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THE IMPACT OF NEW EU REGULATIONS ON LAY SUMMARIES

ECONOMY AND TRADE

Changes to the management and documentation of clinical trials in the European Union will begin to accelerate on January 31, 2022 when the **Clinical Trials Regulation (CTR) EU 536/2014** comes into application along with the requirement to use the new **Clinical Trials Information System (CTIS).**

In addition to the CTR, new requirements of the **Medical Device Regulation (MDR) EU 2017/745** will be in full effect with the completed deployment of the **European Database on Medical Devices (EUDAMED)** planned for May 2022. The delayed **In-Vitro Diagnostics Regulation (IVDR) EU 2017/746** will also come into application concurrently or soon after on May 26, 2022.

All three EU regulations bring new requirements for documenting clinical trial data as well as requiring the use of new databases for distributing this information to both healthcare professionals and patients.

CTR

The Clinical Trials Regulation is intended to align assessment and supervision processes for clinical trials conducted within the European Union and to provide a central point of data storage and distribution via the new Clinical Trials Information System administered by the European Medicines Agency (EMA).

The new CTIS website will be available in all official member state languages and allow access to clinical trial statistics and the downloading of related data and reports.
The CTR will replace the existing EU Clinical Trials Directive (EC) 2001/20, and any member state national legislation created to implement this directive. Any clinical trials approved under the prior directive and ongoing more than three years after the CTR comes into application will need to follow the new regulation.

EU member states will continue the authorization and oversight of clinical trials within the requirements of the CTR.

According to Article 37 of the regulation, within one year of the end of a clinical trial the sponsor is required to submit a summary of the results to the CTIS database. This summary is to be accompanied by another summary "written in a manner understandable to lay persons." CTR does not define the term "layperson," but MDR offers this useful definition - "an individual who does not have the formal education in the relevant field of healthcare or medical discipline."

Article 29(6) states that trial participants must be told during the informed consent phase of the trial that a "lay summary" will be made available.

Annex V lists ten elements that must be included in the lay summary. They may be combined, or their order changed as needed:

Element 1: Clinical trial identification – trial title, protocol number, EudraCT number, and any other relevant identifiers.

Element 2: Name and contact details of the sponsor.

Element 3: General information about the clinical trial. Location and dates when the trial was conducted, objectives and rationale for conducting the trial.

Element 4: Population of subjects. Number of subjects per member state, within the EU and within third countries, age and gender demographics, and the inclusion/exclusion criteria.

Element 5: Investigational medicinal products used. Investigational products and treatments should be named the same as in the trial protocol and registration without the use of any promotional language. The regimen(s) and route of administration should be detailed together.

Element 6: Description of adverse reactions and their frequency. Any adverse reactions must be listed with severity, frequency, and other relevant details.

Element 7: Overall results of the clinical trial. At a minimum, the results of the primary endpoint(s) must be included along with any important additional safety data.

Element 8: Comments on the outcome of the clinical trial. The most important limitations and results, including those that may apply to specific populations, should be included.

Element 9: Indication whether follow-up clinical trials are foreseen. This element may be combined with Element 8 and may include publicly available information about related trials and other non-promotional information.

Element 10: An indication of where additional information can be found. Links to websites and registries containing additional non-promotional material may be provided.

The CTR does not specifically request translation of the lay summary, but recommendations from the EU CT Expert Group suggest that the summaries should be made available in the official local languages of each country where the clinical trial was conducted.

A review of the summary prior to translation and the use of approved glossaries and pre-defined terminology should expedite the translation process and aid in its success.

Where practical, trial sponsors are advised to employ readability testing by native-language patients to uncover any potential misunderstanding and any additional terminology or cultural expressions not already identified.

MDR / IVDR

Among the many new requirements of the MDR is the need to supply a Summary of Safety and Clinical Performance (SSCP) for implantable devices and Class III devices, other than custom-made or investigational devices. The SSCP is new to the medical device industry with a structure that may include information analogous to the lay summary used in clinical trials for investigational medicinal products and treatments. The document is intended to include exhaustive detail on the medical device that is comprehensible to both healthcare professionals and patients with no medical background and must be validated by a notified body.

The regulation indicates that patients should be part of the target audience for SSCP information for any implantable devices for which patients receive implant cards and for any Class III devices intended for direct use by the patient. In these instances, a separate SSCP section should be included that is specifically intended for patients, omitting any performance claims or "promotional language" that may mislead patients. In this section, medical terminology and industry acronyms should be kept to a minimum and only used with a plain language explanation preceding the technical terms.

The IVDR has added a similar documentation requirement called a Summary of Safety and Performance (SSP) for Class C and D in-vitro devices.

There is currently no separate guidance on SSPs other than the details listed in Article 29 of the IVDR. But the EU Medical Device Coordination Group (MDCG) has issued guidance related to MDR SSCPs and notified body expectations that should adapt well to IVDR SSP creation.

Referencing MDR Article 32, the MDCG advises that device technical documentation such as the Clinical Evaluation Report (CER), Post-Market Surveillance (PMS) and Post-Market Clinical Follow-up (PMCF) should be the sole source for information included in the SSCP. The IFU may also be used as an SSCP information source if deemed appropriate.

For IVDR SSPs, general information for the IVD, a performance data summary, and possible therapeutic alternatives should be included. Supporting data from technical documentation such as the Performance Evaluation Report (PER) and Periodic Safety Update Report (PSUR) should also be used. The SSP must be validated by a notified body as well.

Both SSCPs and SSPs are required to be kept updated and available in the EUDAMED system.

According to MDR Article 32, the following elements should appear in the SSCP at a minimum:

- Device identification and manufacturer, including Basic UDI-DI and SRN, if available.
- Device intended purpose with indications, contraindications, and target populations.
- Device description, including previous generations or variants if they exist. Other devices, accessories, or products intended for use in combination with the device.
- Possible diagnostic or therapeutic alternatives.
- Reference to any harmonized standards and common specifications.
- A summary of the clinical evaluation as referenced in Annex XIV and relevant information on post-market clinical follow-up.
- Any residual risks and undesirable effects, warnings, or precautions.
- Suggested profile and training for users.

The SSCP and SSP should be provided in English and translated into languages accepted in EU member states where the device is intended to be sold. The documents should include a statement as to which language was used for validation by the notified body.

REFERENCE:

- MDCG 2019-9: Summary of safety and clinical performance. A guide for manufacturers and notified bodies
- Clinical Trials Regulation and Overview
- Clinical Trials Regulation and Overview [2]
- Good Lay Summary Practice
- European Commission. Summaries of Clinical Trial Results for Laypersons. Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use. Version 2.
- MDR
- IVDR
- European Medicines Agency - List of official Languages per country
- European Medicines Agency - Clinical Trial Information System (CTIS)
- EUDAMED

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