ISSN: 2641-2020
DOI: 10.33552/APPR.2024.04.000584
Archives of
Pharmacy & Pharmacology Research
Iris Publishers

Mini Review

Copyright © All rights are reserved by Clara M Rosso-Fernández

Challenges On New Requirements for Non-Commercial Investigator- Driven Clinical Trials to The Management of Safety Events Within the New European Pharmacovigilance System

María Ángeles Lobo-Acosta[1], Silvia Jiménez-Jorge[1], Elena María, Pérez López[2] and Clara M Rosso-Fernández[1]*

[1]*CTU-HUVR (Clinical Trials Unit-Hospital Universitario Virgen del Rocío), Spain*

[2]*Internal Medicine Resident of Clinical Pharmacology (Hospital Universitario Virgen del Rocío), Spain*

***Corresponding author:** Clara M Rosso-Fernández, Clinical Trials Unit-Hospital Universitario Virgen del Rocío, Spain.

Received Date: March 15, 2024

Published Date: March 22, 2024

Abstract

The new changes in the current European Union legislation regarding the reporting of adverse events for clinical trials complicates pharmacovigilance tasks in non-commercial proposals. The new reporting system implies a greater workload and time commitment for independent researchers who already have fewer economic resources, personnel, and infrastructure.

Keywords: Pharmacovigilance; Non-Commercial; Investigator-Driven; Clinical Trials; Safety Reporting

Abbreviations: AE: Adverse Events; CIOMS: Council for International Organizations Of Medical Sciences CRO: Clinical Research Organizations; CTIS: Clinical Trials Information System DSUR: Data Safety Update Report; EMA: European Medicine Agency EU: European Union; ICH: International Council for Harmonization MedDRA: Medical dictionary for regulatory activities; SUSAR: Suspected Unexpected Serious Adverse Reaction

Introduction

Investigator-driven clinical studies with drugs have become a common situation for non-commercial studies to be performed in response to clinical questions on which there is no economic interests coming from private investors [1]. The development of a pragmatic study must accomplish with ethical and legal requisitions ([2] but even with local and international rules ((ICH E6 section 6.8) [3]) to ensure excellence and quality of data, for both publications and, above all, for clinical questions answers. Pharmacovigilance is a sponsor's responsibility. A very specific activity to be performed in a clinical trial with drugs is the notification of adverse events (AE) occurred during the trial (from the signature of informed consent form to a specific time depending on the drug specific characteristics). This pharmacovigilance activity is to be organized within the study team organizing the study with the aim of gather the AE, graduating (severity/intensity), assessing according to definitions (serious/not serious), considering the suspicion to be related or not with the study drug of interest (comparing with the official information in the Summary of Product Characteristics or Investigator brochure document) and finally to arrive to the classification of SUSAR: suspected Unexpected Serious Adverse Reaction. Only adverse events classified as serious and unexpected

This work is licensed under Creative Commons Attribution 4.0 License

are to be communicated (with specific data) to the EU system, the sponsor (commercial and non-commercial) is responsible to have a detailed description of any other AE and to communicate annually to European Medicine Agency (EMA)-National Regulatory authority via DSUR (Data Safety Update Report).

Lately there has been a specific change in European Medicine Agency trials system organization [4] that has clearly changed the conditions and possibilities of a non-commercial institution to be able to perform adequately an expedited notification. This is the objective of this review for considering new requirements for non-commercial sponsor to report SUSARs to EudraVigilance (European specific system for managing adverse reaction,) Clinical Trial Module and concerns for a non- industry/CRO (Clinical Research Organizations) subcontracted.

Discussion

Up to June 30, 2022, sponsors who may not have the resources and experience for reporting had two options, where this possibility is provided for by a Member State where the SUSAR has to be reported the correspondent case completed in a CIOMS-1 form [3] is sent to the National Competent authority (NCA) affected (simply with a fax connection). The second option was to delegate reporting to another person, for example, the marketing authorization holder of the Investigational Medicinal Product [5]. After 2022, the first option is not available anymore in some EU countries (e.g. Spain). European Union legislation regarding pharmacovigilance and clinical trials clearly defines specific obligations in this matter. The system is not only prepared for reporting but even for receiving confirmation notices. Notification through the electronic submission and exchange of SUSARS case reports (ISO ICSR/ICHE2B [3]) must be completed with the acknowledgment messages and electronic information related to the drug used into the eXtended EudraVigilance Medicinal Product Report Message [6].

This mandatory form of transmission of information on SUSARS cases has meant that non- commercial sponsors must comply with a series of pre-requisites that are described below [7].

1. Generate a clinical trial application in CTIS (Clinical Trials Information System) or in the European Union Drug Regulating Authorities Clinical Trials.

2. Active EMA accounts generated through EMA Account Management portal [8].

3. Sponsoring as public institution must be officially registered in EMAs Organization Management Service [9].

4. Qualified Person Responsible for Pharmacovigilance is to be designated as responsible contact with EMA for regulatory objectives. Even an EudraVigilance responsible person is to be named.

5. Official Training certificates must be provided for Individual Case safety reporting [10]and the use of Extended EudraVigilance medicinal product dictionary [11].

6. A reporting mode must be selected for notifications. Nevertheless, there is a simple reporting module for institutions with a low number of SUSARs and low risk profile of trials, the EudraVigilance website mode is preferably used by non-commercial sponsors.

7. Medical dictionary for regulatory activities (MedDRA) license is required for any sponsor, however a non-Profit / non-Commercial waiver is possible under request [12].

Conclusion

The performance of investigators-driven clinical trials, sponsored by public institutions is a common situation, moreover, is the normal scheme for public funded studies. In this mini review the intention is to highlight the difficulties for a non-Marketing Authorization Holder- sponsor, no funding options for subcontracting a CRO with specialized departments to comply with all these specific requests. The panorama for non-commercial sponsors has changed radically in terms of complexity regarding notification to EudraVigilance. Despite the numerous pages, manuals, and online help services for registration and training this becomes a difficult task for institutions (especially public hospitals).

In the common example of a clinician willing to perform a pragmatic trial, the challenges to accomplish with safety reporting make completely indispensable the participation of research units departments. Specialized personnel (Pharmacist, Clinical Pharmacologists) are needed to be able to put in place a major complex organization which involves official institution registries, specific training and named responsible for safety reporting. A more deeply review adding the comparison with another systems (American Food Drug Administration, or United Kingdom - Medicines and Healthcare products Regulatory Agency) would be needed to reflect the problem.

Acknowledgement

Clinical Trials Unit staff, University Hospital Virgen del Rocío, Seville.

Conflict of Interest

No conflict of interest.

References

1. Gisbert JP, Chaparro M (2021) Retos y desafíos de la investigación clínica independiente. Gastroenterol Hepatol [Internet] 44(8): 599-610.
2. (2001) Directive 2001/20/EC of the European parliament and of the council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. Official Journal of the European Union.
3. (1995) International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Tripartite Guideline. Clinical Safety Data Management: Definitions and Standards for Expedited Reporting. CPMP/ICH/377/95. European Medicine Agency.
4. (2024) European Medicines Agency. EudraVigilance [Internet]. European Medicines Agency; updated June 2016.

5. (2011) Communication from the Commission-Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3'). Official Journal of the European Union.

6. (2014) eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) Data-Entry Tool (EVWEB) user manual [Internet]. European Medicines Agency.

7. (2024) EudraVigilance: how to register [Internet]. Europa.eu.

8. (2024) European Medicines Agency account management [Internet]. Europa.eu.

9. (2024) SPOR Web UI [Internet]. Europa.eu.

10. (2024) EudraVigilance training and support [Internet]. Europa.eu.

11. (2024) Extended EudraVigilance medicinal product dictionary (XEVMPD) training [Internet]. Europa.eu.

12. (2024) Medical Dictionary for Regulatory Activities (MedDRA) [Internet]. Meddra.org.