

COURTNEY M. PRICE  
VICE PRESIDENT  
CHEMSTAR

October 22, 2002



Phillip J. Phillips  
Deputy Director for Science and Regulatory Policy  
Office of Device Evaluation  
Food and Drug Administration  
9200 Corporate Boulevard, HFZ 400  
Rockville, MD 20850

Re: Draft Guidance Pertaining to Medical Devices Made with PVC  
Containing DEHP, Docket No. 02D-0325

Dear Mr. Phillips:

This letter is submitted on behalf of the American Chemistry Council Phthalate Esters Panel, which includes the major U.S. producers and some processors of di-(2-ethylhexyl) phthalate (DEHP) and other phthalate esters.<sup>1</sup> The Panel appreciates the opportunity to meet with you and members of your staff on October 10, 2002, to clarify the intent of the above-referenced draft guidance document (Draft Guidance). Based on discussions at that meeting, the Panel now understands that CDRH did not intend the Draft Guidance to have the broad reach that one might infer from a literal reading of the draft document.

For reasons explained in this letter, the Panel believes CDRH should withdraw the Draft Guidance. If CDRH continues to feel that a guidance document is necessary, then the Panel believes CDRH should issue a revised draft and allow additional opportunity for public comment. Further, if CDRH elects to pursue that course of action, the Panel urges CDRH to announce its intentions as soon as reasonably possible, so that interested parties will not expend resources commenting on a draft document that does not accurately reflect CDRH's intentions.

As described at the recent meeting, the Draft Guidance is causing confusion in the marketplace because of inconsistencies within the document and between the document and the underlying safety assessment. The Draft Guidance acknowledges up front that "DEHP is recognized as an important chemical ingredient that affords PVC many of the physical properties that make the material optimally suited for use in many of today's medical devices." The Draft Guidance also acknowledges that while adverse effects have been observed in animal studies, "there are no human studies that show such effects." Further, the Draft Guidance states, "FDA recognizes that many devices with PVC containing DEHP are not used in ways that result in significant human exposure to the chemical." Elsewhere, however, the Draft Guidance contains

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<sup>1</sup> Members of the Panel include: BASF Corporation, Eastman Chemical Company, ExxonMobil Chemical Company, Ferro Corporation, PolyOne Corporation, Sunoco Inc., and Teknor Apex Company.



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very broad statements and recommendations that, read literally, appear to suggest that all medical devices made with PVC containing DEHP are a concern and should either be replaced or labeled. As stated, the Panel now understands that such a broad interpretation of the Draft Guidance was not intended by CDRH. Unfortunately, the Agency's intent is not clear from the literal language in the Draft Guidance.

Moreover, the overly broad statements in the Draft Guidance are not consistent with CDRH's underlying safety assessment. The concerns identified in the safety assessment pertain largely to *potential hazards* from use of specific medical procedures with specific potentially sensitive subpopulations (e.g., ECMO procedures applied to male neonates). The safety assessment does not demonstrate a likely safety concern for most uses of medical devices made with PVC containing DEHP.

Under the circumstances, the Panel believes CDRH should withdraw the Draft Guidance. The Panel does not believe a guidance document in fact is necessary; the Panel believes CDRH's safety assessment and related Public Health Notification dated July 12, 2002, which also contains recommendations, are adequate to inform medical device manufacturers of the scientific issues pertaining to use of PVC containing DEHP in medical devices.

If CDRH continues to believe a guidance document is necessary, then the Panel believes CDRH should issue a new draft that more accurately reflects CDRH's intentions and allow additional opportunity for public comment, as contemplated by 21 CFR 10.115(g)(1)(v) (procedures for developing and issuing guidance documents). Further, CDRH should promptly announce that it intends to take that action, and at the same time withdraw the current draft or suspend the comment period, so that interested parties will not spend time responding to a draft that will be superseded.

If CDRH decides to issue a new draft guidance document, the Panel urges CDRH to consider the following points:

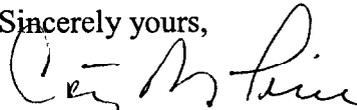
1. Any guidance document should direct attention to the *medical procedures* that CDRH believes pose a potential concern. A list of devices, without a clear connection to specific medical procedures, is misleading, because many medical devices are used in a wide variety of procedures, including both procedures that CDRH has identified as potentially of concern, and procedures that are expected to produce very low exposures relative to the tolerable intake (TI) calculated by CDRH.
2. Any guidance document should include greater recognition of the conservative nature of the TI in the underlying safety assessment. The TI is intended to represent a safe exposure level assuming repeated daily exposures for an extended period, which is not realistic for most medical procedures. The TI also is based on animal studies, in the absence of human data demonstrating adverse effects, and assumes that humans may be more sensitive than laboratory animals, even though primate data

suggest the opposite. For these reasons, even if use of a medical device in a particular procedure might result in exposures above the TI on the days that the procedure is performed, that does not mean there is a significant health risk to the patient.

3. Any guidance document should state clearly that if medical device manufacturers consider alternatives to PVC made with DEHP, they should give adequate consideration to all performance, exposure or safety issues associated with any alternative materials that might be considered. As reflected in the DEHP safety assessment, DEHP has undergone extensive testing and there is an enormous amount of scientific information available to support that safety assessment. Medical device manufacturers should be cautioned about moving to alternative products that might lead to decreases in performance and exposures to substances about which considerably less is known.<sup>2</sup>

Thank you for your consideration of this letter and the Panel's requests. The Panel respectfully urges prompt action by CDRH to alleviate the confusion in the marketplace caused by the overly broad statements in the Draft Guidance. If you have questions concerning this letter, please have your staff contact Marian K. Stanley, Manager of the Phthalate Esters Panel, at 703-741-5623 or [Marian\\_St Stanley@americanchemistry.com](mailto:Marian_St Stanley@americanchemistry.com).

Sincerely yours,



Courtney M. Price  
Vice-President, CHEMSTAR

cc: Daniel G. Schultz, M.D.  
Director, Office of Device Evaluation

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<sup>2</sup> As explained by Peter Galland of Teknor Apex during the meeting, Teknor Apex can supply both alternative polymers and PVC made with alternative plasticizers. However, as Mr. Galland explained, these materials do not share all the performance advantages of PVC (and, in this era of rising health care costs, typically cost more). Further, in the case of alternative plasticizers that might be used in PVC, these materials generally present similar opportunities for human exposure (or perhaps in some cases greater potential for exposure, because of greater solubility compared to DEHP), and much less toxicology data typically is available to support a safety assessment of those exposures.