



Sandra Gallina  
Director General – DG SANTE  
European Commission  
Rue de la Loi 200 - 1049 Brussel  
Belgium

22 December 2023

**Ref.: Rare diseases diagnostics (i.e. “orphan diagnostics”) should be exempt from the Vitro Diagnostic Medical Devices Regulation (EU) 2017/746 in its Article 5.5**

Dear Ms. Gallina,

We are jointly writing you on behalf of the [European Society of Human Genetics](http://www.eshg.org) (ESHG), [EURORDIS-Rare Diseases Europe](http://www.eurordis.org) and the **European Reference Networks (ERNs) Coordinators Group** to express our concerns on the impact of certain provisions of the In Vitro Diagnostic Medical Devices Regulation (EU) 2017/746 (henceforward IVDR) on our community and urge the European Commission to take action.

As we will illustrate below, in its current form the IVDR negatively impacts the diagnosis and treatment of patients with rare diseases in Europe and hampers the development of rare disease diagnostics by the European private and public sector.

We also share a more general concern raised by Member States at the last EPSCO meeting that the transition to the new regulatory IVDR is not as advanced as necessary and there is a consequent, serious risk of shortages of devices, especially class D devices, which may seriously hinder the availability of in vitro devices in the Union.

We therefore call on the European Commission to:

- **Grant an exemption of rare diseases/rare cancers diagnostics (or, as we propose, “orphan diagnostics”) from IVDR regulation in Article 5.5;**
- **Take all necessary measures, including those of legislative nature where appropriate, to reduce or avoid shortages of classes of devices that are essential for patients. This may include a further postponement of IVDR implementation.**

Accessibility to medical devices necessary for diagnostics of rare diseases is of crucial importance to reduce the protracted journeys towards diagnosis that people living with rare disease experience, as recently confirmed by the Rare Barometer global survey on diagnosis (*pending publication of results*).

More than 70% of clinical decisions and therapy guidance are based on laboratory examinations. This is particularly impactful in the field of rare diseases, with more than 80% of them being of a genetic nature. Rare disease diagnostics are also highly relevant for the entire field of rare cancers where delayed diagnosis could have disastrous consequences. The number of EU citizens needing these tests is not small: with rare diseases affecting less than 1 in 2,000 inhabitants, cumulatively these individuals constitute around 5% of the general population, an estimated over 30 million citizens in Europe with a risk of developing one of the 6,000 rare diseases. In paediatrics, rare disease patients constitute a major part of all hospital admissions and are responsible for a substantial part of morbidity and mortality in minors.

**www.eshg.org**  
**European Society  
of Human Genetics**  
Administrative Office:  
ESHG c/o Vienna Medical Academy  
Alser Strasse 4  
1090 Vienna

Phone: +43 1 405 13 83 20  
Fax: +43 1 405 13 83 23  
Email: [office@eshg.org](mailto:office@eshg.org)  
[Austriamembership@eshg.org](mailto:Austriamembership@eshg.org)

**EURORDIS-Rare Diseases Europe**  
Plateforme Maladies Rares ♦ 96 rue Didot  
♦ 75014 Paris ♦ France  
Tel. + 33 1 56 53 52 10 ♦ Fax +33 1 56 53 52 15  
♦ [eurordis@eurordis.org](mailto:eurordis@eurordis.org)

We praise **the rationale behind the IVDR aiming for “a robust, transparent, predictable and sustainable regulatory framework that ensures a high level of safety and health while supporting innovation”**. Yet, as geneticists, clinicians, people and families of the rare disease community, we are afraid that **neither health nor innovation will be supported when it comes to rare diseases**. We observe concerning major shortcomings deriving from the application of the IVDR provisions, which are bound to have a detrimental impact on the health care systems of the EU Member States and on patients and people living with a rare disease:

- While laboratory-developed tests (in-house IVDs, IH-IVDs) could fill the “CE gap”, several aspects of IVDR affect their development, in particular the requirement of no equivalence to IVDR commercial tests now and (Article 5.5) additional administrative burden. This uncertainty of sustainability for IH-IVDs discourages their development for both administrative and economic reasons.
- IVDR calls for large and longitudinal cohorts, which are unavailable for most rare diseases because of their rarity (the largest group has a prevalence of less than 1 in a million per disease), thereby precluding fulfilment of several IVDR requirements that have not considered this specific aspect.
- Since CE labelling has so far come with a significant price increase of the commercially offered diagnostic assays, the costs of rare disease diagnostics have increased. Costs of diagnostics is a major issue for most healthcare providers. Most of the players in this area do not have the capacity and financial background to sustain the vast regulatory burden imposed by IVDR to obtain CE labelling.
- This considerable cost increase is likely to hinder indicated tests for economic reasons, as already seen in the USA where rare disease testing is plateauing due to high test costs and the refusal of insurance companies to cover them. Laboratory examinations are crucial for most clinical decisions and therapy guidance in the field of rare diseases, and their lack of availability may significantly impact on the quality and timeliness of rare disease diagnoses.
- Expertise in the field of rare diseases is scarce and individual teams centred around European Reference Networks (ERN) have been facing a high burden of multidisciplinary care, whereby additional administrative burden related to the full implementation of IVDR will challenge the generally understaffed and underfunded ERN Healthcare Providers.
- Companies are re-evaluating their rare disease portfolios and prioritising diseases or techniques used by larger patient groups. In addition, companies are shifting clinical trials and beta-testing to other regions of the world. Consequently, European patients may remain devoid of the latest technological developments and the EU could fall behind in highly competitive fields of genomics and in the development of personalised medicine-based therapies (e.g. gene therapy).

We are seriously concerned that this would result in a **shortage of crucially important genetics diagnostics, and therefore lead to missed, delayed or inaccurate diagnoses. This would roll back advances made in the last decade in the field of rare disease diagnostics and challenge the substantial improvements towards shortening of the diagnostic odyssey of people with rare diseases.**

These serious issues related to IVDR-related diagnostics were fully recognised by the participants of last year's conference organised by the Czech EU Council Presidency “Towards a New European Policy Framework: Building the Future Together for Rare Diseases”<sup>1</sup> (Prague, 25-26 October 2022). The “Call to Action”<sup>2</sup> that ensued the conference was supported by **22 EU Member States, representing over 82% of the EU general population.**

We appreciate the MDCG guidance document on art. 5.5 of the Regulation that would in detail define based on practical experience and including practical ways for their implementation. Nevertheless, this is not sufficient to ensure that in vitro medical devices necessary for proper diagnostics of rare diseases remain available on the market and further action is needed. The MDCG document is a guidance document, which is not legally binding, and in any case the suggested guidance is still administratively very demanding for academic laboratories which bear the brunt of orphan diagnostics for ERNs (at university hospitals).

**The European Union needs a system that supports the innovation of rare disease diagnostics. The IVDR unfortunately leads to opposite outcomes. This is why we collectively call for adequate measures to be taken in the shortest delay to exempt “orphan diagnostics” from IVDR, Article 5.5, and all the necessary measures that are necessary to avoid**

---

<sup>1</sup> <https://www.mzcr.cz/towards-a-new-european-policy-framework-building-the-future-together-for-rare-diseases/>

<sup>2</sup> [https://www.mzcr.cz/wp-content/uploads/2022/12/CZPRES\\_Expert\\_Conference\\_on\\_Rare\\_Diseases\\_brochure.pdf](https://www.mzcr.cz/wp-content/uploads/2022/12/CZPRES_Expert_Conference_on_Rare_Diseases_brochure.pdf). In particular, the Call to Action states: which, amongst others, states- “The CZ PRES appreciates the ongoing work of the Medical Device Coordination Group MDCG guidance document concerning the art. 54 of the Regulation that will include a clear statement when it comes to possible derogation from the Regulation for medical devices necessary for rare disease diagnostics. Calls upon the MDCG and the European Commission to prepare without any further delay guidance documents on art. 5.5 of the Regulation that would in detail define based on practical experience and including practical ways for their implementation”.



**shortages of diagnostic devices of crucial important for EU patients, which may include a further postponement of IVDR implementation.**

We would welcome any opportunity to discuss these issues and remain available for further in-person or e-mail discussions on this very important topic for European health care.

Yours sincerely,

**The ESHG working group on the IVDR regulation**

Gert Matthijs, prof. PhD

Els Dequeker, prof. PhD

Gunnar Houge, prof. MD PhD

Milan Macek, prof. MD

**For the ERN Coordinators Group**

Alexis Arzimanoglou, Prof. M.D

Holm Graessner, PhD

**For EURORDIS-Rare Diseases Europe**

Yann Le Cam  
Chief Executive Office

**[www.eshg.org](http://www.eshg.org)**

**European Society  
of Human Genetics**

Administrative Office:  
ESHG c/o Vienna Medical Academy  
Alser Strasse 4  
1090 Vienna

Phone: +43 1 405 13 83 20  
Fax: +43 1 405 13 83 23  
Email: [office@eshg.org](mailto:office@eshg.org)  
[Austriamembership@eshg.org](mailto:Austriamembership@eshg.org)

**EURORDIS-Rare Diseases Europe**

Plateforme Maladies Rares ♦ 96 rue Didot  
♦ 75014 Paris ♦ France  
Tel. + 33 1 56 53 52 10 ♦ Fax +33 1 56 53 52 15  
♦ [eurordis@eurordis.org](mailto:eurordis@eurordis.org)