

# Safety of DEHP: Role of the Bureau of Biologics

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The position of the Bureau of Biologics (BoB) relative to the issue at hand is unique on several counts. First, Bureau of Biologics is formally interested in the phthalate issue only in connection with containers for blood and blood products. The authority to regulate the nature of such containers derives from specific regulations. For example, regarding plasma, 21 CFR, Section 648.68(b) states: "Final containers and their components shall not interact with the plasma contents under conditions of storage and use so as to alter the safety, quality, purity or potency of the plasma."

Second, the subjects involved are exposed to the highest doses of DEHP, and it is delivered via the intravenous route. Most of these subjects are patients undergoing treatment, although the increased interest in pheresis procedures will result in similar exposure for more and more normal donors.

Finally, BoB has considered the DEHP in vinyl plastics to be a problem for a number of years. That is, we have been aware that DEHP, a biologically active material, was leached by blood and plasma in considerable quantities from the PVC bags. We were also aware that the available data on toxicity did not support a regulatory demand for immediate change. Members of the blood-banking community were similarly concerned, and this concern was shared by the manufacturers of blood bags, as indicated by the considerable research expenditures dedicated to the quest for a substitute plastic.

At BoB the concerns which derived from the presence of DEHP were balanced by an appreciation of the need for a flexible container. The entire science of blood component preparation in a sealed system is dependent upon a flexible container. The Bureau of Biologics would therefore consider that reversion to a system based on glass bottles is not a viable alternative.

As far as actions that have been taken and will be taken, I would like to refer to the interesting dialogue at this conference between Drs. Peck and Kevy regarding the ability to show that any of the deposition of DEHP in mammalian organs led to demonstrable toxicity. I believe that both Drs. Peck and Kevy would agree that another question is appropriate and that is, rather than asking, "Is it toxic?" the question might be, "Is it possible to demonstrate toxicity in the clinical situation?" I further believe they would both agree that, given the difficulties of clinical investigation, it is not possible to answer that question. So, for the immediate future, the BoB will not await a definitive answer to the toxicity question, but will address other approaches to the problem.

We are aware that there is some concern about the rapidity with which submissions are reviewed and approved. Accordingly, we have already undergone some discussion, namely, blood and blood product containers, both dry and with anticoagulant. Specifically, after a period of about two years of investigating and holding conferences on the subject of testing blood platelets, we have simplified the procedures which were being demanded of the manufacturer for obtaining approval of a container used for storage of platelets. It had been the opinion of many in the community that this particular type of testing was the most onerous. We have developed a new set of guidelines which are available to any interested person and can be obtained by writing to the Director, Bureau of Biologics.

We will encourage accumulation of data on the content of DEHP in various blood products and hope, some time in the foreseeable future, to be able to encourage the development of guidelines for blood banking practice. Since we need a flexible bag, and the currently available systems have large amounts of leachable plasticizers, we would hope to limit exposure by some simple expedient such as using the shortest storage time possible for those components where this is practical. Knowledge of the DEHP content of various components, corre-

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lated with the conditions for their preparation and storage, should suggest a variety of maneuvers which would decrease patient exposure to infused DEHP.

We certainly agree that more fundamental data regarding carcinogenicity of DEHP are needed. Given the problems with the assay system, the variations in the literature stated, and species differences that we have heard about, we believe that any quantitative assessments of risk are premature at this time. We have been opposed to

disseminating such details to patients, such as hemophiliacs and leukemics, whom we feel are sufficiently burdened, and need not be concerned with questionable numbers at this time.

Finally, regarding the question that was asked in the previous session about a timetable for action. In addition to what has been said, I can only state that the Bureau of Biologics will take further action when we feel that there is a consensus within the scientific community that it is time to do so. At this time, we do not feel that there is such a consensus.