ASSOCIATION FOR EUROPEAN PAEDIATRIC AND CONGENITAL CARDIOLOGY

To WHOM it may concern

June 14 2022

BACKGROUND

The European Medical Device Regulation (EU-MDR, 2017/745) from 05.04.2017 was designed in order to improve the safety of medical products and follows the **Medical Device Directive** (**MDD 93/42/EWG, 1983)**. This new EU-MDR became applicable from 26.05.2021 in all the European countries. The regulation has little impact on large companies with high volume well-priced devices. However, it has become apparent that in several niche markets consisting of highly specialized small volume low-to-medium cost devices (for example congenital heart disease interventions), the consequences for the patients and physicians are likely to be enormous. Although the intention of EU-MDR was commendable and idealistic, it will have significant impact on the availability of **Medical Products (MP)** within niche subspecialties, such as Pediatric Cardiology and Pediatric Heart Surgery.

All previously registered medical products (MP) will have to undergo a review process **within 3 years** (from 26.05.2021 to 26.05.2024) regardless of prior certification, in accordance with MDD, including technical review and reports on clinical data. This process is carried out by **Notified Bodies (NB)**, which as private institutions, also have to be certified for this procedure. As they now have to organize certification of all medical products class I-III in accordance with EU-MDR by 2024, and there are approximately 25.000 MPs, the timeline for this process is too short and there are inadequate number of NBs dealing with the vast number of MPs. As each new MP also has to be certified by NB in accordance with the EU-MDR, this will additionally reduce the number of new or available MPs reaching Europe in our field, thus having a significant impact for our patients in foreseeable future.

CONTEXT

The new EU-MDR was designed in order to increase the safety and the efficacy of MPs for all the patients. The field of Pediatric Cardiology is very small and highly specialized, compared with the adult specialties (overall < 1%), and the doctors have been using MPs in newborns, infants, babies, children and adults in order to perform life-saving treatments for decades. The treatment of Congenital Heart Disease, therefore, includes many MPs with a high specification (such as guidewires, catheters, stents, balloons, implants and devices), with most of them having been used clinically for many years. Due to the relatively low incidence of congenital heart disease, and the extremely high variability of the disease spread over different age and weight groups, there is a need for many MPs that may have wide applications. Moreover, due to the wide distribution of numbers over different pathologies and the range of sizes, many MPs may be used in only a few cases each year, and are typically used in “off label” application (estimation 20-30% of applications).

Today and with the expiration date for the EU-MDR of 26.05.2024 approaching, many devices used in congenital heart diseases have already been withdrawn or may not be available in the future. This will have

a huge impact on the treatments we can offer for babies and children with congenital heart defects and raises a major concern in all the European physicians, who offer high quality treatments with extremely low mortality, as was highlighted recently during the Annual AEPC meeting in Geneva.

CURRENT SITUATION AND PROBLEMS

1. The majority of MPs, certified in the MDD process, are not yet recertified in accordance with the new EU-MDR.
    a. Many guidelines and interpretations became available only in 9/21, and notifying bodies are still uncertain about interpretation and application of the of some aspects of MDR.
    b. NBs will not be able to complete these assessments for all MPs by 2024 and recommend the companies to set forward “priorities”.
    c. Delays in recertification imply non-availability of the MPs.
2. Due to various factors such as the complexity of certification and recertification and Brexit, t**he number of notified bodies (NBs)** for cardiac MDs has significantly decreased from >120 under MDD to approximately 20 under MDR. Some NB got their certification as late as November 2021. The current number of NBs is insufficient for timely re-certification or certification of MPs, in accordance with the new EU-MDR.
3. NBs do not differentiate between re-certification of MPs transitioning from MDD to EU-MDR and a completely new clinical study for a new individual MP. The interpretations and guidelines for EU-MDR should distinguish these in a clear manner, so as to reduce the impact on the clinical use of these MPs.
4. Clinical data, needed for recertification, should be defined in collaboration with the physicians in order to achieve realistic possibilities for achievement of the deadlines, such as time, logistics, and financial impacts in the field of pediatric cardiology.
    a. Many MPs have been used “off-label” under MDD with very good clinical results.
    b. Re-certification under MDR will be extremely difficult and almost impossible due to the low volume of cases (typically an ‘orphan’ device) and frequent use in off-label indication;
5. Costs and efforts needed for re-certification are very high, exceeding factor of >10x of the costs compared with the previous MDD or for FDA-approval. Recertification under MDR is repeated every 5 years, with the associated costs.
    a. In a small-volume niche market, such increases are detrimental for marketing such devices.
    b. Due to the costs likely to be incurred, many companies have already decided to stop several ranges of MPs.
    c. This is already having an impact on our ability to perform complex life-saving procedures on babies and children with congenital heart defects.
    d. Such high costs will push all the small companies out of the market, leaving few monopolies to big companies who typically are NOT interested in low-volume high-risk low-profit MD. This will also lead to monopoly position of medical companies for certain classes of MDs.
    e. The very limited number of NB leaves little leverage on service, timing, efficiency;
6. The process of re-certification in accordance with EU-MDR should be faster, in order to reach the important timelines for that purpose. The current timeframe for recertification in USA is 30-180 days, in Canada 47-180 days, but in Europe 18-24 months.
7. The development of new and clinically useful MPs must have a chance to be launched into the European market within a reasonable time.
    a. the backlog due to the new EU-MDR makes this impossible.
    b. Currently any new life-saving MPs are likely to be released in the US or Canada, and not in Europe. Up to a decade ago, the doctors in USA were envious of our ability to use new MPs many years earlier than the FDA allowed them to do so. They campaigned for the FDA to develop their processes such that speedy approvals are now faster obtained in our specialty.

Already in 2022 and certainly by 2023, an increasing number of MPs will no longer available in Europe. This is because the companies manufacturing MPs for our specialty cannot have these certified in accordance with EU-MDR, as highlighted in points 1-7 above. This means that we will be unable to offer many life-saving treatments to babies and children with congenital heart defects and so there will be a huge impact on patient safety, with possibly more complications, increased mortality rates and costs. This needs to be brought to attention widely and steps taken to prevent this impact by MPs either disappearing from the market or not being available until re-certification is completed.

The goal of MDR is to protect the European citizen by improving the safety of medical products. This goal probably will be reached in high-volume MD. However in niche fields with low-volume MDs, MDR will result in either withdrawal of MD from the market, or availability at a much higher price. This will not be beneficial for the European patient with an orphan disease.

For this purpose, we have prepared a list of MP at risk for discontinuation in accordance to the EU-MDR within the community of Paediatric Cardiologists in Europe (**see table 1**). This list was prepared in cooperation with the MP companies and derives from information, as good as is currently available. The time-frame for recertification is currently not predictable by the NBs for many MPs, changes might occur during application or evaluation by NB. Overall re-certification seems to be extremely difficult and time consuming especially for class 3 products.

THE WAY FORWARD

1. The EU has to define those products that should be eligible for a simplified EU-MDR re-certification, because they are **critical or essential** in niche fields, such as **treating children**, have sufficient clinical experience but low volume of cases.
2. Timeline for re-certification in accordance with EU-MDR may have to be modified for “critical” MPs due to inadequate number of NBs, in accordance with article 97.
3. Overall **costs** and **efforts** should be clarified and must be rationalised by NBs; healthy competition between NB on basis of efficiency, service and prices must be possible; monopoly or price-setting must be avoided; the cost may not be dissuasive for marketing MDs in Europe.
4. The relevance and proportion of clinical data requirements for re-certification should be clarified and defined in collaboration with the users (doctors). This is critically important for orphan diseases with orphan solutions;
5. The role of ‘**LEGACY devices’** should be defined and re-certification may have to be facilitated so that it is easier and faster.
6. Reciprocal acceptance of FDA-data or FDA approval should be evaluated for devices with small clinical volume or small turn-over.
7. The higher and continuous cost for recertification will create reimbursement issues for treatments with MPs.

ACTION BY THE EUROPEAN UNION

There is a need for an immediate response by the EU, especially for all Medical Products (MP) widely in the field of Pediatric Medicine and especially in Pediatric Cardiology. Diseases in this specialty are included within the list of the European research Network Heart Guard; EU-MDR creates a huge contrast between the need of care for these patients and the difficulties to provide it in a proper way. Doctors from all the

European countries including UK and USA have already raised their concerns about the possible lack of availability of MPs in Europe currently and in the near future during the Annual Meeting of the Association for European Paediatric and Congenital Cardiology (AEPC) held in Geneva between 25.05.2022 and 28.05.2022. Some of the companies have already stopped the production or marketing in Europe of several "life-saving" MPs. Many other MPs are also at risk of being completely withdrawn from the European market within the next 12 months. This will have a huge impact on the treatment strategies and risks to babies and children with congenital heart defects, not only in Europe, but also surrounding countries in Africa and Asia.

Therefore, the EU-MDR application needs to be modified and adapted to prevent children with congenital heart defects being denied treatments, which have a very positive track record over the last three decades.

The AEPC has created a task force for EU-MDR, which is available for further discussions and negotiations with the representatives of EU-MDR in the EU.

Please do not hesitate to contact us, if you need further clarification or any other information.

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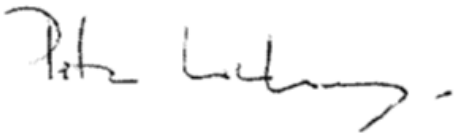

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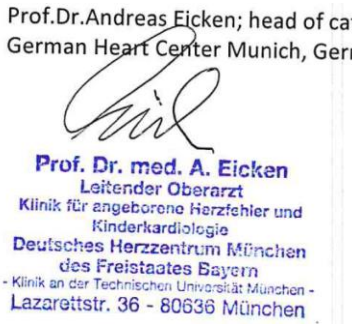

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