

*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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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*Ex parte* CHRISTER JAN MATTSSON, CARL M.E. SVAHN  
and MICHAEL P. WEBER

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Appeal No. 1996-1009  
Application No. 07/949,551

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ON BRIEF

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Before WILLIAM F. SMITH, GRON, and SPIEGEL, *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 16 and 18 and refusing to allow claims 15 and 17 as amended subsequent to the final rejection.<sup>1</sup>

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<sup>1</sup>The amendment filed November 8, 1994 (Paper No. 10), amending claims 15, 17, 19 and 21, was entered by the examiner in the advisory action mailed November 17, 1994.

Claims 19 through 22, the only other claims pending in this application, have been withdrawn from appeal (brief, page 1). Claim 15 is representative of the subject matter on appeal and reads as follows:

15. A method for treatment of angina pectoris by administration of a heparin derivative from bovine or porcine heparin characterised by:

- having a molecular weight equal to or larger than standard bovine or porcine heparin,
- showing a sulfur content which is equal to or higher than that of said bovine or porcine heparin,
- having an anticoagulant activity in the anti-FXa assay of less than 10% of said bovine or porcine heparin it was made from,

showing a ratio of APTT activity over anti-FXa activity of 3-35,

showing a reduced prolongation of bleeding time compared to said bovine or porcine heparin it was made from as measured in the rat tail after i.v. administration, and

showing enhancement of the rate of development of coronary collaterals in dogs equal to or better than clinically used heparin,

in a therapeutic dose to a patient in need of said treatment.

The references relied on by the examiner are:

Naggi et al. (Naggi '063)	4,727,063	Feb. 23, 1988
Naggi et al. (Naggi '881)	4,948,881	Aug. 14, 1990
Petitou et al. (Petitou)	5,013,724	May 7, 1991 (filed Jul. 11, 1986)
Conti et al. (Conti)	5,164,378	Nov. 17, 1992 (filed Nov. 26, 1990)

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WEBSTER'S NEW COLLEGIATE DICTIONARY 85 (9th ed. 1983).

Appellants rely on the following reference supplied with their reply brief:

A. Lane and Ulf Lindahl (Lane), BIOSYNTHESIS OF HEPARIN AND RELATED POLYSACCHARIDES 164 (Chemical and Biological Properties Clinical Applications Ed., Edward Arnolds, London, 1989).

*ISSUES<sup>2</sup>*

Claims 15-18 stand rejected under 35 U.S.C. § 103 as being unpatentable over any of Naggi '063, Naggi '881, Petitou or Conti. 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. 15, mailed April 17, 1995) for the examiner's reasoning in support of the rejections and to the appellants' brief (Paper No. 14, filed February 15, 1995) and to the appellants' reply brief (Paper No. 17, filed June 16, 1995) for the appellants' arguments thereagainst.

*OPINION*

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<sup>2</sup> According to the advisory action mailed November 17, 1994 (Paper No. 11), the amendment filed November 8, 1994 (Paper No. 10) overcame the final rejection of claims 15-22 under 35 U.S.C. § 112, second paragraph, as being indefinite.

**Naggi '063** describes reacting a heparin of natural origin with a sulfuric acid/chlorosulfonic acid mixture to produce depolymerized and supersulfated heparin products having molecular weights between 2000 and 9000, with good fibrinolytic and hypolipemic activity joined to a weak anticoagulant activity (col. 4, line 67 - col. 5, line 2; col. 5, lines 41-45), and which are useful for prevention of thrombolytic diseases and treatment of atherosclerosis (col. 10, lines 58-66). Naggi '063 explicitly describes at least the relative molecular weights and degree of sulfation (a measure of sulfur content) between various starting heparin materials and their resulting product(s) and, in some cases, results of activated partial thromboplastin time (APTT), activity towards blood coagulation factor Xa (anti-Xa activity), and the ratio anti-Xa/APTT. A summary of this data follows, with calculated APTT/anti-Xa ratios where data was available.

	mol. weight	degree of sulfation	APTT	anti-Xa activity	anti-Xa/APTT	(calc.) APTT/anti-Xa
<b>starting heparin D212</b>	13,500	1.95	1.000	1.20	1.20	0.83
<i>product AH-16</i>	6,000	3.0	0.06	0.18	3.0	0.33
<i>product AH-19</i>	6,000	3.0	0.05	0.22	4.4	0.23
<i>product AH-104</i>	6,000	2.9	0.078	0.30	3.84	0.26
<i>product AH-103</i>	6,000	2.8				
<i>product AH-105</i>	6,000	3.0				
<i>product AH-106</i>	6,000	2.8	0.080	0.31	3.87	0.26
<i>product AH-107</i>	6,000	3.0				

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<b>starting heparin D212/B</b>	16,500	2.0				
<i>product AH-18</i>	3,000-5,000	2.6				
<b>starting heparin D212/A</b>	10,000	1.5	0.212	0.324	1.61	0.65
<i>product AH-17</i>	3,000-5,000	2.5	0.05	0.17	3.4	0.29
<b>starting heparin D470</b>	11,000	2.1				
<i>product AH-108</i>	6,000	3.1				
<i>product AH-109</i>	6,000	3.0				
<i>product AH-110</i>	6,000	2.9				
<i>product AH-111</i>	6,000	3.0				
<b>starting heparin D98</b>	13,500	1.8				
<i>product AH-118</i>	6,000	2.8				
<b>starting heparin D479</b>	11,000	2.1				
<i>product AH-67</i>	4,000	2.5				
<i>product AH-65</i>	3,800	2.5				
<i>product AH-68</i>	4,500	2.8				
<b>starting heparin Parke-Davis</b>	19,200	2.27				
<i>product DS-16</i>	8,600	3.33	10% of starting heparin	60% of starting heparin	>3	

**Naggi '881** describes a depolymerization and sulfation process of polysaccharides, including heparin (col. 3, lines 3-7; col. 4, lines 4-5) and shows a pattern of relative molecular weights and degree of sulfation similar to that in Naggi '063. For example, starting heparin D212 has a molecular weight of 13,500 and a 1.95 degree of sulfation while products AH-16, AH-19, AH-104, AH-103, AH-105, AH-106 and AH-107 have molecular weights of 6,000 and degree of sulfations of 3.0, 3.0, 2.9, 2.8, 3.0, 2.8 and 3.0, respectively.

**Petitou** describes a process of preparing highly sulfated or "sursulfated" heparin (col. 6, lines 40-49). According to the examiner, Petitou "does teach a product having molecular weight higher than 9000 daltons" (answer, page 10). However, Petitou also discloses that standard heparin has a molecular weight of 15,000 (line 4 in the table bridging cols. 17-18).

**Conti** describes a process of preparing a *low molecular weight* supersulfated heparin by reacting standard heparin with oleum (col. 1, lines 33-35; col. 2, lines 33-35; col. 3, lines 49-55).

**According to the examiner,**

Although it is acknowledged that none of the references explicitly mentions angina pectoris, the references all deal with the treatment of cardiovascular disorders directly related to angina. The examiner notes that angina pectoris is "chest pain precipitated by deficient oxygenation of the heart muscles" (see "Websters' Ninth New Collegiate Dictionary", page 85). Thus the treatment of the described conditions would result in alleviation of the pain associated with such cardiovascular disorders. While no single reference teaches each and every limitation of claim 15 regarding properties of the heparin derivative, including the ability to enhance development of coronary

collaterals in dogs, there has been no showing that the sulfated heparins of the references do not possess these properties. [Answer, page 5, first full paragraph.]

**According to appellants**, “[t]he prior art does not suggest treating patients for angina pectoris as recited in the claims now on appeal. In addition, the heparin derivatives employed pursuant to the present invention are quite different from the products suggested by the prior art” (brief, page 4, lines 1-3).

As to treatment of angina pectoris, the examiner’s position is two-fold. First, “appellant’s specification acknowledges that it is known in the art to use derivatives of heparin for treatment of angina (see page 1 of the Background)” (answer, page 7). Secondly, since “[a]ngina is a symptom directly related to an atherosclerosis situation. If the references teach prevention or treatment of the underlying cause of angina, it therefore follows that prevention or treatment of angina itself is inherently taught” (answer, page 7). First, the specification states that heparin, not derivatives of heparin, has been found to improve collateral circulation in patients with effort angina (page 1, lines 14-19). Secondly, the claimed invention requires treating a patient that has already has angina pectoris.<sup>3</sup> Atherosclerosis is not angina pectoris, just as angina pectoris is not myocardial infarction. That is not to

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<sup>3</sup> While the record in this appeal indicates that the examiner performed a database search of the PTO’s automated patent search system (USPAT) and of chemical abstracts (CAS) for oxidized, reduced and/or sulfated heparin derivatives, it does not appear that a database search linking heparin to angina pectoris was ever performed. Therefore, in the event of further prosecution, the examiner should consider conducting a database search, e.g., in MEDLINE, CAS, BIOSIS (biological abstracts) and the PTO’s own automated patent search system, linking at least “heparin” to “angina pectoris,” e.g., within 10 words, and to publication years of 1992 or earlier, given the filing date of this application.

say that these different diseases are not related, i.e., are not all cardiovascular diseases. However, a treatment for one cardiovascular disease may or may not be indicated as the treatment for another cardiovascular disease any more than a treatment for a first-degree burn may or may not be indicated for the treatment of a third-degree burn. Therefore, while it may be plausible to use heparin/heparin derivative therapy to treat a patient with angina pectoris because it can be used to treat a patient with a less severe cardiovascular disease, i.e., atherosclerosis, the examiner has not established that one of ordinary skill in the art would have reasonably expected such therapy to be successful in the treatment of angina pectoris.

Assuming *arguendo* that it would have been obvious to treat a patient with angina pectoris with a heparin derivative, the question becomes whether the specific heparin derivatives recited in the claimed invention would have been obvious over the heparin derivatives described by Naggi '063, Naggi '881, Petitou or Conti. Insofar as the examiner appears to making an *In re Best* type of analysis,<sup>4</sup> we answer this question in the negative. While the heparin derivatives of the prior art do

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<sup>4</sup>As stated in *In re Best*, 562 F.2d at 1255, 195 USPQ at 433-34 (CCPA 1977):

Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. ... Whether the rejection is based on 'inherency' under 35 U.S.C. § 102, on 'prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products.

show a sulfur content, i.e., degree of sulfation, equal to or higher than the starting heparin from which they were derived, they have molecular weights *lower* than that of the starting heparin. In fact, both the anti-Xa activities and APTT/anti-Xa ratios of the derivatives of Naggi '063, to the extent that they are disclosed, do not meet the limitations of the heparin derivatives in the claimed invention. Thus, the examiner has not met her burden of establishing that the heparin derivatives of the prior art are identical or substantially identical to those of the claimed invention and, therefore, the burden has not switched to appellants to prove that the prior art heparin derivatives do not necessarily or inherently possess the characteristics of the heparin derivatives of the claimed invention.

Furthermore, it is well established that inherency and obviousness are different concepts. *In re Shetty*, 566 F.2d 81, 86, 195 USPQ 753, 756 (“inherency is quite immaterial if ... one of ordinary skill in the art would not appreciate or recognize that inherent result.”); *In re Spormann*, 363 F.2d 444, 448, 150 USPQ 449, 452 (“the inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.”). A conclusion of obviousness must be based on evidence, not unsupported arguments.

Based on the foregoing, we conclude that the examiner has not established a *prima facie* case of obviousness as to claim 15. Since all the limitations of independent claim 15 are not disclosed or suggested by the applied prior of Naggi '063, Naggi '881, Petitou or Conti, we will not sustain the

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rejection of dependent claims 16-18 under § 103. Dependent claims are nonobvious under § 103 if the independent claims from which they depend are nonobvious. *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

Having concluded that the examiner has not established a *prima facie* case of obviousness, we do not reach appellants' discussion of rebuttal evidence on pages 5 and 6 of the brief and on pages 2-4 of the reply brief.

#### *CONCLUSION*

To summarize, the decision of the examiner to reject claims 15-18 under 35 U.S.C. § 103 is reversed.

**REVERSED**



