

SUMMARY MINUTES - MEETING 7  
PANEL ON REVIEW OF BLOOD AND BLOOD DERIVATIVES

June 25, 1976  
Bethesda, Maryland

Bureau of Biologics  
Food and Drug Administration

Present:

Official Members

Scott Swisher, Chairman  
Joseph R. Bove  
John A Collins  
William S. Howland  
Robert D. Langdell  
Jacob Nusbacher  
Sherrill J. Slichter

FDA Participants and Observers

Morris Schaeffer  
Lewellys Parker  
Pinya Cohen  
Joan Roelands  
Elizabeth Paul  
E. R. Simon  
M. Crouch  
Sam Gibson  
John Finlayson  
Joyce Bagley

Liaison Representatives

Karl Bambach - Industry  
Louis Aledort - Consumer

Panel Executive Secretary

Clay Sisk

Observers

R. Ben Dawson, M.D. - U. Md.  
P. Hajduk - Abbott  
M. Wickerhauser - ARC

These summary minutes for the June 25-26, 1976 meeting of the Panel on Review of Blood and Blood Derivatives were approved and adopted on August 16, 1976.

Positions taken during the meeting are provisional in nature and may be modified or otherwise revised during subsequent deliberations of the Panel.

Whenever there is a lack of unanimity on any given point, the vote will be given. Regulations permit only the official panel members to vote.

"I certify that I attended the June 25-26, 1976 meeting of the Panel on Review of Blood and Blood Derivatives and that these minutes accurately reflect what transpired."

GRO-C: Scott Swisher MD

Chairman

1. The meeting was opened at 9:00 a.m. June 25, 1976, by Dr. Scott Swisher, the Panel Chairman. The minutes of the 6th meeting were approved with the following correction. The word "plasma" should be deleted in line 3 of paragraph 15.

2. In the open session, a letter from R. Ben Dawson, M.D., Baltimore, Maryland, was discussed. Dr. Dawson was present for the discussion. He requested that consideration be given to the use of Rh (D) Immune Globulin by the intravenous (I.V.) route rather than the presently approved intramuscular route. He cited experience and practice in Europe which has occurred subsequent to the licensing of the U.S. products. The issue of the I.V. route of administration is pertinent to all types of gamma-globulin. It was stated that studies would probably have to be done by the manufacturers to demonstrate the safety and effectiveness by the I.V. route. One study was mentioned with another globulin preparation in which there was a high rate of hepatitis transmitted when administered I.V. It was agreed that this is an important issue which deserves further study and discussion since the I.V. route should permit a much smaller dose and better utilization of specific immune globulin resources. The cost and practicalities of such studies, even if the European experience is utilized, may preclude a speedy resolution to the problem.

3. Additional data submissions were received from Hyland Laboratories and Cutter Laboratories in response to Panel requests. These will be considered when the products are reviewed in closed session.

4. In closed session, reviews of specific manufacturers' products were begun for Fibrinogen (Human), Normal Serum Albumin (Human), Plasma Protein Fraction (Human), Antihemophilic Factor (Human) and Factor IX Complex (Human). Panelists' draft reviews for these products will be further revised for discussion at the November meeting. Rh<sub>0</sub>(D) Immune Globulin was deferred until that time.

5. For Fibrinogen (Human), several risks and complications were identified. Fibrinogen is prepared from the plasma of large numbers of donors. Because of this and because fibrinogen will not tolerate those pasturization processes used to inactivate the hepatitis virus in other blood fractions, fibrinogen administration has been associated with a significant risk of transmitting viral hepatitis. The present risk is, however, almost impossible to evaluate since:

- a. Most studies do not have a careful follow-up of recipients.
- b. In almost all cases, recipients of fibrinogen have also received other blood products.
- c. There are no reports of the hepatitis incidence in patients who have received fibrinogen prepared from donor plasma that is negative when tested for hepatitis B surface antigen by third generation methods.

Therefore, the position stated in the minutes of the last meeting was reaffirmed. The consensus is that the product licenses should be withdrawn because the benefit-to-risk ratio is low. The Panel invites any physicians, manufacturers, or others interested in fibrinogen therapy with the presently available Fibrinogen products to present any data or opinion in support of or in opposition to its continued availability for certain well defined, limited uses. The subject will be considered at the November 12-13, 1976 meeting of the Panel. Persons interested in appearing should contact the Panel Executive Secretary in advance of the meeting.

6. Normal Serum Albumin, (Human) and Plasma Protein Fraction (Human) were generally considered to be safe and effective for their primary uses if the products are properly prepared and properly used. The Panel has difficulty in assessing whether the methods of preparation used by the different manufacturers are adequate. If possible, a consultant will be engaged to provide a detailed analysis of the fractionation methods to help determine if there are any identifiable deficiencies. Panel members expressed concern that many physicians using these products may be poorly informed about the clinical indications and the necessary dosages. One statement taken from the literature, "Albumin is used in too many patients in quantities too small to do many of them much good if they did need it," may summarize the Panel's opinion. The Panel report and labeling recommendations will address this issue. Also, basic research is needed on in vivo albumin persistence, distribution, metabolic fate, and transport competence of the proteins. The Panel recommends that such studies be undertaken by the National Heart, Lung and Blood Institute.

7. Antihemophilic Factor (Human) used to control spontaneous bleeding episodes in patients with congenital factor VIII deficiency was considered by the Panel to have benefits which vastly outweigh the risks presented by the product. When used to provide hemostatic levels in patients with congenital factor VIII deficiency who require surgery, the risk of the surgical procedure is made equivalent to that of an individual with normal hemostatic function. When used to treat acquired factor VIII deficiency, the benefit is less predictable. Prophylactic use in patients with congenital factor VIII deficiency poses safety considerations which have not been well evaluated. The risks may outweigh the benefits. Recommendations are to be developed upon further study by the Panel. There was an opinion that in selected patients prophylactic therapy may be indicated, but for most patients, therapy should be reserved to treat clinically apparent disease. A similar situation applies to recommendations for home therapy either in chronic low dose prophylactic use or for intermittent, episodic home therapy. Antihemophilic Factor (Human) usage is limited because of risk of transmitting viral hepatitis. The role of high purity or high potency concentrates also needs to be better defined.

8. Because of the high risk of hepatitis and thromembolic complications, the current sense of the Panel is that Factor IX Complex (Human) should be restricted to situations where the patient cannot be appropriately managed with fresh frozen plasma. These situations would include: 1) major surgery in patients with severe congenital deficiencies of the clotting factors contained in the concentrates and 2) life-threatening bleeding in patients with either Factor VIII or IX inhibitors or in patients with multiple deficiencies of the prothrombin complex factors where fresh frozen plasma is not available or where the recipient could not tolerate the volume of plasma administered.

9. The next meeting is scheduled for October 1 and 2, 1976 in Conference Room 10, Building 31, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland. A subsequent meeting is scheduled for November 12-13, 1976.

10. The agenda for the October 1-2, 1976 meeting will be devoted to the use of adenine in red blood cell preservation. The Panel will consider the evidence that an adenine preservative solution should be licensed by the Bureau of Biologics. The meeting will be conducted as a joint seminar with the National Heart, Lung and Blood Institute and will be open to the public.

11. The meeting adjourned at 5:15 p.m. June 25, 1976.