SPRAYS claiming virucidal and antimicrobial actions - notice to manufacturers and notified bodies

The Health and Youth Care Inspectorate as market surveillance authority for medical devices in The Netherlands, would like to remind manufacturers, of some essential points to be considered before placing sprays on the European market. This notice applies to sprays which have claims of virucidal and antimicrobial actions, for example against SARS-CoV-2, that are intended to be placed on the European market as medical devices according to Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC. This notice has been jointly developed by the European market surveillance authorities.

Qualification and classification

It is the responsibility of the manufacturer to ensure that their product is appropriately qualified and classified[1] in line with the relevant legislation, and in accordance with the intended purpose and the principal mode of action of the product.

- sprays which achieve their **principal intended action by pharmacological[2], immunological or metabolic means** are not medical devices. These maybe medicinal products according to Article 1(2) of Directive 2001/83/EC which would require a marketing authorisation.
- Sprays which fall under the definition of Article 2(1) of Regulation (EU) 2017/745 and which achieve their **principal intended action by physical or mechanical means** are medical devices. Their classification into one of the medical device risk classes needs to be determined according to the rules of Annex VIII of Regulation (EU) 2017/745. Generally, Rule 21 will apply if these sprays are composed of a substance or a combination of substances that are intended to be introduced into the human body via a body orifice and that are absorbed by or locally dispersed in the human body.
- Sprays which fall under the definition of Article 2(1) of Regulation (EU) 2017/745 and incorporate a substance, which if used separately would be considered to be a medicinal product according to Directive 2001/83/EC, should be classified according to rule 14 of Annex VIII of Regulation (EU) 2017/745 providing that this substance has an **ancillary action** to the principal physical or mechanical mode of action of the device.

Manufacturers are reminded that with the implementation of Regulation (EU) 2017/745[3], the conformity assessment route for all sprays that meet the definition of a medical device will require the involvement of a notified body[4]. This is because sprays are classified as class IIa medical devices at a minimum, pursuant to Rule 21 of Annex VIII. If manufacturers have not already begun engaging with a notified body, it is highly advisable to do so as soon as possible to ensure timely certification.

Furthermore, a procedure in the case of devices that are composed of substances or of combinations of substances that are absorbed by or locally dispersed in the human body shall be followed as described in Annex IX, section 5.4 of Regulation (EU) 2017/745.

Clinical Data

Before placing a spray on the European market as a medical device, the manufacturer shall specify and justify the level of clinical evidence necessary to demonstrate conformity with the relevant general safety and performance requirements laid down in Annex I of Regulation (EU) 2017/745. The depth and extent of the clinical evaluation shall be proportionate and appropriate to the intended purpose and risks of the device and to the manufacturer's claims in respect of the device. For example, claims

against a human pathogenic virus in the context of a global health crisis should be considered as a high risk situation.

The technical documentation[5] shall contain the relevant clinical data[6] to demonstrate each of the claims in respect of the device.

Article 61 of Regulation (EU) 2017/745 specifies the requirements for the clinical evaluation.

The device must have an acceptable benefit/risk ratio. This must be based on meaningful, measurable and relevant clinical outcomes. These clinical outcomes must be defined in terms of the (primary) endpoints in clinical investigations and these endpoints must also be achieved.

Laboratory tests simulating the conditions of the (nasal) cavity are not sufficient and need to be supplemented by substantial clinical data.

The clinical data should verify not only the safety of the device, but also its clinical effectiveness and performance, whilst there should also be sufficient evidence to support the mode of action and the site where the action is performed. Clinical investigations in which the results may be contested due to presence of bias, lack of statistical robustness, or adequate controls are not considered to have scientific validity[7] for demonstration of adequate clinical performance. . In particular, clinical data shall provide evidence of the duration of action claimed by the manufacturer.

When manufacturers choose to demonstrate the equivalence of their device to another comparable device, any technical, biological and clinical characteristics must be considered and documented. According to Annex XIV of Regulation (EU) 2017/745, the use of a clinical demonstration by equivalence to a spray that has not previously demonstrated performance against the same infection/condition is inappropriate. For example, clinical data for a spray against seasonal influenza cannot be used as clinical equivalence to demonstrate clinical performance against Covid-19 disease. Considerations on the equivalence of devices shall be based on proper scientific justification considering technical, biological and clinical characteristics.

Notified bodies should verify the presence of relevant and appropriate clinical data to demonstrate the claimed performance before any EU certificate of conformity with Regulation (EU) 2017/745 is issued.

During the transitional period until 26 May 2024, sprays which are placed on the European market in conformity with Directive 93/42/EEC, shall also have a clinical evaluation based on “sufficient clinical data”, as described in the MDCG 2020-6 guidance on sufficient clinical evidence for legacy devices[8]. Both Directive 93/42/EEC and Regulation (EU) 2017/745 require the quantity and quality of clinical data to be sufficient to demonstrate the safety, performance and acceptability of the benefit-risk ratio. Post-market clinical data together with the clinical data generated for the conformity assessment under the Directive 93/42/EEC will be the basis of the clinical evaluation process for legacy devices.

Claims

The manufacturer shall ensure that the device is supplied with the required safety and performance information according to Annex I, Chapter III, point 23 of Regulation (EU) 2017/745. The manufacturer should provide a description of the expected performance of the device and include the exact information on the label, in order to ensure that the user understands the intended purpose and the claims regarding the proven device benefit.

An action against COVID-19 shall not be indicated if the performance of the spray has not been proven specifically on the SARS-CoV-2 virus.

As a reminder, Article 7 of Regulation (EU) 2017/745 it is prohibited to mislead the user with regard to the performance of the device, in the labeling, instructions for use[9] and also in the advertising of devices.

The manufacturer should communicate residual risks (limitations, contra-indications, precautions, warnings) to the user, according to Annex I, Chapter III, point 23.1 g of Regulation (EU) 2017/745.

The information supplied with the device shall not suggest that the use of a virucidal or antimicrobial spray would exempt the users from following public health recommendations for protection against infection with SARS-CoV-2 or from respecting the measures that are recognised as being effective for reducing the spread of SARS-CoV-2 infection (e.g. hand washing, wearing masks, keeping distance). It is important to note that contamination with SARS-CoV-2 can also occur by mouth and eyes.

References

[1] The MDCG 2021-24 Guidance on classification of medical devices can be used in addition to the rules of classification given in the Annex VIII of the Regulation (EU) 2017/745.

[2] See MDCG 2022-5 Guidance on borderline between medical devices and medicinal products under Regulation (EU) 2017/745 on medical devices for definitions of 'Pharmacological means', 'immunological means', 'metabolic means' and 'principal intended action'.

[3] Regulation (EU) 2017/745 applies from 26 May 2021. Under Article 120 (3), amended on 27 December 2019, a device which is a class I device pursuant to Directive 93/42/EEC, for which the declaration of conformity was drawn up prior to 26 May 2021 and for which the conformity assessment procedure pursuant to this Regulation requires the involvement of a notified body, may be placed on the market until 26 May 2024, under certain conditions.

[4] list of notified bodies: https://ec.europa.eu/growth/tools-databases/nando/

[5] Annex II section 6 of Regulation (EU) 2017/745 specifies the content of the documentation concerning the product verification and validation.

[6] According to Article 2 (48) of Regulation (EU) 2017/745, 'clinical data' means information concerning safety or performance that is generated from the use of a device and is sourced from the following:
— clinical investigation(s) of the device concerned,
— clinical investigation(s) or other studies reported in scientific literature, of a device for which equivalence to the device in question can be demonstrated,
— reports published in peer reviewed scientific literature on other clinical experience of either the device in question or a device for which equivalence to the device in question can be demonstrated,
— clinically relevant information coming from post-market surveillance, in particular the post-market clinical follow-up.

[7] Examples of studies that lack scientific validity for the demonstration of adequate clinical performance and/or clinical safety are described in appendix A6 of the guideline MEDDEV 2.7/1 rev. 4. MDCG guides could later specify this point.

[8] As defined in MDCG-25 guidance: "Legacy devices should be understood as devices, which, in accordance with Article 120(3) of the MDR, are placed on the market after the MDR's date of application (DoA) and until 26 May 2024 if certain conditions are fulfilled. Those devices can be:

- devices which are class I devices under Directive 93/42/EEC (MDD), for which an EC declaration of conformity was drawn up prior to 26 May 2021 and for which the conformity assessment procedure under the MDR requires the involvement of a notified body;
- devices covered by a valid EC certificate issued in accordance with Directive 90/385/EEC (AIMDD) or the MDD prior to 26 May 2021."

[9] See Article 2, paragraphs 12 to 14 of Regulation (EU) 2017/745 for definitions of intended purpose, label and instructions for use.