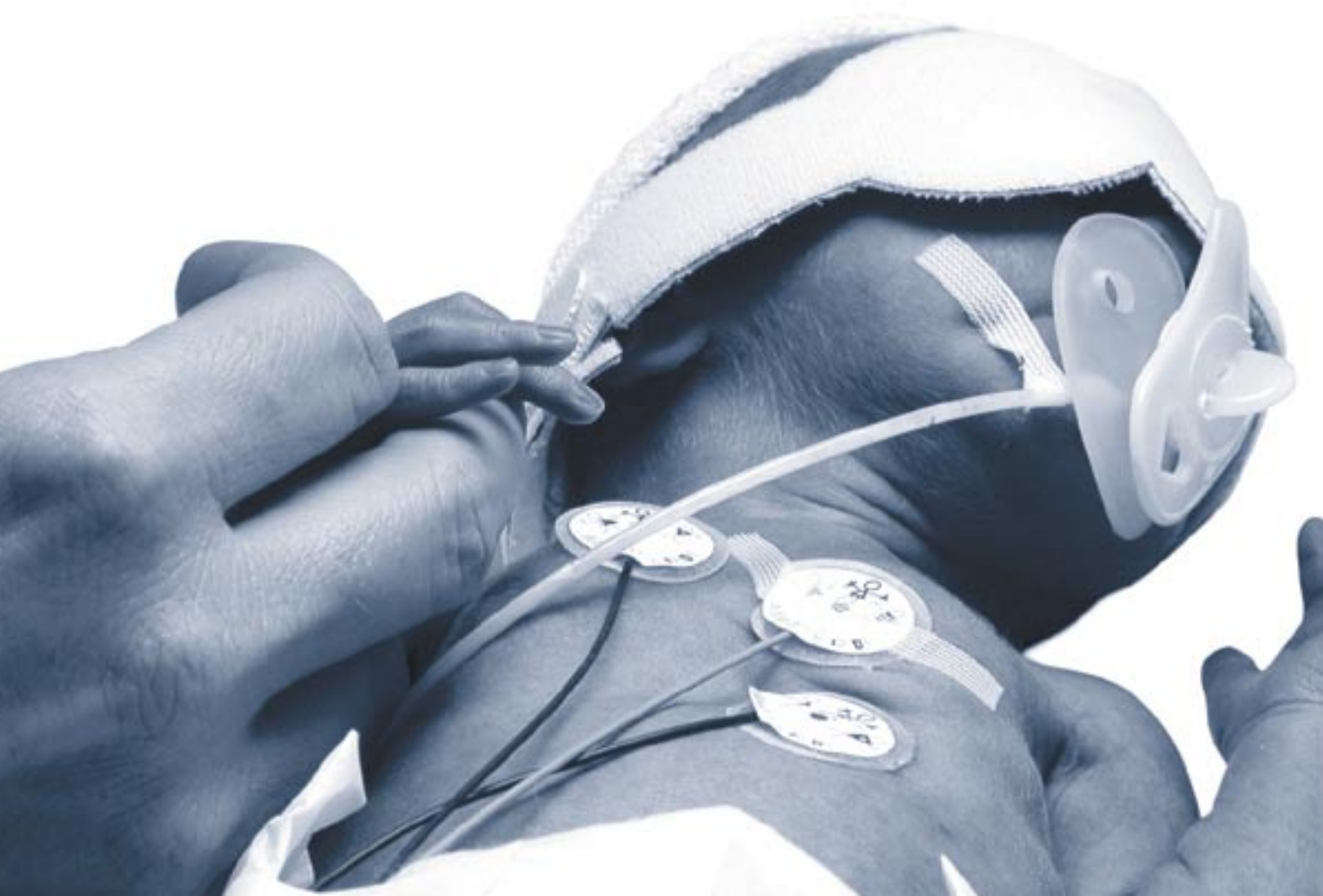




Preventing Harm from Phthalates, Avoiding PVC in Hospitals

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Executive Summary

Across the European Union, hospital patients, including newborn children, are unnecessarily being exposed to the phthalate DEHP from medical devices made from polyvinyl chloride (PVC) plastic, according to new product tests detailed in this report. In April 2004, Health Care Without Harm tested 48 common medical devices used in hospitals in Austria, the Czech Republic, France, Germany, Poland, Spain and Sweden for the presence of DEHP. Thirty-nine out of the 48 products contained between 17 and 41 % DEHP by weight. All of the DEHP-containing products -- which include infusion and nutrition sets, tubing and masks, mostly from neonatal and pediatric units -- were made of PVC plastic.

DEHP - di (2-ethylhexyl) phthalate or bis (2-ethylhexyl) phthalate - is a known reproductive toxin that causes birth defects and infertility in animal studies. Many hospitals are still using PVC medical devices that leach DEHP despite the fact that non-PVC medical devices are readily available on the market. The product tests found that eight of the products tested contained no DEHP. These DEHP-free products were made of plastics other than PVC, including ethylene vinyl acetate, polypropylene, polyethylene, polyurethane and silicon.

The report also shows that hospitals across Europe and the United States are phasing out PVC medical devices in order to protect patients from DEHP. Leaders in this effort include the Vienna Hospital Association, Sweden's Karolinska University Hospital, Hospital Na Homolce in Prague, Czech Republic, and Kaiser Permanente, the largest non-profit health care system in the United States. The leadership of these health care institutions comes in response to the recommendations of government bodies in the European Union, Japan, Canada and the United States that pregnant women, fetuses, infants, children and other high-risk patient groups should be protected from DEHP-containing medical devices when alternatives are available. But the absence of clear and consistent government policies is harming the ability of health care providers to fully protect their patients from unnecessary exposure to DEHP and other dangerous chemicals.

The EU has banned DEHP from cosmetics, personal care products and certain toys. But the EU continues to allow the use of DEHP in medical devices, which are used on sick infants and other vulnerable populations, and which can result in far higher levels of exposure. The EU has drafted a DEHP Risk Assessment and Risk Reduction Strategy recommending that pregnant women and infants are immediately protected from DEHP-containing medical devices, and a Directive concerning Medical Products that would restrict phthalate exposure from medical devices when alternatives are available. But chemical industry pressure has prevented the finalisation of these protective measures.

The DEHP problem illustrates the urgent need to change the way chemicals are regulated in order to protect public health. The proposed reorganisation of European Union chemicals regulation (REACH) would give the public greater protection from manmade, hazardous chemicals such as DEHP. Under REACH, chemicals would be identified as "substances of very high concern" if they can cause cancer, damage genetic material or, like DEHP, are toxic to the reproductive system. These high-concern chemicals will require a special authorisation to continue use, even if they have already been on the market for many years. The addition of the substitution principle (a mandatory substitution of hazardous chemicals when safer alternatives are available) to the current REACH proposal would institutionalise the best practices of the hospitals and health care institutions that are already replacing DEHP-containing PVC medical devices with safer alternatives.

European governments can also play a vital role by immediately restricting the use of DEHP in medical devices. The DEHP Risk Assessment and Risk Reduction Strategy, begun in 1997, must be finalised now, followed by the amendment of the EU Directive concerning Medical Products.

Health care providers have a unique chance to take precautionary action by eliminating DEHP from use in hospitals. The experience of the Vienna Hospital Association, Sweden's Karolinska University Hospital, Prague's Hospital Na Homolce and Kaiser Permanente in the United States show that such change is possible. The initial higher cost of PVC-free products is justified by the avoidance of potential adverse health effects in high-risk patient groups. As health care professionals pledge to first do no harm, it is their responsibility to avoid the use of reproductive toxicants during medical care if safer alternatives perform equally well and exist on the market.

It is also up to the manufacturers to make it their corporate responsibility to sell only safe products and to offer PVC-free alternatives that are price-competitive.

From Foetus to Toddler: Exposure to DEHP during a Critical Period of Development

DEHP is part of a family of chemicals called phthalates. It is the most widely used phthalate as well as the phthalate most widely found in the environment. 90% of DEHP consumed in Europe is used as a plasticiser in polymers, mainly PVC. PVC softened with DEHP is used in a variety of consumer products from cosmetics to toys, packaging and medical devices as well as building materials, such as wallpaper, flooring, films, sheets and coated products, cables, hoses and profiles.¹

DEHP is used to soften the inherently rigid PVC and improve its flexibility and workability, i.e. change the polymer into a soft material suitable for production of a variety of products, including medical devices. Polyvinyl chloride has been until recently the predominant plastic used in medical devices. However, DEHP is not chemically bound to the PVC matrix and can be released throughout the lifecycle of the medical product.

Human exposure to DEHP – Bis (2-ethylhexyl) phthalate – begins at conception. Pregnant women, like the general population, are exposed to DEHP and similarly acting phthalates everyday. Flexible vinyl products made with DEHP are so pervasive that the plasticiser is a regular contaminant in food products, ambient air, and drinking water, which are all potential exposure sources for pregnant women. Blood samples from Members of the European Parliament found DEHP to be among the most common contaminants in the human body.² Adults are exposed to DEHP from food, water, outdoor air, as well as medical devices, with food being the primary source of exposure for the average adult.³ Fatty foods such as oils, milk, cheese, meat, and fish typically contain considerably higher DEHP residues than other foods⁴ because DEHP readily dissolves in fat.

Baby food is another source of exposure, with DEHP concentrations ranging from 0.01 to 0.63 mg DEHP/kg baby food.^{5 6} In addition, babies and small children are exposed to DEHP from house dust. The natural inclination of babies to put hands and toys in their mouths, adds ingestion to inhalation as another exposure pathway to DEHP in the home. Children absorb chemicals more efficiently, process them more slowly and eliminate them less efficiently than adults.⁷

Recent research by Koch, et al. (2003)⁸ indicates that the levels of DEHP exposure for the highest exposed populations are greater than expected. They concluded that the median intake of DEHP in the general German population is 13.8 µg/kg bw/day, but for those receiving the highest levels of exposure (the 95th percentile) it is 52.1 µg/kg bw/day. The highest exposure levels exceed by almost 100% the estimated

average adult exposure to DEHP of 3.8-30 µg/kg bw/day (for the United States) from food, water, and outdoor air.⁹

Aggregate exposure to phthalates is of additional concern. Excluded from estimates of average adult exposure has been exposure to other phthalates with similar reproductive and developmental effects as DEHP: including di-(n-butyl) phthalate (DBP), butyl benzyl phthalate (BBP), and di-isononyl phthalate (DINP). When analysed as a class of chemicals with similar adverse health effects, the aggregate levels of phthalates for the highest exposed (95th percentile) women of reproductive age in the United States will be considerably higher than for individual compounds.¹⁰

The Toxicity of DEHP

DEHP causes abnormal sexual development in laboratory animals. In particular, the developing male reproductive tract is most sensitive to monoethylhexyl phthalate (MEHP), the toxic monoester metabolite of DEHP, and is far more sensitive than the reproductive tract of juvenile or adult male mammals.^{11 12 13 14} Within the developing male reproductive tract, the Sertoli cells are the most sensitive target tissue,^{15 16 17} with other adverse effects including: 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 vesicle, and glans penis.^{18 19 20} As Moore, et al. (2001), conclude, in utero and lactational “DEHP exposure can profoundly alter male reproductive system development (including sexual behaviour) in rats”.²¹

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 postnatal growth; ovarian changes; and infertility in males and females.²²

The lowest observed adverse effect level (LOAEL) from DEHP exposure varies across studies and depends upon the effects being observed. The lowest LOAEL reported was by Arcadi, et al. (1998),²³ who observed testicular damage in the male offspring of female rats exposed to an estimated 3.0-3.5 milligrams per kilogram body weight per day (mg/kg bw/day) in drinking water. Testicular damage included the disorganization of the seminiferous tubule structure and the absence of spermatocytes. Poon, et al. (1997),²⁴ reported testicular lesions and changes in liver enzymes at exposures

of 38-42 mg DEHP/kg bw/day in young adult rats (4-6 weeks old at the start of the study). The expert panel of the National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (2000)²⁵ concluded that the LOAEL is 38-144 mg/kg bw/day and the NOAEL (no observed adverse effect level) is ~ 3.7-14 mg/kg bw/day for reproductive effects in rodents by the oral route.

Other adverse effects of DEHP exposure in animal studies include suppressed or delayed ovulation, suppressed estradiol production, and polycystic ovaries,²⁶ reduced kidney function,²⁷ kidney atrophy,²⁸ reduced liver function,²⁹ respiratory distress,³⁰ and decrease in heart rate and blood pressure.³¹

DEHP Exposure during Specific Medical Treatment Therapies

Particularly troubling is the potential for exposing foetuses, premature infants (<35 weeks), and neonates to DEHP at critical points in their development. For pre-term babies requiring intensive care, the intensity of DEHP exposures differs markedly in comparison to the healthy full term newborn.

Pregnant women undergoing medical treatment may be exposed to DEHP at substantially higher doses than the general population. In addition to episodic exposures that may occur during periods of acute illness, women on dialysis because of renal failure are exposed to 0.01-7.2 mg DEHP/kg bw per session.³² According to one survey of 930 units, 2.4% of female hemodialysis patients of childbearing age became pregnant over a 4-year period.³³

DEHP can cross the placenta, resulting in foetal exposures.³⁴ In a study of cord blood of 84 human babies, Latini, et al. (2003)³⁵ found that 88% of the newborns had detectable levels of either DEHP or MEHP, with a mean concentration of DEHP of 1.19 µg/ml. Babies with MEHP in their cord blood showed a significantly lower gestational age (27-42 weeks) in comparison to the MEHP negative infants (37-42 weeks).³⁶ As noted above, foetal and newborn rodents were adversely affected by maternal DEHP exposures lower than those potentially received by women on hemodialysis.

Not chemically bound to PVC, DEHP leaches and off-gasses from PVC products. The rate of DEHP leaching varies widely depending on a variety of factors, including storage and use temperatures, storage time, handling practices (whether agitated or not), contact with lipophilic solutions, and percent DEHP in a product. High lipid (fat) content products, such

as blood, blood products, breast milk, and parenteral and enteral formulas, are of particular concern because DEHP is fat soluble. High lipid products more readily extract the plasticiser from vinyl bags and tubes.³⁷

Blood Transfusions

Pre-term babies, especially low weight babies,¹ often require many medical treatments that use DEHP-plasticised PVC products. DEHP concentrations in blood and blood products are of particular concern for premature babies who receive regular blood transfusions. These children may receive one or more blood transfusions per week. The most commonly used blood products, packed red blood cells and fresh frozen plasma, are typically packaged in DEHP-plasticised bags and conveyed to the patient through DEHP-plasticised tubes. DEHP has been detected at levels as high as 174 mg per litre (mg/l) of packed red blood cells and 889 mg/l of plasma.¹¹

Total Parenteral Nutrition and Enteral Nutrition

Total parenteral nutrition (TPN) and enteral nutrition are another set of potentially significant sources of DEHP exposure. Pre-term babies and infants that cannot breast or bottle-feed receive their nutrition either intravenously (TPN) or enterally (through tubes passed into the intestinal tract). Loff, et al. (2000) estimate that infants receiving TPN through DEHP-plasticised tubing can be exposed to 5 mg DEHP/kg/day.¹¹¹ This exposure includes DEHP contamination in the TPN formula itself: DEHP in lipid emulsion 20% ranged from 0.75-4.05 µg/mL with a mean of 1.6 µg/mL. When combined with additional infusions of plasma stored in DEHP-plasticised PVC bags and medications the exposure doubles and reaches 10 mg DEHP/kg/day. This indicates how readily DEHP leaches from PVC into lipid solutions. The TPN is in contact with the tubing for only a short period, unlike red blood cells that can sit in DEHP-plasticised PVC bags for weeks.

While no studies have been published on DEHP exposure during enteral feeding, it is reasonable to expect similarly high exposure levels given the lipid content in enteral formula and the common use of DEHP-plasticised PVC tubing and bags. Enteral feeding for infants involves delivering formula or breast milk from a syringe, through an extension tube, to a nasogastric tube. The extension tubes may be, and the short-term (3 days or less) nasogastric tubes are, manufactured with DEHP-plasticised vinyl. Mothers may also express breast milk through DEHP-plasticised PVC tubes. An unpublished study of leaching from DEHP-plasticised nasogastric tubes at Stockholm University "showed that the section of the tube which had been inside the infant's stomach contained only

Polyvinyl Chloride (PVC) Products in Hospitals

Disposable Health Care Products

Blood Products and Transfusions

- apheresis circuits
- blood bags and tubing
- extracorporeal membrane oxygenation circuits

Breast Pumps

- tubing used with collection kits

Collection of Bodily Fluids

- dialysis, peritoneal: drainage bags
- urinary collection bags, urological catheters, and irrigation sets
- wound drainage systems: bags and tubes

Enteral Feeding Products

- enteral feeding sets (bags and tubing)
- nasogastric tubes
- tubing for breast pumps

Gloves, Examination

Intravenous (IV) Therapy Products

- catheters
- solution bags
- tubing

Kidney (Renal Disease) Therapy Products

- hemodialysis: blood lines (tubing) and catheters
- peritoneal dialysis: dialysate containers (bags) and fill and drain lines (tubing)

Packaging, Medical Products

- film wrap
- thermoformed trays for admission and diagnostic kits, and medical devices

Patient Products

- bed pans
- cold and heat packs and heating pads
- foot orthoses
- inflatable splints and injury support packs
- patient ID cards and bracelets
- sequential compression devices

Respiratory Therapy Products

- aerosol and oxygen masks, tents, and tubing
- endotracheal and tracheostomy tubes
- humidifiers, sterile water bags and tubing
- nasal cannulas and catheters
- resuscitator bags
- suction catheters

Office Supplies

- notebook binders
- plastic dividers in patient charts

Durable Medical Products

- testing and diagnostic equipment, including instrument housings

Furniture Products and Furnishings

- bed casters, rails, and wheels
- floor coverings
- furniture upholstery
- inflatable mattresses and pads
- mattress covers
- pillowcase covers
- shower curtains
- thermal blankets
- wallpaper
- window blinds and shades

Construction Products

- doors
- electrical wire sheathing
- pipes: water and vent
- roofing membranes
- windows

half as much plasticiser as the rest of the tube" (which had 40% DEHP by weight to begin with) after only 24 hours of use.³⁸ Enteral exposures to DEHP are of more concern than equivalent intravenous exposures because DEHP delivered into the intestine is more readily and completely converted to the toxic metabolite, MEHP, than DEHP delivered intravenously.

Blood Exchange Transfusions

Less common treatments that involve potentially high DEHP exposures are blood exchange (or replacement) transfusions^{IV} and extracorporeal membrane oxygenation (ECMO).^V The sources of DEHP exposure in blood exchange transfusions are the bags containing blood products and the tubes conveying the blood to the patient. Based on the volume of blood transfused and the mean concentration of DEHP in serum, researchers estimate that blood exchange transfusions result in DEHP exposures ranging from 0.5 to 22.6 mg DEHP/kg bw/treatment (see Table 2).^{39 40 41}

Extracorporeal Membrane Oxygenation (ECMO)

In ECMO, the source of DEHP exposure is the tubing circuit. Schneider, et al. (1989), calculated that after 3 to 10 days of ECMO treatment an infant would be exposed to 42-140 mg DEHP/kg bw. Karle, et al. (1997)⁵⁷, reported a lower level of exposure that ranged from non-detect to 34.9 mg DEHP/kg bw/treatment. The non-detect level resulted from the use of a DEHP-plasticised PVC circuit that was coated with heparin. In addition to the heparin coated tubing, Karle, et al., attributed the differences between their study and Schneider, et al.,⁵⁸ to the smaller surface area of the newer ECMO configurations and varying percentages of DEHP composition in each type of tubing.

The highest DEHP exposures from ECMO, TPN delivery, and blood exchange treatments resulted in exposures greater than the LOAEL observed by Arcadi, et al. (1998)⁵⁹ and approach the low end of the LOAEL range (38-144 mg/kg bw/day) set by the NTP-CERHR Expert Panel (2000).⁶⁰ The highest ECMO exposure (14 mg DEHP/kg bw/day), TPN exposure (10 mg DEHP/kg bw/day), and blood exchange transfusion exposure (22.6 mg DEHP/kg bw/treatment) are two to three orders of magnitude greater than average general population exposures (0.003 - 0.030 mg DEHP/kg bw/day).

Rais-Bahrami, et al. (2004)⁶¹ sought to study the vulnerability of humans to DEHP exposure by analysing adolescents (13 males and six females) who received ECMO treatments as neonates. The males were studied for testicular volume,

phallic length, and testosterone levels. Their conclusion: all had normal growth for their age and testosterone levels appropriate for the stage of pubertal maturity.

These are welcome data, but the study has several important limitations. First, the level of DEHP exposure from the ECMO treatments is unknown (and unknowable since it was not measured during the treatment). Second, the endpoints examined are limited. As the authors note, normal testosterone levels vary widely in adolescents. Finding a testosterone level within "normal" range is useful information, but the level would need to be dramatically reduced to fall outside of "normal." As a result, it is impossible to know if the observed levels are actually lower than they might otherwise have been without DEHP exposure. Moreover, the reported hormone levels give no indication as to their values shortly after ECMO treatments. Measurable endpoints for semen quality, such as sperm concentration, sperm motility, and morphology were not measured, nor was the development of accessory organs of the reproductive tract.

Infusions

In addition to blood infusions, patients may receive medications, nourishment (such as total parenteral nutrition), and other fluids, such as dextrose or electrolyte solutions through infusion. An IV set-up includes a bag containing a solution and tubing that conveys the solution from the bag to the catheter inserted into the patient's vein. Approximately 80% of IV sets are manufactured with DEHP-plasticised PVC bags and tubes.⁶²

The leaching of DEHP into IV medications and products is well established. Trissel (1998),⁶³ for example, has identified a range of drugs, including the cancer drug Taxol, that have been shown to increase DEHP leaching. DEHP leaching into standard IV products -- such as glucose (sugar) solutions, or electrolyte (saline) solutions -- is more likely when the bags have been agitated or warmed. DEHP concentrations have been found as high as 0.36 mg/l in glucose solutions and 0.16 mg/l in electrolyte solutions. An infusion of one litre of glucose solution could result in 0.005 mg DEHP/kg bw.^{64 65 66 67}

Breast Milk and Infant Formulas

Breast milk is another potential source of DEHP exposure. The Swedish National Chemicals Inspectorate (KemI) estimated the average daily intake of DEHP from nursing at 0.021 mg/kg/day for infants 0-3 months old and at 0.008 mg/kg/day for 3-12 month old children. This is from healthy

Table 2

Potential Exposures to DEHP from Medical Procedures and Nutrition

Source of DEHP Exposure	Exposure (mg DEHP/kg body weight)	Unit	Total Exposure or Concentration in Product	Source
Artificial ventilation in preterm infants (PVC respiratory tubing; not polyethylene)	NR	Hour (inhalation)	0.001-4.2 mg (estimated exposure)	Roth et al., 1988 ⁴²
Neonatal blood replacement transfusion; short-term, acute	0.3 (0.14-0.72)	treatment period	NR	Sjoberg, et al. 1985a ⁴³
Neonatal blood replacement transfusion; double volume; short term, acute	1.8 (0.84-3.3)	treatment period	NR	Sjoberg, et al. 1985a ⁴⁴
Platelet concentrates in newborns	1.9	treatment	NR	Huber et al., 1996 ⁴⁵
Enteral feeding	0.035	day	0.14 mg/kg (estimated exposure for 4 kg neonate)	US FDA, 2001 ⁴⁶
Extracorporeal membrane oxygenation (ECMO) in infants	42-140	treatment	NR	Schneider et al., 1989 ⁴⁷
ECMO in infants	4.7-34.9	Treatment	NR	Karle et al, 1997 ⁴⁸
Congenital heart repair (neonates)		1-4 hours	0.3-4.7 µg/mL/hr (change in level in whole blood during procedure)	Barry et al., 1989 ⁴⁹
IV glucose solution	0.005 (maximum)	one liter of solution	NR	Roksvaag et al., 1990 ⁵⁰
Total parenteral nutritional formula (TPN)	NR	NR	3.1 µg/mL (concentration in TPN formula)	Mazur et al., 1989 ⁵¹
TPN/IV Tubing	5	day	10 mg/2-kg baby/day	Loff et al., 2000 ⁵²
Multiple IV Sources: packed red blood cells, platelet rich plasma, fresh frozen plasma, and medications	5	day	10 mg/2-kg baby/day	Loff et al., 2000 ⁵³
Breast milk	0.0015-0.0165	Day	0.01-0.11 mg/kg (concentration in breast milk)	Pfordt and Bruns-Weller, 1999 ⁵⁴
Infant formula	0.015	Day	0.004-0.06 mg/kg wet weight	Petersen and Breindahl, 2000 ⁵⁵
Infant formula	0.0087-0.035	NR	0.33-0.98 mg/kg dry weight	MAFF, 1998 ⁵⁶

NR = Not Reported

mothers.⁶⁸ For nursing mothers on hemodialysis, exposures to DEHP could be quite high. The US FDA (2001)⁶⁹ estimated exposures “could be as much as 90 mg/kg/day” (p. 18).

DEHP has also been detected in infant formula.^{70 71 72 73} Studies from the United Kingdom estimated exposures to DEHP from infant formula (at birth) at 0.0087-0.035 mg DEHP/kg bw/day.^{VI 74}

Respiratory Therapy

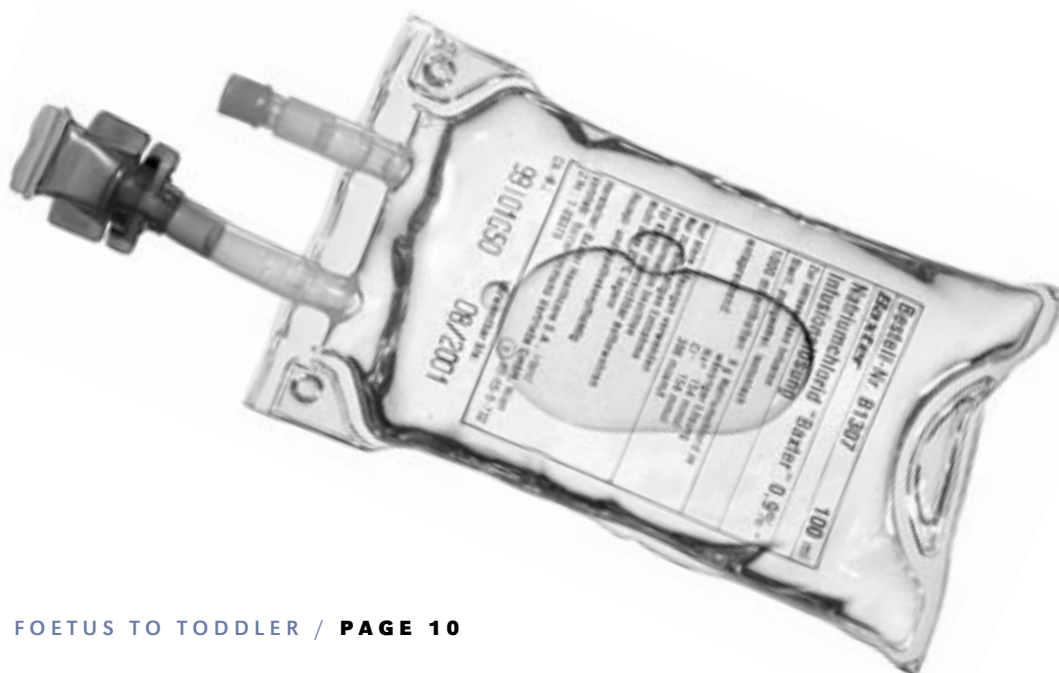
DEHP-plasticised PVC is commonly used during respiratory therapy in the following products: respiratory masks, oxygen tubing, cannulas, suction catheters, endotracheal tubes, bags to contain sterile water for humidifiers, and humidifier tubing. It has also been used in ventilator tubing, although that is uncommon today.

Latini and Avery (1999)⁷⁵ documented the leaching of DEHP from endotracheal tubes, finding a loss of 0.06-0.12 mg DEHP per mg of tube sample (6%-12%) after use.^{VII} They also noted that the material degraded and became less flexible, after a few hours of use. Hill et al also measured DEHP in gases passed through DEHP-containing PVC tubing used for respiratory therapy.⁷⁶ Other potential respiratory exposures to DEHP include off-gassing from vinyl floorings, wallcoverings, mattress covers, drainage tubes and bags, and privacy dividers for mothers expressing breast milk.

Aggregate Exposures to DEHP from Medical Procedures

No published studies have measured exposure to DEHP from enteral feeding bags and tubing, nasogastric tubes, breast milk pumps and tubing, respiratory tubing, endotracheal tubes, oxygen masks, or all sources combined. Individual studies of DEHP exposure from specific medical treatments, when viewed as a whole, reveal the potential for multiple exposures to DEHP through multiple pathways. The highest individual exposures -- blood exchange and replacement transfusions, ECMO treatments, and TPN infusions -- exceed the average daily adult exposure to DEHP by two to three orders of magnitude and approach the LOAEL for DEHP exposure in animal studies set by the expert panel of the US National Toxicology Program, Center for the Evaluations of Risks to Human Reproduction (see Table 2).

A result of the use of flexible PVC products that contact human tissue, such as nasogastric tubes, endotracheal tubes, and umbilical vessel catheters is product degradation over time. They become brittle as the softening agent (DEHP or any other plasticiser) leaches out. Thus it should come as no surprise that staff at the Infant and Child Clinic at a Stockholm hospital “noticed that the discarded [nasogastric] tubes were brittle and hard, when removed after just 24 hours’ use”.⁷⁷ Or that Latini and Avery (1999)⁷⁸ “confirmed materials degradation in endotracheal tube after usage.” Because flexible PVC products become brittle in the body and expose patients to DEHP (or any other plasticiser), medical device manufacturers do not market flexible PVC products for long-term use in the body.⁷⁹



Results from Analytical Survey of Phthalates in Medical Products

To demonstrate the potential risks of DEHP leaching out into the patient's body, HCWH tested 48 medical devices for phthalates content.

Samples

48 products from 7 European countries were collected at hospital units in:

- Austria
- Czech Republic
- France
- Germany
- Poland
- Spain
- Sweden

More than half of the products are used at paediatric and neonatology units. The emphasis in product selection was on products that transfer oxygen and various solutions including nutritional formulas, drug solutions, glucose and saline solutions into the patient's body. The risk of DEHP exposure increases when patients receive the solutions over long periods of time, especially when the product is used invasively with fatty solutions.

Tubing products were the most common medical device tested and included:

- infusion tubing system
- feeding tubes
- nasogastric tubes
- catheters
- endotracheal tubes

The bags tested were:

- IV bags
- enteral nutrition bag
- parenteral nutrition bag

Oxygen masks were tested as well.

These products devices are made by many of the major manufacturers in Europe, including:

- B.Braun
- Fresenius
- Baxter
- Vygon (Tyco Health Care group)
- Maersk Medical
- Nutricia
- Codan
- Beckton Dickinson
- Dahlhausen

These corporations are among the producers that distribute their products to variety of European countries in Western as well as Eastern Europe.

Methods

Products were tested by the Institute for Testing and Certification, a.s, Czech Republic that has accredited testing laboratories according to CSN EN ISO/IEC 17 025 including accreditation for raw materials and semi-finished products testing (polymers, chemicals) and the products from them. The testing was performed according to CSN EN ISO 6427. 48 samples of medical devices were tested by FTIR spectroscopy to identify the polymer used. The content of extractable compounds was tested by Soxhlet extraction and the extractable compounds (plasticisers) were identified by Gas Chromatography-Mass Spectroscopy. The results are expressed as a percent of the total weight of the product.

Results

Out of 48 products, 40 were made of softened PVC. In all but one case, the softener used was identified as Bis (2-ethylhexyl) phthalate = DEHP.^{VIII} In 39 PVC-containing products, DEHP accounted for 17 to 41% of the total weight of the product. In 8 remaining products, alternative materials including co-polymer Ethylene Vinyl Acetate (EVA), polyethylene, polyurethane and polyamide were tested for phthalate content. Here DEHP was not detected with the exception of one product made of EVA where traces of phthalates were found (0.02% by weight). Phthalates could have accidentally contaminated the product during the manufacturing process or during storage with other PVC products.

For product containing multiple components, such as infusion set, the tubing was typically selected for testing because the liquid could come into contact with the DEHP and result in patient exposure to DEHP. For example, small amounts of fatty solutions can be transferred through 30 to 80 cm long tubing made of softened PVC for extended periods of time.

Only in two cases where tubing was attached to an oxygen mask and a nutrition bag, both the product and the tubing were tested. In the case of the nutrition bag manufactured by Nutricia, the bag was made of copolymer EVA but the tubing attached to the bag was made of PVC containing 32% DEHP. Consequently, although some of the equipment such as IV bags is often substituted, the patients are still exposed to DEHP via tubing that transfers the liquids to the patient.

Comparison with other studies

In two previous studies on the presence of DEHP in medical devices,⁸⁰ the quantities of DEHP found were broadly similar

Table 3

DEHP Content by Weight in Medical Devices Tested

Country	Device type	Manufacturer	Material	Phthalates content (%) by weight
France	Infusion Set	Codan	PVC softened with DEHP	34,5
France	Oxygen Catheter	Maersk Medical	PVC softened with DEHP	31,9
France	IV Administration Set for Gravity Infusion	B. Braun	PVC softened with DEHP	32,6
France	Airway Tubus	PharmaPlast - Maersk Medical	Co-polymer Ethylene Vinyl Acetate	0,02
France	Winged Infusion Set	Surflo Terumo Europe	PVC softened with DEHP	37,3
France	Set for Epidural Anaesthesia	B. Braun	Polyamide	<0,01
France	Solution Administration Set	Baxter	PVC softened with DEHP	31,9
France	Toddler Size Inflatable Face Mask	King Systems Corporation	PVC softened with DEHP	16,6
Sweden	IV-bag with Solution	Baxter	Polyethylene	<0,01
Sweden	IV-bag Solution, NaCl	Baxter	Polyethylene	<0,01
Sweden	Tubing, Parenteral for Dialysis	Hospamed (Bioster)	PVC softened with DEHP	33,8
Sweden	Extension Tube For Blood Warmer	MediPlast AB	PVC softened with DEHP	28,8
Sweden	Infusion Aggregate with Dropcounter	B. Braun	PVC softened with DEHP	31,5
Austria	Hotline Fluid Warming Set	Level 1 (Smiths Medical)	PVC softened with DEHP	21,2
Austria	IV bag with NaCl 0,9% Infusion Solution	Baxter	PVC softened with DEHP	31,1
Austria	IV bag with Glucose 5% Solution	Baxter	PVC softened with DEHP	30,7
Austria	IV Bag with NaCl Solution	Fresenius	Polypropylene modified with polystyrene	<0,02
Austria	Perfusor Tubing	Clinico	PVC softened with DEHP	34,7
Austria	Intrafix Air (infusion)	B. Braun	PVC softened with DEHP	33
Austria	Catheter CH10 for Neonates	Dahlhausen	PVC softened with DEHP	30,1
Austria	Catheter CH12 for Neonates	Dahlhausen	PVC softened with DEHP	31,9
Austria	Oxygen Mask for Neonates incl. Safety Tubing 2,1m	Dahlhausen	PVC softened with DEHP	30,8

for most products, with the exception of tubing, which was as high as 81%, and a blood bag at 65% DEHP. The analysis of tubing in the present study found levels of DEHP between 26% and 41%, which are significantly lower but still substantial.

Previous studies have also investigated other PVC products and have found a range of phthalates as well as other chemical additives. A study on children's toys, found that phthalates comprised a sizeable proportion (10-40%) of the total weight of the product, and that DINP had replaced DEHP as the most commonly used phthalate.⁸¹ Other

phthalates were also identified at lower levels – Di-(n-butyl) phthalate (DBP) and butyl benzyl phthalate (BBP).⁸²

The levels of DEHP found in this present study show that DEHP is still widely used in large quantities for softening PVC medical devices. Their use represents a significant potential for exposure of patients to chemical hazards, of particular concern to foetus and young

children who are going through sensitive periods of development. The fact that DEHP can leach into intravenous solutions is acknowledged by many, including medical device manufacturers.⁸³

⁸⁴ Exposure to such hazards is clearly unacceptable for vulnerable populations, particularly when medical products, which don't contain DEHP are available for many applications.

Austria	Suction Catheter / Funnel	Unomedical	PVC softened with DEHP	38,1
Austria	Infusomat Tubing/Line	B. Braun	PVC softened with DEHP	31,3
Austria	Nutrition Bag (nutrition bag)	Nutricia	Co-polymer Ethylene Vinyl Acetate	<0,01
Austria	Flocare Tubing Attached to the Bag	Nutricia	PVC softened with DEHP	32,6
Austria	Tubing Leading from Oxygen Mask	Intersurgical	PVC softened with DEHP	26,7
Austria	Oxygen Mask	Intersurgical	PVC softened with DEHP	33,6
Austria	Minify Perfusion Set Tubing	Duschek	PVC softened with DEHP	41,2
Poland	Total Parenteral Nutrition (TPN) Sets - Universal Set Gravity	Nutricia	PVC softened with DEHP	32,2
Poland	Enteral Feeding Set	Galmed	PVC softened with DEHP	28,4
Poland	Enteral Feeding Set	Margomed	PVC softened with DEHP	31,8
Poland	Stomach Gastric Tube	Sumi	PVC softened with DEHP	34,6
Spain	Enteral Nutrition Bag	Oiarso (Bexen)	PVC softened with DEHP	34,5
Spain	Filter Catheter Court IV	Pall Medical	PVC softened with unidentified phthalates	39,1
Spain	Transfer Pack	Baxter	PVC softened with DEHP	30
Spain	Multiplayer Parenteral Nutrition Bag	Oiarso (Bexen)	Co-polymer Ethylene Vinyl Acetate	<0,02
Spain	Administration Set	Baxter	PVC softened with DEHP	27,9
Germany	Suction Catheter	Maersk Medical	PVC softened with DEHP	36,6
Germany	Paediatric Feeding Tube	Mallinckrodt	PVC softened with DEHP	33,4
Germany	Infusion Set	Becton Dickinson	Co-polymer Ethylene Vinyl Acetate	<0,02
Germany	Infusion Set	Becton Dickinson	PVC softened with DEHP	34,6
Czech Republic	Uncuffed Tracheal Tube (oral, nasal)	Kendall -Gammatron (Tyco Health Care group)	PVC softened with DEHP	27,3
Czech Republic	Catheter for Neonates with Low Birth Weight	Gama Czech Republic	PVC softened with DEHP	32,9
Czech Republic	Infusion Set	Gama Czech Republic	PVC softened with DEHP	34,4
Czech Republic	Paediatric Endotracheal Tube	Vygon (Tyco Health Care group)	PVC softened with DEHP	33,7
Czech Republic	Suction Catheter	Maersk Medical	PVC softened with DEHP	33,9

Source: Institute for Testing and Certification, a.s. Test Report No. 472100491. 2004.

Solution at Hand - Replacing PVC with Alternative Materials

Most exposure to DEHP can be avoided by using PVC-free and DEHP-free alternatives. Since the leaching of DEHP from PVC products is an uncontrollable source of contamination, contributing to the human body burden of DEHP, the problem needs to be solved through a precautionary approach, by eliminating the DEHP at source.

Using a PVC-free product eliminates the concern of DEHP exposure because alternative polymers do not contain phthalates or any other softeners. They are inherently flexible, thus do not require a softening agent. Among these alternative materials medical devices manufacturers regularly use polyethylene, polypropylene, polyurethane and other polyolefins, silicone, ethylene vinyl acetate and multi-layer laminate plastics. PVC-free polymers also pose less danger of becoming brittle after long-term use.

In addition, using non-PVC medical alternatives avoids the life-cycle hazards associated with PVC. During manufacture emissions of carcinogens such as vinyl chloride monomer and ethylene dichloride pose a threat to workers and local communities living around the chemical plants. One of the most serious concerns associated with PVC appears during the disposal phase. Due to the high chlorine content, disposed PVC medical devices are a major source of dioxins and hydrochloride acid during the combustion of medical waste in incinerators.⁸⁵ Dioxins are toxic at extremely low levels of exposure and can cause cancer, birth defects and damage to the immune system.^{IX 86 87 88 89 90}

Hospitals have the option of choosing PVC-free medical devices. On the European market, many manufacturers offer products of same category in both versions – made of PVC or the alternative material. Table 4 gives some examples of PVC-free products that are currently available on the market in Europe.^X There are product categories where the patient exposure is critical due to large DEHP amounts leaching from the product during medical procedures as the liquid or air passing through the tubing and bags gets contaminated with DEHP and is transferred into the patient's body.⁹¹

Intravenous, enteral feeding and respiratory therapy products are among those to be substituted as a priority. However, there are many other products made of PVC, including examination gloves, aprons, body collection bags and bottles where manufacturers have already substituted PVC with alternatives due to the undesired environmental side effects.

For nearly every product made of PVC, there are currently PVC-free alternatives on the market. A notable exception

is for packaging of red blood cells. In the case of red blood cells, the DEHP in PVC offers the advantage of being an unintentional preservative of red blood cells.

In addition, there are PVC products softened by other plasticisers available on the market. The alternative softening agents use include citrates, benzoates, trimellitates and adipates. However, alternative plasticisers suffer from the same problem as DEHP – softening agents will leach out of the product during medical treatment. Citrates are generally recognised as less hazardous than DEHP. However, potential health risks associated with these alternative plasticisers are not well documented, as there is poor toxicological data available.

One of the concerns associated with the substitution to PVC-free materials are higher costs of alternative materials. Prices differ based on the national market and also according to individual contracts between hospitals and suppliers. Hospitals that have purchased large volumes of products were able to negotiate cost-competitive prices for alternatives to PVC. On the European market, the prices of IV bags are generally similar for PVC and non-PVC products as in these applications downgauging is possible – making a similar product with less material.⁹² As the specific density of PVC is higher than that of polypropylene, a polypropylene product needs less material by weight compared to a PVC product. Tubing typically costs more but there is the advantage of longer-term use. PVC gloves are another example of a high volume product: when purchased in large quantities, nitrile gloves are price-competitive with PVC.

In the light of possible developmental damage to children from DEHP exposure of high-risk patient groups including neonates on intensive care units, pregnant women, and pre-pubescent children, higher costs are justifiable. Recent trends on the medical devices market show that as the demand for non-PVC products grows, manufacturers lower the prices of alternatives and they become more cost-competitive. Lastly, manufacturers will have to adapt to new regulatory situation as phthalates are identified as unsuitable for medical devices for patient consumers in the Risk Assessment for DEHP.

Manufacturers also bear responsibility for preventing DEHP exposure to patients. In the majority of cases, where alternatives are available, the manufacturers sell both products – PVC and PVC-free. Due to the fact that many alternatives are currently more expensive, hospitals are not yet using the safer alternatives and are purchasing products that may be harmful to patients.

Table 4

PVC-free Medical Products on the Market in Europe

PRODUCT CATEGORY	PRODUCT	MATERIAL	MANUFACTURERS
Body Fluids Collection	Bladder Catheter	Polyurethane or Silicon	Astra, B. Braun, Rüsç, Tyco Healthcare, Coloplast
	Collection Bags or Bottles (f.e. Urine Bags)	Polypropylene Bags or Reusable Polyolefin Bottles, Ethylene Vinyl Acetate	B. Braun, Benesch, Dahlhausen, Odelga, Sterimed, Coloplast, Terumo Europe
Dialysis Products	Peritoneal Dialysis Sets	Polyolefins or Silicon	Fresenius, Gambro, Meise GmbH, Tyco Healthcare
Enteral Feeding Products	Enteral Feeding Bags	Ethylene Vinyl Acetate	Nutricia Pfrimmer
	Feeding Tubes	Polyurethane, Rubber	Tyco Healthcare (Vygon), Oiarso, Nutricia Pfrimmer, Rüsç
	Nasogastric Tubes	Polyurethane, Silicon	Tyco Healthcare (Vygon)
Gloves	Examination Gloves	Polyethylene or Polyethylene Copolymer, Nitrile	B. Braun, Odelga, Dahlhausen
Intravenous (IV) Products	IV Bags	Ethylene Vinyl Acetate, Polyolefin Laminates, or Polypropylene/Styrene Ethylene, Butadiene Styrene Laminate	Baxter, B Braun, Fresenius, Haemotronic S.p.A., Nutricia Pfrimmer, Sengewald Verpackungen GmbH
	IV Tubing	Ethylene Vinyl Acetate, Copolymers, or Polyolefins (Polyethylene)	B. Braun, Clinico, Maersk Medical (Unomedical), Nutricia Pfrimmer, Smiths Medical, Tyco Healthcare (Vygon)
	Parenteral Nutrition Bags	Polyolefin Laminates, EVA	B. Braun, Oiarso (Bexen)
	Platelet and Fresh Frozen Plasma Bags	Polyolefins	Baxter
	Red Blood Cell and Whole Blood Containers	DEHP-free PVC Bag Plasticised with Citrates	Baxter
	Umbilical Vessel Catheters	Polyurethane	many (f.e. Tyco Healthcare - Vygon)
Respiratory Therapy Products	Endotracheal Tubes	Rubber or Reinforced Silicon, Polyurethane	Rüsç, Smiths Medical
	Humidifier, Sterile Water Bag,	Polypropylene	Tyco Healthcare, Smiths Medical
	Humidifier, Tubing	Silicon	Dräger GmbH, Tyco Healthcare, Rüsç Medical
	Oxygen Masks	Rubber or Silicon	Rüsç Medical, Smiths Medical
Aprons		Polyethylene	Dahlhausen
Catheters	Urinary Catheters	Silicon, Polyurethane	B. Braun, Rüsç Medical, Maersk Medical (Unomedical)
	Peripheral Vessel Catheters	Polyurethane	Beckton Dickinson, B. Braun
	Epidural Vessel Catheters	Polyethylene, Polyurethane, Polyamide	B. Braun, Vygon, Smiths Medical
Syringes		Polypropylene, Polyamide	B. Braun, Terumo Europe, Beckton Dickinson, Vygon, Smiths Medical

Disclaimer: The listing of products in this table does not constitute an endorsement of the products nor were the products tested for safety or efficiency by the authors or Health Care Without Harm. Products should be tested and evaluated before purchasing to ensure they meet required performance specifications. The table lists only examples of products offered on the European market and does not aim to cover all manufacturers operating in Europe. Sources: Lichtman, 2000; Tickner, et al., 1999; Greenpeace, 1995; and interviews with company representatives.

Case Studies

There are several examples of hospitals and health care facilities that have already taken the necessary steps to eliminate PVC use in medical devices.^{93 94} To move away from PVC, these hospitals began with identifying products containing PVC. This can be a complicated process because manufacturers are not required to label their products or indicate what material they have used. However, as the demand for non-PVC devices grows and health concerns with DEHP clarified, manufacturers have started to label products 'PVC-free' or 'DEHP-free' or positively such as 'made from PP' (polypropylene).

As described below in the individual case studies, PVC elimination usually began at units where the most sensitive patients to DEHP are treated. The highest risk procedures were identified where exposure to DEHP poses the greatest threat to the patient. Neonatal intensive care units (NICUs) and dialysis clinics were among the most frequent departments where audits were first performed.

The next step consisted of identifying and evaluating the alternatives. This also meant ensuring that these alternatives perform equally well and that there are no other safety or environmental concerns.

Finally, the hospitals developed programs that favour alternative products and require manufacturers to offer PVC-free products or justify the use of PVC when individual bids for new products are made. Individual clinics then continuously move from the use of PVC-containing products to alternatives.

Vienna Hospital Association Phase Out Policy on PVC

The Vienna Hospital Association operates 18 hospitals, nursing homes and geriatric care centres, employing 32 000 people in total. In 2002, the Vienna Hospital Association looked after 3.4 million patients in ambulant and 400 000 patients in stationary care annually with a turn over of 2.3 billion Euro. The Vienna Hospital Association adopted a policy of eliminating PVC from packaging, building materials and medical devices in 1992 when Vienna City Council decided to phase out PVC from all city funded projects and institutions.

Two of the Vienna Hospital Association Hospitals - Glanzing Paediatric Hospital and Preyer Paediatric Hospital - serve as examples of PVC and phthalate elimination. They have succeeded in becoming almost completely PVC-free.

At first, hospital staff conducted a PVC audit to identify PVC containing products and to quantify the amount of PVC waste generated. Among the PVC containing products were respiratory therapy products, catheters and tubing, urinary drainage catheters, blood pressure seals and ECG electrodes. Approximately half of these PVC products were replaced, and for the remaining ones, alternatives were tested or researched. Measured by weight, the share of PVC products amounted to 14.6% (Glanzing) and 9.8% (Preyer) of the total weight of examined products. The PVC share of the entire medical ward waste was 0.9% in the Preyer Hospital and 0.37% in the Glanzing Hospital.

By June 2003 the Neonatology Unit of the Paediatric Clinic Glanzing had almost completely phased out PVC/DEHP disposable products. Currently, almost all the invasive medical products, such as catheters and tubing used in the Paediatric Clinic, are PVC-free. Pacifiers, IV bags, blood filters, respiratory therapy equipment, feeding tubes and other tubing used at the Clinic are made from non-PVC materials. PVC is used only for a few non-invasive products, because there are currently no alternatives on the market. However, even with those products, hospital management expects that PVC-free products of the same performance quality will be on the market within one to two years.

Currently, the three other neonatology clinics of the Vienna Hospital Association (two located in the Vienna General Hospital, one in the Danube Hospital) are also successfully phasing out PVC / DEHP containing devices based on the experiences gathered by the Glanzing Clinic.

In addition to PVC-free medical devices, the Vienna Hospital Association strategy also involves construction work, where PVC has been avoided for flooring and window frames since 1990. In the last two years, pilot renovation projects for three hospital pavilions have been initiated where the use of PVC will be avoided in all sectors, including all electrical installations such as cables and wires.^{XI}

Stockholm County Council PVC Elimination Policy

Stockholm County Council passed a resolution to phase out PVC in 1997. PVC was identified as a priority to be avoided in the procurement of new products as part of a sustainable purchasing policy. The program prohibits the

use of PVC unless a very strong, written explanation for its purchase and use is provided as part of the purchasing process. In many disposable medical products, PVC has been avoided, with a few exceptions such as tubing and blood transfusion bags. For blood transfusion in small children fresh blood is used, i.e. blood that has been kept in the blood bag for only a few days. Alternatives for blood transfusion bags have been tested but due to the fact that DEHP acts as a stabiliser of the red blood cell membrane and thus preserves the blood, DEHP-softened PVC is still in use. Although there are no legal restrictions on the use of DEHP, hospitals try to avoid DEHP-softened tubing for use with small children. For example, at 32 neonatology units in the country, feeding tubes used for the long-term treatment of babies are made of non-PVC materials.

While the testing of medical devices from Karolinska University Hospital showed that although IV bags tested for phthalates were made of polyethylene and did not contain any traces of phthalates, hemodialysis tubing and blood transfer tubing were made of PVC and contained DEHP. Suitable alternatives are not yet available for these applications.

In addition, Karolinska University Hospital has just finalised a procurement contract for gloves for the entire complex of Stockholm County Hospitals. PVC gloves softened with phthalates are to be substituted with nitrile gloves and PVC gloves softened with citrates.

Na Homolce Hospital

The Czech Hospital Na Homolce has switched to PVC-free IV bags as of November 2003. The initiative came from the renal unit because dialysis patients belong to the group of patients exposed to high levels of DEHP due to long-term medical procedures. Patients on dialysis receive multiple treatments with intravenous liquids; therefore the exposure from these IV bags is significant. The initial costs of PVC-free bags were higher, however the hospital managed to negotiate a fairly competitive price with one of the major IV bags suppliers. After 3 years, the hospital pharmacy - the central purchasing unit - completely switched to PVC-free IV bags and safer alternatives made of multi-layer plastic from polyethylene (PE), polyamide (PA) and polypropylene (PP) are now used in majority of hospitals units. IV Bags represent the group of medical devices that is most easily substituted as they are purchased in large quantities and bags made of safer alternatives are generally price competitive.⁹⁵

Kaiser Permanente: Successful Approach towards DEHP Elimination at Neonatology Intensive Care Units

Kaiser Permanente is the largest non-profit health care provider in the US, serving 8.4 million people. Kaiser Permanente operates 29 medical centres, and 423 medical office buildings. There are 129 000 employees and 11 000 physicians. Beginning in July 2001, after learning of the potential hazards to neonatal patients from DEHP exposure, Kaiser Permanente staff underwent a process of identifying DEHP-containing medical devices used in the Neonatal Intensive Care Units. Kaiser Permanente staff conducted an inventory of NICU products. The nurse manager of one Kaiser Permanente neonatal unit gathered products from the unit and asked experts to help identify products that potentially contained PVC/DEHP, products that were high risk for exposure, and products for which alternatives to PVC/DEHP were readily available that would meet quality and performance criteria.

Based on the results of the trials and evaluations, staff recommended to switch to non-PVC/DEHP products for three commonly used NICU devices: umbilical vessel catheters (PVC-free), peripherally inserted central catheters (PICC) lines (PVC-free) and enteral feeding products (DEHP-free). The fourth product identified for replacement, neonatal endotracheal tubes, was not recommended for a switch because a suitable alternative was not identified. As a follow-up to the process, Kaiser Permanente engaged in a discussion with its supplier, Baxter International Inc., to conduct an analysis of Baxter's products and to focus on other non-DEHP containing Baxter products that could be adapted for NICU use.^{xii}

Review of Regulatory Initiatives to Limit DEHP Exposure in Humans

DEHP has been under pressure from scientists, NGOs and some governments for many years due to the health and environmental risks it poses throughout its life cycle. Therefore there are many critical statements from governments and / or their scientific bodies around the world, which emphasise their concern. The recent decision of the EU to classify DEHP as a health hazard and therefore label it as "toxic" with "skulls and crossbones" gave this discussion additional momentum and confirmed the growing concern about DEHP.

In the following chapter the most important and recent statements are summarised:

DEHP is classified as toxic to reproduction according to the EU Directive 67/548/EEC on Classification and Labelling of Dangerous Substances. 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. ^{xiii}

Unfortunately for DEHP/PVC product users, 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 20 - 40% of DEHP on average. This turns PVC products, which consume approximately 90 % (!) of all DEHP in the EU, into an unlabelled and therefore unnoticed use area!

Contradictorily, DEHP has been already banned in cosmetic 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. There is a proposal to replace this temporary ban with permanent legislation, which is likely to impose wider restrictions on DEHP, DBP and BBP because of their classification as reprotoxic substances.⁹⁶ 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."⁹⁷

The EU and the Swedish Chemical Inspectorate (KemI), as Rapporteur, have been working on the risk assessment and risk reduction strategy for DEHP since 1997. The Risk Assessment on DEHP recommends limiting risks for consumers from medical equipment for long term haemodialysis in adults, long term blood transfusion and extra-corporeal oxygenation in children, and transfusion in neonates, as there is concern about adverse effects on fertility, testes and reproductive function.

The European Parliament published a resolution on the Commission Green Paper on environmental issues of PVC⁹⁸ where the Parliament suggests that the Commission and the PVC industry should look into the possibility of setting targets for reducing the use of phthalates, particularly in medical equipment. Parliament called on the Commission to examine alternatives to the uses of phthalates as plasticisers.

The European Union is also re-organising the way that chemicals are regulated in general. There is a proposal for a new European chemicals regulation, intended to give the public greater protection from manmade, hazardous chemicals. It is the biggest and most important regulation in 20 years. REACH (Registration, Evaluation and Authorisation of Chemicals) will completely change the way chemicals are controlled.

Chemical companies will have to provide basic health and safety data on the chemicals they produce, which has not been a legal requirement to date for the majority of chemicals. REACH will then identify extremely hazardous chemicals and give them a special classification as 'substances of very high concern'. A chemical is classified as of very high concern if it can cause cancer, damage genetic material or is a reproductive toxin. These chemicals will require a special authorisation to continue use, even ones that have already been on the market for many years. Environment NGOs and some progressive industries are pressing for the substitution principle to take effect; if a safer alternative is on the market authorisation would not be given. DEHP would be a candidate for a substance of very high concern.



Because of the vast number of chemicals for which adequate safety data is currently not available (100 000 chemicals), REACH will prioritise. About 30 000 chemicals will be included in the system. Those produced in the highest volumes and those already known to have dangerous properties will be dealt with first. REACH will also reduce the complexity of current chemicals legislation. New and old chemicals will be brought under the same regime and will replace over 40 pieces of current legislation.^{99 100}

There have been a number of recommendation issued by authorities outside the European Union, especially in Japan, USA and Canada:

1) 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.^{xiv} Companies that use DEHP in their products have to warn consumers of potential exposure or reformulate their products as of October 2004. This covers not only medical devices but also consumer products. Now manufacturers either have to produce medical devices without Prop 65 reproductive toxins, or they can notify health care providers that their products contain DEHP and may pose reproductive hazards.

2) The United States National Toxicology Program (USNTP) concluded 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 concern 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.”¹⁰¹

3) The United States Food and Drug Administration (USFDA), 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.¹⁰²

4) 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.”¹⁰³

5) The Japanese Ministry of Health, Labour and Welfare has 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.¹⁰⁴

Despite these strong recommendations, the use of DEHP in medical devices continues. It is therefore scandalous that in Europe the Risk Assessment and Risk Reduction Strategy has been weakened and delayed as a result of chemical industry pressure over four years, and still has not been finalised. The use of DEHP in medical devices continues without restrictions.

Conclusions and Recommendations

This study found that the reproductive toxicant DEHP is present in large quantities, reaching up to 41% by weight of the PVC medical devices. The fact that DEHP can leach out of PVC plastic is well known. Therefore the continued use of DEHP in medical devices means that hospitals are probably exposing patients to this reproductive toxicant, risking permanent health effects, particularly for foetus and young children who are going through sensitive stages of development.

Exposure to such hazards is clearly unacceptable for vulnerable populations, particularly when medical products, which don't contain DEHP, are available in many applications. The many examples of PVC/DEHP free products available on the European market and of hospitals using these products show that there is no reason to delay action to prevent DEHP exposure in hospitals.

Real changes in legislation and the market are needed to reduce patient exposure to DEHP. Rather than taking precautionary measures, policy makers continue to delay taking effective measures to protect the most vulnerable consumers, despite having implemented such measures in the case of toys and cosmetic products.

It is time for health care professionals to act and substitute products containing phthalates with safer alternatives that are equally effective without the potential for harm. As the European Union debates a completely new approach to the regulation of chemicals used in everyday products, doctors and nurses have the opportunity to show that they can prevent the exposure of patients to chemicals considered as harmful by substituting safer alternatives.

Health Care Without Harm (HCWH) recommends that health care providers:

- **Adopt and implement a PVC phase out policy and follow the examples of the Vienna Hospital Association and Karolinska University Hospital in Sweden. Avoid purchasing medical devices made of PVC where alternatives are readily available on the market. All other PVC or DEHP-containing products used in hospitals such as office supplies, furniture and building materials should be substituted wherever possible.**
- **As the first step towards a PVC phase out, contact manufacturers and ask them to specify clearly which products are made of PVC and/or contain DEHP and to request lists of products made of alternative materials.**

The whole population has the right to be protected from exposure to phthalates. 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 in the EU, Japan, and the US. However, instead of acting on 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 continue to delay.

HCWH recommends that European and national regulatory authorities:

- **Finalise the Risk Assessment and Risk Reduction Strategy on DEHP with the concluding recommendation to limit risks from DEHP exposure in medical devices.**
- **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 causes certain patient groups to undergo a risk of developmental and reproductive disorders for themselves or their offspring and where safer alternatives are already on the market.**
- **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.**
- **To reduce our general exposure to hazardous chemicals in the environment and from consumer products, 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 the absence of regulation, the Medical Devices Industry should be encouraged to apply the substitution principle themselves and phase out PVC from use in health care. The health of patients must take priority over the economic interests of the PVC and DEHP industries, who despite sufficient scientific data on adverse health effects caused by plasticisers, dioxins and other toxic byproducts, continue to produce and market DEHP-containing products to hospitals.

HCWH recommends that manufacturers:

- **Stop offering DEHP-softened PVC devices where they also offer PVC-free alternatives. Actively promote the choice of PVC-free products in the company's marketing strategy.**
- **Label PVC products and products made from alternative polymers, so that hospitals can recognise the risk and choose products that are safer for patients.**
- **Develop products made of alternative materials for medical devices where they are currently not available on the market.**

Appendix

Contacts to Major Manufacturers of PVC-free Medical Devices in Europe

ALARIS Medical Nordic AB,
Box 452,
SE-191 24 SOLLENTUNA,
Sweden
Tel: +46 8 544 43 200
Fax: +46 8 544 43 225

B.Braun Melsungen AG
Carl Braun Strasse 1
D-34209,
Germany
Tel: +49 (5661) 71-4772,
Fax: +49 (5661) 75-4515

Baxter Deutschland GmbH
Edisonstr. 3-4
85716 Unterschleissheim
Germany
Tel: +49 89 31701-777
Fax: +49 89 31701-720

Beckton Dickinson (BD)
Tullastrasse 8-12
69126 Heidelberg
Germany
Tel +49 6221 3050
Fax +49 6221 3038 04

Clinico
Robert Koch Strase 5,
D- 36251 Bad Hersfeld
Germany
Tel. +49 6621/16 8-168
Fax +49 6621/168 111

Codan Medizinische Geräte GmbH & Co KG
Grüne Straße 11
D-23738 Lensahn
Germany
Tel.: +49 / 43 63 / 51 12 00
Fax:+49 / 43 63 / 51 12 09

Fresenius AG
Konzern-Kommunikation
61346 Bad Homburg
Germany
tel. +49/6172/608-0
Fax: +49/6172/608-2294

Intersurgical - Marketing Dept
Molly Millars Lane
Wokingham
Berkshire
RG41 2RZ
United Kingdom
Tel: +44 (0)118 9656 300
Fax: +44 (0)118 9656 356

Gambro AB
Jakobsgatan 6
PO Box 7373
SE-103 91 Stockholm
Sweden
Phone: +46 8 613 65 00
Fax: +46 8 611 28 30

Tyco Healthcare - Basingstoke
3 Elmwood, Chineham Business Park
Basingstoke, Hampshire RG24 8WG
United Kingdom
Phone: 44-1256-708-880
Fax: 44-1256-379-501

Oiarso, S.Coop.
Pol Ibarluce 57-F 20.128 Hernani
Apartado 52
Spain
tel.: +34 943 33 50 20
Fax: +34 943 33 52 10

P.J.Dahlhausen & Co. GmbH,
Emil Hoffmann Strase 53,
50996 Köln
Germany
Tel: +49 (2236) 3913-0
Fax: +49 (2236) 3913-109

Pall Medical
Division of Pall Europe Ltd.,
Havant Street - Portsmouth
Hampshire, England PO1 3PD
United Kingdom
Phone: +44 (0)23 9230 3303
Fax: +44 (0)23 9230 2509

Pfrimmer Nutricia GmbH
Am Weichselgarten 23
91058 Erlangen
Germany
Tel.: +49 (0 91 31) 77 82-0
Fax: +49 (0 91 31) 77 82-10

Smiths Medical Division
765 Finchley Road
London NW11 8DS
United Kingdom
Tel. +49 8091 551 143
Fax +49 8091 551 161

Unomedical a/s
Maersk Medical
Engmosen 1
3540 Lyngø
Denmark
Phone: +45 4816 7000
Fax: +45 4816 7045

VYGON GmbH & Co.KG
Prager Ring 100,
D-52070 Aachen
Germany
Tel.: 0049 241 9130,
Fax: 0049 241 9130-106

Willy Rüsç GmbH
Willy-Rüsç-Str. 4-10
Kernen, D-71394
Germany
Tel: +49 7151 4060
Fax: +49 7151 406200

Footnotes

ⁱ A “low weight baby” is 2,500 grams or less at birth. Seven percent of all babies were low weight in 1996. (National Center for Health Statistics. 1998. Health, United States, 1998. Hyattsville, MD: Public Health Service).

ⁱⁱ In some blood products, varying amounts of DEHP are converted to the metabolite, mono-ethylhexyl phthalate (MEHP), by enzymes present in the blood (Cole, 1981; Rock 1978³¹). This metabolic transformation may be reduced when storage time and temperature are reduced.

ⁱⁱⁱ The TPN bag was non-PVC, therefore it was a non-DEHP containing bag.

^{iv} In a blood exchange transfusion all of the blood of a newborn is replaced with new blood.

^v During ECMO a patient’s blood is circuited outside of the body through PVC tubing. ECMO has become standard treatment for severe neonatal respiratory failure. At the University of Michigan Medical Center, of the 6,000 newborn infants treated for severe respiratory failure in the neonatal intensive care units, eight percent (460 patients) were treated with ECMO (Shanley, et al., 1994).

^{vi} Estimated exposures to DEHP from infant formula decline with age, with an exposure range of 0.0061-0.023 mg DEHP/kg bw/day at six months (MAFF, 1998⁵⁶).

^{vii} An endotracheal tube delivers oxygen to the trachea: it is inserted through the nose or mouth, through the larynx, into the trachea.

^{viii} In one of the PVC products (IV CATHETER from Pall Medical) contained 39% of unidentifiable type of phthalate.

^{ix} 2,3,7,8,TCDD, the most toxic form of dioxin has been classified by International Agency for the Research of Cancer, a body of the WHO, as a class 1 human carcinogen, and other dioxins are classified as likely human carcinogens. See McGregor, et al 1998. Dioxins have been estimated by the US EPA to increase the risk of contracting cancer by 1 in 1,000. See US EPA, 2000.

^x The table lists primarily producers whose products were tested for phthalates content (see Table 4). There are additional manufacturers included whose PVC-free products are used in hospitals where PVC elimination has already began such as the Vienna Hospital Association or Karolinska University Hospital.

^{xi} The project is documented in the XCHANGE database available at www.greeninghealthcare.net

^{xii} HCWH. PVC and DEHP in Neonatal Intensive Care Units, Kaiser Permanente www.noharm.org/details.cfm?ID=811&type=document

^{xiii} Added in the amendment from 2002 of the Directive on Classification and labelling of dangerous substances 67/548/EEC

^{xiv} 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

Endnotes

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