Rocket Medical Statement on the use of Phthalates (POL58)

Brief Background

At Rocket Medical, with regards to our poly (vinyl chloride) (PVC) products, we use one type of Phthalate:

Di(2-ethylhexyl)phthalate (DEHP)

PHT
DEHP

Clinical Benefits of Phthalates

Medical devices containing PVC with Di(2-ethylhexyl)phthalate (DEHP) have important clinical benefits. For certain medical procedures such as drainage of the pleural or mediastinal space the flexibility of certain parts of a medical device is essential. This flexibility allows a medical device to fulfil its function in treating patients whilst allowing for the comfort of the patients and reducing the risk of damage to tissues. Various substances are used to ensure this flexibility, among which DEHP is the most frequently used plasticizer in PVC medical devices.

Potential of DEHP Exposure

Medical procedures using PVC medical devices containing DEHP have the potential to lead to DEHP exposure due to DEHP leaching from the device. The extent of exposure largely depends upon the medical treatments administered, the duration of the treatment, and in the case of plastic blood bags, by the length of storage and the storage temperature. Lack of research in humans means it is difficult to predict the adverse effects of DEHP because certain animal models may not apply to humans. Most studies utilise mice and rats, however breakdown of DEHP in the human body differs to the mechanism observed in these animals. These effects are also seen only at levels far in excess of normal human exposure.

The following procedures have been shown to have the potential for high exposure to DEHP:

- Exchange transfusion of blood in neonates
- Extracorporeal membrane oxygenation (ECMO) treatment of neonates and of adults
- Total Parenteral Nutrition (TPN) in neonates
- Multiple procedures in preterm neonates
- Haemodialysis
- Enteral nutrition in neonates and adults
- Heart transplantation or coronary artery bypass graft surgery
- Massive blood transfusion of red blood cells and plasma
- Peritoneal dialysis

The exposure during the aforementioned procedures is caused by various types of medical devices including blood bags; tubing like catheters, intubation tubes and intravenous catheters; and other medical devices made of PVC.

In adults, the highest short-term exposure may result from transfusions of blood components in trauma patients and in patients undergoing ECMO, whereas the highest chronic treatment is represented by haemodialysis. Rocket Medical does not produce equipment for haemodialysis which poses the greatest risk of exposure to DEHP. Voluntary medical treatments such as the apheresis procedure to separate and donate blood products can cause exposure to DEHP, however Rocket Medical do not manufacture this type of equipment.

Long-term total parenteral nutrition corresponds to higher exposure for infants and children, implying that the lower the body weight, the higher the exposure. Pleural catheters, the main DEHP-containing product manufactured by Rocket Medical, are utilised to drain fluid from the lungs easily and painlessly, avoiding the need for injections and chest tubes. In infants and neonates ECMO is the medical treatment which may give the highest daily exposure over repeated exposure for a short period of time, however Rocket Medical does not produce equipment for this type of medical procedure.

Scientific Opinion on the Use of DEHP in Medical Devices

In September 2002, the Scientific Committee on Medicinal Products and Medical Devices adopted an opinion on "Medical Devices containing DEHP plasticized PVC; Neonates and Other Groups Possibly at Risk from DEHP toxicity" according to which "there is no evidence that any of these groups do experience DEHP related adverse effects".

The 2015 review by the Scientific Committee on Emerging and Newly-Identified Health Risks found that there was no, weak or inconsistent evidence for the effect of DEHP across a number of epidemiological and clinical studies. Further research is required to confirm the definitive adverse effects following exposure of consumers through medical equipment.

In February 2016 the Scientific Committee on Emerging and Newly-Identified Health Risks stated that "the benefit of medical devices must also be considered" when assessing the risk of DEHP exposure. It could be viewed that the benefit of pleural catheters outweighs the risk of DEHP exposure.

Rocket Devices Containing Phthalates

The Rocket devices containing phthalates are documented in a version-controlled phthalates matrix. The devices contain between 0.2% and 28% DEHP, which have been calculated to ensure the device is fit for use, this is documented in the design files for the devices. The use of phthalates and biocompatibility will be reviewed in the Risk Assessment in line with ISO 14791 and ISO 10993 and will be addressed in the essential requirements. Where in the Risk Assessment and the Clinical Evaluation Report the clinical need for phthalates in the product outweighs the potential risks of the device, this will be considered acceptable. Where the clinical benefit of the use of phthalates does not outweigh the risks of the exposure the phthalates, this risk will be considered unacceptable and the product will not be considered viable.

The devices in the Rocket portfolio which include phthalates can be split in to two.

The first are critical to preserving life. Thoracic Catheters or Chest tubes are required to drain the pleural or mediastinal space of air or fluid in pleural effusion, pneumothorax, empyema, or haemothorax in spontaneous, trauma, iatrogenic and surgical scenarios. These occurrences can inhibit the breathing of the patient, causing shortness of breath, chest pain, and if left untreated, can be fatal

to the patient. Patients who undergo chest drainage are on a critical treatment path to ensure lung re-inflation and resolve from the clinical condition. Pneumothorax, pleural effusion and haemothorax can occur spontaneously, due to trauma to the chest lung disease or malignancy. These conditions are not likely to be reoccurring and pre-exposure is not likely, specifically in the event of trauma to the chest. In the circumstance of malignancy, it is likely that the disease is at a progressed stage and exposure to phthalates is unlikely to be a contributing factor to any existing illness or instigate new toxicity in the patient.

- Thoracic Catheters
- Seldinger Chest Drainage Sets
- Pleural Vent Pneumothorax Device (component containing DEHP is non-patient contacting)

Although in the majority of patients the catheters would be in situ for up to 72 hours, the devices are for short term use. Whilst it is acknowledged that the use of phthalates in the Rocket devices which are for short term use is not ideal, these devices are only used for critical procedures where the risk of phthalate exposure is clearly outweighed by the benefit to the patient.

Phthalates maintain the plasticity of the chest drainage tubes. This is essential avoiding additional damage to surrounding tissues when the lung re-inflates, allowing positioning for optimum drainage and patient comfort as when the tubes contain phthalates, they are more pliable, and subsequently easier to insert and place.

The second, oocyte aspiration, part of In Vitro Fertilisation as a treatment for infertility.

The material is non-patient contacting in this application.

- Filter Sets
- Filter sets contained in Oocyte Aspiration Packs

The material is utilised to connect a suction unit via a barrier hydrophobic filter to an oocyte aspiration set. This component must be flexible and able to withstand the application of high vacuum.

Additional information on the use of Phthalates in Rocket Devices

Safety concerns have been expressed for high-risk patient groups, such as neonates, infants, pregnant and breast-feeding nursing women exposed to DEHP.

The Rocket Medical devices would be used on these patient groups for critical procedures where the risk of phthalate exposure is clearly outweighed by the benefit to the patient as shown in the statements above.

Rocket Medical is working to review the phthalate status of the devices they supply to ensure the inclusion of phthalates is essential to the devices supplied. Where alternative ingredients are available to ensure plasticity of the device, these are being considered on a case by case basis. As the current literature demonstrates that sufficient evidence has not been presented to suggest that medical devices which contain DEHP phthalates pose an unacceptable public health risk to patients, the use of phthalates in life critical devices is currently considered acceptable.

Alternatives to DEHP phthalates which can be used in medical devices include ATBC (Acetyl tributyl citrate) however this has been demonstrated to affect the central nervous system in animal models.

There have been additional studies which indicate that ATBC inhibits the proliferation of lymph node T cells and may cause irritation. DINCH (Di-isononylcyclohexane-1, 2-dicarboxylate) may also be used in medical devices, specifically tubing, however again, DINCH poses its own risks as studies in animals have demonstrated effects of the testes, liver and thyroid stimulating hormone. Alternative new plasticisers such as “Grindsted soft-n-safe” are becoming more available, however the safety profile of these newer alternatives, whilst promising, are not yet fully established and subsequently could pose further risks.

Additional data and information will be proactively sought by Rocket Medical on a six-monthly basis. Where additional data becomes available, this will be reviewed and taken into consideration for the Risk Benefit profile of the devices that contain phthalates, to ensure the most up to date safety profile is available and subsequently appropriate decisions can be made.

Conclusion

In conclusion:

- Rocket Medical has shown the benefits of using DEHP in its products outweighs the risk.
- Rocket Medical does not produce equipment for extracorporeal oxygenation in children.
- Rocket Medical does not produce equipment for haemodialysis, infusion of platelets and apheresis.
- The FDA has identified a risk which may be present during bypass surgery where blood passes through PVC bypass tubing and is then reinfused into the patient - Rocket Medical manufactures chest drainage tubes as a conduit for draining blood from the mediastinum or pleural space. Fluid drained in this manner may be re-infused into the patient but storage of the collection of cells is not performed by the catheter itself.
- Should Rocket Medical consider entering the neonate market for chest drains, then the above guidelines will be reviewed during the design process as part of our normal Risk Management procedures.

References

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