Letter to the Editor

Incidental events in spontaneous reports – a proposal for filtering ‘noise’

Louisa Walsh

Clinical Drug Safety, AstraZeneca LP, Wilmington, Delaware, USA

One of the goals of spontaneous reporting systems is to protect the public health by providing an early warning system for previously unknown serious adverse drug reactions (ADRs). A driving principle of these systems is the suspicion of possible causal relationships between adverse events (AEs) and drugs, which prompts the reporter to submit a spontaneous report. In the course of investigating these reports, drug safety personnel may receive information on events, adverse or otherwise, that occurred after the drug was administered, but were not the intended subject of the spontaneous report. These events which did not prompt contact with the pharmaceutical company or regulator and for which there is no indication of drug causality are proposed to be defined as ‘incidental events’ by the Council for International Organizations of Medical Sciences (CIOMS) V Working Group [1]. The CIOMS V group endorses reporting incidental events as either medical history or concurrent conditions, and not as suspected ADRs on which regulatory reporting decisions are made, unless a causal relationship is implied or stated by the reporter, the medical records, or company review staff. However, regulatory agencies do not currently recognize incidental events, and there is no field or category for recording ‘concurrent events’ on spontaneous report forms or electronic file formats.

Additionally, the International Conference on Harmonization (ICH) Endorsed Guide for Medical Dictionary for Regulatory Activities (MedDRA) Users instructs users to code every reported ADR/AE or medical concept described by the reporter, regardless of perceived relationship to drug product [2]. The rationale for this is that by not coding all AEs, there is a risk of missing adverse events that were thought to be unrelated to a drug, but were later determined to be drug-related. If

this reasoning were followed, then by not coding all concomitant drugs as suspect drugs, there is a risk of missing drugs that were thought to be unrelated to the adverse event, but were later determined to be causal for the AE.

What is happening in practice is that drug manufacturers must report AEs and ADRs in such a way that they are indistinguishable from each other in the database. In addition, seriousness is recorded on reporting forms and electronic file formats at the case level and not at the event level, resulting in the inability to distinguish serious from nonserious adverse events in the database. Both of these issues result in an abundance of potential ‘noise’ in spontaneous reporting databases, that is nonserious and/or incidental adverse events, which detracts from the ability of reviewers to detect true potential serious ADR signals and protect the public health.

One solution would be to create a new field on reporting forms and electronic files for suspect and concomitant event, just as there is such a field for suspect and concomitant drug. By convention, no causal relationship would be assumed for concomitant events that were not the subject of a spontaneous report. If the reporter, the medical records, or company reviewer indicated a causal relationship for the event(s), the event would be listed as a suspect and not a concomitant event. This practice would satisfy all concerned parties by maintaining current reporting obligations, while allowing the ability to distinguish suspect ADRs from AEs. This modification would enhance signal detection activities in large regulatory spontaneous report databases by allowing for the ability to search and data mine for the ‘gold’, i.e. potential serious suspect ADRs, while maintaining the ability to filter in or filter out potential ‘noise’, i.e. concomitant and nonserious AEs, as is currently practised with suspect and concomitant drugs. In the future, electronic files will have the ability to record seriousness at the event level, and spontaneous report forms could be modified to allow this important distinction.

References

- 1 Council for International Organizations of Medical Sciences (CIOMS). Report of CIOMS Working Group V. Current Challenges in Pharmacovigilance: Pragmatic Approaches, 2001 :86–9. Available at: <http://www.cioms.ch>.
 - 2 MedDRA Term Selection: Points to Consider – Application to Adverse Drug Reactions /Adverse Events & Medical and Social History & Indications 18 November, 2004. Available at: <http://www.ich.org/cache/compo/276–254–1.html>.
-

Received

10 June 2005

Accepted

13 July 2005

Correspondence

Dr Louisa Walsh, MD, Clinical Drug Safety, AstraZeneca LP, 1800 Concord Pike, Wilmington, Delaware 19850–5437, USA. Tel.: +1 302–886–5380; Fax: +1 302–886–4320; E-mail: louisa.walsh@astrazeneca.com