Scientific Committee on Health, Environmental and Emerging Risks

SCHEER

Hearing on the preliminary Guidelines on benefit-risk assessment of Phthalates in Medical Devices

BRUSSELS - 4 April 2019

SUMMARY RECORDS

European Commission:

Philippe Roux, Natacha Grenier (SANTE C2)
Deirdre Fehily, Paolo Catalani (SANTE B4)
Erik Hansson, Paul Piscoi, Olga Tkachenko (GROW D4)

Experts from the SCHEER Working Group:

Scientific Committee on Health, Environmental and Emerging Risks - SCHEER members:

Teresa Borges
Rodica Mariana Ion
Wim H. de Jong (Chair and Rapporteur)
Demosthenes Panagiotakos
Theo Vermeire

Scientific Committee on Consumer Safety - SCCS member:

Ulrike Bernauer

External experts:

Hilde B. M. Kopperud (Nordic Institute of Dental Materials, Oslo, NO)
Tanja Schmidt (University of Applied Science, Hochschule Ansbach, DE)

Registered participants:

8 ORGANISATIONS WERE REPRESENTED

1. Rainer Otter, BASF SE Germany
2. Dorota Napierska, HEALTH CARE without HARM Europe
3. Nigel Talboys, MPPE - MedPharmPlast Europe
4. Nathalie Buijs & Christian Whitney, MEDTECH Europe
5. Perry Walters, CEFIC - European Plasticizers
6. Wieneke Bil, RIVM, National Institute for Public Health and the Environment, NL
7. Susanne Marschner, TERUMO BCT Belgium
8. Jan Mervart, DEZA, a.s. Czech Republic

(EASTMAN Company UK Ltd - was unable to participate as planned due to unforeseen circumstances)

1. WELCOME AND OPENING (DG SANTE)

The Chair, Philippe Roux, Head of Country Knowledge and Scientific Committees Unit from the European Commission's DG SANTE, welcomed the nine participants representing eight organisations from several EU countries and briefly explained the role of the SCHEER Committee as an independent advisory body on scientific matters.
The Chair passed on apologies from the representative from the EASTMAN Company UK, who had to cancel his attendance at the Hearing at the last moment.
The Chair introduced the agenda and explained that the purpose of the Hearing was to present the preliminary version of the Guidelines and to provide an opportunity for various stakeholders to take part in an open scientific discussion with the scientists involved in producing the Opinion.
He reminded the participants that the Hearing was not replacing the public consultation opened until 29 April 2019, and reminded them that only the comments submitted in writing via the on-going public consultation would be taken into account by the SCHEER in the finalisation of the Guidelines.

2. PRESENTATION OF THE MANDATE (DG GROW) - EU POLICY

Erik Hansson, deputy Head of Health Technology and Cosmetics' Unit from the Director-General for Internal Market, Industry, Entrepreneurship and SMEs (DG GROW), welcomed the participants before giving the floor to his colleague, **Paul Piscoi**, who introduced to the audience their mandate to the Committee.

He explained that the Medical Device Regulation (MDR), Regulation (EU) 2017/745 allows the use of Carcinogenic Mutagenic Reprotoxic (CMR) 1A/1B and/or Endocrine Disrupting (ED) substances in medical devices above a concentration of 0.1% by weight (w/w) when a proper justification can be provided (Annex I, Chapter II point 10.4). Before a justification can be accepted as valid, several steps need to be taken, including giving consideration to the possible use of alternative substances, materials, designs, and medical treatments. In addition, the risk in terms of hazards associated with such alternatives should be weighed against the risk of the use of CMR 1A/1B and/or ED identified phthalates covered under MDR Annex I Chapter II point 10.4.1. However, the risk by itself is not the only parameter to consider an evaluation must also be made of the impact

of the possible alternatives on the functionality, the performance and the overall benefit-risk ratio of the medical device.

DG GROW asked SCHEER to provide Guidelines on the benefit-risk assessment of the presence, in the medical devices specified below, of phthalates, which have one or more of the following properties: carcinogenic, mutagenic, toxic to reproduction or endocrine-disrupting, according to the criteria outlined in the mandate.

The devices covered, or those parts thereof of those materials used therein, are those which:

- are invasive and come into direct contact with the human body,
- (re)administer medicines, body liquids or other substances, including gases, to/from the body, or
- transport or store such medicines, body fluids or substances, including gases, to be (re)administered to the body.

The Guidelines shall include guidance on how, for an individual device, to:

- analyse and estimate potential patient or user exposure to the substance,
- analyse possible alternative substances, materials, designs, or medical treatments,
- to justify why possible substance and/or material substitutes, if available, or design changes, if feasible, are inappropriate in relation to maintaining the functionality, performance and the benefit-risk ratios of the product, including taking into account if the intended use of such devices includes treatment of children or treatment of pregnant or breastfeeding women or treatment of other patient groups considered particularly vulnerable to such substances and/or materials.

In addition, the Scientific Committee is requested to

- identify any relevant knowledge gap; and
- to give consideration to what extent of new evidence would be deemed appropriate to justify an update of these Guidelines before the maximum period of five years.

In order to ensure the appropriateness of this guidance the Scientific Committee should inter alia:

- involve at the appropriate level the notified bodies active in the field of medical devices, or other relevant stakeholders such as Competent Authorities, professional and patient associations, industry associations, while maintaining scientific independence;
- involve to the necessary extent the relevant EU Agencies and Scientific Committees;

The preliminary version of these Guidelines is now published and the final version shall allow manufacturers to implement them before the legal deadline (i.e. May 2020).

These Guidelines are not a usual SCHEER Opinion including a risk assessment of a specific phthalate used in a certain medical device, which would be beyond the mandate's scope. As foreseen by the Medical Device Regulation, adherence to these Guidelines will become mandatory.

3. PRESENTATION OF THE PRELIMINARY GUIDELINES (SCHEER)

Wim de Jong, the Chair and the rapporteur of the SCHEER WG, gave an overview of the composition of the experts of the SCHEER WG and provided a summary of the content of the Guidelines on benefit-risk assessment of Phthalates in Medical Devices and SCHEER conclusions.

These Guidelines describe the methodology on how to perform a benefit-risk assessment (BRA) for the justification of the presence of CMR 1A or 1B and/or ED phthalates (CMR/ED phthalates) in medical devices and/or or parts or materials used therein at percentages above 0.1% by weight (w/w).

They also consider the evaluation of possible alternatives for these phthalates used in medical devices. The global structure and the stepwise approach were presented. Most of the information and the data is already available but needs to be assembled and the justification needs to be well described. Complete biocompatibility studies are not needed again. Examples on how to describe risks are provided in the document. The conclusion should be drawn by manufacturers, taking into account that phthalates can have different functionalities.

These Guidelines are intended to be used by the relevant stakeholders, e.g. manufacturers, notified bodies and regulatory bodies.

The approach taken in these Guidelines may also be used for a BRA of other CMR/ED substances present in medical devices.

During the preparation of these Guidelines for BRA of the use of CMR/ED phthalates in medical devices, SCHEER noticed that a number of BRA methodologies are theoretically available. In addition, there is a considerable lack of data for potential alternatives to be used in medical devices. Therefore, manufacturers are encouraged to produce (semi)quantitative data on the use of alternatives for CMR/ED phthalates in medical devices.

Pending on new scientific evidence, it is recommended that the use and usefulness of these Guidelines be evaluated after an experience period of three years.

4. QUESTION AND ANSWER SESSION

Nine representatives from eight organisations asked questions and made comments or presentations during the "Question and Answer" session. The Chair asked that issues raised during this session, in addition to supporting evidence, be submitted through the public consultation process to ensure that the SCHEER will examine them in more detail for the finalisation of the Guidelines. A summary of the main points raised orally is provided below:

A majority of representatives from the participating organisations welcomed the SCHEER's preliminary Guidelines and its structure, although the majority of the stakeholders would like a better explanation of how notified bodies will assess their files. The Guidelines should also make clearer, also in the title, that only the legal text applies.

Representatives of plasticisers companies argued that the Guidelines do not provide alternatives to phthalates. However, the Chair of the SCHEER Working group clarified that the task of the SCHEER is to focus on the questions asked in the mandate and not to provide a comprehensive review of the field. It would not be necessary to use these Guidelines should the manufacturer stop using a CMR/ED-designated phthalate. It is up to the manufacturer to decide what type of plasticiser to use and to formulate a justification and perform a risk assessment of the substances used for the manufacturing of the MD.

An issue was raised about the Guidelines focusing exclusively on the oral route, while medical devices are also used in the intravenous route and in air supply (tubing). The SCHEER should therefore address this comment.

Blood bag companies raised the issue of the uniqueness of blood bags and their components as medical devices. An additional expert in blood has been requested to help SCHEER WG finalise and review the Guidelines.

Many organisations pointed out that some clearer definitions are still needed (e.g. realistic "worst-case" scenario) and that some references are not used correctly in the preliminary Guidelines. In response to these issues, the SCHEER representatives agreed to ensure that definitions in the final version of the Guidelines would be improved and adequate references used correctly.

One participant was astonished that the "uncertainty" chapter was bigger than other chapters of the Guidelines, but the chair of the SCHEER WG stressed that the length of the text does not reflect the importance of the section. Guidelines are divided by two: 10 steps are provided, and examples. Uncertainty and Benefit-Risk Assessment are just chapters that needed more explanation.

A generic question was raised about the validity period of the manufacturers' technical files and the mandating DG replied it should be for the duration of the certification process (i.e. 5 years) unless there is an urgent request for taking the medical device off the market.

Near the close of the Hearing, the timeline for the rest of the process was requested. The chair of the SCHEER WG announced that the plan is to finalise these Guidelines, taking into account comments received through the public consultation process, at a mid-May meeting, so that members of SCHEER would be able to adopt them at their plenary meeting in June. Publication is foreseen before the summer.

5. CLOSING (DG SANTE)

The Chair thanked participants for their contributions and reiterated that the deadline for the submission of written contributions and supporting evidence through the public consultation process would be on 29 April 2019.

The Chair explained that according to the Rules of procedures, contributions to the consultation process should not be about policy or risk management issues, but should aim at improving the scientific basis of the Guidelines.

The Chair reiterated that only submissions directly referring to the content of the preliminary Guidelines and relating to the issues that the document addresses would be considered during the consultation period of six weeks (which was considered too short by some participants).

The SCHEER will consider all the relevant submissions related to the scope of the public consultation and will decide if and to what extent each of the contributions should be taken into account in the formulation of the final version of the Guidelines.

The Chair concluded by thanking the members of the SCHEER for their work and expressing his wishes for their continued support.

Note: presentations are published on the same webpage, in agreement with the respective speakers.
