BVMed-Positionspapier | 05.06.2020

Ethylenoxid / Einstufung nach Biozidverordnung (BPR)

1. Vorbemerkung und Sachverhalt

Ethylenoxid wird als Agens zur Sterilisation von Medizinprodukten verwendet. In vielen Fällen ist es nicht durch andere Sterilisationsmethoden (gesättigter Wasserdampf, Gammastrahlen, etc.) zu ersetzen, weil diese zu Materialschäden oder einer kürzeren Lebensdauer der Medizinprodukte führen würden. Ethylenoxid ist gemäß der 14. Anpassungsverordnung (Adaption to Technical Progress – ATP) der Verordnung (EG) Nr. 1272/2008 über die Einstufung, Kennzeichnung und Verpackung (CLP) von Stoffen und Gemischen als karzinogen, mutagen und reproduktionstoxisch (CMR) Klasse 1B gekennzeichnet. Außerdem wird geprüft, ob es als potentiell endokriner Disruptor eingestuft wird.

Daher erfüllt Ethylenoxid die Ausschlusskriterien der Biozidverordnung (Biocidal Products Regulation (EU) No 528/212 (BPR)) und ist ein „candidate for substitution".

Wirkstoffe, die die Ausschlusskriterien erfüllen, werden grundsätzlich nicht zugelassen. Ausnahmeregelungen sind vorgesehen, insbesondere wenn der Wirkstoff aus Gründen der öffentlichen Gesundheit oder des öffentlichen Interesses benötigt wird, wenn keine Alternativen zur Verfügung stehen. In diesem Fall wird die Genehmigung eines Wirkstoffs für maximal fünf Jahre erteilt.

Bevor eine Entscheidung über die Genehmigung oder Nicht-Genehmigung gefällt wird, wurde für die Erstellung der „ECHA[1] Biocidal Products Committee opinion" ein öffentliches Konsultationsverfahren eröffnet (Eingabefrist 9.4. bis 8.6.2020), an dem MedTech Europe, aber auch der BVMed teilgenommen haben. Die BVMed Stellungnahme finden Sie im Anhang.

Derartige Konsultationen sind im Zusammenhang mit den Zulassungsverfahren für Biozidprodukte keine Ausnahme. Wenn ein Stoff die Ausschlusskriterien gemäß BPR Artikel 5(1) – in dem Fall CMR 1B - erfüllt, kann er dennoch – gemäß einer Ausnahme von den Ausschlusskriterien/ Artikel 5(2) – für den Einsatz in Biozidprodukten genehmigt werden, und zwar, wenn

- das Risiko für Mensch, Tier oder die Umwelt unter realistischen Worst-Case Verwendungsbedingungen vernachlässigbar ist (z.B. Anwendung in geschlossenen Systemen, Kontakt mit Menschen und Freisetzung in die Umwelt sind ausgeschlossen)
- der Wirkstoff ist nachweislich unbedingt erforderlich um ernsthafte Gefahr für die Gesundheit von Mensch Tier oder für die Umwelt zu vermeiden, oder
- die Nichtgenehmigung – verglichen mit dem Risiko aus der Verwendung – unverhältnismäßige negative Folgen für die Gesellschaft hätte.

Um herauszufinden, ob diese Bedingungen erfüllt sind, führt die ECHA eine entsprechende Konsultation durch, in der Alternativen geprüft werden. Dies insbesondere auf Basis technischer und wirtschaftlicher Machbarkeit, eventueller Gefahren und Risiken sowie deren Verfügbarkeit ab.

Nach Beendigung des Konsultationsverfahrens erstellt das ECHA Biocidal Products Committee innerhalb von 270 Tagen eine Stellungnahme mit der Entscheidung über Zulassung oder Nicht-Zulassung (und ob die Bedingungen nach Art. 52 (2) erfüllt sind), die dann im Anschluss (spätestens 60 Tage nach der Stellungnahme) von der EU-Kommission mit dem Standing Committee on Biocidal Products angenommen wird.

Berlin, 5. Juni 2020

[1] European Chemicals Agency

2. Anhang: Inhalt der Eingabe beim ECHA Konsultationsverfahren

Im Folgenden finden Sie den beim ECHA Konsultationsverfahren eingegeben Text des BVMed auf Englisch.

General information:

BVMed is an industry association that represents more than 220 industry and trade companies. Among the members of the association are 20 of the largest medical device manufacturers worldwide in the durables and consumer goods sector.

Sterilisation with ethylene oxide (EO) is an important sterilisation method for medical devices (MD). This method is chosen because of the low process temperature and good compatibility for e.g. electronic devices and polymers.
MD which are made of polymers, contain sensitive electric parts or certain adhesives or have either a hydrophilic, polymeric, or medicinal coating cannot be sterilised with other sterilisation methods. Sterilization processes have a large effect on performance and shelf life of the devices and they must maintain the integrity of all the components of the devices.

The Change of sterilization methods creates high efforts in terms of process validations and might also require significant effort in modifying certain materials used in order to resist e.g. sterilization by radiation without degradation of technical performance for electronics and material properties of plastics. In addition, changing the sterilization method would mean revised regulatory submissions and approvals for several worldwide sales markets. Especially with regard to the change of the regulation within the MD sector.

1. Alternative Identity and Properties

All alternative sterilisation methods like dry heat, ozone, steam, gamma irradiation sterilisation, hydrogen peroxide (with or without plasma) or others have significant effects to the material used in the MD. Even if irradiation (gamma and e-beam) methods occur at relatively low temperature ranges compared to other sterilizing techniques, it can cause some physical and chemical degradation to the devices.

2. Technical Feasibility

The technical feasibility need a full validation of all processes, including product and packaging testing and accelerated aging tests. The foreseen timeline would be at least two to five years.

3. Economic Feasibility

In terms of the economic feasibility the whole process of regulatory approvals have to be considered. Substantial changes especially in high class MD (class III implantable devices) take a long time. Additionally the change of the regulation ((AI)MDD to MDR) has another effect to regulatory approvals. In the case of a non-approval decision for EO a lot of products will be lost because most of them cannot be sterilised with other methods without losing their performance and/or safety. This has a major impact to patient safety.

4. Hazards and Risks of the Alternative

Due to possible material damage and the resulting reduction of product life time the risk for patients would be high. This has a major impact to patient safety.

5. Availability

There is no adequate alternative to EO available.

6. Conclusion on suitability and availability of the alternative

It is very unlikely that EO can be replaced due to specific (product) material specifications.

7. Other Comments

The sterilization with EO is highly standardised in Europe. The manufacturing of the sterilizer must be done acc. DIN EN 1422. The sterilization process for MD must be validated acc. to DIN EN ISO 11135. The EO residuals are defined in ISO 10993-7. Especially in Germany, the work safety must be acc. to TRGS 513 and the exhaust air must keep the EO-limits acc. “TA-Luft”.

Furthermore not only the sterilisation itself has to be considered. But also in case of external sterilisation very small quantities are used in the analysis (e.g. batch release) for the analysis of residual EO gas of MD sterilized with EO.

In addition, we would like to mention that a ban of EO sterilisation for medical devices will have a huge effect of jobs within Europe and transfer them to Asia which make us more dependent on manufacturer from China or India.
We should learn from the Covid-19-crisis and try to keep the economic knowledge in Europe. All medical device manufacturers behave responsibly with EO by investing large amounts in safety of the process for the environment and workers and other stakeholders around our facilities.

BVMed-Position paper | 05th June 2020

Ethylene oxide / Classification according the Biocidal Products Regulation (BPR)

1. Preliminary observation and facts

Ethylene oxide is used as an agent for the sterilization of medical devices. In many cases it cannot be replaced by other sterilization methods (saturated steam, gamma rays, etc.) because these would lead to material damage or a shorter life span of the medical devices.

Ethylene oxide is classified as carcinogenic, mutagenic and toxic for reproduction (CMR) class 1B according to the 14th Adaptation to Technical Progress (ATP) of Regulation (EC) No. 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures. Moreover, ETO is under assessment as a potential endocrine disruptor.

Ethylene oxide therefore meets the exclusion criteria of the (BPR) Art. 5 (1) and is a "candidate for substitution".

In principle, active substances meeting the exclusion criteria will not be approved. Derogations are foreseen, in particular when the active substance may be needed on the grounds of public health or of public interest when no alternatives are available. In this case, approval of an active substance is granted for a maximum of 5 years.

Before a decision on approval or non-approval is made, a public consultation procedure has been opened for the preparation of the "ECHA Biocidal Products Committee opinion" (submission deadline 9.4. to 8.6.2020), in which MedTech Europe, but also BVMed participated. Please find attached the final submission of BVMed.

Such consultations are normal processes within the authorisation procedures for biocidal products. If a substance fulfils the exclusion criteria according to BPR Article 5(1) - in the case of CMR 1B - it may nevertheless be authorised - according to an exception to the exclusion criteria/ Article 5(2) - for use in biocidal products, if

- the risk to humans, animals or the environment is negligible under realistic worst-case conditions of use (e.g. use in closed systems, contact with humans and release into the environment are excluded)
- it has been shown that the active substance is essential to prevent serious risks to human health, animal health or the environment; or
- the non-approval would have disproportionate negative consequences for the company compared to the risk arising from its use.

In order to evaluate whether these conditions are met, ECHA will carry out a consultation where alternatives will be examined. This is based in particular on technical and economic feasibility, possible hazards and risks and their availability.

At the end of the consultation process, the ECHA Biocidal Products Committee prepares an opinion within 270 days with the decision on authorisation or non-authorisation (and whether the conditions according to Article 52 (2) are fulfilled), which is then going to be adopted by the EU Commission with the Standing Committee on Biocidal Products (at the latest 60 days after the opinion).

Berlin, 05. Jun. 2020

2. Appendix: submitted information to the public consultation on potential candidates for substitution

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