

## GC-MS Identification of Phthalate and Alternative Plasticisers in Medical Devices

Malarvannan G<sup>1\*</sup>, Onghena M<sup>1</sup>, Verstraete S<sup>2</sup>, van Puffelen E<sup>3</sup>, Jacobs A<sup>2</sup>, Vanhorebeek I<sup>2</sup>,  
Verbruggen S<sup>3</sup>, Joosten K<sup>3</sup>, Van den Berghe G<sup>2</sup>, Jorens PG<sup>4</sup>, Covaci A<sup>1</sup>

<sup>1</sup>Toxicological Centre, University of Antwerp, Universiteitsplein 1, Wilrijk, Belgium

<sup>2</sup>Clinical Division and Laboratory of Intensive Care Medicine, Department of Cellular and Molecular Medicine, KU Leuven, Herestraat, Leuven, Belgium

<sup>3</sup>Intensive Care, Department of Pediatrics and Paediatric Surgery, Erasmus MC, Sophia Children's Hospital, Rotterdam, The Netherlands

<sup>4</sup>Department of Intensive Care Medicine and Clinical Pharmacology, Antwerp University Hospital and University of Antwerp, Edegem, Belgium

Intensive care relies heavily on the use of soft and flexible indwelling medical devices. These devices are mostly made of polyvinyl chloride (PVC), an inherently rigid polymer. To increase flexibility and softness, phthalates, and in particular di(2-ethylhexyl) phthalate (DEHP), have been historically used as plasticisers (or softeners) for plastic indwelling medical devices [1]. DEHP is not chemically bound to plastics and can leach from medical devices during the use. Recently, DEHP metabolites have been found at high levels of up to 10 µM in urine and blood of adult/and paediatric patients in the ICU following the use of indwelling medical devices [2-3]. In neonatal ICU patients, the urinary levels of DEHP metabolites have been correlated with the number of DEHP-containing medical devices and even exceeded the average daily adult exposure by 1-2 orders of magnitude [4-5].

Due to its carcinogenic, mutagenic, or reprotoxic properties, the use of DEHP in medical devices has recently been challenged by the European authorities [6]. This action has forced manufacturers to replace DEHP with alternative plasticizers, such as tri-octyltrimellitate (TOTM), di-(2-ethylhexyl) terephthalate (DEHT), di(isononyl)-cyclohexane-1,2-dicarboxylic acid (DINCH), di-(2-ethylhexyl) adipate (DEHA), acetyl tri-n-butyl citrate (ATBC), diisodecyl phthalate (DIDP), di-isononyl phthalate (DINP), and di(2-propylheptyl) phthalate (DPHP)). Currently, toxicity data and information regarding leaching from medical devices for these alternative plasticizers are hardly available [7-8].

The principal aim of the study was to identify the major plasticizers present in medical devices commonly used in the paediatric intensive care unit (PICU). Plasticizers were extracted from PVC medical devices using Hexane:Ethyl acetate (1:1) and the supernatant was injected into a GC-EI/MS system. For identification, standard solutions were injected separately to know the retention times and specific fragmentation patterns and ions. Further, the identification was done using the Mass Spectral database of WILEY2009. We have analysed a wide range of PVC medical devices (n=97) daily used in the PICU of two academic hospitals. Identified compounds varied between the samples, leading to a wide variety of chemicals. This may also be due to different product types, companies or year of manufacture. In some samples (n= 4), no chromatographic peaks could be seen or identified. Results indicated still a predominant use of DEHP as plasticizer, followed by DEHA, DEHT and TOTM. Other plasticizers were respectively used in < 5% of the investigated samples. DEHP was detected in 60 samples out of a total of 97 samples, followed by DEHA (32 of 97), DEHT (24 of 97), TOTM (20 of 97), ATBC (10 of 97), DPHP (4 of 97), DiNP (4 of 97), DIDP (2 of 97) and DINCH (2 of 97). The higher frequency of contamination observed for DEHP/DEHT/DEHA could be explained by the use of raw materials (plasticizers) of low purity, e.g. devices containing TOTM contained also DEHP and DEHT. The levels of impurities depend on the nature and the purity of the plasticizer used.

These results are in good agreement with results obtained in PVC medical devices tested earlier by Gimeno et al. (2014) and suggest that children hospitalised in the ICU are exposed to a wide range of plasticizers, including the contested DEHP.

### References

1. Gimeno et al. (2014) *Journal of Chromatography B*, **949-950**: 99-108.
2. Huygh et al. (2015) *Environment International*, **81**: 64-72.
3. Verstraete et al. (2016) *Intensive Care Medicine*, **42**: 379-392.
4. Weuve et al. (2006) *Environmental Health Perspectives*, **114**: 1424-1431.
5. Green et al. (2005) *Environmental Health Perspectives*, **113**:1222-5.
6. European Union Directive (2007) <http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX:32008R1272>
7. Danish EPA (2014) <http://www2.mst.dk/udgiv/publications/2014/03/978-87-93178-27-4.pdf>
8. SCENIHR (2016) [https://ec.europa.eu/health/scientific\\_committees/emerging/docs/scenihr\\_o\\_047.pdf](https://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_047.pdf)