

The Weight of Evidence on DEHP

Overview of Legal Actions to Restrict the Use of Phthalates, Particularly in Relation to Medical Care

Introduction

Although DEHP (di(2-ethylhexyl) phthalate) is hazardous to people's health, it is still widely used in medical devices within many European hospitals and health care facilities. Due to the environmental health risks it brings throughout its life cycle, DEHP-softened PVC has been criticised by the scientific community, governments and NGOs for more than 10 years, and many statements exist expressing this concern.

When the EU decided to classify DEHP as a health hazard and label it as "toxic" with a "skulls and crossbones" symbol, global discussions on reducing exposure to DEHP gained further momentum. Studies undertaken by US, Canadian and EU governments have all concluded that DEHP exposure is a real concern to certain patient populations and subsets of the general population. In particular, healthy infants and toddlers, pregnant and lactating women, and patients undergoing certain medical procedures are vulnerable. All of the government-led studies recommended action to reduce DEHP exposure in vulnerable populations.

Despite the results of these scientific studies, the use of DEHP-softened PVC medical devices continues. As is the case with many other chemicals, the lack of evidence of harm in humans is used as proof of safety and the European regulatory authorities have so far failed to protect citizens. For high-risk patient groups, scientific evidence has already led to a recommendation to limit DEHP use in certain medical procedures. However, instead of implementing this recommendation and using the precautionary principle to limit the use of phthalates in medical devices and other consumer products for the whole population, the EU authorities have not acted.

This paper aims to highlight where the EU and its member states, as well as other global actors, have taken action in relation to restricting the use of DEHP. It also provides some concrete actions that European and national governments can take immediately to reduce the health risks.

Recommendations for Action

HCWH and EPHA Environment Network recommend that European and national regulatory authorities:

- 1. Finalise the Risk Assessment and Risk Reduction Strategy on DEHP and include a recommendation to limit risks from DEHP exposure in medical devices.**
- 2. Restrict the use of DEHP in medical devices by amending EU Directive 93/42/EEC concerning medical devices.**
Immediately ban the use of DEHP in products used for medical procedures where long-term exposure can lead to an increased risk of developmental and reproductive disorders for certain patient groups, or to their offspring, and where safer alternatives are already on the market.
- 3. Implement the substitution principle and phase out the use of DEHP in all medical devices where safe alternatives are readily available on the market.**
The same precautionary approach that was taken with certain toys and cosmetics, where DEHP has been banned from use, should be applied to medical devices.
- 4. Ensure that the REACH proposals for the regulation of chemicals will require the mandatory substitution of 'substances of very high concern' when a safer alternative is already available on the market,** in order to reduce the public's general exposure to hazardous chemicals in the environment and from consumer products.

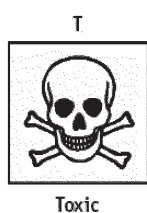
The difficulties of using DEHP as a softener in PVC medical devices must be viewed in the context of a wider problem. Substituting DEHP with another type of plasticiser does not resolve the health risks of using plasticisers, that is, their properties of leaking into the solutions (especially fatty solutions and blood) which are then transferred directly to the patient's body.

Therefore, HCWH and EEN recommend the substitution of PVC materials in general when possible, not just DEHP. PVC leads to a number of other environmental problems throughout its entire life cycle including the release of dioxins during combustion of PVC medical waste.

Restriction on DEHP Use in European Union:

European Union Directives restricting the use of DEHP in products

DEHP is classified as toxic to reproduction according to the EU Directive 67/548/EEC on Classification and Labelling of Dangerous Substances.¹ To indicate the danger so called "risk phrases" are used: R60 - "May impair fertility" and R61 - "May cause harm to the unborn child." DEHP as such and chemical preparations containing more than 0,5% of DEHP must be labelled with the "skull and crossbones" symbol and warning text reading TOXIC.



Unfortunately for DEHP/PVC users and consumers, this directive is limited to chemical preparations and does not restrict the use of DEHP in products such as medical devices made out of soft PVC containing 30 - 40% of DEHP by weight on average.²

In contrast, DEHP has been already banned in cosmetics and certain toys and children's products. The risks posed by toys and childcare articles have to an extent been covered by the European Commission (Decision 1999/815/EC) temporary ban on DEHP and five other phthalates; DIDP, DINP, DBP, BBP and DNOP in toys and childcare articles intended to be put into the mouth by children under three years of age. In September 2004, the EU Competitiveness Council agreed to replace this temporary ban with permanent legislation within the framework of

Directive on Restrictions on the Marketing and Use of Certain Substances and Preparations (76/769/EEC), which banned DEHP, DBP and BBP in toys and children's articles for ALL children because of their classification as reproductive toxicants. The revision also bans DIDP, DINP and DNOP in the same products intended for children under 3 years of age. This decision clearly demonstrated the EU's ability to act in precautionary manner and protect our children from hazards posed by phthalates.

Similar restrictions on DEHP, as one of many substances classified as Carcinogenic, Mutagenic and Reproductive Toxicants (CMR), have been already adopted in the Cosmetics Directive 2003/15/EEC by European Parliament in February 2003. "The Scientific Committee on Cosmetics concluded that CMR substances pose a significant threat to the health of consumers when used in cosmetic products. Although the exposure routes are not the same, toys, food packaging materials and medical devices may be seen as parallel cases giving rise to direct exposure of (the) consumers."³

EU Risk Assessment and Risk Reduction Strategy on DEHP

The EU has been working on the risk assessment and risk reduction strategy for DEHP since 1997. The Risk Assessment on DEHP concluded in 2004 that there is a need to limit risks for consumers from medical equipment for specific medical procedures:

- for long term haemodialysis in adults⁴
- long term blood transfusion in children
- and transfusion in neonates

This concern is based on adverse effects on fertility, testes and reproductive function.⁵ DEHP can leach out from medical devices such as catheters, tubing and intravenous sets during repeated long-term procedures when liquids circulate through the tubing for many hours and therefore the exposure to the reproductive toxin may be quite significant.

The recent draft of Risk Reduction Strategy on DEHP therefore includes several legislative actions to limit these

risks in patients. It recommends restricting the use of DEHP in medical devices giving rise to exposure of neonates and identified groups of concern. Urgent and immediate action is needed in order to avoid yet more delays before measures are taken to limit the exposure of neonates from medical devices.

The practicality of such steps is being currently discussed by the Medical Devices Expert Group under the DG Enterprise. Additionally, there are suggestions to amend the Medical Devices Directive (93/42/EEC), including generic limitations on the use of CMR substances, category 1 and 2 and in the relevant legislation for toys (88/378/EEC), food packaging material (2002/72/EEC) and medical devices.⁶ Such a measure would stimulate the development of alternative materials for medical devices, and at the same time avoid undesirable substitution of DEHP with other substances of similar severe properties.

The newly proposed chemicals legislation reform known as REACH (Registration, Evaluation and Authorisation of Chemicals) should institutionalise this substitution principle and require substitution of chemicals of high concern (which include all CMR substances) in the majority of products. Substances such as DEHP will have to be authorised for continued use only if there are no safer alternatives available. Although medical devices are not included in REACH, similar principles of evaluation, authorisation and substitution are suggested to be applied in a long-term.

European Parliament's Resolution on DEHP

In 2001, the European Parliament adopted a resolution in response to the Commission Green Paper on environmental issues of PVC⁷ and called for the Commission and the PVC industry to examine how targets might be set to reduce the use of phthalates, particularly in medical equipment. The resolution also asked the Commission to examine alternatives to the uses of phthalates as plasticisers.

In February 2005, the European Parliament brought this issue again to the forefront by adopting a resolution on the European Environment & Health Action Plan 2004-2010 and called for

action specifically in the area of phthalates and vulnerable groups. "Considers that, without prejudice to existing legislation and following the opinion of the Scientific Committee on Health and Environment Risks, urgent consideration needs to be given to restricting the marketing and/or the use on the European market of the following dangerous substances, to which new-born babies, children, pregnant women, elderly persons, workers and other high-risk sections of the population are heavily exposed, as safer alternatives become available: Six products from the phthalate family (DEHP, DINP, DBP, DIDP, DNOP, BBP) in domestic products for indoor use and in medical devices, except where such a restriction would have a negative impact on medical treatment, ..."8

German Federal Institute for Drugs and Medical Devices (BfArM)

In 2004, the German Federal Institute for Drugs and Medical Devices (BfArM) issued a warning to health care professionals in order to minimise exposure primarily for the high-risk patient groups. These include foetuses, premature infants and newborns as well as children in pre-puberty age.

It was recommended that:

- medical devices manufacturers actively engage and strive for further development of safer DEHP-free alternative products;
- manufacturers consequently provide users with a comprehensive explanation on the risks of DEHP in medical devices as well as label correspondingly their products;
- in neonatology intensive care, alternative products are used if available and suitable for the relevant procedure in order to act with precaution and therefore avoid the DEHP exposure for premature infants and newborns.

Additionally, BfArM urged consumers in health care facilities to ask for alternative products whenever substitution is possible without compromising the quality of medical care. BfArM follows the assumption that increasing consumers' demand will have a lasting positive influence on the market development of safer alternatives. Likewise, BfArM urges producers to develop DEHP-free alter-

native high-quality products and to recommend their use to customers, especially the high-risk patient groups mentioned above.⁹

Recommendations to Limit the Use of DEHP Outside of EU

Proposition 65 California

Proposition 65: The Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency added DEHP to the list of more than 750 chemicals known to the state to cause reproductive toxicity for the developmental and male reproductive endpoints.¹⁰ Companies that use DEHP in their products are required to warn consumers of potential exposure or reformulate their products by October 2004. This covers not only medical devices but also consumer products. Manufacturers today must either produce medical devices without these reproductive toxins, or notify health care providers that their products contain DEHP and may pose reproductive hazards.

The United States National Toxicology Program (US NTP)

The United States National Toxicology Program (US NTP) concluded in 2001 that DEHP is a reproductive and developmental toxicant in animals; the animal studies are relevant to humans; and current exposure levels are of concern for three distinct human populations:

Critically ill infants:

"The available reproductive and developmental toxicity data and the limited but suggestive human exposure data indicate that exposures of intensively-treated infants/children can approach toxic doses in rodents, which causes the Panel serious concern that exposure may adversely affect male reproductive tract development [in humans]."

Healthy infants and toddlers: "If healthy human infant/toddler exposure is several-fold higher than adults [it will approach levels found to be toxic in rodents, therefore], the Panel has con-

cern that exposure may adversely affect male reproductive tract development [in humans]."

Pregnancy and lactation: "[T]he panel has concern that ambient oral DEHP exposures to pregnant or lactating women may adversely affect the development of their offspring."¹¹

The United States Food and Drug Administration (US FDA)

The United States Food and Drug Administration (US FDA), which assessed the safety of DEHP use in medical devices, concluded that exposures to patients during the following medical procedures may exceed the Agency's tolerable intake level for DEHP:

- All patients receiving enteral nutrition;
- Infants receiving total parenteral nutrition (TPN);
- Infants undergoing exchange transfusions;
- Adults and infants undergoing extra-corporeal membrane oxygenation (ECMO) therapy;
- Adults undergoing cardiopulmonary bypass; and
- Nursing infants of mothers on haemodialysis.¹²

Health Canada

In 2002, an Expert Advisory Panel proposed a risk management strategy to Health Canada to address the hazards posed by DEHP to human health in medical devices. The Panel recommended that "DEHP containing devices should not be used in the following circumstances (i.e., only devices containing an alternative to DEHP should be used in these situations):

- In all newborns and in pre-pubertal males, for high exposure procedures such as ECMO (except where the kits are heparin coated to prevent leaching), during cardiac surgery, during TPN and for double volume exchange transfusions;
- In some adults such as heart transplant patients, those undergoing cardiac bypass, haemodialysis

patients, and pregnant and lactating women;

- When administering lipophilic drug formulations;
- In adult trauma patients who fall into a potentially sensitive population (heart transplant recipients, pregnant or lactating women)."

Therefore:

- "The Panel recommends that labelling of products always indicate that DEHP is present in a particular product."
- "As alternative products are already available (albeit at significantly elevated cost), the Panel recommends that total parenteral nutrition solutions be administered to newborns and infants only via products which do not contain DEHP."¹³

Japanese Ministry of Health, Labour and Welfare

In 2002, the **Japanese Ministry of Health, Labour and Welfare** recommended that healthcare professionals do not use medical devices made of PVC in which the plasticiser DEHP is used; alternative devices should be used instead.¹⁴

on haemodialysis are required to undergo this procedure for approximately 12 hours a week.

⁵ Risk Assessment: Bis(2-ethylhexyl) phthalate, June 2004. CAS-No.: 117-81-7, EINECS-No.: 204-211-0

⁶ KEMI, op.cit.

⁷ European Parliament 2001, Environmental Aspects of PVC, A5-0002/200, European Parliament resolution on the Commission Green Paper (COM(2000) 469 - C5-0633.2000 - 2000/2297 (COS).

⁸ European Parliament, 2005. REPORT on the European Environment & Health Action Plan 2004-2010(2004/2132(INI)), Committee on the Environment, Public Health and Food Safety.

⁹ Bundesinstitut für Arzneimittel und Medizinprodukte. Recommendations available at http://www.bfarm.de/de/Medizinprodukte/mp_akt/index.php?pv=&more=dehp.php.

¹⁰ Chemical Listed Effective October 24, 2003 as Known to the State to Cause Reproductive Toxicity: Di(2-ethylhexyl) phthalate (DEHP) [10/24/03]. For more info see www.oehha.ca.gov/prop65.html

¹¹ National Toxicology Program (NTP), Center for the Evaluation of Risks to Human Reproduction (CERHR). 2000. NTP CERHR Expert Panel Report on Di (2-ethylhexyl) Phthalate. Alexandria, VA: NTP CERHR.

¹² US FDA, 2001. United States Food and Drug Administration (FDA), Center for Devices and Radiological Health. 2001. Safety Assessment of Di(2-ethylhexyl)phthalate (DEHP) Released from PVC Medical Devices. Rockville, MD: U.S. FDA.

¹³ Health Canada, 2002. Health Canada, Medical Devices Bureau, Therapeutic Products Directorate, Health Products and Foods Branch. 2002. Health Canada Expert Advisory Panel on DEHP in Medical Devices: Final Report 2002 January 11. Ottawa: Health Canada.

¹⁴ Japan Chemical Week, 2002. Ministry Advises Hospitals to Use Alternatives to Medical Devices Using DEHP, Japan Chemical Week, 2002/11/21.

¹ Classification established by Commission Directive 2001/59/EC - 6 August 2001.

² Rubin RJ and Schiffer CA, 1976. Fate in Humans of the Plasticiser, di-2-ethylhexyl phthalate, arising from transfusion of platelets stored in vinyl plastic bags. *Transfusion*, 16(4): 330-335. See also

Ruzickova K, Rossi M, Cobbing M, Belazzi T, 2004. Preventing Harm from Phthalates, Avoiding PVC in Hospitals. HCWH Prague.

³ KEMI, 2005. RISK REDUCTION STRATEGY: Bis(2-ethylhexyl)phthalate, DEHP. CAS No: 117 - 81 - 7. EINECS No: 204 - 211 - 0. Draft.

⁴ Patients suffering chronic renal failure undergo this medical procedure when blood is circulated through a set of PVC tubes and a dialyser (a filtering system) that removes chemicals from patient's blood. Once cleaned the blood is returned to the patient's body. Patients



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You can find more information about the issue of DEHP/PVC in health care at Health Care Without Harm website (www.noharm.org/pvcDehp).