GE Healthcare

# Di2-ethyhexyl phthalate (DEHP) in medical devices

## Examining the potential patient risks and what hospitals are doing to minimize exposure

White Paper

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# Introduction

## DEHP in Healthcare: Examining Risks and Safeguards

In the past decade, and increasingly in recent years, hospitals have reacted to concerns about the potential health effects of di2-ethylhexyl phthalate (DEHP), a plasticizer used in many medical devices. Some government agencies in the United States, Canada and Europe have found that newborns in Neonatal Intensive Care Units (NICUs) may be exposed to levels of DEHP that have been found to cause harm to the male reproductive tract in laboratory animals. Some researchers believe the animal studies are relevant for predicting impacts in humans. At the same time, the agencies have also noted that there is no human data to determine whether male babies are actually affected.[1]

News reports and GE Healthcare observations show that some hospitals are requiring certain devices used in the NICU to be DEHP-free, and that some are insisting on DEHP-free products even more broadly. For example, some hospitals now require all NICU devices to be DEHP-free. Also in 2005, the Catholic Healthcare West system based in San Francisco, CA., transitioned to DEHP-free products for all of its intravenous solution bags, solutions and tubing.[2]

GE Healthcare is sensitive to these concerns and has developed cuffs that do not contain DEHP, even though to our knowledge no research has cited cuffs as a significant source of DEHP exposure in the NICU or elsewhere. To help our customers understand the potential issues surrounding DEHP, we offer this review of literature. It draws upon journal articles and reports from government agencies and non-profit organizations that present a wide range of perspectives on DEHP, its potential risks, and practical safeguards. We encourage readers to review in their entirety any or all of the items referenced at the end of this document. Each hospital must evaluate the available data and make its own informed choices about DEHP and the use of DEHP-free products.

[1] Rossi, M. Neonatal Exposure to DEHP (di-2-ethylhexyl phthalate) and Opportunities for Prevention. Health Care Without Harm, Third edition, October 2002.

[2] Catholic Healthcare West: www.chwhealth.org/Who_We_Are/Environment/index.htm.

## What is DEHP?

DEHP is a manufactured chemical from a family called phthalates (pronounced THA'-lates). This chemical is used to make plastics soft and flexible. One such plastic is PVC, which is used in many medical devices. DEHP is a colorless liquid with almost no odor and is used in a wide range of products, including wall coverings, tablecloths, floor tiles, upholstery, shower curtains, garden hoses, baby pants, dolls, toys, and packaging materials.[3] In healthcare, DEHP is used in items such as blood storage bags, IV bags, enteral nutrition feeding bags, umbilical artery catheters, and a wide variety of tubing,[4] including the tubing found in some blood-pressure cuffs.

The oral route is the main pathway for DEHP exposure.[5] Skin contact with products containing DEHP is less likely to cause harmful effects because the chemical cannot be absorbed easily through the skin.[6]

## Why are there concerns about DEHP?

Concerns about DEHP have risen because animal studies indicate that the chemical is a reproductive and developmental toxicant. One of the biggest concerns focuses on the developing male infant's reproductive tract. DEHP is used in a wide variety of products, it is everywhere in the environment, and everyone is exposed to it on some level every day. However, during medical procedures, people can be exposed to more DEHP than they would encounter in daily life. Because the developing male reproductive tract is the most sensitive area, there is special concern about DEHP exposure in fetuses, infants, and boys before puberty.[7] Also potentially vulnerable are healthy infants, and toddlers and pregnant and lactating women.[8]

Medical procedures can expose patients to higher levels of DEHP because the chemical can leach out of plastic medical devices and into solutions that come into contact with the plastic. Seriously ill patients may have multiple medical procedures, increasing their exposure to DEHP.[9] Apart from the number of procedures, some additional factors that may cause more DEHP to leach out of medical products are higher temperatures, higher lipid content in the liquid (because DEHP is fat soluble), higher DEHP content in the plastic, and prolonged contact between the liquid and the plastic.

Medical procedures that pose the highest risks of DEHP exposure include:

- Exchange transfusion, Extracorporeal Membrane Oxygenation (ECMO), Total Parenteral Nutrition (TPN) and multiple procedures in neonates.
- Hemodialysis in peripubertal males and lactating women.
- Enteral nutrition in neonates and adults.
- Heart transplantation or coronary artery bypass graft surgery.
- Massive infusion of blood to trauma patients.
- Transfusion in adults undergoing ECMO.[10]

Neonates in the NICU are likely to be among the most exposed patients because of their low body weight and the many different DEHP-containing products used regularly in that setting.[11] Human fetuses, pre-term babies, and other neonates may be more vulnerable to DEHP exposures because of their lack of mature metabolic pathways used to break down DEHP. This prolongs their exposure when compared to adults.[12]

[3] Di(2-ethylhexyl) phthalate (DEHP), CAS # 117-81-7, Fact Sheet from Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Social Services, September 2002.

[4] Medical Devices: FDA Public Health Notification: PVC Devices Containing the Plasticizer DEHP, U.S. Food and Drug Administration, July 2002.

[5] "Toxicological Profile for Di(2-Ethylhexyl)Phthalate," U.S. Department of Health and Human Services, Public Health Service, Agency For Toxic Substances And Disease Registry, September 2002.

[6] Di(2-ethylhexyl) phthalate (DEHP), CAS # 117-81-7, Fact Sheet from Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Social Services, September 2002.

[7] Rossi, M. Neonatal Exposure to DEHP (di-2-ethylhexyl phthalate) and opportunities for prevention. Health Care Without Harm, Third edition, October 2002.

[8] The weight of the evidence on DEHP: Exposures are a cause for concern, especially during medical care. Going Green: A Resource for Pollution Prevention in Health Care, Health Care Without Harm, March 2009.

[9] Medical Devices: FDA Public Health Notification: PVC Devices Containing the Plasticizer DEHP, U.S. Food and Drug Administration, July 2002.

[10] Medical Devices: FDA Public Health Notification: PVC Devices Containing the Plasticizer DEHP, U.S. Food and Drug Administration, July 2002.

[11] Schettler, T, DEHP exposures during the medical care of infants: A cause for concern, Going Green: A Resource for Pollution Prevention in Health Care, Health Care Without Harm, November 2002.

[12] Rossi, M. Neonatal Exposure to DEHP (di-2-ethylhexyl phthalate) and Opportunities for Prevention. Health Care Without Harm, Third edition, October 2002.

## What does the research say about the health effects of DEHP?

The U.S. Food and Drug Administration reports, "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 effects 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."[13]

Effects on the male reproductive system found in animal studies include undescended testes, abnormal sexual development, penile abnormalities, prostate agenesis, nipple retention, hypospadias, atrophy of the seminiferous tubes, changes in sperm production, and reductions in the weight of the testes, epididymis, prostate, seminal vessicle, and glans penis. Other reproductive and development effects in laboratory animals include skeletal, cardiovascular, eye and neural tube defects; intrauterine death and increased post-natal death; decreased intrauterine and post-natal growth; ovarian changes; and infertility in males and females. Also observed were suppressed or delayed ovulation, suppressed estradiol production, polycystic ovaries, reduced kidney function, kidney atrophy, reduced liver function, respiratory distress, and decreased heart rate and blood pressure.[14]

To date, no studies have shown that DEHP in medical devices harms humans. In 1999, a panel convened by the American Council on Science and Health and chaired by former U.S. Surgeon General C. Everett Koop reviewed scientific literature and risk assessments published by government agencies. The panel concluded that DEHP in medical devices is not harmful even to people who are highly exposed to the chemical, and that physical characteristics in products containing DEHP are critical to the function of medical devices, such that the elimination of the chemical in these products could cause harm to some patients.[15]

One scientific study followed up with 13 boys and six girls ages 14 to 16 who had undergone ECMO as neonates. It concluded that there were no significant negative effects on their physical growth, pubertal maturity, and that functionality of key organs and gonadal functions were within a normal range for age and sex distribution.[16]

## What do government agencies say about the risks of DEHP?

According to a summary report from Health Care Without Harm, "Assessments conducted for the governments of the United States, Canada and the European Union have all concluded that exposures to DEHP are of concern to some patient populations and subsets of the general public…All of the government-sponsored assessments point to the need for action, with the Canadian and Swedish studies recommending specific action to reduce DEHP in health care and other vulnerable populations. The FDA has recommended that medical device manufacturers reformulate products to remove DEHP and that hospitals use alternatives to DEHP-containing products, whenever possible, for high-risk populations."[17] The summary cites these reports:

- U.S. National Toxicology Program Expert Panel, 2000, 2005, 2006. The panels concluded that DEHP is a reproductive and developmental toxicant in animals, that the animal studies are relevant to humans, and that current exposure levels were of particular concern for critically ill infants, healthy infants and toddlers, and pregnant and lactating women.
- U.S. FDA Safety Assessment, 2001. The assessment listed several procedures in which patients' exposure to DEHP may exceed the agency's tolerable intake level.
- U.S. FDA Public Health Notification, 2002. The FDA issued a public health notification that advised considering alternatives to DEHP-containing products, if available, for certain procedures involving male neonates, pregnant women who are carrying male fetuses, and peripubertal males.
- American Medical Association, 2006. The AMA approved a resolution encouraging hospitals and physicians to phase out PVC medical devices, especially those containing DEHP, and urging use of safe, cost-effective alternatives where available.
- Consumer Product Safety Improvement Act of 2008. The U.S. Congress passed this law, which includes a federal ban on DEHP and five other phthalates in toys and children's products.
- National Academy of Sciences. The academy's report, Phthalates and Cumulative Risk Assessment: The Task Ahead, recommended that risks of phthalate exposure be considered in the context of cumulative exposure to all phthalates and anti-androgens.
- Health Canada Expert Advisory Panel on DEHP, 2002. The panel recommended that DEHP-containing devices not be used in certain specific procedures.[18]

[13] Medical Devices: FDA Public Health Notification: PVC Devices Containing the Plasticizer DEHP, U.S. Food and Drug Administration, July 2002.

[14] Rossi, M. Neonatal Exposure to DEHP (di-2-ethylhexyl phthalate) and Opportunities for Prevention. Health Care Without Harm, Third edition, October 2002.

[15] American Council on Science and Health, Review and consensus statement: A scientific evaluation of the health effects of two plasticizers used in medical devices and toys, June 1999.

[16] Khodayar R, Nunez S; Revenis ME; Luban N, Short B, "Follow-up study of adolescents exposed to di(2-ethylhexyl) phthalate (DEHP) as neonates on extracorporeal membrane oxygenation (ECMO) support, Environmental Health Perspectives, 2004.

[17] The weight of the evidence on DEHP: Exposures are a cause for concern, especially during medical care. Going Green: A Resource for Pollution Prevention in Health Care, Health Care Without Harm, March 2009.

Recommendations and restrictions on the use of DEHP in the European Union include:

- European Union Directives Restricting the Use of DEHP in Products, 2001.
- European Union, Draft Risk Assessment, prepared by Swedish Chemical Inspectorate, 2004.
- European Union, Draft Risk Reduction Strategy, prepared by Swedish Chemical Inspectorate 2005.
- European Parliament's Resolution of DEHP, 2001, 2005.
- European Chemicals Agency, Support Document for Identification of DEHP as a Substance of Very High Concern, 2008.
- German Federal Institute for Drugs and Medical Devices, warning to healthcare professionals, 2002.

On the other hand, in 2007, the European Union Scientific Committee on Emerging and Newly-Identified Health Risks (SCENIHR) published a report on "the safety of medical devices containing DEHP-plasticized PVC or other plasticizers on neonates and other groups possibly at risk."

The Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom reviewed the report and concluded:

- No new evidence suggested that medical devices plasticized with DEHP present an unacceptable health risk to humans, and in particular DEHP exposure had no proven effect on male reproductive health.
- Medical devices containing DEHP-plasticised PVC had important clinical benefits, and therefore it would be premature to recommend a change to other plasticizers.[20]

## Are there alternatives to medical devices containing DEHP?

There are various ways to eliminate or limit patients' exposure to DEHP. The U.S. FDA states that for some procedures with high-risk patients, PVC devices that do not contain DEHP can be substituted, or devices made of non-PVC materials can be used.[21]

Alternative polymers such as ethylene, vinyl acetate, polyethylene, polypropylene, polyurethane and silicone are inherently flexible and so do not need a phthalate softening agent. Another approach is to use DEHP-containing products coated with a thin layer of another material to prevent or reduce leaching.[22]

Another way to minimize exposure is to use, for example, the freshest possible blood products stored at the lowest possible temperatures.[23]

The number of PVC- and DEHP-free medical products continues to grow, and makers of PVC-free medical-grade plastics are experiencing increased demand.[24]

## What are hospitals doing to minimize DEHP exposure?

A first step to eliminating DEHP is to identify which products contain it. Once that is done, alternatives must be evaluated. It can be helpful to create a committee of stakeholders to perform the evaluation and devise a plan for replacing DEHP-containing products with alternatives.[25]

Direct, specific health risks are not the only reason hospitals are considering replacement of DEHP-containing devices: Some are doing so as part of overall green initiatives that include efforts to decrease the use of chemical pollutants.[26]

Hospitals take a variety of approaches to dealing with DEHP. Many hospitals and health systems are transitioning away from DEHP, especially in the NICU.[27] Here are a few representative examples:

- At John Muir Medical Center in Walnut Creek, CA, the Intensive Care Nursery (ICN) staff evaluated the NICU product list and identified which ones contained DEHP and which did not. The hospital's clinical nurse specialist then led a DEHP-reduction effort, working with the medical and nursing staffs. The facility announced a virtually DEHP-free NICU within six months of beginning the effort.[28]
- Kaiser Permanente, the nation's largest nonprofit health plan, undertook a process to identify DEHP-containing medical devices used in NICUs and evaluate alternatives. Staff used a risk-management process to target products and ran clinical trials to test alternatives. In the end, the system switched to non-DEHP products for three common NICU devices: umbilical vessel catheters, PICC lines, and enteral feeding products.[29]
- Miller Children's Hospital in Long Beach, CA, made TPN bags and tubing the top priorities for reducing DEHP exposure to neonates, followed by IV sets. With help from the pediatric department medical staff, clinical products committee, central supply products manager, and the risk management attorney, the facility reached its target of 100% DEHP elimination in IV and TPN products.[30]

[18] The weight of the evidence on DEHP: Exposures are a cause for concern, especially during medical care. Going Green: A Resource for Pollution Prevention in Health Care, Health Care Without Harm, March 2009.

[19] The weight of the evidence on DEHP: Exposures are a cause for concern, especially during medical care. Going Green: A Resource for Pollution Prevention in Health Care, Health Care Without Harm, March 2009.

[20] "Phthalates/DEHP in PVC medical devices," Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom, 2007.

[21] Medical Devices: FDA Public Health Notification: PVC Devices Containing the Plasticizer DEHP, U.S. Food and Drug Administration, July 2002.

[22] Rossi, M. Neonatal Exposure to DEHP (di-2-ethylhexyl phthalate) and opportunities for prevention. Health Care Without Harm, Third edition, October 2002.

[23] Medical Devices: FDA Public Health Notification: PVC Devices Containing the Plasticizer DEHP, U.S. Food and Drug Administration, July 2002.

[24] Rossi, M. Neonatal Exposure to DEHP (di-2-ethylhexyl phthalate) and opportunities for prevention. Health Care Without Harm, Third edition, October 2002.

[25] Gilmore Hall A, Nurses: taking precautionary action on a pediatric environmental exposure: DEHP. Pediatr Nurs 2006;32(1):91-93.

[26] Sattler B, Hall K, Healthy choices: transforming our hospitals into environmentally healthy and safe places. Online Journal of Issues in Nursing, Aug 29, 2007.

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This review draws on information from industry associations, government agencies, and clinical journal articles that provide a range of information, recommendations and viewpoints on DEHP in medical devices and its potential effects on sensitive patient populations. The sources are:


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- "Nurses: Taking Precautionary Action on a Pediatric Environmental Exposure: DEHP," Anna Gilmore Hall, *Pediatric Nursing*, 2006.
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[27] Gilmore Hall A, Nurses: taking precautionary action on a pediatric environmental exposure: DEHP. Pediatr Nurs 2006;32(1):91-93.

[28] Gilmore Hall A, Nurses: taking precautionary action on a pediatric environmental exposure: DEHP. Pediatr Nurs 2006;32(1):91-93.

[29] Gilmore Hall A, Nurses: taking precautionary action on a pediatric environmental exposure: DEHP. Pediatr Nurs 2006;32(1):91-93.

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GE Healthcare provides transformational medical technologies and services that are shaping a new age of patient care. Our broad expertise in medical imaging and information technologies, medical diagnostics, patient monitoring systems, drug discovery, biopharmaceutical manufacturing technologies, performance improvement and performance solutions services help our customers to deliver better care to more people around the world at a lower cost. In addition, we partner with healthcare leaders, striving to leverage the global policy change necessary to implement a successful shift to sustainable healthcare systems.

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