

# CONTROLLING THE HEALTH RISKS ASSOCIATED WITH DEHP EXPOSURE



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**Abstract:** DEHP is one of the most commonly used plasticizers in the world and is utilized in many medical devices. Both the FDA and the European Chemicals Agency (ECHA) have issued advisories or statements regarding DEHP and its potential risks to patients.<sup>1,2</sup> This paper discusses DEHP; why it is used; its potential risks, particularly in medical devices; the patient populations at risk; and a new non-DEHP product option for oxygen delivery to patients in the hospital and the home.

## INTRODUCTION

Medical devices are commonly made from polyvinyl chloride (PVC) because it is durable, cost effective and easily manufactured. However, PVC is inherently rigid and is made tougher and more flexible through the addition of plasticizers.<sup>3,4</sup> DEHP (di(2-ethylhexyl)phthalate) is the most common plasticizer in PVC products and is part of a family of chemicals called phthalates. Many PVC medical products typically contain approximately 30% DEHP.<sup>3</sup> When PVC is formulated using DEHP, no bonds form between the DEHP and PVC chemicals, allowing DEHP to exist as free molecules between polymer fibers. These molecules can leave the plastic and migrate to the surrounding environment. This process is referred to as “leaching”, and is of greater concern from soft plastic components, such as tubing, when exposed to liquids or moisture.<sup>1,3</sup>

The amount of DEHP that will leach depends on the temperature, the lipid content of the liquid, the duration of contact with the plastic, and the percent of DEHP in the product.<sup>2</sup> It has been known for a long time that DEHP can leach out of PVC, resulting in exposure to body tissues and fluids.<sup>1</sup> Medical products such as IV bags and tubing, blood bags and infusion tubing, enteral nutrition feeding bags, nasogastric tubes, peritoneal dialysis bags and tubing, tubing used in cardiopulmonary bypass procedures, extracorporeal membrane oxygenation (ECMO) and hemodialysis, and tubing used for oxygen delivery typically contain DEHP as a softening agent in the PVC.<sup>5</sup>

Studies with laboratory animals have shown that exposure to DEHP may produce a range of adverse effects. Thus, the subject of DEHP and its potential health risks is being debated worldwide based on the possibility of plasticizers leaching from PVC.<sup>5</sup>

## RISKS ASSOCIATED WITH DEHP

Although there have been no documented reports of adverse events in humans, the FDA reported that exposure to DEHP has produced a range of adverse effects in laboratory animals, with the effects on the development of the male reproductive system and production of normal sperm in young animals being of greatest concern. The FDA issued a public health notification that provides steps to reduce the risk of exposure to DEHP in certain patient populations and released an advisory recommending that precautions should be taken to limit exposure of the developing male to DEHP.<sup>2</sup> The FDA also issued a safety assessment that reported that DEHP is released from a wide variety of medical devices, including nasal cannula tubing.

The European Chemicals Agency (ECHA) has identified DEHP as a substance of very high concern (SVHC), as it is classified as toxic to reproduction, category 2. As such, it was included on the organization’s Registration, Evaluation, Authorization, and Restriction of Chemical Substances (REACH) candidate list in October, 2008. ECHA has called for the progressive substitution of the chemicals on this list when suitable alternatives have been identified.<sup>1,6</sup>

## POPULATIONS AT RISK

The amount of DEHP that a patient might be exposed to is largely determined by the patient’s sensitivity to DEHP<sup>2,5</sup>, the type of procedure performed,<sup>5</sup> and the frequency and duration of these procedures.<sup>2</sup> Based on evidence that the FDA, ECHA and other credible studies have found, the male fetus (through exposure to his mother), male neonate, and peripubertal male would appear to be high-risk groups, as they have a higher sensitivity.<sup>2,6,7</sup> The National Toxicology Program, a component of the National Institutes of Health, has recently reached a similar conclusion.<sup>8</sup> Neonates in the NICU environment are exposed to multiple devices containing DEHP and it is possible to estimate that a 4 kg infant could receive a DEHP dose on the order of 3 mg/kg/day for periods of weeks or months.<sup>5</sup> Children are also at increased risk for the effects of DEHP because they absorb chemicals more efficiently, process them more slowly, and eliminate them with less efficiency than adults.<sup>5</sup>

The type, duration and frequency of the procedures performed directly affect the dose of DEHP received by a patient.<sup>2,5</sup> The following procedures have been identified as possibly posing the highest risk for exposure to DEHP: exchange transfusion,<sup>5</sup> ECMO,<sup>5</sup> enteral and total parenteral nutrition in neonates;<sup>5</sup> multiple procedures in sick neonates;<sup>5</sup> nursing infants of mothers on hemodialysis,<sup>5</sup> heart transplantation or coronary artery bypass surgery (aggregate dose),<sup>2</sup> transfusion of blood,<sup>5</sup> and transfusion in adults undergoing ECMO.<sup>2</sup> Seriously ill patients may require more than one of these procedures, thus potentially exposing them to higher levels of DEHP.<sup>2</sup>

A study conducted with the National Research Council of Italy determined that human exposure to DEHP can begin in utero, suggested that phthalate exposure is significantly associated with shorter pregnancy duration, and found detectable cord blood DEHP concentrations in 88.1% of samples, thus suggesting pregnant women are at increased risk for the health effects of DEHP exposure.<sup>7</sup> Another population that may be at increased risk for the effects of DEHP exposure are patients who use oxygen for prolonged periods, such as those suffering from Chronic Obstructive Pulmonary Disease (COPD), as they are exposed to DEHP for extended periods.<sup>4</sup>

## THE CHALLENGE AND A SOLUTION

Medical products made with PVC require a softening agent (plasticizer) when pliability and flexibility are required. For decades, DEHP has been used as the plasticizer in a myriad of devices. The challenge has been to find a non-DEHP plasticizer that could be used as a viable alternative.

A case in point is the Nasal cannula, which has traditionally been manufactured using PVC with DEHP as the plasticizer, and is used to deliver supplemental oxygen to patients in need of respiratory support. Because of its comfort, convenience and ability to deliver low to medium concentrations of oxygen, the nasal cannula is one of the most frequently used oxygen delivery devices across the patient spectrum. Flexibility, toughness and pliability are necessities with this product, which required the use of a plasticizer; and for decades DEHP was the only option.

Recent advances in medical device design and materials have now allowed Hudson RCI® to produce the new Softech® Plus nasal cannula product offering which uses a new material blend with a non-DEHP plasticizer. With this new breakthrough in material science, the non-DEHP Softech® Plus cannulas are exceptionally soft and set a new standard in patient care; ensuring a comfortable fit for both short and long-term use, without the potential risks posed by DEHP.

## CONCLUSION

While the FDA recommends that you should not avoid procedures or devices simply because of the possibility of health risks associated to DEHP exposure in patients at increased risk for the effects of DEHP, they do recommend considering alternatives for the treatment of those patients, including PVC devices made with non-DEHP plasticizers. For other patient groups, the decision to use DEHP alternatives must take into account the medical advantages and drawbacks of the substitute and their availability.<sup>2</sup>

The Softech® Plus cannulas offer an exciting option for providing oxygen therapy to populations identified as at increased risk for the health effects attributed to exposure to DEHP, such as male neonates,<sup>2</sup> pregnant women who carry male fetuses,<sup>2</sup> peripubertal males,<sup>2</sup> children,<sup>5</sup> patients undergoing multiple high risk procedures,<sup>5</sup> and patients who use oxygen for prolonged periods.<sup>4</sup>

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