Recommendations on medical devices for use in infants, children and adolescents

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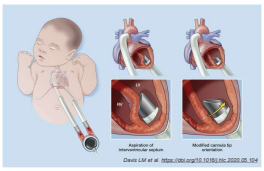

Declarations

- I declare NO CONFLICT of interest
  (no funding provided by any commercial entity related to medical devices)
- My work in this area is financially supported in part by the EU Horizon 2020 research & innovation programme, project CORE-MD *(Coordinating Research and Evidence for Medical Devices, grant agreement 965246)*
- On behalf of the European Academy of Paediatrics, I serve as task leader for the work on paediatric medical devices in the CORE-MD project

Background

- The EU MDR 745/2017 aims to strengthen clinical evaluation and safety, particularly of high-risk MD
- EU MDR **markedly increases time & costs** for bringing MD to or keeping them on the market; particularly challenging for MD sold in small numbers
- **Paediatric & orphan MD increasingly disappear** from the EU market
- **Loss of essential MD** needed for appropriate care of sick children and other patients with orphan disease

Developing recommendations

- Based on systematic review on current status of clinical investigation of MD intended for children, review of current approaches to support R&D, and review of current approaches to certification for market introduction
- Invitation to paediatric and other related medical associations, regulators, European Commission, and renown experts to join expert panel
- Sharing information, invitation to a face to face panel meeting and an additional online meeting, plus digital communication
- Conclusions adopted by consenses, publication & dissemination

Recommendations on clinical investigation & evaluation

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ACTA PAEDIATRICA WILEY

European expert recommendations on clinical investigation and evaluation of high-risk medical devices for children

Experts from various child health specialties, representatives of **24 medical associations** (Eur Acad Paediatrics, Child Health Foundation-Stiftung Kindergesundheit, Assoc Eur Paed Congen Cardiol, Biomed Alliance Eur, Cardiovasc Intervent Radiol Soc Eur, conect4children, Eur Ped Dialysis WG, Eur Ped Surgeons Assoc, Eur Rare Kidney Dis Ref Network, Eur Ref Network Rare Endocrine Conditions, Eur Ref Network Hereditary Metabol Disorders, Eur Soc Cardio, Eur Soc Developm Perinatal Paed Pharmacol, Eur Soc Emergency Med, Eur Soc Endocrinol, Eur Soc Ped Nephrol, Eur Soc Paed Neonatal Intens Care, Eur Soc Paed Gastro Hepatol Nutrition, German Soc Paed Adolescent Med, Int Ped Nephrol Ass, Royal College Paed Child Health UK, Royal College Physicians Ireland, Int Ped Nephrol Assoc, Soc Study Inborn Errors Metabol) a **regulatory authority** (Health Products Regulatory Authority Ireland) and the **European Commission** Directorate General Health and Food Safety - Health Technology Unit B6

Clinical investigation: recommendations

- No “one size fits all” solution – one and the same approach to clinical investigation of all MD intended for children patients cannot be applied
- **Different levels of clinical evidence** are required depending on
  - specific research question
  - type of MD
  - identification of potential hazards and expected risks
  - nature and prevalence of conditions treated with the MD
  - intended age group

Clinical investigation: recommendations

The approach to clinical investigation of MD in children should consider

- **RCTs are the gold standard** for evaluating therapeutic benefits of medical interventions and should be performed whenever feasible.
- **RCTs in children are mostly not feasible** to evaluate MDs for ethical or practicality reasons. Other study designs must be considered to generate clinical data on device performance and safety. Generally, one should **strive for the highest level of clinical evidence** that is achievable

- Hierarchy of evidence: 1) RCT (highest level); 2) Comparative prospective study with concurrent controls (experimental or observational); 3) Comparative study without concurrent controls (e.g. with historical control); 4) Prospective case series with documentation of either post-test or pre-test/post-test outcomes

Gürlich K et al. European expert recommendations on clinical investigation and evaluation of high-risk medical devices for children. Acta Paediatr. 2023 Jul 24. doi: 10.1111/apa.16919.

Clinical investigation: recommendations

- **Mixed population studies** (both adults & children) can optimize sample sizes and resource use in case of a shared indication for MD use (include subgroup analyses)
- **Extrapolation** of data obtained from trials in adults can be considered for devices with the same intended use in children, if the condition being treated is similar and if there is no indication for different effectiveness and safety of the device in children
- For post-marketing surveillance, European **patient registries supervised by competent paediatric associations** systematically collecting relevant and informative data on paediatric patients treated with MD of interest
- **Define and enhance quality** of existing registries, establish new registries
- **Funding** to be secured from public and private sources

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Clinical evaluation: recommendations

- Establish an **expert panel on paediatric MD**, with **paediatric experts** to provide scientific and clinical advice
  - to developers of new and high-risk MD according to MDR Art. 61(2)
  - to EU MD Coordination Group with respect to consistent application of the MDR on MD for children according to MDR Art. 106
- **Require notified bodies** certifying paediatric MD to **seek advice from competent paediatric experts**
- **Transparency** needed regarding 1) **advice** of expert panels re clinical evidence expectations provided to MD developers according to MDR Art. 61(2), and 2) **clinical data** relied upon by manufacturers for paediatric MDs to ensure predictable evidence requirements, and clinicians have access to MD related data

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Clinical evaluation: recommendations

- **Designation of "orphan MD" status** should be based on a case by case evaluation, taking the following criteria into account
  - Intended use in a life-threatening or chronically debilitating disease with a prevalence of <1 per 2,000 people, based on the accepted definition of rare diseases in the EU
  - Existence of an unmet medical need, and
  - Absent or insufficient suitable / equivalent alternative therapeutic options with similar clinical safety

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Interim solutions for paediatric and orphan MD

- **Ensure continued access** to essential paediatric and orphan MD
- **Establish systematic monitoring** on MD that are about to disappear or have already disappeared from the market
- Implement efficient & fast process to assign a "paediatric device" or "orphan device" status, leading to a **simplified, fast and low-cost conformity assessment**
- Proactively support bringing MDs to market also for small and particularly vulnerable patient groups, e.g. **public funding, other incentives** *(cf. drugs for children)*
- **Until final solution is achieved:** paediatric or orphan MDs that have been marketed for at least 3 years without reported problems to get permission for continued use; MDs approved with credible evaluation in other jurisdictions to be permitted for market access, to support patient safety and well-being with access to essential MDs

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Increasing awareness, support political decisions

- Clinical experts to work together with paediatric associations in Europe to increase awareness on consequences of the EU MDR and its implementation for medical care of sick children, due to increasing unavailability of essential MD for children

Open Letter to EU Health Commissioner signed by 27 organizations

copy by e-mail:
cab-kyriakides-contact@ec.europa.eu

Commissioner Stella Kyriakides
European Commissioner for
Health and Food Safety
European Commission
Rue de la Loi / Wetstraat 200
1049 Brussels, Belgium

Date 27/6/2023
Open letter: Urgent action needed to secure continued access to essential medical devices for children and for patients with orphan diseases

Response by European Commission President

EUROPÄISCHE KOMMISSION
Kabinet der Präsidentin Ursula von der Leyen

Brüssel, 04. September 2023
Ares (2023) 4514166

Sehr geehrter Herr Professor Koletzko,

Präsidentin von der Leyen dankt Ihnen für die Übermittlung des an Kommissarin Kyriakides gerichteten offenen Briefes, den Sie gemeinsam mit 28 anderen europäischen Verbänden im Bereich der Kindermedizin und der medizinischen Versorgung unterzeichnet haben. Sie äußern darin Ihre Besorgnis über die Auswirkungen der Umsetzung der Verordnung (EU) 2017/745 über Medizinprodukte (MDR) auf die Verfügbarkeit bestimmter Medizinprodukte, insbesondere solcher zur Behandlung von

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Motion for a resolution of the Eur. Parliament on ensuring access to medical devices in paediatric care in the EU

pursuant to Rule 143 of the Rules of Procedure - Sunčana Glavak MEP, December 2023

European Parliament, - having regard to the "EU for Health" program 2021-2027, - having regard to the Medical Devices Regulation (EU 2017/745), - having regard to article 143 of its Rules of Procedure,

A. Whereas the provisions of the **Medical Devices Regulation may lead to the unavailability of key medical devices, putting paediatric and rare disease patients at risk**;

B. Whereas maintaining **uninterrupted access to vital medical devices is essential for optimal health care and protection**;

C. Whereas the **EU does not have an effective surveillance mechanism** to actively monitor the availability and potential withdrawal of essential medical devices from the market;

Motion for a resolution of the Eur. Parliament on ensuring access to medical devices in paediatric care in the EU

1. Calls for the **amendment of the EU Medical Devices Regulation** to ensure continued access to devices essential for advanced paediatric care and treatment of rare diseases;

2. Calls for the **expansion of monitoring** of shortages and the availability of certain medical devices, with the aim of avoiding potential shortages;

3. Calls for the **establishment of temporary measures** to protect patients during the transition, including automatic authorization for the continued use of high-risk paediatric medical devices that have been proven safe in the EU for at least 3 years;

4. Recommends that **conformity checks for devices for paediatric patients** be carried out by **subsidized public bodies** or by **limiting the fees** charged by private bodies;

5. Instructs its President to forward this Resolution to the Commission, the Council and the Governments and Parliaments of the Member States.

Continued advocacy needed

EAP and it's paediatric member associations need to and will continue advocacy activities at the European and at national levels

While EU Medical Device Coordination Group (MDCG) task force members have been open to conversations on an individual basis, MDCG so far has refused to establish formal collaboration with the paediatric community

We need to continue making the voice of children heard