IPAC-RS
International Pharmaceutical Aerosol Consortium on Regulation & Science

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**BY MAIL AND EMAIL**

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August 20, 2019

**RE: Impact of Rule 20 of Annex VIII of Regulation (EU) 2017/745 of the European Parliament and the Council on medical devices.**

Dear Mr D'Acunto and Dear Dr Rys,

International Pharmaceutical Aerosol Consortium on Regulation & Science (IPAC-RS) is a non-profit association of companies that manufacture, develop or market orally inhaled and intranasal drug products, which typically include a delivery device, and therefore IPAC-RS members have a keen interest in MDR implementation. IPAC-RS also contributed to a previous letter to the European Commission regarding the impact of Article 117 of the MDR on drug-device combination products, and very much appreciate the responses received and subsequent guidance provided. On behalf of the IPAC-RS, we would like to highlight the challenges manufacturers are facing in complying with Rule 20, Annex VIII of the Council Regulation (EU)2017/745 Medical Device Regulation (MDR).

*Rule 20:*

*All invasive devices with respect to body orifices, other than surgically invasive devices, which are intended to administer medicinal products by inhalation are classified as class IIa, unless their mode of action has an essential impact on the efficacy and safety of the administered medicinal product or they are intended to treat life- threatening conditions, in which case they are classified as class IIb.*

It is our concern that without changes to the timing of implementation, industry will not be able to comply with Rule 20 for currently marketed (Class I) inhalation devices used for essential medicinal products. Our objective in highlighting this concern is that Industry and the Commission can work in partnership to agree a mutually acceptable way forward that meets the needs of the patients we both serve.

IPAC-RS member companies are concerned that upon application of the MDR in May 2020 inhalation devices within scope of Rule 20, which do not have a Certificate of Conformity issued by a Notified Body (NB) and have been CE marked by the manufacturer, will no longer be authorized to be supplied to the European market. This will have a potentially negative impact on the health of patients who are dependent on the medicines that is delivered though these devices and for which the safety profile would not have changed. The impact of this to medicines and patients is that manufacturers will no longer be able to market the currently self-certified medical devices. The documentation is required to be updated and devices which are up-classified will also need physical changes to labelling, packaging and in some cases even tooling to implement the NB number, which was not required for a Class 1 device. These changes cannot be completed until the chosen NB has been officially designated under the MDR.

In a recent survey of IPAC-RS members, to which 7 of the 14 IPAC-RS member companies responded, it was found that six companies have a total of 28 non-integral devices on the European market. 6 devices out of these 28 will require a physical change to update the labelling of the device due to the up-classification. Outside of IPAC-RS, it can be expected that more devices are impacted, including essential medicinal products for treatment of asthma and flu epidemics. IPAC-RS seeks reassurance that this issue is currently being considered by both medicines and medical device regulators and that guidance will also be forthcoming to ensure consistent interpretation of classifications. The wording of Rule 20 allows room for different interpretations across manufacturers and NBs.

The two major challenges industry and the EU Commission need to address to be compliant with the new regulations are as follows:

1. To date, only 3 NBs (one of which is located in the UK) have been designated to undertake the additional workload as defined by the revised regulatory framework. This challenge has been magnified as the Regulation is both prospective and retrospective (i.e., there is no grandfathering clause). The first two designated NBs have advised industry that they will not be able to take on any new clients before the date of application of the MDR. Furthermore our understanding is that in short to mid term it is unlikely that the number of NBs certified to undertake such a review will not increase significantly. In that context, whilst industry can prepare the necessary paperwork there is not the sufficient NB capacity to complete the review process. With other NBs withdrawing their designation applications, others not applying for designation, manufacturers are left with little or no choice to have their technical file reviewed by a designated NB to meet the timelines.

2. Whilst industry is preparing themselves as much as possible, it is not possible to fully comply with MDR and CE mark the devices within scope of the Regulation until a NB has provided a valid Certificate of Conformity. The requirements of Article 20 for the CE marking to be indelible and Annex 1 specific to labelling requirements will require industry to change either the design or packaging and the Instructions for Use. For example, any change to the design of an injection mould tool could take up to 12 months to implement based upon the scale of the installed manufacturing capacity.

The perspective from industry is that to maintain supply of the medicines that are dependent upon the device that are now within scope of Rule 20 all parties need to agree a way forward. Industry would propose the following options, in order of preference:

a) Rule 20 is not to be applied retrospectively. This would be in line with the approach taken for compliance with the amended Medicinal Product Directive 2001/83/EC, whereby compliance with Article 117 of the MDR is only applicable to new Marketing Authorization Applications, as clarified in the recent EMA and CMDh Q&A[1]. Any new medicines seeking approval in the EU would be required to comply.

b) Legacy devices falling under Rule 20 are allowed to have the transition period extended to May 2024. This would be in line with Art 120.2 which states that certificates issued by NBs in accordance with Directive 93/42/EEC shall remain valid or become void latest on 27 May 2024 for higher risk devices.

c) There would be recognition that devices may continue to be placed on the market while under review or while stock phasing physical changes to the device in terms of MDR labelling requirements (e.g., NB number) after May 2020.

IPAC-RS agrees that inhalation devices can have an essential impact on the efficacy and safety of the administered medicinal product and are often used in treatment of life- threatening conditions. Therefore, as an industry representative group we are keen to continue to work with both medicines and medical device regulators to ensure that these products have a suitable safety and performance profile. Our cross-industry collaborations on a science and risk-based approaches to application of the new MDR[2] and human factors testing[3] have been shared and discussed with regulators at conferences, in publications and meetings at agencies. We would be very happy to discuss further and arrange a workshop on this topic.

Yours Sincerely,

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## References:


1 European Medicines Agency (EMA), Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh). **Questions & Answers on Implementation of the Medical Devices and In Vitro Diagnostic Medical Devices Regulations ((EU) 2017/745 and (EU) 2017/746).** 27 February 2019 EMA/37991/2019 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/questions-answers-implementation-medical-devices-vitro-diagnostic-medical-devices-regulations-eu/745-eu-2017/746_en.pdf Accessed August 7, 2019

2 European Biopharmaceutical Enterprises, European Federation of Pharmaceutical Industries and Associations. **EBE-EFPIA Reflection Paper: An Industry Perspective on Article 117 of the EU Medical Devices Regulation and the Impact on how Medicines are Assessed**. 12 July 2018. https://www.ebe-biopharma.eu/wp-content/uploads/2018/07/EBE-EFPIA_-Reflection-paper_-Industry-Perspective-on-Art-117-of-MDR_Final_2018.07.12-copy.docx Accessed August 7, 2019

3 N. Roche, G. Scheuch, J. N. Pritchard, C. Nopitsch-Mai, D. A. Lakhani, B. Saluja, J. Jamieson, A. Dundon, R. Wallace, S. Holmes, D. Cipolla, M. B. Dolovich, S. A. Shah, and S. Lyapustina. **Patient Focus and Regulatory Considerations for Inhalation Device Design: Report from the 2015 IPAC-RS/ISAM Workshop.** Journal of Aerosol Medicine and Pulmonary Drug Delivery Vol. 30, No. 1, February 2017. https://www.liebertpub.com/doi/abs/10.1089/jamp.2016.1326 Accessed August 7, 2019