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RICHARD W. HENNING  
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U.S. DISTRICT COURT  
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IN THE UNITED STATES DISTRICT COURT  
NORTHERN DISTRICT OF CALIFORNIA

GENENTECH, INC., ) Case Number C 94-01379 BAC  
Plaintiff, )  
) AFFIDAVIT OF  
) JOHN GHRAYEB, Ph.D.  
)  
CENTOCOR, INC., )  
) Date: August 26, 1994  
Defendant. ) Time: 9:00 a.m.  
Dept: Courtroom 5, 17th Floor

COMMONWEALTH OF PENNSYLVANIA :  
: ss  
COUNTY OF CHESTER :

DR. JOHN GHRAYEB, being duly sworn, deposes and  
says:

1. I am the Vice President of Pharmaceutical  
Research of Centocor, Inc. I make this affidavit in support  
of Centocor's motion for summary judgment. While my job  
title has changed over the years, I have been personally

AFFIDAVIT OF JOHN GHRAYEB, Ph.D.

1 involved with Centocor's research and development efforts in  
2 the monoclonal antibody field since 1984.

3 2. The c7E3 product is a fragment of a chimeric  
4 antibody which is intended to inhibit the formation of blood  
5 clots in the cardiovascular system. A chimeric antibody is  
6 a protein molecule which derives certain portions of its  
7 structure from one mammalian species (here a mouse) and  
8 other portions from a second species (here a human).

9 3. Centocor first began work on the anti-  
10 clotting drug ultimately known as c7E3 in 1986. In March of  
11 that year, it received a live culture of the murine (or  
12 mouse) hybridoma cell, 7E3, from Dr. Barry S. Collier of the  
13 State University of New York at Stony Brook ("SUNY"). This  
14 hybridoma cell resulted from a fusion of a mouse antibody-  
15 producing cell and a mouse myeloma cell, a cell capable of  
16 immortalizing the resulting fusion, that is, making it  
17 capable of continued cell division under culture. The  
18 antibody secreted by 7E3 binds specifically to a  
19 glycoprotein found on human blood platelets and thereby  
20 inhibits a step involved in the formation of blood clots.  
21 Centocor licensed 7E3 from SUNY to pursue research in the  
22 area of anti-clotting agents of potential benefit to  
23 patients at risk of the injurious consequences of blood  
24 clots. More generally, Centocor's focus has been on various  
25 antibody-derived diagnostic and therapeutic products since  
26 its founding.

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1 demonstrated to have the capability of secreting an intact  
2 and biologically active (or functional) four chain antibody.  
3 The antibody was chimeric; that is, the variable regions  
4 were derived from the mouse 7E3 and the constant regions  
5 were of human antibody derivation.

6 8. The transfectoma from which c7E3 is derived  
7 was created on September 19, 1988. This represented a  
8 continuation of the work begun at the end of 1987; and the  
9 same vectors were used. The September 19, 1988 transfectoma  
10 cell was subsequently subcloned to select a cell line  
11 capable of high level production of c7E3 to be used in  
12 clinical trials. The actual clinical product used by  
13 Centocor is an antibody fragment which retains the binding  
14 characteristics of the whole antibody. It is produced by  
15 cleaving the whole antibody with an enzyme which correctly  
16 selects the desired fragment. All of this research and  
17 development activity occurred prior to the issuance of the  
18 Genentech '567 patent.

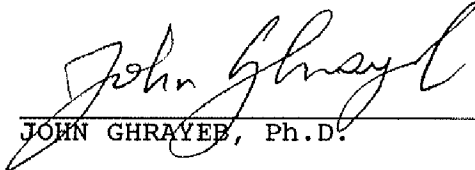
19 9. Shortly after receiving the 7E3 cell line,  
20 Centocor commenced toxicologic, pharmokinetic and  
21 pharmacologic testing of the 7E3 antibody and fragments  
22 thereof, including testing in animal models. Upon creation  
23 of transfectoma cell lines, similar testing began with c7E3  
24 and fragments thereof. Such testing is required by the FDA

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prior to the commencement of any clinical trials with human subjects.

  
JOHN GHRAYEB, Ph.D.

Sworn to and subscribed  
before me this 13<sup>th</sup>  
day of June, 1994.

  
NOTARY PUBLIC

Notarial Seal  
Beverly C. Halvorsen, Notary Public  
Malvern Boro, Chester County  
My Commission Expires July 21, 1997