Health Care Without Harm Workshop

3rd December 2019 in Brussels

FRESENIUS KABI

caring for life

Progress and challenges in substituting DEHP in a broad portfolio

Stefan Kolb

VP European Governmental Affairs

Fresenius Kabi

Fresenius SE

The Fresenius Health Care Group

FRESENIUS KABI
caring for life

FRESENIUS MEDICAL CARE

- Dialysis Products
- Dialysis Care
- Extracorporeal Therapies

FRESENIUS KABI

- IV Drugs
- Clinical Nutrition
- Infusion Therapy
- Devices
- Transfusion Medicine & Cell Therapies (TCT)

FRESENIUS HELIOS

- Operation and management of acute clinics and rehabilitation centers

FRESENIUS VAMED

- Planning, constructing and managing health care facilities

FRESENIUS MEDICAL CARE

Fresenius Medical Care Dialysis Portfolio Non-DEHP

Status for Dialysis Centers and Home Care

FRESENIUS
MEDICAL CARE

WE ALL OWN COMPLIANCE

- We will conduct business with integrity and honesty in compliance with all laws, company policy, and our values.
- We are committed to produce products and deliver services that are safe and of the highest quality for our customers.

Fresenius Medical Care Product Portfolio

FRESENIUS KABI
caring for life

Bloodlines

- All Fresenius bloodlines distributed in EMEA market are made of DEHP-free material, i.e. TOTM
- Our innovative 6008 CAREset has less plasticiser compare to standard bloodline due to Biofine components (plasticiser-free)

Needles

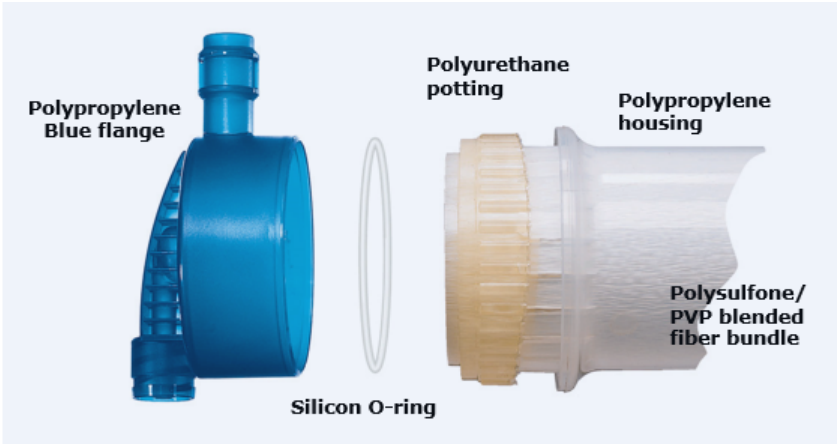
- In beginning 2018, Fresenius Medical Care has decided to switch all its fistula needle products from DEHP to DEHP-free material to comply with new MDR requirement (implementation ongoing)

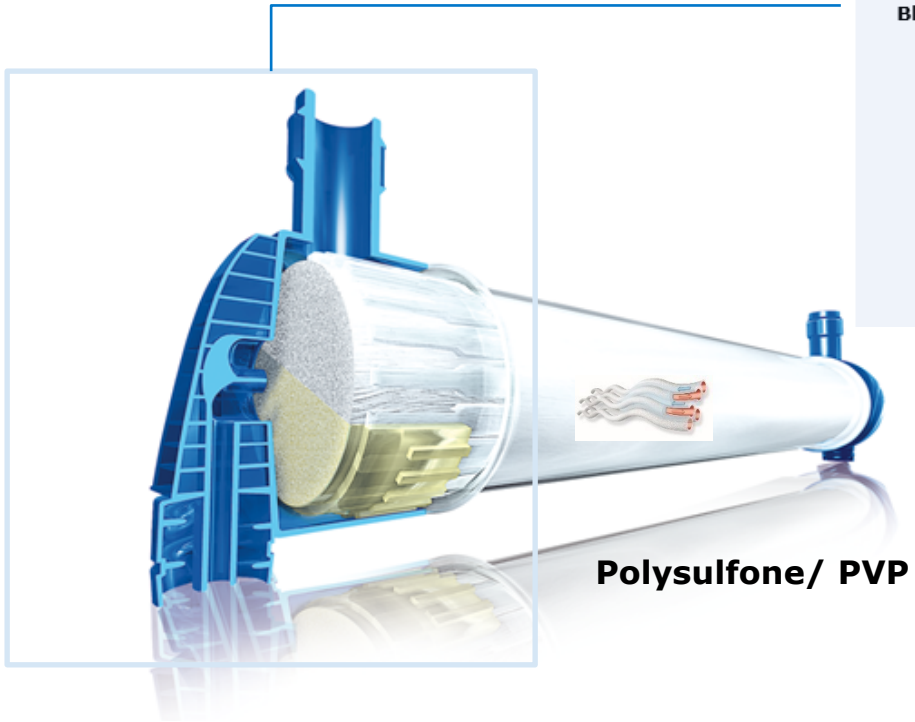
FX Dialyser components

FRESENIUS KABI
caring for life

Dialysers

- All Fresenius dialysers are made of completely DEHP-free material, for details see pictures





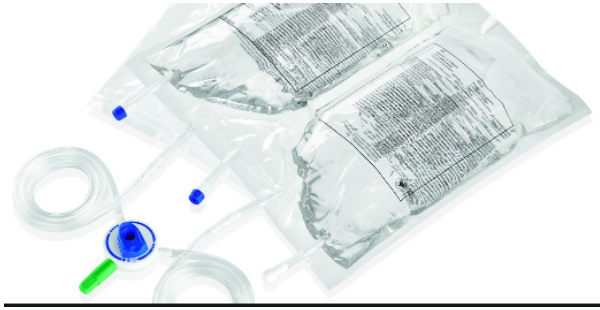
Polysulfone/ PVP blended fiber bundle

Fresenius Medical Care Product Portfolio

FRESENIUS KABI
caring for life

Portfolio for peritoneal dialysis

- PVC-free (thus also DEHP free) material Biofine® used for PD fluids since 1996
- Biofine® is recycled to into carbon dioxide and water during incineration
- Less waste material generated due to thinner foil1
  - ~88kg/year for a CAPD (Continuous Ambulatory Peritoneal Dialysis) patient
  - ~29 kg/year for an APD (Automated Peritoneal Dialysis) patient
- 1st healthcare company certified by Nordic Ecolabel (SWAN label) in 2008/2009
- Phase out of DEHP materials, e.g. currently still in waste with MDR implementation during the cause of 2022



1. EDTA 2019, Budapest, Poster (FP573)

Fresenius SE

The Fresenius Health Care Group

FRESENIUS KABI
caring for life

FRESENIUS MEDICAL CARE

- Dialysis Products
- Dialysis Care
- Extracorp…
  Th…

Summary: Vastly DEHP free disposable portfolio

FRESENIUS KABI

- IV Drugs
- Clinical Nutrition
- Infusion Therapy
- Devices
- Transfusion Medicine & Cell Therapies (TCT)

FRESENIUS HELIOS

- Operation and management of acute clinics and rehabilitation centers

FRESENIUS VAMED

- Planning, constructing and managing health care facilities

Fresenius SE

The Fresenius Health Care Group

FRESENIUS KABI
caring for life

FRESENIUS MEDICAL CARE

- Dialysis Products
- Dialysis Care
- Extracorporeal Therapies

FRESENIUS KABI

- IV Drugs
- Clinical Nutrition
- Infusion Therapy
- Devices
- Transfusion Medicine & Cell Therapies (TCT)

FRESENIUS HELIOS

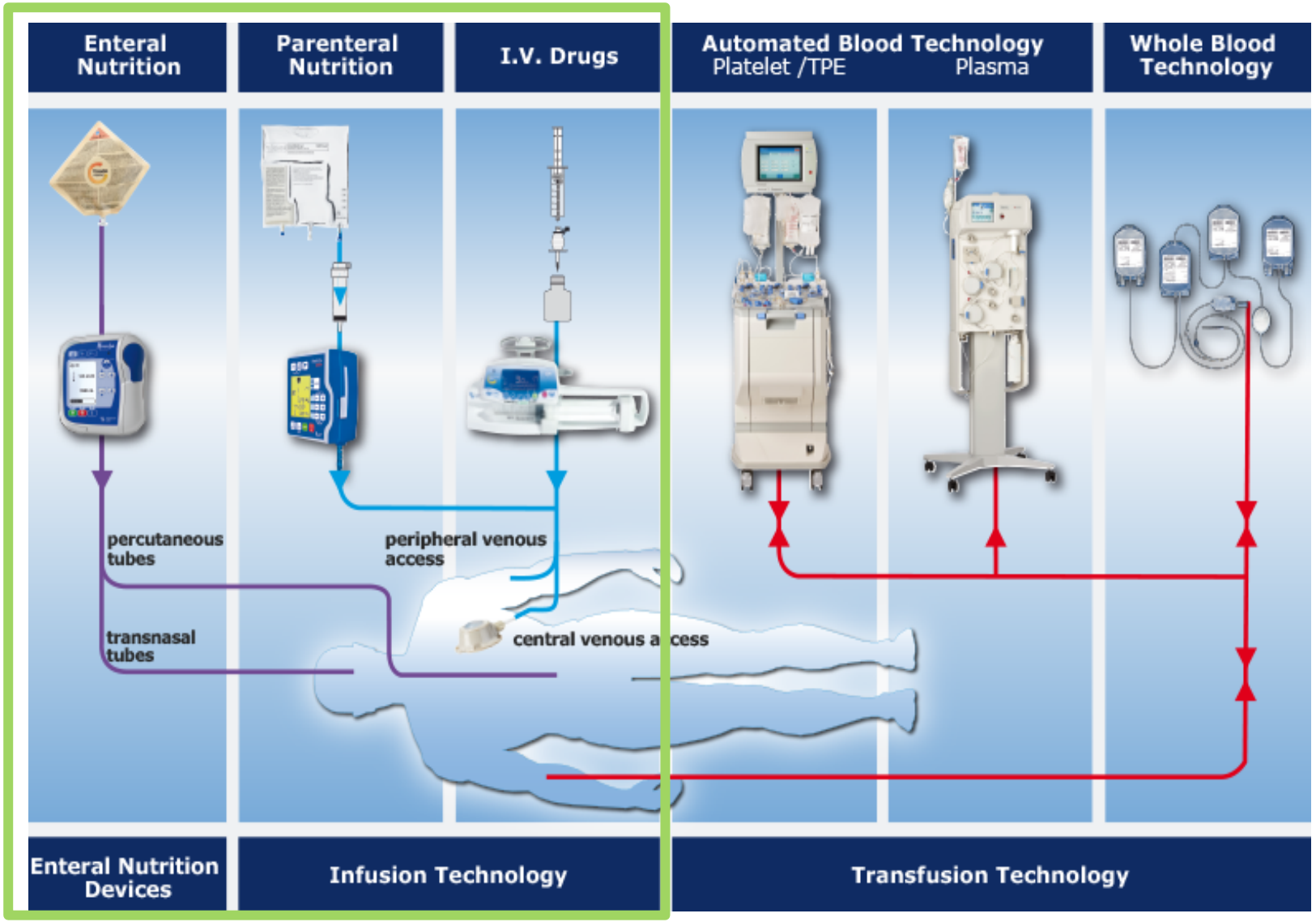
- Operation and management of acute clinics and rehabilitation centers

FRESENIUS VAMED

- Planning, constructing and managing health care facilities

Fresenius Kabi
Medical Device Devision

FRESENIUS KABI
caring for life



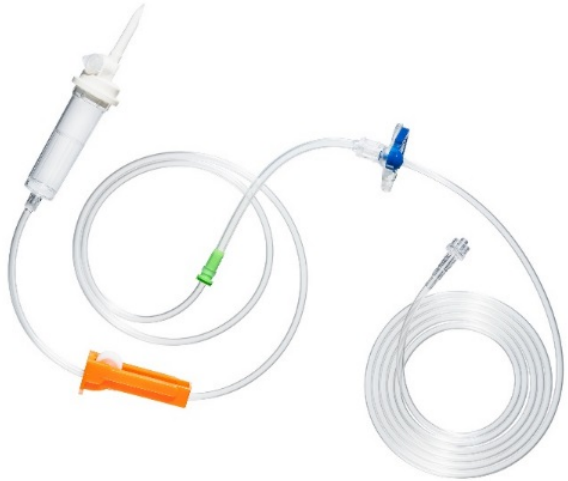
Infusion Therapy Portfolio

Volumat Lines are not made with DEHP

From the start, Fresenius Kabi has developed a PVC tubing **without using DEHP plasticizer** for our IV Dedicated Set portfolio.

Instead, TOTM is used as a plasticized agent.

Some Volumat Lines also use **PVC-free alternatives** for special applications.



In conclusion, with Volumat Lines, the potential risks of DEHP are therefore eliminated.

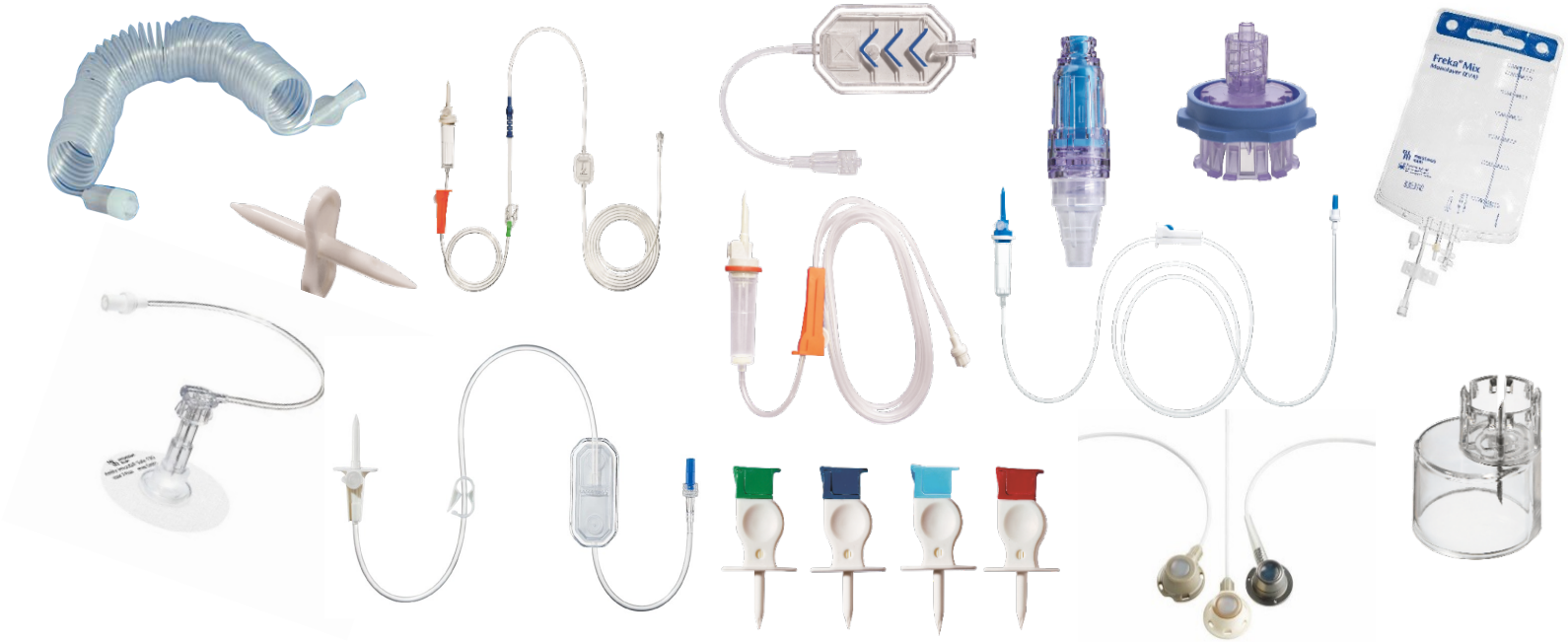
Devices & Disposables
Infusion Therapy Portfolio

FRESENIUS KABI
caring for life

In our continuous mission for Medication Safety,

Fresenius Kabi is constantly working to replace DEHP with alternative plasticizers.

We offer a wide selection of products in our Infusion Therapy portfolio using TOTM plasticizer.

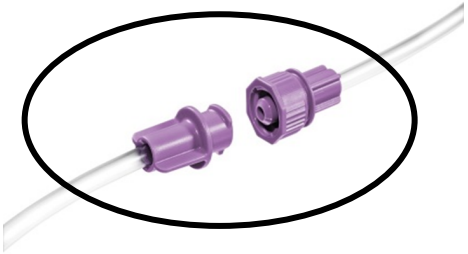


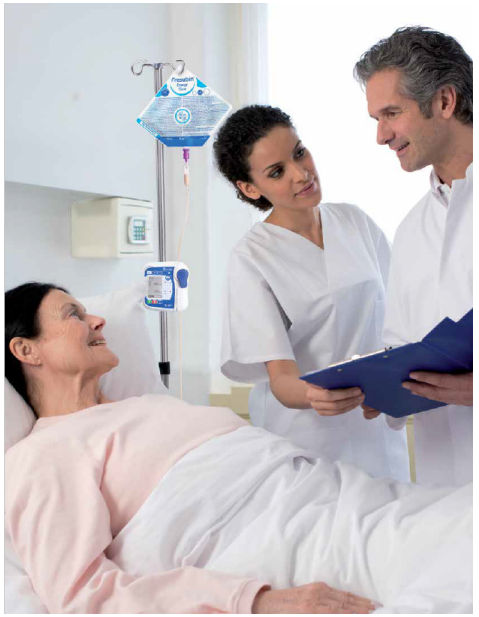
Enteral ENFit and ProNeo Portfolio

FRESENIUS KABI
caring for life

The safe side of enteral nutrition!

Since 2017, ENFit has been globally promoted as the new standard for enteral connectors for enteral feeding application according to ISO 80369-3.



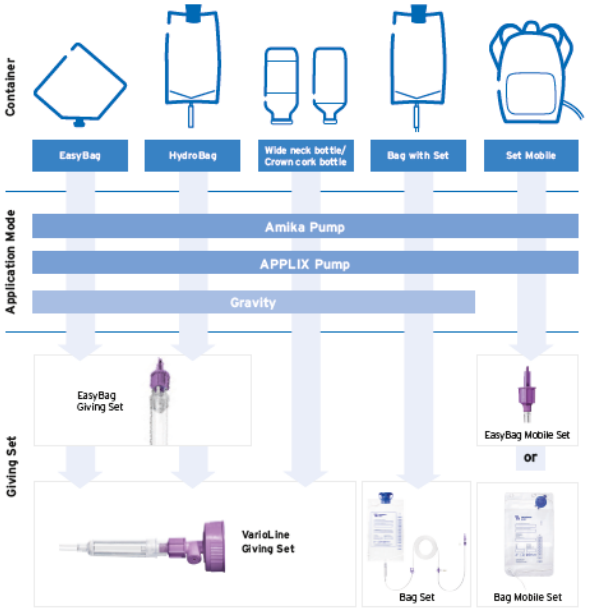


Fresenius Kabi provides a comprehensive enteral portfolio including giving sets, feeding tubes and accessories with the safe ENFit connector.
For the neonatal and paediatric application, a special offering has been developed with the ProNeo range.

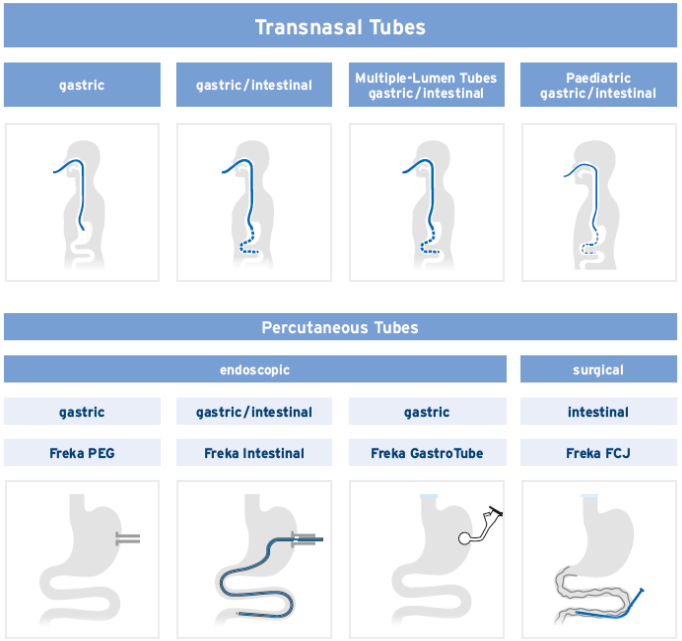
ENFit and ProNeo giving sets, feeding tubes and accessories are free of DEHP in accordance with REACH.

Enteral ENFit Portfolio Overview

Giving Sets (incl. HydroBag)



Feeding Tubes



14

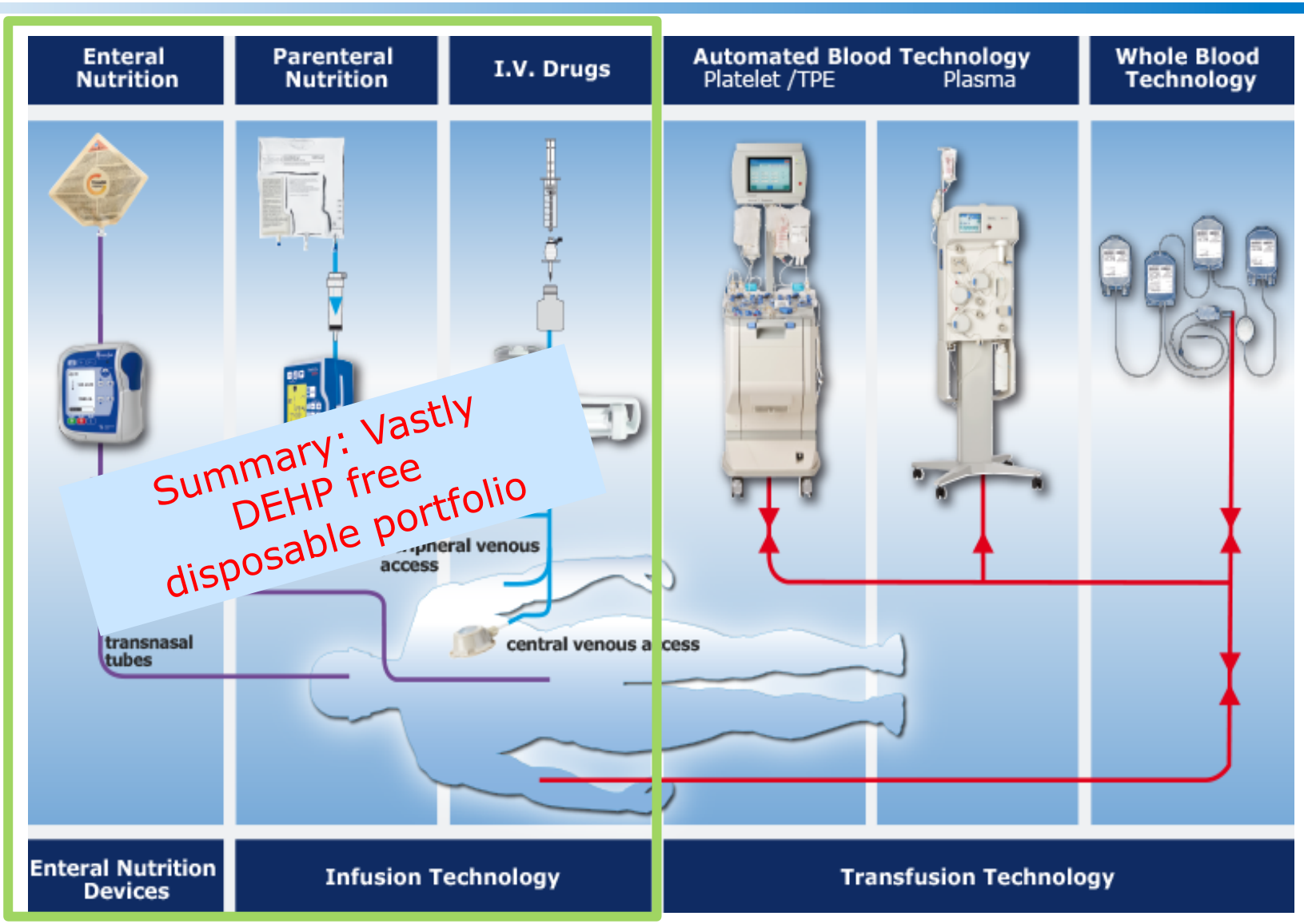
ProNeo Portfolio

The **ProNeo portfolio** includes a **complete** product range to cover all necessary steps in the enteral nutrition workflow: **from nutrition preparation to safe administration.**

Entire portfolio is Non-DEHP

Fresenius Kabi
Medical Device Devision

FRESENIUS KABI
caring for life



Regulatory challenges in the Blood Transfusion Industry

FRESENIUS KABI
caring for life

Piling up regulatory challenges could negatively impact the availability of blood supply within the EU

Regulatory challenges in the Blood Transfusion Industry

FRESENIUS KABI
caring for life

Piling up regulatory challenges could negatively impact the availability of blood supply within the EU

1. **Transition from MDD to MDR** till deadline May 2020, leading to **major efforts for all manufacturers** in updating their broad global portfolio with 1.000s of articles

2. **Newly implemented BRA** according to SCHEER guidelines

3. **Risk of up-classification of blood bag systems** from class IIb → III (!!)

4. **Sunsetting DEHP for blood bag systems** according to ECHA Annex XIV update from 06/2019, with no viable alternative plasticizer to maintain full Red Blood Cell (RBC) storage period of 42/49 days.

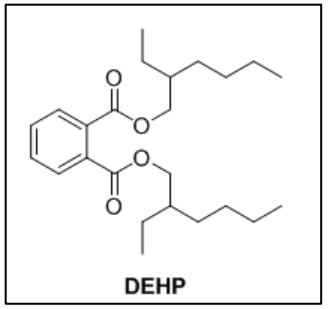
   A full RBC storage period is essential for a safe national blood supply during all periods of a year!

Why does DEHP stabiles Ery membranes?

FRESENIUS KABI
caring for life

DEHP helps to extend the shelf life of the stored red blood cells (RBCs)

- Interaction between the membrane of the red blood cell and the plasticizer



Hemolysis:

- If free hemoglobin (fHb) is too high it can not be removed completely via kidney and will aggregate in the renal tubules.
- **Potentially hazardous health risk: Renal failure with uremia can cause multi organ failure (!)**
- Resulting in a severe patient health risks

Alternative plastizicers are inferior

- All manufacturers studied alternatives like DINCH, DEHT etc. and partially even launched them
- Outcome: elevated fHb / hemolysis levels in comparison to DEHP in RBC storage

RBC storage requirements per PVCMed Alliance

Why is a storage period for up to 49 days necessary?

PVC blood bags allow a long shelf life for the blood. Under refrigeration, the blood can last for up to 49 days. While much blood is used within a few weeks, there are several reasons why a storage period of up to 49 days is crucial:

1. The warehousing and distribution of the national blood supplies in Europe are based on up to 49 days shelf life. Patients' safety depends on this stability of supply of blood components stored in blood bags, especially of Red Blood

2. A shorter storage period would have dramatic consequences in the national supply chain for RBCs. A reduced storage time could only be compensated by an increase amount of RBC´s including an extension of warehouse capacity and furthermore in increase of donations. To increase the number of donations will be very difficult as the motivation of the population to donate blood is typically low and is thus a challenge in many of the European countries already today. This would increase the risk of blood shortages, an increase in discarding outdate RBCs and pose a threat to patients. Last but not least, an increase in discards of voluntarily donationed blood is also an ethical problem for the public.

3. Rare blood types are often in low stock. Thus, the shelf life of the blood must be as long as possible to have enough supply.

4. Unforeseen events, big social events, seasonal volatilities such as holiday periods, distribution of blood groups, and compatibility of blood groups are some of the factors that can impact blood supplies. Typically holiday period do already today pose a supply risk, this would dramatically increase in case the storage period is reduced to only 28 days. A shorter shelf life would heighten the risk of shortages.

It is essential that any attempts to develop blood bags with alternative materials take these considerations into account.

Link: https://pvcmed.org/healthcare/safe-and-innovative-pvc-blood-bags/

Logistical challenges on RBC supply

FRESENIUS KABI
caring for life

Reasons for bottlenecks in Blood Supply

Unforeseen events

Blood group compatibility

Big social events

Distribution of Blood groups

Individual volatilities

Seasonal volatilities

Long term Developments

Aging population

Tentative timeline of Annex XIV amendment on 4 phthalates (DEHP, BBP, DBP, DIBP)

FRESENIUS KABI
caring for life

Date (TENTATIVE!)	Step/Action
June 24-27 2019	**ECHA Member State Committee (MSC) meeting** (Discussion and adoption of MSC Opinion, taking into account comments submitted in both consultations that ran from June 2018-March 2019)
July 2019	ECHA to submit final **recommendation to the EU Commission** (including their recommendation on transition times, exempted uses and review period lengths)
(3-4 months)	Preparation of draft delegated act by EU Commission (*no legal deadline*)
End of 2019	**4-week stakeholder consultation on Commission draft delegated act**
Q1 2020?	**Vote by Member States in REACH Committee**
TBC	Finalisation of delegated act by EU Commission
Q2 2020?	**Start of scrutiny by EU Parliament + Council** (3 months according to Art. 5a, Decision 1999/468/EC)
Q3 2020?	**Publication in the EU Official Journal**
Q3 2020?	**Entry into force** (20 days after publication in EU OJ)
Q1 2022?	**Latest application date** (EU COM proposal: 18 months after entry into force)
Q3 2023?	**Sunset date** (EU COM proposal: 36 months after entry into force)

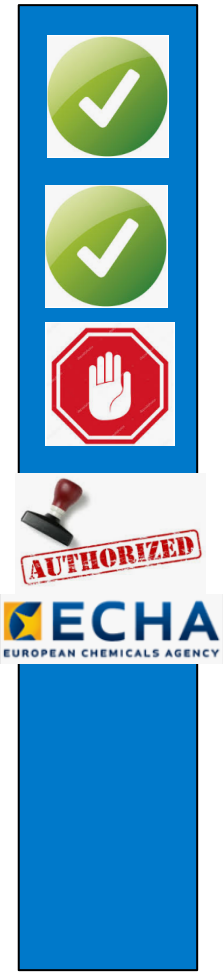
Apply for authorization for blood bags containing DEHP
→ anyway environmental DEHP exposure considered to be low
→ limited patient exposure
→ substitution plan in preparation

Conclusions for the Blood Transfusion Industry

FRESENIUS KABI
caring for life

Piling up regulatory challenges could negatively impact the availability of blood supply within the EU

1. **Transition from MDD to MDR** with deadline May 2020, leading to **major efforts for all manufacturers**
2. **Newly implemented BRA** according to SCHEER guideline
3. **Risk of up-classification** of blood bag systems from class IIb → III MDR(!)
4. **Sunsetting DEHP for blood bag systems** according to ECHA Annex XIV with no viable alternative plasticizer to maintain full RBC storage period



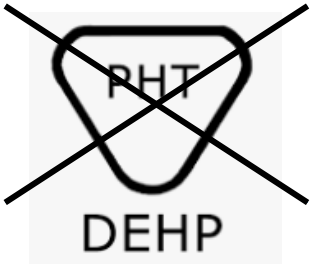
Summary for Fresenius

Fresenius is on a good way to phase out DEHP where ever feasible

- Substantial progress towards a DEHP free portfolio has been reached for the
  → Fresenius Medical Care Dialysis portfolio, for both Dialysis Center and Peritoneal dialysis
  → Fresenius Kabi IV drugs, enteral and parenteral nutrition portfolio, incl. focus on the pediatric products

- Challenges only remain for the blood transfusion products where no viable alternatives do exist today. However, DEHP exposure seams limited. Class IIb for blood bags must remain.

- We are committed to substituted DEHP also in future where ever possible.



FRESENIUS KABI
caring for life

Thank You!

caring for life

The people of Fresenius Kabi are driven by a common purpose: to put life-saving medicines and technologies in the hands of people who care for patients, and to find answers to the challenges they face.

Caring for Life