May 29, 1997

Responsible Head
Plasma Fractionator
City, State, Zip

Dear Responsible Head,

The purpose of this letter is to provide all manufacturers of licensed plasma derivative products with an understanding of FDA's Center for Biologics Evaluation and Research (CBER) view on product recalls conducted by the plasma fractionation industry.

Recently, several different manufacturers of plasma derivatives have characterized a number of product retrievals as market withdrawals, which upon review CBER determined to warrant recall. CBER advised these manufacturers that these situations met the definition of a recall and subsequently the manufacturer initiated a recall of their products and provided instructions to secondary distributors for extension of the recall to their customers. In some instances, a re-issuance of letters to consignees was needed. Two of these situations were assigned Class I recall classifications by FDA. A Class I recall is "a situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death" [21 CFR 7.3 (m)(1)].

FDA defines a market withdrawal as "a firm's removal or correction of a distributed product which involves a minor violation that would not be subject to legal action by the Food and Drug Administration or which involves no violation, e.g., normal stock rotation practices, routine equipment adjustments and repairs, etc." [21 CFR 7.3 (j)]. Thus, it is FDA's viewpoint, that the characterization of any recall, particularly Class I recalls, as a market withdrawal can mislead the public as to the public health significance of the violative product.

When such characterization occurs, there is: (1) a misrepresentation of the health hazard; (2) a reduced sense of urgency; (3) a less extensive notification of secondary distributors, wholesalers, or retailers; and (4) an unnecessarily prolonged exposure of users to potentially unsafe products.

Prompt action to retrieve products is important as is the need to accurately describe the reason(s) for retrieval. We therefore believe that it is necessary to advise product manufacturers of the importance of removing violative products from distribution channels. Manufacturer's responsibilities and the consequences of inadequate implementation are discussed at length in FDA's

Enforcement Policy as published in the Federal Register of June 16, 1978 [43 FR 26202-26221], a copy of which is enclosed. In the preamble to the recall regulations, FDA noted that the Federal Food, Drug and Cosmetic Act and the Public Health Service Act had no specific recall provisions for foods, drugs and cosmetics and biologics. Since then, Congress amended the PHS Act, section 351(d)(2)(A) and added provisions for an FDA ordered recall of biological products. The order may be given when a licensed product presents an imminent or substantial hazard to the public health.

It is important to note that this "Enforcement Policy" recognizes that manufacturers have the primary responsibility for assuring that the products they manufacture and distribute comply with the law. They have the added responsibility of removing any product that does not so comply. When manufacturers do not appropriately or effectively conduct product recalls, FDA may initiate legal action, including seizures and injunctions [21 CFR 7.40 (c)].

In addition, FDA may request a firm to initiate a recall (FDA-requested recall) based on the following determinations: (1) that a distributed product presents a risk of illness or injury or gross consumer deception, (2) that the firm has not initiated a recall of the product, or (3) that an agency action is necessary to protect the public health and welfare.

Key provisions of these procedural guidelines that are pertinent to conducting proper plasma derivative recalls include the following:

I. Recall Strategy [21 CFR 7.42]

Firm-initiated recalls should be conducted in accordance with a recall strategy developed by the recalling firm. While a firm-initiated recall may proceed without FDA review and approval of the strategy, FDA will assess the adequacy of the strategy and recommend changes as appropriate. If a firm chooses to proceed with a recall without involving FDA, the Agency may request the re-issuance of recall letters, expansion of the recall, or other corrective action should the initial strategy be found inadequate. FDA places a high priority on recalls and is committed to working closely with manufacturers to expedite review and proper implementation of this important consumer protection measure.

It is also important to report recall information to the appropriate FDA personnel so that accurate information is obtained and prompt guidance can be provided. This should prevent erroneous advice and unnecessary delays. In the past, many plasma derivative manufacturers have communicated recall information to FDA personnel not assigned recall responsibility. In this regard, it is important that requests for recall guidance and assistance be directed to the proper FDA District Offices who have the responsibility for the day-to-day management and monitoring of recalls. Within CBER, recalls are the

responsibility of the Division of Inspections and Surveillance which coordinates the health risk assessment and classification, and disseminates this information to the appropriate district office(s).

II. Health Hazard Evaluation [21 CFR 7.41]

The evaluation of the health hazard presented by a product being recalled is an important part of the recall strategy. While the manufacturer should make a preliminary health hazard evaluation in the development of its recall strategy, FDA has the ultimate responsibility for assigning a health hazard. Factors used in assigning a health hazard are listed in 21 CFR 7.4l. It is important to note that FDA assesses the hazard of the product on various segments of the population who are expected to be exposed to the product, emphasizing those individuals who may be at greatest risk [21 CFR 7.41 (a)(3) & (4)].

For example, certain factual situations may pose a greater risk of adverse effects for hemophiliacs than for other populations. Manufacturers should pay particular attention to the unique health conditions of various users of these products in evaluating potential health hazards.

III. Depth of Recall [21 CFR 7.42 (b)(1)] and Effectiveness Checks [21 CFR 7.42 (b)(3)]

Depending upon the degree of hazard and extent of distribution, products may need to be recalled from the wholesale, retail, or consumer level. The recalling firm should ensure that the product is recalled from the level of distribution appropriate to the degree of hazard and conduct effectiveness checks to ensure that notification was received. In the preamble to the recall regulations [43 FR 26214, June 16, 1978], FDA advised that the purpose of effectiveness checks is to verify that all known, affected consignees have received notification about a particular recall and have taken appropriate action. The Agency further concluded that unless a firm follows through by checking the effectiveness of its recall, the firm is not meeting its obligation and responsibility to consumers.

FDA may regard a firm's recall as inadequate if the recall does not go to the proper depth in the distribution chain, thus necessitating the re-issuance of recall letters or FDA initiated legal actions.

IV. Recall Communications - Content and Inappropriate Promotional Statements [21 CFR 7.49].

Recall communications refer to letters and other forms of notification between the recalling firm and its customers. These notifications should be clear and

concise to assure that sufficient information is provided for removing violative product from distribution channels. The recall communication should not be diluted or camouflaged by irrelevant qualifications, promotional statements, or other information that may detract from the message [21 CFR 7.49 (c)(2)]. In the preamble to the recall regulations [43 FR 26215 - 26216, June 16, 1978], the Agency noted that a firm's recall communication has as its objectives to notify affected customers: (1) that the product in question is subject to recall, (2) that further distribution or use of any remaining product should cease immediately, (3) in certain cases, that the customer should in turn notify others known to have received the product, and (4) with instructions as to what to do with the product. For a firm's recall communication to achieve the above objectives, it is necessary to include a concise statement regarding the reason the product is being recalled and the hazard associated with that defect.

FDA has observed that recall notifications from plasma derivative manufacturers frequently have been found to be deficient and ineffective due to the inclusion of extraneous information that detracts from the message.

V. Public Notification of Recalls [21 CFR 7.50] and Public Warnings [21 CFR 7.42 (b)(2)]

The FDA makes available to the public in the weekly FDA Enforcement Report a descriptive listing of each new recall and its classification and the specific action being taken by the recalling firm. The report does not include a firm's product removals or corrections which the agency has determined to be market withdrawals or stock recoveries.

Public Warnings are different from Recall Communications in that the former are targeted to the ultimate consumer (i.e., user) while the latter are targeted to direct accounts, secondary distributors, wholesalers, or retailers. The purpose of a public warning is to alert the public that a product being recalled presents a serious hazard to health. It is reserved for urgent situations where other means for preventing use of the recalled product appear inadequate. Public Warnings may issue through the general news media (i.e., either national or local), and/or the specialized news media (e.g., professional or trade press), or to specific segments of the population (e.g., physicians, hospitals, etc.).

Recent public concern focusing on the importance of plasma derivatives to specific segments of the population suggest the need for rapid communication of recalls and/or market withdrawals. FDA has started to address this issue by: (1) convening a public workshop in November 1996, to discuss and obtain public input on notification of the public on recalls, and (2) the use of electronic communications, such as the CBER World Wide Web Home Page that has a special section for recalls and market withdrawals of fractionated blood and plasma

products.

Conclusions:

Plasma derivative manufacturers must be vigilant in exercising their recall responsibilities to restore public confidence in their products and avoid FDA initiated legal action. FDA is fully committed to the use of all available legal sanctions to assure removal of violative products not promptly removed through an effective recall.

This letter is written to urge your personal attention to this important public health matter. The enclosed Enforcement Policy is particularly relevant to this situation. I am available for further discussion with individuals or professional associations interested in cooperative efforts to enhance consumer protection through a more effective recall process for violative products.

Sincerely,

James C. Simmons
Director, Office of Compliance
Center for Biologics Evaluation
and Research