MDR/IVDR – SO YOU THINK YOUR PLASTICS SUPPLY CHAIN CAN HELP?

HOW MEDPHARMAPLAST IS HELPING OVERCOMING THE POTENTIAL CHALLENGES

MedPharmPlast
A sector group of EuPC

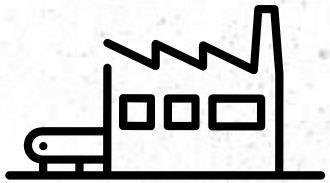
4th March 2020

Steve Duckworth (Clariant) & Jo Belshaw (Albis)

CLARIANT

Who is: Clariant Healthcare Polymer Solutions ?

- **Dedicated Healthcare experts:** global and regional team of technical specialists are able to support multiple projects, trouble shooting and develop the right **compound or concentrate solution** for each need and transfer globally.



- **Global EN: ISO13485-2016 manufacturing footprint since 10 years. Validated back-up supply reduces your supply chain risk**.

- **Comprehensive regulatory testing and documentation.** Pre-testing of the raw material ingredients to pharma industry standard, DMF, formulation disclosure

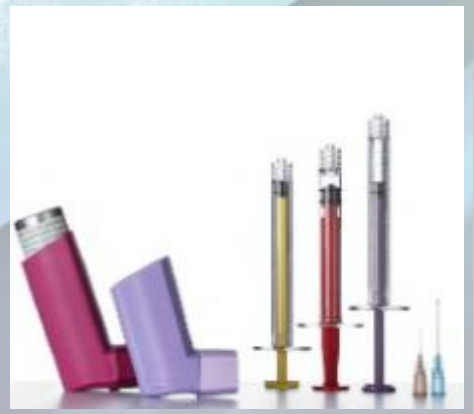
- **Minimizing risk of changes:** Incoming batch control of ingredients versus a finger-print to monitor changes. Change Control agreements.

CLARIANT

‘Medical grade’ MEVOPUR® / REMAFIN® -EP color and functional concentrates and compounds used in:

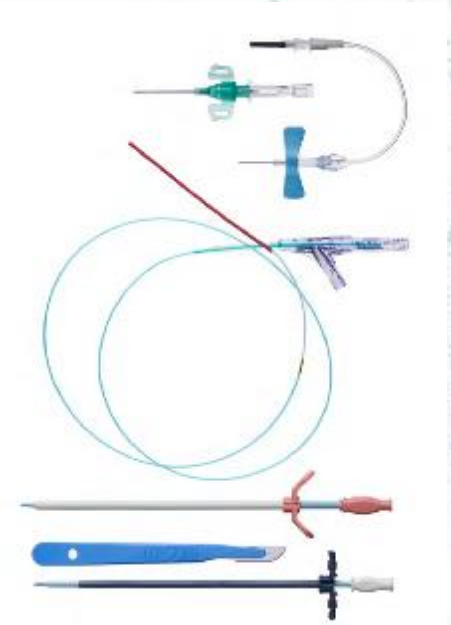
Drug delivery

– Colors for identification / branding
– Function (examples):
  - Lubrication - metering
  - γ protection
  - Laser welding / marking
  - Nucleation
  - Anti-counterfeit PLASTIWARD



Invasive

– Colors and compounds in
  - Polyolefins to PEBA, TPU, PA11/12, and Liquid Silicone
– Function:
  - Radiopacity;
  - Lubrication;
  - Anti-microbial

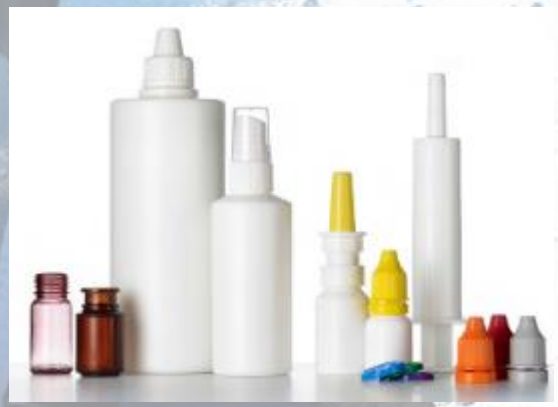


Diagnostics

– Colors for identification
– Function:
  - Laser-welding / marking
  - Hydrophobic
  - Conductivity;
  - Clarifiers

Pharma packaging

– EP ‘white +’ and colors e.g. ophthalmic standard range
– Function
  - γ protection
  - UV protection
  - Productivity enhancing
  - Anti-counterfeit PLASTIWARD



Who is: MedPharmPlast Europe (MPPE)?

- Sector group of European Plastics Converters (EuPC)
- Companies representing the complete supply chain of plastics used in medical devices, IVD & pharmaceutical packaging in Europe
- Has a Regulatory Task Force – cross industry experts
- Provides
  - Updates of developments in Eu Regulations and their impact
  - A forum for members to share their views & years of expertise
  - Prioritisation of patient safety
  - An opinion former and route to legislators to support delivery of work-able final regulations

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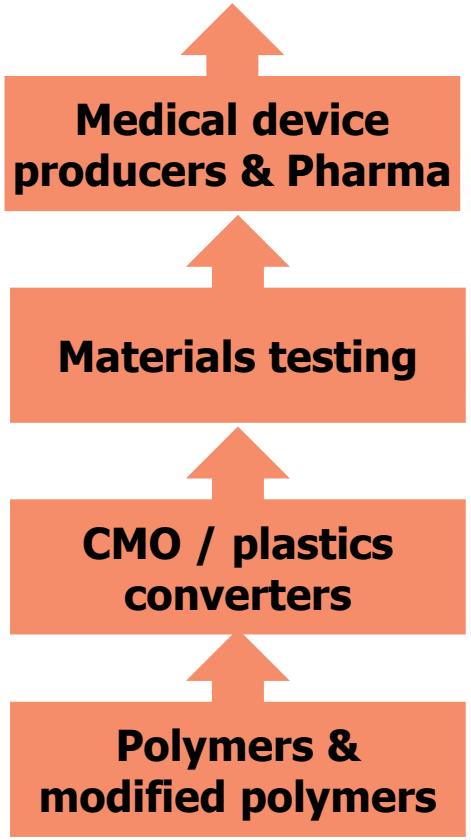
MPPE - the only vertical organization that represents the whole healthcare value chain



ALBIS
BOREALIS
CLARIANT
covestro
ELIX POLYMERS
EMI
EUPC
INEOS STYROLUTION
MELITEK
Nelson Labs.
Nemera
Polynt
PolyOne
nakan
sabic
SANOFI
Sealed Air Re-imagine
STYROLUTION Driving Success. Together.
TERUMOBCT
TOTAL
TRINSEO
VELOX

100s of years of plastics application and regulatory know-how

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What do we do and how we create value for our members?

- Participate in Medical Device Coordination Group
  - Influence the interpretation of regulations and practical guidelines
- Regular information and updates –
  - e.g. substance check tool covering CLP, REACh, biocides
- MPPE networking events (GA & conference)
- Position papers
  - TiO2, Animal-derived content, Update of Annex XIV –Phthalates, Reprocessing single-use medical devices
- Out-reach to other associations, stake-holders, and notified bodies e.g. TEAM-NB, VDE, EuP, IPAC-RS, USP

You don’t need to be a plastics expert…you’ll become one!

Interested ?

Come and talk to us about membership or attending the summer conference

You don’t need to be a plastics expert, you’ll become one!

MDR / IVDR AND PLASTICS RAW MATERIALS

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So you think your plastics supply chain can help?

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MDR & IVDR is only one of a complex series of 'healthcare' regulations - focus is on having 'well-characterized' materials

Drug formulations and metal contaminants ICH Q3D = USP<232>

USP <661.1> construction plastic materials used in pharmaceutical packaging (revised) & USP <661.2> 'packaging systems' & USP 1661 'Extractables' (revised)

USP<661.4> for drug delivery 'combination' devices planned

USP<665> 'Polymeric Components and Systems Used in the Manufacturing of Pharmaceutical and Biopharmaceutical Drug Products'

Updates to USP<87>, <88> Bio-reactivity and ISO10993

Europe: MDR /IVDR - applicable starting May 2020 ……

How well is the industry prepared to meet the changes and challenges ?

- 2018 survey* of device makers' regulatory and quality professionals [78% said they did not sufficiently understand the MDR /IVDR law](#).

- And perhaps fewer have a strategy for:
  - 'no-grandfathering' = new dossiers for previously used materials?
  - realistic view on how to get necessary information from the supply chain?
  - inevitable changes?

*Regulatory Affairs Professionals Society (RAPS) & KPMG

Specific requirements on materials used … and the issues.

- For all medical devices the 'Brand-owner'* must determine if their final device contains >0.1% of:
  - Carcinogenic, Mutagenic or Reproductive toxic substances ('CMR' 1A/1B')
  - Endocrine Disrupters (ED)
  - Nano-materials (definition issue)

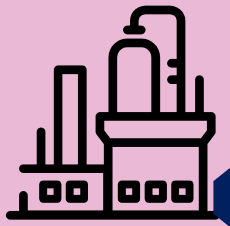
  ~150 substances listed ….will get longer… in scope is approx. 1500 substances.
- List is similar to, but not the same as, the REACh SVHC
  - There is 'limited obligation' for a substance-producer to test / provide information
  - How to keep up to date ?
    - MedPharmPlast Europe has developed a comparison tool - updated every quarter (members only)
  - Requests (already) coming from medical brand owners to the supply chain already suggest some problems ahead ….for the device brand-owner*.

*in this context = the company placing the device on the Eu market

Simplified supply-chain for plastic parts … and market interest

Chemicals

- Monomers
- Stabilizers
- Pigments
- Slip agents
- Surfactants



<0.1%

Polymers 5%

Concentrates & Compounds

- 1-2 polymers
- +1-3 pigments
- + stabilizers
- + others

3%

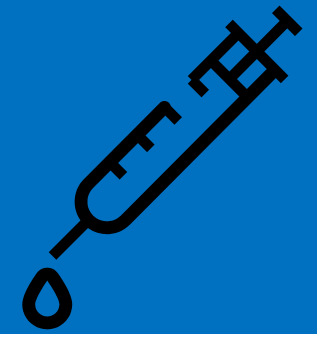
Plastic Processor(s) (CMO etc) components & assembly

- Multiple materials

Final assembly / filling

Brand / Licence Holder*

- Medical Devices
- IVD
- Pharmaceuticals



- The simplicity hides the complexity ….e.g. 1 'color' formula can contain 5 substances with multiple suppliers
- The healthcare industry is 'interesting' but has little importance because the volume consumed is low.
- Information flow is going to be determined by balance of 'interest' vs 'risk' (lesson of REACh)

*in this context = the company placing the device on the Eu market

The real supply chain is not a straight line !

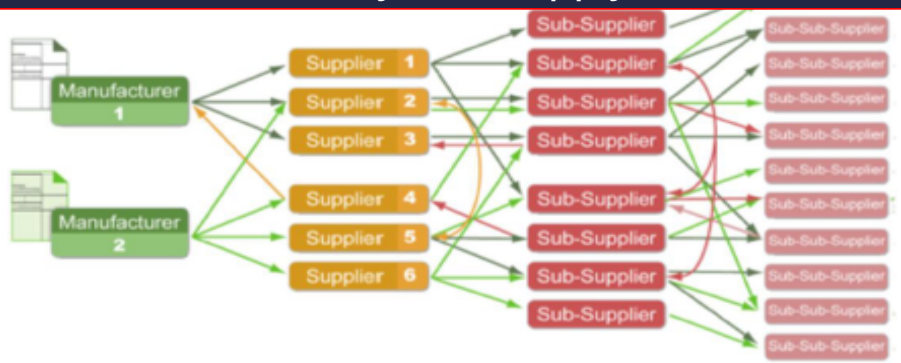
Challenges in Substance Management

Complex supply chain; number of regulated substances is increasing continuously

SIEMENS

- Permanent changes in regulations require constant actualization
  - → Every six months new queries have to be communicated trough the whole supply chain
- Each manufacturer is querying different substances in a different way
  - → Companies like EPCOS or INTEL are receiving hundreds of different queries
- Many suppliers do not understand or even know regulations
  - → Only big companies have material-specialist and processes in place
  - → Quality and trustworthiness of material information is very low

The reality of a supply chain



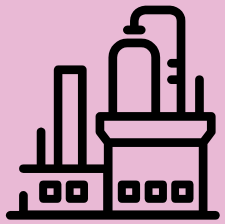
The manual gathering and providing of substance declarations is time consuming, expensive and error-prone

Source: presentation by Siemens Healthcare at BOMCheck seminar

Information required by brand-owner for MDR is not readily available

Chemicals

- Monomers
- Stabilizers
- Pigments
- Slip agents
- Surfactants



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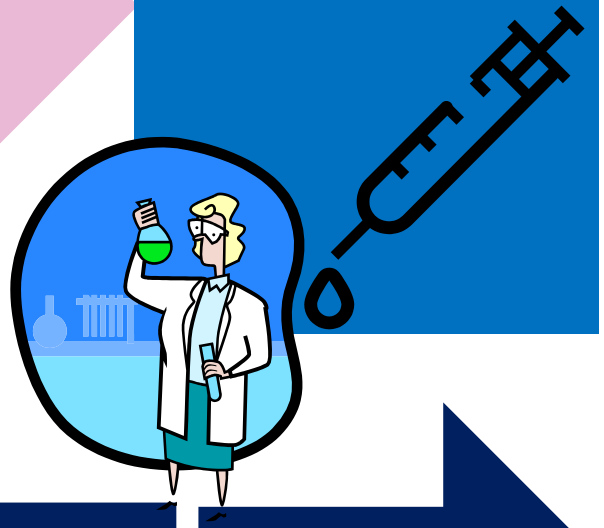

- **Trade secret**
- **Test ONLY for substances - expected to be found or legally required**
- **Multiple sources for ingredients**
- **Legal departments 'Limit liabilities'**

'Not intentionally added'

'Tell me what is in'

Risk assess / test /dossier

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So you have some declarations / did your tests and have a 'well-characterized material'…. through-out the life-cycle?

- Risk of change is ever present and needs to be managed (QbD)
- 'Grand-fathering' of devices and their materials characterization will be more challenged by regulators in EU and USA
- And reprocessing of 'single-use' devices; impact on original materials?

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Some requests we already receive ….. and potential issues

Request	Potential issue
Confirm your plastic product is <u>compliant</u> to MDR /IVDR	• **A raw material cannot be 'compliant'** because it the device that has to be compliant and not a raw material. • Raw material is potentially mixed and downstream processed….i.e. it is changed.
Statement on 'does not contain' (150 + substances….plus perhaps a few others that are customer specific…..)	• **We do not / cannot test for 150+ substances-neither does our supplier** ! • **Relies on information from the substance supplie**r: 'Declarations' • Declarations = '**Not Intentionally Added'** • Potentially 'confidential / proprietary information' • '**One-time test' …. Batch to batch variations?** Change Notifications ?
Contains 'Y/N' ? - tick the boxes in our spreadsheet /data-base	• **'Y/N' (because of above) is not possible**. Legal departments will not permit this type of input. • Every medical device company **has a custom list.** • We have Product Stewardship professionals – but not enough for this
Additionally **please inform us if 'something changes'**	**Potentially the biggest issue….** • 'Change Notification' is not generally offered (certainly not from substance suppliers) • 'Change Management' can only offered for specific 'Medical Grade Material'

So what can we do (jointly) ?

We are committed as MedPharmPlast members to explain what can be offered …. practically

- Continue to engage in the EC Stakeholder meetings to help all get better understanding and practical solutions
- Developing a cross-member ‘position paper’ on information support for MDR and IVDR (see next slides)
- Further work with, and develop VDI ‘Medical Grade Polymer’ guideline to cover <u>what goes into</u> the polymer
  - ‘Medical Grade Plastic Materials’

MPPE members* commitment to support MDR /IVDR

- Bring knowledge of your market, the regulations and how they impact plastics
  - MedPharmaPlast members will continue to share knowledge; based on cross-industry expertise from dedicated Healthcare teams and regulatory specialists. It is the only 'one-stop shop'
- Open-ness
  - We will attempt to answer your questions based on best information, and if we can't …..we will tell you why not.
- Supporting documentation (see next slide)
  - For products defined as 'medical', 'pharma' or 'healthcare' specific declarations based on testing* where available.
- Change notification for designated Healthcare* products
  - Implementation of change control and risk management process in our raw materials, processes

Note: we can only manage and reduce risk of change; not eliminate it

*Availability of documentation and Healthcare industry policy may vary from company to company and limited to specific products designated for Healthcare applications. Please check with individual companies

What we can provide for Healthcare designated products*

- Composition disclosure to the 'brand-owner' – CAS Number & %

Note: normally restricted to brand-owner only, and based on signature of confidentiality agreement.

- Information on certain substances regulated in the MDR / IVDR
  1. Declaration on CMR/ED substances listed that are also SVHC defined in REACh EC1907/2006 Annex XIV
  2. Declaration of CMR/ED substances that are not SVHC but are intentionally added.
  3. For all other substances not fitting 1 or 2 ; a 'Not Intentionally Added' statement

Note: The above is in almost all cases derived from declarations from substance suppliers. It does not mean 'tested'

- Declaration of content of 'animal-derived' substance
- Summary of Healthcare specific tests performed on products /ingredients where available.

*Note: these **help with risk assessment and reduce risk of non-compliance,** but not replacing final device testing*

*In addition to standard declarations such as 'food contact' RoHS. Availability other documentation and Healthcare industry policy may vary from company to company and limited to specific products designated for Healthcare applications. For Clariant these are available for MEVOPUR® and REMAFIN®-EP product-lines only; other products certain information selectively

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For Clariant MEVOPUR & REMAFIN-EP products we can provide declarations based on testing ingredients to 'healthcare' standards

- ICH-Q3D (USP<232>) – extractable metals
- European Pharmacopeia 3.1 relevant sections polymers
- USP <661.1> (2016)
- Biological evaluation
  - USP<87> <88> (according to Class VI devices and /or ONID standard)
  - ISO10993 pt 4 haemolysis; pt 5 cytoxicity; pt10 irritation; pt12 acute systemic toxicity; pt18 extractable evaluation

With change control management process based on EN:ISO13485-2016 QMS

Note: these do not replace final device testing but support overall risk management and decision whether further testing is necessary.

In summary one strategy could be .....

.... however we believe there is a better way with a common understanding

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In summary - for a successful implementation of MDR/IVDR we believe the EU med-tech industry needs to:

- Understand and accept what is possible to provide …… and what not.
- Understand plastic materials are not automatically 'medical grade' and in most cases doesn't cover 'modifications'
- Understand 'well-characterized material' probably does not mean one used for the last XX years .
- Consider for MDR /IVDR the weakest links will be 'substance' supplier and lack of change control.
- Consider supply-chain 'risk / reward' balance may mean the *'provide…or else'* tactic will back-fire.
- Consider an industry standard 'input database' that stakeholders are prepared to use:
  - The earlier slide (Siemens Healthcare) concluded that:
    - 'manual' collection of data will not succeed – and supply chain will eventually say 'no'
    - need for permanent actualization to deal with additions / updates
  - Systems exist (automotive, electronics industry) – better to 'adopt' than 'create'.
    - Auto companies invested and estimated Euros 20m over time to get their system to where it is today.

If we haven't convinced you why you need to be part of MedPharmPlast ……

Come and talk to us at our stand or register to attend the summer conference June 17-18 Hamburg

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