DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

SEP 5 2001

Sanford J. Lewis, Attorney
P.O. Box 79225
Waverly, MA 02179

Re: Docket Number 99P-2077/CP1

Dear Mr. Lewis:

This letter is in response to the citizen petition that you submitted to the Food and Drug Administration (FDA) on behalf of Health Care Without Harm (HCWH). FDA filed the petition on June 15, 1999. In the petition you requested that FDA (1) initiate a rulemaking or issue a guidance requiring that all polyvinyl chloride (PVC) medical devices that leach phthalate plasticizers include a prominent, clearly worded warning label as to the potential for di-(2-ethylhexyl) phthalate (DEHP) or other phthalate plasticizers to leach out the PVC and to enter the body, potentially causing detrimental health effects, and (2) establish a program to expedite the development and usage of substitutes for PVC medical devices that leach phthalate plasticizers.

In our two previous interim responses, we informed you that FDA was conducting a safety assessment of the DEHP used in medical devices (12/2/99) and that because of the complexity and extent of the analysis, we anticipated that the agency's review would take several months (3/29/00). We have since completed the safety assessment and the internal review of this document. The results of the safety assessment serve as the basis of the response to this petition. In addition, you can view the safety assessment on line at http://www.fda.gov/cdrh/ost/dehp-pvc.doc (Word version) or http://www.fda.gov/cdrh/ost/dehp-pvc.pdf (PDF version).

For the reasons outlined below, we are denying most of the specific actions you requested in your petition. We are, however, implementing a risk communication strategy to notify health care providers of the results of the safety assessment, available via the FDA website.

99P-2077

PDN 1

Labeling

In order to issue a regulation or guidance containing the labeling statement that you requested, FDA would need to determine that, without such a statement, the device would be misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352)(the Act)). Specifically, FDA would need to determine that the absence of such a statement would render the labeling of the device false or misleading or that, without such a statement, the labeling would not contain adequate directions for use of the device.

Patients undergoing medical procedures such as blood transfusions, hemodialysis and peritoneal dialysis, and cardiopulmonary bypass (CPB) may be exposed to DEHP, a compound used as a plasticizer for medical devices made from PVC. DEHP has been shown to produce a wide range of adverse effects in experimental animals. Although the toxic and carcinogenic effects of DEHP are well established in experimental animals, the ability of DEHP to produce adverse effects in humans is inconclusive and continues to be a topic of discussion and debate in the scientific and regulatory communities.

Because patients undergoing medical procedures may be exposed to DEHP, the Center for Devices and Radiological Health (CDRH) conducted a safety assessment to provide risk managers with information necessary for informed decision-making regarding the safety of DEHP released from PVC in medical devices. We are providing a copy of the safety assessment to you as part of this response.

After careful review of the petition and the supporting documents, we believe the evidence provided does not support your request that FDA require all PVC devices to include labeling that would warn users of the potential for DEHP leaching and potential adverse health effects from DEHP. For example, there is little concern for DEHP-mediated effects occurring in adult patients receiving intravenous solutions and there is little risk posed by exposure to DEHP in patients undergoing peritoneal dialysis. However, based on the results of the safety assessment, we recognize that risk reduction strategies may

be necessary for some medical procedures that employ PVC devices, and new labeling for selected devices is one possible regulatory option. Therefore, we may issue such guidance, or undertake other regulatory initiatives to address potential risks from DEHP associated with individual devices in the future.

Alternative Materials

In your petition, you also request that FDA establish a program to expedite the development and usage of phthalate-free alternatives to medical devices that leach plasticizers. We do not believe it is FDA's responsibility to establish programs to expedite the development of alternative materials. Any device manufactured from an alternative material would be required to go through the same review process as a device containing PVC to establish its safety and effectiveness.

However, the agency has discretion to apply expedited review procedures to its review of product applications and CDRH has published a guidance document on expedited review of premarket approval applications and premarket notifications (see www.fda.gov/cdrh/modact/expedite.html). CDRH will apply its expedited review policy to any applications for phthalate-free medical devices that meet the parameters of the guidance.

FDA is implementing a risk communication strategy to notify health care providers of the results of the safety assessment, available via the FDA website. In addition, we have posted a Q & A document on the FDA webpage, "Consumer Update – DEHP in Plastic Medical Devices" that you may see at http://www.fda.gov/cdrh/ocd/dehp.html to communicate the risks of DEHP exposure from medical devices to health care providers and to the general public.

Conclusion

FDA appreciates your client's interest in the safety of medical devices that leach phthalate plasticizers and the effort you have made to submit and support this petition. Although we are denying your petition, we

recognize that risk reduction strategies are appropriate for some medical procedures that employ PVC devices, and we are currently exploring options to reduce exposure of some patient populations to DEHP. These options, as mentioned above, may include new labeling for selected devices. If you have any questions on the information given above, please contact Dr. Mel E. Stratmeyer at 301-443-7130.

Sincerely yours,

Linda S. Kahan

Linda S. Kahan
Deputy Director
Center for Devices
and Radiological Health