *Hahn v. Wong*, 892 F.2d at 1032, 13 USPQ2d at 1317.

C. Non-inventor witness, Dr. Goeddel

Hitzeman et al. argue that Dr. Goeddel corroborates the February 3, 1981, planning session to express HBsAg in yeast using the ADH and PGK promoters.

Hitzeman Brief, p. 34; HR2359; HR2386-87. Dr. Goeddel states, in relevant part:

I remember working closely with Dr. Hitzeman and Mr. Hagie at the time the alcohol dehydrogenase (ADH) promoter system was successfully used to express leukocyte interferon in yeast. I recall having a conversation with Dr. Hitzeman within a few days after the successful expression of interferon, where he and I talked about using the ADH and the yeast 3-phosphoglycerate kinase (PGK) gene to express other heterologous *proteins* in yeast, including the hepatitis surface antigen [emphasis added] [HR2359, last para.].

We have analyzed Dr. Goeddel's statement under the guidelines set forth in *English v. Ausnit*, 18 USPQ2d 1625, 1632 (Bd. Pat. App. & Inter. 1994), and we accord it little evidentiary weight. Corroboration must be to that point in time during which the inventor alleges he conceived of the invention. Here, Dr. Goeddel recalls having a discussion with Dr. Hitzeman, but he does not appear to recall the date.

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conclusions. Dr. Goedel does not indicate that Dr. Hitzeman described a plan to construct a DNA vector having the characteristics of the count as set forth in limitations (1)-(5), above. Nor does Dr. Goedel provide any of the underlying facts or a description as to Dr. Hitzeman's "scheme" to use "the ADH and ... PGK gene to express other heterologous proteins in yeast." Thus, we find that, at best, Dr. Goedel's statement suggests that Dr. Hitzeman had a general goal to express the hepatitis surface antigen *protein* in yeast, and *not HBsAg particles*. To establish conception, however, Dr. Hitzeman must demonstrate that he had "a specific, settled idea ... and not just a general goal or research plan he hope[d] to pursue." *Burroughs v. Wellcome Co. v. Barr Labs., supra*.

D. Hitzeman et al.'s possession of all the DNA fragments set forth in the count by February 3, 1981

Hitzeman et al. argue that a DNA expression vector capable of replication and phenotypic selection in yeast host cell strain was known and in the possession of Hitzeman prior to February 25, 1981. Brief, p. 51. According to Hitzeman et al., Dr. Hitzeman and his collaborators worked on and created eight different derivatives of the "pFRL4" vector, known as the "pFRPn" series, prior to February 3, 1981. *Id.*, p. 52.

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expression in yeast prior to February 3, 1981, *viz.*, a vector using the PGK promoter. *Id.*, p. 53. According to Hitzeman et al., the gene encoding the yeast PGK protein was cloned and the location of the site for initiating transcription was known prior to February 3, 1981. *Id.* For support, Hitzeman et al. point to a 1980 publication (HX26) authored by Dr. Hitzeman. Hitzeman et al. still further argue that co-inventor “Mr. Daniel G. Yansura created a vector containing the HBsAg gene, the plasmid pHS94, encoding the 226 amino acids of HBsAg, useful for further studies in yeast prior to February 3, 1981 (HX8). . . . The HBsAg gene was tested for transcription and translation in *E. coli* (Yansura, HR1872).” Hitzeman Brief, pp. 54-55.

We have reviewed the exhibits proffered by Hitzeman et al.²³ which describe various projects that the Hitzeman co-inventors were involved with prior to February 3, and prior to February 25, 1981, but we do not find that the exhibits establish that Dr. Hitzeman, Dr. Levinson and Mr. Yansura had a definite and permanent idea of a complete and operative invention within the scope of the count on the alleged date. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1376, 231 USPQ2d 81, 87 (Fed. Cir. 1986) . The exhibits describe independent research projects and fail to demonstrate that Dr. Hitzeman, Dr. Levinson and Mr. Yansura had a complete

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combined in the manner required by the count.²⁴

For example, RX BH3 is a copy of Hitzeman Application 06/237,913, filed February 25, 1981, entitled "Expression of Polypeptides in Yeast." The patent application is directed to a DNA expression vector capable of expressing heterologous proteins in a transformed yeast host cell, methods of transforming a yeast host cell with said vector, and a yeast strain transformed with said vector. See claims 1-15. The vector is said to be useful for the expression of heterologous genes such as normal and hybrid human interferons, human proinsulin, the A and B chains of human insulin, human growth hormone, somatostatin and thymosin alpha 1. See, e.g., p. 2 and claim 12. We find no mention of the expression, in yeast, of a DNA sequence encoding HBsAg, or the production of HBsAg particles having a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles, using any of the vectors, including the pFRPn series of vectors.

²⁴ We have considered the evidence proffered as corroboration for the interferon/yeast and HBsAg/*E. coli* projects of the Hitzeman co-inventors; i.e., the testimony and/or accompanying exhibits of Mr. Hagie (HX6, 7, 10, 11, 18 and 27-28); Ms. Chen (HR1990-92, 2006-09, 2019-34, 2041-57); Dr. Kleid (HR1528-35; HX40, 32, 41, 8, 42 and 43), Dr. Goeddel (HR2359, 2386087; 2380-82, HX23 and HX16, p.51); and Ms. May (HR2323-26; HR2343-53; HX70). However, we do not find that any of the

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As to the PGK work described in the 1980 Hitzeman publication entitled "Isolation and Characterization of the Yeast 3-Phosphoglycerokinase Gene (PGK) by an Immunological Screening Technique" (HX26), we find no mention of (i) the PGK promoter, (ii) the use of the PGK promoter to express a DNA sequence encoding HBsAg in yeast, (iii) the production of HBsAg particles in yeast, or (iv) the production in yeast of HBsAg particles having a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles. Moreover, contrary to Hitzeman et al.'s argument that the transcription initiation site of the PGK protein was known prior to February 3, 1981, the publication merely indicates that the entire PGK gene is located on a 3.1 kb DNA fragment; there is no delineation of the promoter from the structural gene. No nucleotide sequence information or restriction map of the PGK gene is disclosed. Thus, we find that Hitzeman et al.'s argument has not been supported with objective evidence and, therefore, is of no probative value. We point out that argument of counsel cannot take the place of objective evidence. ***Meitzner v. Mindick, supra.***

With respect to the exhibit, HX8- "Fourth Quarter Scientific Progress Report November 1, 1979- February 25, 1980," which was provided to demonstrate that Hitzeman et al. were in possession of a DNA fragment encoding HBsAg, we point out

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(ii) the expression of the DNA sequence encoding HBsAg in yeast, (iii) the production of HBsAg particles in yeast, or (iv) the production of HBsAg particles having a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles.

In sum, Hitzeman et al. have not met their burden of establishing that they had a complete mental picture of the **combination** of limitations set forth in the count.

Evidence suggesting that Hitzeman et al., perhaps, had possession of several DNA fragments which eventually might have been used to construct an expression vector encoding HBsAg, does not establish they had envisioned the specific **combination** of those DNA fragments in the manner required by the count.

E. Dr. Hitzeman's "hope"

Hitzeman et al. argue that Dr. Hitzeman had

a hope that particles would be produced (Hitzeman, HR1116-18), and he certainly expected that transcription and translation would occur in yeast. It is clear that Dr. Hitzeman expected that HBsAg protein would be expressed in yeast based upon his previous success with interferon (Hitzeman, HR1113) [Hitzeman Brief, p. 57].

Dr. Hitzeman's expectation that transcription and translation of the DNA

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that of authentic 22 nm HBsAg particles.

Moreover, Dr. Hitzeman's testimony of his "hope," ten years after it was discovered that HBsAg particles having a sedimentation rate which is virtually identical to that of authentic 22 nm HBsAg particles could be produced in yeast, is of little probative value since it is self-serving and requires corroboration.

Accordingly, when considering the evidence as a whole, we do not find that Dr. Hitzeman's laboratory notebook page (HX16, p. 51), Dr. Goeddel's or Mr. Hagie's testimony establishes that Dr. Hitzeman had conceived of an invention within the scope of the count on February 3, 1981. Neither Dr. Goeddel nor Mr. Hagie states that Dr. Hitzeman had disclosed to them his "completed thought expressed in such terms as to enable those skilled in the art to make the invention" described in the count, on the critical date. *Coleman v. Dines, supra*. See also; *Burroughs Wellcome Co. v. Barr Labs., Inc., supra*, ("Conception analysis turns on the inventor's ability to describe his invention with particularity. Until he can do so, he cannot provide possession of the complete mental picture of invention"). Rather, at best, the evidence suggests that Dr. Hitzeman had a general goal, or research plan, to express a DNA sequence encoding HBsAg in yeast. HR2359. Hitzeman et al. have failed to establish conception of a

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burden of proving, by a preponderance of the evidence, that they had a definite and permanent idea of the invention on February 3, 1981.

V.

Simultaneous Conception and Reduction to Practice

In reviewing the record before us, we find that this case is one which falls under the doctrine of simultaneous conception and reduction to practice. ***Amgen, Inc. v. Chugai Pharmaceutical Co.***, 927 F.2d at 1207, 18 USPQ2d at 1021 (Fed. Cir.), ***cert. denied***, 502 U.S. 856 (1991) (“In some instances, an inventor is unable to establish a conception until he has reduced the invention to practice through a successful experiment”); ***cf. Alpert v. Slatin***, 305 F.2d 891, 894, 134 USPQ 296, 299 (CCPA 1962)(with some types of research, “the inventor’s mind cannot formulate a completed invention until he finally performs a successful experiment”).

It is well established that “evidence of record relative to conception and reduction to practice should be ... considered in conformity with the character of the invention”. ***Smith v. Bousquet***, 111 F.2d 157, 162, 45 USPQ 347, 352 (CCPA 1940).

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sucrose and/or cesium chloride gradient centrifugations were obtained was a definite and permanent idea of the yeast-derived HBsAg particle envisioned by the inventors of either party. That is, because it was not possible to predict or determine the results in advance of actual experimentation, conception and reduction to practice in the present case are necessarily concurrent.

The record shows that the only previous use of recombinant DNA technology to express a DNA sequence encoding hepatitis B surface antigen in a transformed unicellular host cell (*E. coli*) resulted in the production of protein monomers, and not particles. Hitzeman Brief, pp. 7-11; Rutter Brief, pp. 17-18. With respect to the expression of heterologous proteins in yeast, in general, the record shows that this art was still in its infancy. We direct attention to Rutter Application 06/289,915, p. 4 (RIX 3) which states:

Yeast has never previously been used for expression of the genes of a virus which normally multiplies in a different organism. Prior art attempts to express heterologous proteins in yeast have yielded mixed results. An attempt to express rabbit globin, under control of its own promoter appears to have been unsuccessful in translation of the protein (Beggs, J.D. et al. *Nature* **283**, 835 (1980)). A gene coding for a *Drosophila* gene has been reported capable of complementing a yeast *ade 8* mutant, under conditions

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We also direct attention to the *ex parte* prosecution of the applications involved in the present interference proceeding. Hitzeman et al. argued that in view of the poor results obtained using recombinant DNA technology to express HBsAg in *E. coli*, one of ordinary skill in the art would not have expected (i) that a DNA sequence encoding HBsAg could be expressed in yeast, and (ii) that in the event the DNA sequence encoding HBsAg was expressed in yeast, that the process and assembly of HBsAg particles would occur.²⁵

²⁵ For example, Hitzeman et al. argued during the prosecution of Application 06/599,387 that

The items referred to by the Examiner as showing HBsAg cloned in *E. coli* (Rutter *et al.*, Murray *et al.* and Tiollaies *et al.*) do not teach that bacteria are able to assemble and secrete HBsAg particles. On the contrary, Mackay *et al.* (newly cited) point out that HBsAg from bacteria comigrates in electrophoresis gels with bacterial polypeptides (p. 4512). Thus the results obtained by applicants herein were unexpected and surprising. **One skilled in the art at the time this application was filed would not have been able to reasonably predict that HBsAg could be expressed by yeast and, even if this was reasonably predictable, would not have expected yeast to process and assemble HBsAg particles having substantially the same buoyant density as HBsAg particles from virally-infected sources.** [Emphasis added] [HX20, p. 7].

* * *

Bacterial expression of poorly immunoreactive HBsAg cast a pall

Rutter et al. agree that the prosecution history demonstrates that the particulate nature and sedimentation characteristics of the yeast-derived HBsAg product could not have been predicted prior to reduction to practice of the invention. Rutter Brief, pp. 34-35, 43-45, and 58-62. In addition, Dr. Rutter points out that:

44. . . . It is noteworthy that as late as 1983 Hitzeman et al. in reporting the expression of HBsAg in yeast still speculated that expressed HBsAg was monomeric in form, and that particle formation resulted from the glass bead extraction procedure rather than from intracellular assembly (Hitzeman, R. et al., *Nucleic Acids Research* 11:9 (1983) (Rutter Exhibit RS-2)) [RR136, paras. 43 and 44].

At the time the Hitzeman et al. and Rutter et al. patent applications were filed, the record indicates that, in yeast, only one heterologous protein (interferon) had been successfully expressed, and the expression of another heterologous protein (rabbit globin) had failed. Thus, it reasonably follows that one of ordinary skill in the art would not have been able to predict, prior to testing, whether the expression (transcription and translation) of heterologous proteins in yeast, in general, and therefore, HBsAg, in particular, was possible in 1981.²⁶ Moreover, not only was the expression of the DNA

²⁵(...continued)

was able to process and assemble HBsAg particles. [Emphasis added] [HX20, p. 8].

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encoding HBsAg in yeast unpredictable, but assuming, **arguendo**, said DNA was expressed, it was unpredictable whether such expression would result in the production of (i) HBsAg protein monomers only, or (ii) HBsAg particles of any size, albeit 22 nm particles, 22 nm rods, or a particle size unique to yeast. Accordingly, it is reasonable to conclude that the physical characteristics (particulate form and sedimentation rate) of the HBsAg product made as a result of the expression of the DNA sequence encoding HBsAg in yeast could not have been envisioned by the inventors prior to reduction to practice. Accordingly, we hold that Hitzeman et al. did not have conception of a DNA expression vector comprising the DNA sequence encoding HBsAg wherein expression of the DNA sequence encoding HBsAg resulted in the production of HBsAg particles in a transformed yeast host cell as required by the count until reduction to practice had been achieved. ***Amgen, Inc. v. Chugai Pharmaceutical Co., supra.***

A. *Rutter's actual reduction to practice*

For the sake of completeness, Rutter et al. state that on June 29, they “performed a sucrose gradient centrifugation experiment which, on June 30, 1981,

²⁶(...continued)

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showed that the HBsAg particle produced by yeast (transformed with pHBS16) had a sedimentation rate virtually identical to that of authentic HBsAg 22 nm particles.”

Rutter Brief, pp. 32-33. Thus, Rutter et al. urge that they had reduction to practice of an invention within the scope of the count no later than June 30, 1981. *Id.*, p. 32. We have reviewed the corroborating evidence (testimony and laboratory notebooks) of non-party Ms. Medina-Selby, and we agree. Selby RR96, para. 36; AMS-2, Bates 0113-17.²⁷ Hitzeman et al. do not contest that Rutter et al. had reduction to practice of an invention within the scope of count no later than June 30, 1981 and they concede that they were second to reduce to practice. Hitzeman Reply Brief, p. 24, line 1.

VI. Diligence

The issue of diligence does not arise in (i) this case because Hitzeman et al. have not established conception of an invention within the scope of the count, and (ii) cases which come under the doctrine of simultaneous conception and reduction to practice. Since we hold that Hitzeman et al. did not conceive of an invention within the scope of the count prior to obtaining the results from the sucrose and cesium chloride gradients, the issue of reasonable diligence of the inventors to a reduction to practice is

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VII.
Judgment

Based on the above record, judgment as to the subject matter of the count is hereby awarded to WILLIAM J. RUTTER, PABLO D.T. VALENZUELA, BENJAMIN D. HALL and GUSTAV AMMERER, the senior party.

Accordingly, on the present record, junior party, RONALD A. HITZEMAN, ARTHUR D. LEVINSON, and DANIEL G. YANSURA, are not entitled to their patent 4,803,164 containing claims 1 through 11, corresponding to the count.

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RUTTER et al. are entitled to a patent containing claims 6 through 34
corresponding to the count.

MICHAEL SOFOCLEOUS)	
Administrative Patent Judge)	
)	
)	
)	
MARY F. DOWNEY)	BOARD OF PATENT
Administrative Patent Judge)	APPEALS AND
)	INTERFERENCES
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