5.2 The Role of Narratives

The objective of the narrative is to summarize all relevant clinical and related information, including patient characteristics, therapy details, medical history, clinical course of the event(s), diagnosis, and ADR(s) including the outcome, laboratory evidence (including normal ranges), and any other information that supports or refutes an ADR. The narrative should serve as a comprehensive, stand-alone "medical story". The information should be presented in a logical time sequence; ideally this should be presented in the chronology of the patient's experience, rather than in the chronology in which the information was received. In follow-up reports, new information should be clearly identified.

Abbreviations and acronyms should be avoided, with the possible exception of laboratory parameters and units. Key information from supplementary records should be included in the report, and their availability should be mentioned in the narrative and supplied on request. Any relevant autopsy or post-mortem findings should also be summarized in the narrative and related documents should be provided according to local regulation and if allowed by local data privacy laws.

Terms (e.g., AEs/ADRs, indication, and medical conditions) in the narrative should be accurately reflected in appropriate data fields.

5.3 Clinical Case Evaluation

The purpose of careful medical review is to ensure correct interpretation of medical information. Preferably, information about the case should be collected from the healthcare professionals who are directly involved in the patient's care. Regardless of the source of an ADR report, the recipient should carefully review the report for the quality and completeness of the medical information. The review should include, but is not limited to, the following considerations:

- Is a diagnosis possible?
- Have the relevant diagnostic procedures been performed?
- Were alternative causes of the reaction(s) considered?
- What additional information is needed?

ADR terms should be used consistently and in accordance with recommended standards for diagnosis, if possible. The report should include the verbatim term as used by the reporter, or an accurate translation of it. Any company personnel receiving reports should provide an unbiased and unfiltered report of the information from the reporter. While the report recipient is encouraged to actively query the reporter to elicit the most complete account possible, inferences and imputations should be avoided in report submission. However, clearly identified evaluations by the MAH are considered appropriate and are required by some regulatory authorities.

When a case is reported by a consumer, his/her description of the event should be retained, although confirmatory or additional information from any relevant healthcare professionals should also be sought and included.

5.4 Follow-up Information

The information from ADR cases when first received is generally incomplete. Ideally, comprehensive information would be available on all cases, but in practice efforts

should be made to seek additional information on selected reports, including second – hand reports (see Attachment, Recommended Key Data Elements, of this guideline).

In any scheme to optimize the value of follow-up, the first consideration should be prioritization of case reports by importance. The priority for follow-up should be as follows: cases which are 1) serious and unexpected, 2) serious and expected, and 3) non-serious and unexpected. In addition to seriousness and expectedness as criteria, cases "of special interest" also deserve extra attention as a high priority (e.g., ADRs under active surveillance at the request of the regulators), as well as any cases that might lead to a labeling change decision.

Follow-up information should be obtained, via a telephone call and/or site visit and/or a written request. The company should provide specific questions it would like to have answered. Follow-up methods should be tailored towards optimizing the collection of missing information. Written confirmation of details given verbally should be obtained whenever possible. In exceptional circumstances, if requests for information have been refused by the reporter, a regulatory authority might be able to assist an MAH in obtaining follow-up data.

To facilitate the capture of clinically relevant and complete information, use of a targeted questionnaire/specific form is encouraged, preferably at the time of the initial report. Ideally, healthcare professionals with thorough pharmacovigilance training and therapeutic expertise should be involved in the collection and the direct follow-up of reported cases (particularly those of medical significance). For serious ADRs, it is important to continue follow-up and report new information until the outcome has been established or the condition is stabilized. How long to follow up such cases is a matter of judgment.

It is important that at the time of the original report, sufficient details about the patient and reporter be collected and retained to enable future investigations, within the constraints imposed by local data privacy laws.

5.4.1 Pregnancy Exposure

MAHs are expected to follow up all pregnancy reports from healthcare professionals or consumers where the embryo/foetus could have been exposed to one of its medicinal products. When an active substance, or one of its metabolites, has a long half-life, this should be taken into account when considering whether a foetus could have been exposed (e.g., if medicinal products taken before the gestational period should be considered).

5.5 How to Report

The CIOMS I form has been a widely accepted standard for expedited adverse event reporting. However, no matter what the form or format used, it is important that certain basic information/data elements, when available, be included with any expedited report, whether in a tabular or narrative presentation. It is recommended that the Medical Dictionary for Regulatory Activities (MedDRA) be used for coding medical information. The standards for electronic submission of Individual Case Safety Reports (ICSRs), according to the ICH E2B/M2 guidelines, should be implemented.

The listing in the Attachment of this guideline addresses those data elements regarded as desirable; if all relevant elements are not available at the time of expedited reporting, efforts should be made to obtain them.

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