

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 28

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOHANN HOCK and HERMANN KARGES

Appeal No. 1997-1093
Application No. 08/272,281¹

ON BRIEF

Before WINTERS, SPIEGEL, and ADAMS, Administrative Patent Judges.
SPIEGEL, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner finally rejecting claims 2, 3, 5, 7, 8 and 10 through 14, and refusing to allow claims 1 and 9 as

¹ Application for patent filed July 8, 1994. According to appellants, this application is a continuation of application 08/003,318 filed January 12, 1993, now abandoned.

amended subsequent to the final rejection, which are all of the claims pending in this application.² Claim 1 is illustrative and reads as follows.

1. A processed stable fibrinogen solution, obtained by
 - a) treating a starting fibrinogen solution at least twice with an adsorbent selected from the group consisting of an anion exchanger, a sparingly soluble salt of an alkaline earth metal and aluminum hydroxide,
 - b) removing said adsorbent from the treated fibrinogen solution leaving a supernatant, wherein the fibrinogen remains in said supernatant and
 - c) recovering said supernatant,

wherein the fibrinogen in the supernatant maintains its ability to function when stored at 4-25EC for four weeks.

The references relied on by the examiner are:

Kotitschke et al. (Kotitschke)	4,272,523	Jun. 9, 1981
Rose et al. (Rose)	4,627,879	Dec. 9, 1986
Mathews et al. (Mathews)	4,743,680	May 10, 1988

ISSUES

Claims 1-3, 5, 7, 9, and 11-13 stand rejected under 35 U.S.C. § 103 as being unpatentable over Kotitschke in view of Mathews. Claims 8, 10, and 14 stand rejected under 35 U.S.C. § 103 as being unpatentable over Kotitschke in view of Mathews as applied to claims 1-3, 5, 7, 9, and 11-13, and further in view of Rose.

² The amendment filed October 27, 1995 (Paper No. 19) amending claims 1 and 9 was entered by the examiner in the advisory action mailed December 6, 1995 (Paper No. 21).

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We REVERSE.

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims and to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's answer (Paper No. 23, mailed May 6, 1996) for the examiner's reasoning in support of the rejection and to the appellants' brief (Paper No. 22, filed January 29, 1996) for the appellants' arguments thereagainst.³

OPINION

According to appellants, "the present claims are directed to a process wherein fibrinogen solution is treated at least twice with an adsorbent that does not remove or adsorb the fibrinogen from solution to thereby yield a stable processed fibrinogen solution" (brief, page 12, lines 16-19).

According to the examiner,

The fibrinogen solution obtained by Kotitschke presumably maintains the ability to function for four weeks at 4-25EC since the method taught by Kotitschke and that claimed are nearly identical. This claimed property is an inherent feature of a fibrinogen solution obtained by the method claimed and taught by Kotitschke. [Answer, paragraph bridging pages 4-5.]

³ Appellants' reply brief (Paper No. 24, filed July 8, 1996) was denied entry by the examiner in the communication mailed August 6, 1996 (Paper No. 25). Appellants' petition under 37 CFR § 1.181 to enter the reply brief was denied by the Group Director in the decision on petition mailed November 25, 1996 (Paper No. 27). Therefore, appellants' reply brief was not considered in our decision making.

Furthermore, "[t]he use of aluminum hydroxide to adsorb fibrinogen, an optional method claimed, is taught by Mathews" (answer, page 4, lines 17-18).

However, the method taught by Kotitschke is not "nearly identical" to that claimed. Kotitschke uses a single adsorption onto protein adsorbing anion exchangers, e.g., DEAE-Sephadex or DEAE-cellulose, to remove factors II, VII, IX and X, as well as antithrombin III, from a citrated plasma cryoprecipitate, resulting in a supernatant containing fibrinogen (Fig. 4; col. 4, lines 16-22; col. 6, lines 31-45). The fibrinogen is then adsorbed on colloidal silica, separated from the supernatant, eluted with buffer and ultrafiltered with subsequent alcohol fractionation to obtain coagulable fibrinogen (Fig. 4; col. 5, lines 50-56).

Apparently recognizing the difference in methodology, the examiner opines that "it is well known in the art to use as many purification [i.e., adsorption] steps as are necessary in order to obtain [sic] a product with the desired purity" (answer, page 5, lines 5-7). However, the claimed invention does not require a fibrinogen solution of stated minimum purity, but rather a stable fibrinogen solution which maintains its ability to function when stored at 4-25EC for four weeks. Purity and stability are not synonymous. Purity refers to lack of contaminants or impurities, while stability refers to a resistance to chemical change or physical decomposition.

Further, the claimed "ability to function" refers "in particular [to a fibrinogen solution] without significant change in consistency and coagulation properties" (specification, page 1, lines 5-7). Kotitschke, however, suggests that additional method steps, i.e., at least dialysis or ultrafiltration of the fibrinogen solution, is required to obtain a coagulation-active fibrinogen (see e.g., col. 5, lines 50-56).

Nothing in Mathews⁴ or Rose⁵ makes up for these deficiencies in Kotitschke. According to the examiner, "Mathews was only cited to show that another member of the Markush group, aluminum hydroxide, is known to adsorb fibrinogen" (answer, page 12, lines 14-15) and "whether Rose's fibrinogen component is identical to that claimed is not the issue. It would have been obvious to use any fibrinogen in a fibrin glue since it is a well known critical ingredient" (answer, page 14, lines 13-15).

Thus, we find the examiner has not carried her burden of establishing a prima facie case of obviousness.

Accordingly, the rejections of claims 1-3, 5, and 7-14 under 35 U.S.C. § 103 as being unpatentable over Kotitschke, Mathews and Rose are reversed.

⁴Mathews purifies proteins by column chromatography in the presence of various sugars, polyhydric alcohols, amino acids and salts ("hydration additives") to enhance selective binding of proteins to an ionic chromatography column and selective elution of proteins from a hydrophobic affinity column (col. 4, line 65 - col. 5, line 28).

⁵ Rose describes preparation of a fibrin glue from a cryoprecipitated suspension containing fibrinogen and Factor XIII by adding a sufficient amount of thrombin so as to cause the fibrinogen in the suspension to be converted to fibrin glue which then solidifies in the form of a gel (see e.g., paragraph bridging cols. 4-5).

OTHER MATTERS

Upon return of the application, the examiner should consider whether the claimed invention raises any issues under 35 U.S.C. § 112. It appears that claimed method may be incomplete in failing to recite all critically required method steps to obtain a fibrinogen solution which maintains its ability to function when stored at 4-25EC for four weeks. First, the only disclosure in the specification of a fibrinogen solution having the claimed stability was obtained not after treatment with two adsorbents, but after additional method steps.

According to Example 1 on specification page 5:

Cryoprecipitate from citrate plasma was dissolved in isotonic saline (2.8 l/kg). Subsequently, 5% (volume/volume) of an aluminum hydroxide suspension (1.5% weight/volume) was added, and the mixture was stirred for 15 min. The aluminum hydroxide was removed by centrifugation, and the same amount of aluminum hydroxide plus 5.25 g of QEA-Sephadex A-50 per kg of cryoprecipitate, was again added to the supernatant. Centrifugation was repeated. Glycine was added to the supernatant with stirring until the final concentration was 2.7 mol/l, and the resulting precipitate was removed by centrifugation and dissolved in isotonic saline (1.5 l/kg). The solution was mixed with glycine (final concentration 1.15 mol/l) and stirred for 30 min. This was followed by centrifugation, and the residue was discarded. The supernatant was mixed with glycine (final concentration 2.15 mol/l) and stirred for 30 min. The precipitate was removed by centrifugation, taken up in 0.05 mol/l NaCl, 0.005 mol/l trisodium citrate, 0.02 mol/l arginine, pH 7.5, and dialyzed against the same buffer.

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Second, glycine is a known stabilizer of fibrinogen which can be used to precipitate fibrinogen from supernatant liquid (see e.g., Kumpe et al.⁶ at col. 2, lines 10-40). Third, the file history suggests that a combination of a high salt precipitation of fibrinogen plus at least two adsorption steps may be necessary.⁷ If it is determined that an additional method step(s) is required to obtain a fibrinogen solution which "maintains its ability to function when stored at 4-25EC for four weeks," the examiner should take a step back and reassess the patentability on the claims on appeal.⁸

Secondly, the language of the dependent claims is inconsistent with some claims reciting "processed stable fibrinogen solution as claimed in ... " (e.g., claim 2), while others recite "stable fibrinogen solution as claimed in ... " (e.g., claim 12). We also note that the

⁶Kumpe et al., U.S. Patent No. 4,960,757, was originally submitted with appellants' Information Disclosure Statement filed September 8, 1993 (Paper No. 5).

⁷ According to the amendment filed July 8, 1994 (Paper No. 14),

The presently claimed invention employs a high salt precipitation of fibrinogen combined with at least two adsorption steps using aluminum hydroxide, a sparingly soluble salt of an alkaline earth metal or an anion exchanger. Importantly, the present invention uses a process whereby the fibrinogen is not adsorbed by the adsorbent ... rather it remains in the supernatant during ... all of the adsorption steps This process results in a fibrinogen solution that is stable for at least four weeks when stored at 4-25EC. [Page 5, first full paragraph, emphasis in the original.]

Also see the amendment filed April 19, 1995 (Paper No. 16) at page 5, first full paragraph.

⁸ We also note that Kotitschke et al. U.S. Patent No. 5,009,003 (made of record by the examiner on the PTO-892 accompanying the Office action mailed April 13, 1993 (Paper No. 2)), uses ethyl alcohol and glycine to precipitate fibrinogen and Factor XIII from a supernatant obtained after anion exchange adsorption of citrated plasma.

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Markush group of claim 1 does not include a combination of one or more the recited adsorbent.

CONCLUSION

To summarize, the decisions of the examiner to reject claims 1-3, 5, 7, 9, and 11-13 under 35 U.S.C. § 103 as being unpatentable over Kotitschke in view of Mathews and to reject claims 8, 10 and 14 under 35 U.S.C. § 103 as being unpatentable over Kotitschke in view of Mathews as applied to claims 1-3, 5, 7, 9, and 11-13, and further in view of Rose are reversed.

REVERSED

SHERMAN D. WINTERS)	
Administrative Patent Judge)	
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)	BOARD OF PATENT
CAROL A. SPIEGEL)	APPEALS
Administrative Patent Judge)	AND
)	INTERFERENCES
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DONALD E. ADAMS)	
Administrative Patent Judge)	

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FINNEGAN HENDERSON FARABOW
GARRETT AND DUNNER
1300 I STREET, N.W.
WASHINGTON, DC 20005-3315

CAS/cam

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APPLICATION NO. 08/272,281

APJ SPIEGEL

APJ WINTERS

APJ ADAMS

DECISION: **REVERSED**

Prepared By: Cheryl

DRAFT TYPED: 18 Sep 01

FINAL TYPED: 07/07/00