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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

CERTAIN BIOLOGICAL PRODUCTS

Request for Data and Information Regarding Safety, Effectiveness, and Labeling Review

The Food and Drug Administration is continuing its review of all licensed biological products to determine that they are safe, effective, and not misbranded under prescribed, recommended or suggested conditions of use. This notice is prompted by the elimination of three previously planned panels, namely: The Panel on Review of In Vitro Diagnostic Reagents, the Panel on Review of Immune Serums, Antitoxins, and Antivenins, and the Panel on Review of Miscellaneous Biological Products. Products from these three panels are being distributed to the remaining six advisory review panels, some of which are already constituted and others which are in the process of being formed. Also, eleven products are being transferred from the Panel on Review of Blood and Blood Derivatives.

The final order outlining the procedures and explaining the purpose of this review was published in the FEDERAL REGISTER of February 13, 1973 (38 FR 4319). To facilitate this review and to provide all interested persons an opportunity to present, for the consideration of the reviewing panels, the best data and information available to support the stated claims for this group of miscellaneous biological products, submission of data, published and unpublished, and other information pertinent to the products listed is hereby solicited.

Accordingly, notice is hereby given that all data and information regarding the safety and effectiveness of the following licensed biological products shall be submitted:

I. To be considered by the Panel on Review of Bacterial Vaccines and Toxoids with Standards of Potency:

Botulism Antitoxin.
Collagenase.
Diphtheria Antitoxin.
Fibrinolysin (Human).
Fibrinolysin and Desoxyribonuclease Combined (Bovine).
Fibrinolysin and Desoxyribonuclease Combined (Bovine) with Chloramphenicol.
Gas Gangrene Polyvalent Antitoxin.
Haemophilus Influenzae Typing Serum.
Pertussis Immune Globulin.
Staphylococcus Antitoxin.
Streptokinase.
Streptokinase-Streptodornase.
Tetanus Antitoxin.
Tetanus & Gas Gangrene Polyvalent Antitoxin.
Tetanus Immune Globulin.

II. To be considered by the Panel on Review of Viral and Rickettsial Vaccines:

Antirabies Serum.
Immune Globulin (Human), Pepsin-Modified.
Immune Serum Globulin (Human).
Measles Immune Globulin.
Mumps Immune Globulin.
Vaccinia Immune Globulin.

III. To be considered by the Panel on Review of Allergenic Extracts:

Histamine Azoprotein.

The format of the submission shall be in accordance with § 601.25(b)(3) (21 CFR 601.25(b)(3)), except as changed in this FEDERAL REGISTER notice. The Commissioner has concluded that some changes and clarifications are required for these products if the panel is to obtain the information needed for this review. The data required by these changes are necessary since differences in propagation techniques and manufacturing prosesses are critical in determining the quality and specifications of each particular finished product. Generic descriptions of production methods for a particular biological product, or data and studies relating to the same product processed by a different manufacturer may not always be sufficient to support the safety or effectiveness of any particular product.

Therefore, the submissions for these products shall follow the prescribed format incorporating the following changes and clarifications as applicable:

1. Items I and II are unchanged.

2. For item III, manufacturers of the products shall provide, in addition to the complete quantitative composition:

a. A description of the step-by-step manufacturing procedures currently employed;

b. Data on any preservatives, stabilizers, or adjuncts used either in the final product or employed in the manufacturing process;

c. A complete description of the biologic source(s) of all raw materials giving, where applicable, the species and types of animals used, the current types or strains of microorganisms used including their passage history and cultivation procedures, extraction or concentration techniques, storage methods, and all such pertinent information including any changes in these matters since original product licensure;

d. A description of the test methods used to demonstrate specificity, potency, purity, safety, and stability; and

e. Data indicating the means employed to assure that the culture medium used for the propagation of any microorganism does not contain ingredients capable of producing allergenic effects in human subjects where applicable to the product.

3. For items IV, V, and VI, manufacturers shall provide all existing data which are applicable to, or in direct support of, the specific product as currently produced by the manufacturer. When published literature or other reference data is cited, it shall be made clear whether it refers to the specific studies which apply to the company's product, as described in the submission, or whether it is a part of the general literature pertaining to the product generically. If a manufacturer's current finished product is produced in any manner other than referenced in the literature, or other data submitted in support of a similar product, the equivalency of the qualitative and quantitative compositions shall be identified and compared. A concise summary of the data contained in the reference material and a precise statement of how it supports the claims made for the product shall accompany the list of references.

4. In the matter of documented case reports for item V, "Human safety data," and item VI, "Efficacy data," numerous citations of individual case reports are not necessary. Instead, a tabular summary of data available, including the salient features concerning the patients tested, the results obtained and the types of reactions observed shall be provided for us by the panel. However, the raw data shall be available for inspection, or duplication for submission, should the panel find it necessary at a later date.

5. In submitting pertinent marketing experience as required in item V, paragraph C.4, each manufacturer shall list the number of doses distributed annually for the past 5 years.

6. For item VII the rationale for the recommended dosages shall also be included in the summary.

7. Item VIII is unchanged.

To assure a complete and fully informed review of this category, the panel may request additional data or information from producers of the licensed products under review.

To be considered, 12 copies of the data and information, presented in the prescribed format, must be submitted on or before August 19, 1974, to:

Office of Efficacy Review, Bureau of Biologics (HFB-5), Building 29, Room 124, 8800 Rockville Pike, Bethesda, Md. 20014.

Any other data and information which is available and pertinent to this category of biological products is solicited from all interested persons.

Dated: June 10, 1974.

SAM D. FINE,
Associate Commissioner for Compliance.

[FR Doc.74-14015 Filed 6-18-74;8:45 am]