Editorial

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Complex analytical procedures in diagnostic laboratories and the IVDR

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The *In Vitro* Diagnostic Medical Devices Regulation (IVDR) 2017/746 [1] entered into force in May 2017 and will be fully applicable in all EU member states in May 2022. According to Article 1, this regulation lays down rules concerning placing on the market, making available on the market or putting into service in the European Union *in vitro* diagnostic medical devices for human use and accessories for such devices. The IVDR does not regulate the operation of IVDs or the oversight of their operation. This is done at the member-state level.

The interpretation that the IVDR also regulates the conduct of so-called LDTs (laboratory-developed tests), *in-house tests* or *non-standard tests* in the medical laboratory, is repeatedly expressed [2–4]. This interpretation is fundamentally questionable. It is based on the assumption that the overall process of a laboratory medical examination procedure carried out without, or in part without, the use of commercially available diagnostics represents an *in vitro* diagnostic medical *device*.

Under this interpretation — as an example — the cytomorphological analysis of a bone marrow smear is considered to be an LDT. Here, a product for general laboratory use — namely, a microscope — is used to examine a slide according to a procedure protocol and ultimately to create a medical report. The correct interpretation of blood and bone marrow smears is an integral part of medical education and health care. The measurement of drug levels by means of complex mass spectrometry-based measurement procedures can also be cited as an example of such complex analytical procedures that are implemented under the responsibility of a laboratory manager who is authorized and competent under national law. Here, too, products for general laboratory use are applied in complex, individual procedures (Figure 1). Corresponding medical examination procedures that are not (or are only partially) based on industrially manufactured medical devices but are developed and/or implemented individually in a diagnostic laboratory under the responsibility of a physician are also widely used in human genetics, microbiology, molecular pathology and clinical pharmacology or toxicology and are absolutely indispensable for high-quality laboratory medical care.

Article 2 of the IVDR, Definitions, defines an *in vitro* diagnostic medical device as “… *any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, piece of equipment, software or system, whether used alone or in combination, intended by the manufacturer to be used in *vitro* for the examination of specimens, including blood and tissue donations, derived from the human body …*” Only, and explicitly, software — but not procedures — is mentioned as an *in vitro* diagnostic device of a non-material character.

Article 5, paragraph 5, of the IVDR deals with *devices* that are manufactured and used only within health institutions and are not marketed. The requirements of the IVDR do explicitly not apply to these devices as long as few conditions are met — with the exception of the relevant general safety and performance requirements according to Annex I.

"LDT" may be a common term used worldwide to describe the above-mentioned exemplary non-standard diagnostic procedures. However, it must be clearly stated that the term LDT is not used in the IVDR; the same applies to the term “test” in general, such as in “in-house test” or “test from in-house production”. In the IVDR, the term “*in vitro* diagnostic medical device” is used exclusively. This language does not suggest that protocols for medical laboratory examinations as a process chain are themselves considered medical *devices* in the context of the IVDR.

This is consistent with the Treaty on European Union, Title XIV, Article 168, which clearly states that the Union’s actions shall respect the responsibilities of the member states for the definition of their health policies and for the
organization and delivery of their health services and medical care. The responsibilities of the member states include the management of health services and medical care. Thus, the regulation of processes in medical laboratories, as part of the exercise of the medical profession itself, is not compatible with the EU treaty. The regulation of complex laboratory diagnostic examination procedures by EU legislation would violate this treaty.

Generically formulated standards to assist in the development and implementation of individual laboratory medical examination procedures in a healthcare facility [5] undoubtedly have their justification and value, but such documents or their application cannot be considered a requirement of the IVDR.

The implementation of the IVDR must not misclassify the exercise of the medical profession in laboratory diagnostics as a medical device. The application of a European regulation to an integral part of health care would set a precedent that restricts medical activities. The regulation of complex laboratory diagnostic examination procedures by EU legislation would violate this treaty.

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The implementation of the IVDR must not misclassify the exercise of the medical profession in laboratory diagnostics as a medical device. The application of a European regulation to an integral part of health care would set a precedent that restricts medical activities. The IVDR can only be conclusively applied to material elements used within in-house examination procedures. The regulatory supervision of the IVDR in the member states must be clearly limited to these elements — i.e., calibration materials or reagents, if applicable, that are individually manufactured in a healthcare facility (according to Article 5 and Annex 1) — and must not be concerned with the processes, protocols and procedures of the medical practice.

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References

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