



July 12, 2002

Public Health Notification: PVC Devices Containing the Plasticizer DEHP

(You are encouraged to copy and distribute this information)

Dear Colleague:

This is to inform you that FDA's Center for Devices and Radiological Health completed its safety assessment of Di(2-ethylhexyl)phthalate (DEHP) released from polyvinyl chloride (PVC) medical devices in September, 2001, and to advise you of steps that you can take to reduce the risk of exposure in certain populations.

Devices Affected

PVC is a plastic polymer that is used in a wide array of products. Unplasticized PVC is hard and brittle at room temperature. A plasticizer (softener) is typically added to increase the flexibility of the polymer. DEHP is the plasticizer for most PVC medical devices.

Devices that may contain DEHP-plasticized PVC include:

- intravenous (IV) bags and tubing
- umbilical artery catheters
- blood bags and infusion tubing
- enteral nutrition feeding bags
- nasogastric tubes
- peritoneal dialysis bags and tubing
- tubing used in cardiopulmonary bypass (CPB) procedures
- tubing used in extracorporeal membrane oxygenation (ECMO)
- tubing used during hemodialysis

Nature of the Problem

Everyone is exposed to small levels of DEHP in everyday life. However, some individuals can be exposed to high levels of DEHP through certain medical procedures. DEHP can leach out of plastic medical devices into solutions that come in contact with the plastic. The amount of DEHP that will leach out depends on the temperature, the lipid content of the liquid, and the duration of contact with the plastic. Seriously ill individuals often require more than one of these procedures, thus exposing them to even higher levels of DEHP.

Exposure to DEHP has produced a range of adverse effects in laboratory animals, but of greatest concern are effects on the development of the male reproductive system and production of normal sperm in young animals. We have not received reports of these adverse events in humans, but there have been no studies to rule them out. However, in view of the available animal data, precautions should be taken to limit the exposure of the developing male to DEHP.

Risk determinants

Two factors determine the degree of risk posed by exposure to DEHP in a medical setting. The first is the patient's sensitivity to DEHP. Based on the evidence cited above, the male fetus, male neonate, and peripubertal male would appear to be high-risk groups. The second factor is the dose of DEHP received by the patient. This is determined largely by the type of procedure performed, as well as the frequency and duration of these procedures.

Highest risk procedures

We examined the potential risk of exposure posed to patients by comparing the dose of DEHP that patients might receive during various procedures to a "Tolerable Intake" (TI) value for the compound.

The following procedures have been identified as posing the highest risk of exposure to DEHP:

- exchange transfusion in neonates
- ECMO in neonates
- total Parenteral Nutrition (TPN) in neonates (with lipids in PVC bag)
- multiple procedures in sick neonates (high cumulative exposure)
- hemodialysis in peripubertal males
- hemodialysis in pregnant or lactating women
- enteral nutrition in neonates and adults
- heart transplantation or coronary artery bypass graft surgery (aggregate dose)
- massive infusion of blood into trauma patient
- transfusion in adults undergoing ECMO

In contrast, there is little or no risk posed by patient exposure to the amount of DEHP released from PVC IV bags during the infusion of crystalloid fluids (e.g., normal saline, D5W, Ringer's Lactate). Further, there is little risk posed by exposure to the amount of DEHP released from PVC bags used to store and administer drugs that require a pharmaceutical vehicle for solubilization, when label instructions are followed.

Recommendations

Most importantly, you should not avoid the procedures cited above simply because of the possibility of health risks associated with DEHP exposure. The risk of not doing a needed procedure is far greater than the risk associated with exposure to DEHP.

For some of the above procedures, PVC devices that do not contain DEHP can be substituted, or devices made of other materials (such as ethylene vinyl acetate (EVA), silicone, polyethylene or polyurethane) can be used, if available. If PVC devices containing DEHP must be used, you may be able to minimize exposure to DEHP by, for example, using the freshest possible blood products stored at the lowest possible temperature, or by using heparin-coated ECMO circuits.

We recommend considering such alternatives when these high-risk procedures are to be performed on male neonates, pregnant women who are carrying male fetuses, and peripubertal males. One source for identifying alternative devices that do not contain DEHP-plasticized PVC is <http://www.sustainablehospitals.org>, associated with the University of Massachusetts Lowell.

For other patient groups, who are presumably at lower risk, the decision to use DEHP alternatives must take into account the medical advantages and drawbacks of the substitute materials and their availability.

Reporting Adverse Events to FDA

The Safe Medical Devices Act of 1990 (SMDA) requires hospitals and other user facilities to report deaths and serious injuries associated with the use of medical devices, including the devices cited above. We request that you follow the procedures established by your facility for such mandatory reporting.

We also encourage you to report other adverse events associated with the use of medical devices. You can report these directly to the device manufacturer. You can also report to MedWatch, the FDA's voluntary reporting program. You may submit reports to MedWatch one of four ways: online at <http://www.accessdata.fda.gov/scripts/medwatch>, by telephone at 1-800-FDA-1088; by FAX at 1-800-FDA-1078; or by mail to MedWatch, Food and Drug Administration, HF-2, 5600 Fishers Lane, Rockville, Maryland 20857.

Getting More Information

The complete safety assessment, "Safety Assessment of Di(2-ethylhexyl)phthalate (DEHP) Released from PVC Medical Devices," can be found on the CDRH web site at www.fda.gov/cdrh/ost/dehp-pvc.pdf. Should you have questions concerning this letter, please contact Laura Alonge, Office of

Surveillance and Biometrics (HFZ-510), 1350 Piccard Drive, Rockville, Maryland 20850, by fax at 301-594-2968, or by e-mail at phann@cdrh.fda.gov. Additionally, a voice-mail message may be left at 301-594-0650 and your call will be returned as soon as possible.

All of the FDA medical device postmarket safety notifications can be found on the World Wide Web at <http://www.fda.gov/cdrh/safety.html>. Postmarket safety notifications can also be obtained through e-mail on the day they are released by subscribing to our list server. You may subscribe at <http://list.nih.gov/archives/dev-alert.html>.

Sincerely yours,

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