

# STRATEGIES TO UNCOVER TROUBLESOME EMBEDDED ADVERSE EVENTS

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## Introduction

Understanding the complete safety profile of a drug is dependent upon postmarketing surveillance and spontaneous reports of adverse events (AEs) from both consumers and health care providers. These occur after the drug is approved and begins to be used by a broader population of patients than those studied in the clinical development program.<sup>1-3</sup> In 2009, the last full year for which data are available, the FDA reported receiving over 580,000 spontaneous AE reports from health care professionals and consumers. Fifty-five percent (55%) of these events were reported by health care providers and 47% by consumers. Ninety-four percent (94%) were reported to manufacturers or distributors who are required to report them to FDA. Of the cases reported to FDA, over 330,000 (67%) were serious and unlisted AE reports and, therefore, required a 15-day expedited report.<sup>4</sup>

The vast majority of these spontaneous AE reports are made via phone directly to the manufacturers and distributors of drug products. The most critical component of the report is the ability of the contact center agent to interact and communicate with the reporter effectively during the call to uncover the full story of the AE so that it can be evaluated for medical significance.

## Where are These Embedded Adverse Events (AEs)?

In reporting AEs, consumers and health care providers often do not differentiate an AE from a product complaint. Consumers often say, “I

have a complaint about Product X: it caused a headache whenever I took it.” The consumer is really reporting an AE rather than a complaint. Similarly, the underlying reason for a medical product inquiry can be the occurrence of an AE: the health care provider may ask, “Does Product X cause headaches?” In this case, the health care provider may be asking the question relative to a patient who is experiencing the headache while taking Product X. In both of these cases, the AE is embedded within either the product complaint or the medical inquiry and must be uncovered during the conversation with the reporter in order to be documented and reported as required.

In a sampling of cases reported through a contact center, over 7,600 contacts from consumers and health care providers were made to manufacturers and distributors of various mature pharmaceutical products in several different therapeutic categories.<sup>5</sup> These

contacts generated 3,690 medical inquiries (MI), 748 AE reports and 3,697 product complaint reports (PC). In this sample, 486 (6.4%) of the cases included some combination of reasons for the contact (See Tables 1 and 2).

Of the total 748 AE reports, 415 (56%) were reported with either a MI (25%) or PC (26%) or, in 34 cases (5%) both an MI and PC. Only 333 (44%) of the AE reports gave the AE as the only reason for contact (See Figure 1). In these combination cases, discussion with the reporter uncovered the embedded AE which was, in many cases, the stimulus for the contact. Of these embedded AE reports, 10 (2.4%) were serious AEs: 7 within an MI and 3 within a PC. Of the 10 serious AE reports, 8 were received from consumers and 2 from physicians. Four of the 10 were assessed as serious and unexpected and, therefore, required a 15-day expedited report.<sup>6</sup> All 4 were reported by consumers.

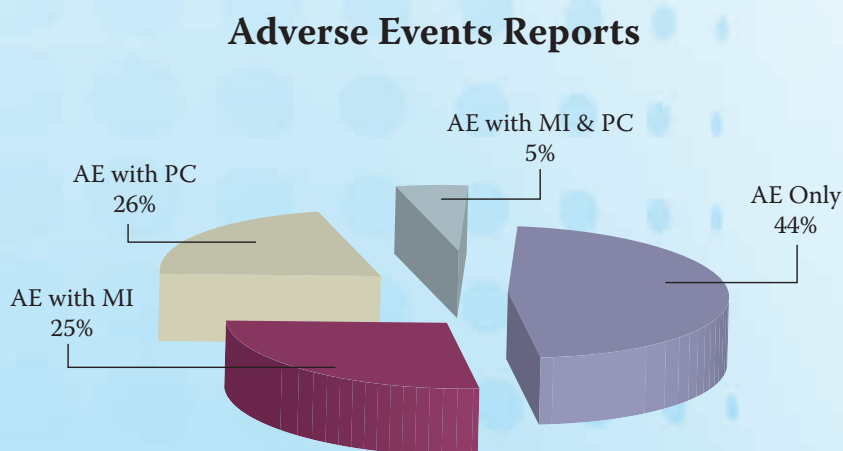
Table 1 - Contact Center Summary

Contact Center Cases	N	%
Case Contacts	7615	
Contact Reasons		
Medical Inquiry (MI) Only	3400	44.6
Product Complaint (PC) Only	3396	44.6
Adverse Event (AE) Only	333	4.4
Cases with Multiple Reasons	486	6.4
Total	7615	100.0

**Table 2 - Embedded Combination Cases**

Cases with Multiple Reasons	N	%
AE with PC	196	40.3
AE with MI	185	38.1
MI with PC	71	14.6
AE with PC and MI	34	7.0
Total	486	100.0

**Figure 1 - Adverse Event Reports**



While the number of product complaints reported in combination with either an AE or MI is fewer than those for AEs, overall 8% of the PCs were reported in combinations. In this series of cases, 88% (172 of 196 AE-PC combination cases) were lack of drug effect reports typically characterized as lack of efficacy by consumers.

Uncovering embedded product quality complaints is also critically important since complaints alleged to include mislabeling; product contamination; significant chemical, physical or other change in the distributed drug product or any

failure of distributed product to meet its specifications are potentially reportable to FDA by the manufacturer within 3 working days as an NDA – Field Alert Report.<sup>7</sup> None of the PCs in this series were NDA – Field Alert reports.

**Strategies to Uncover Embedded Adverse Events**

Timely recognition and identification of embedded AE and product complaint reports become very important since both are related to the safe use of the drug product and are subject to regulatory reporting. The ability to uncover or identify either the AE or PC which

is embedded with another type of case should be focused on the staff member who receives the initial contact and on procedures for review and processing of cases.

**Contact Center Agents**

Contact center agents (CC-Agents) who receive the initial contact from inquirers/reporters must be educated and trained to identify and process all types of cases. Registered nurses are well prepared through their clinical training to interview patients using a friendly, supportive and investigative style to elicit and document a complete medical history. Nurses learn to communicate with patients helping them to feel comfortable and, therefore, willing to share both solicited and unsolicited information. These skills and techniques are readily transferable from the health care setting to telephone interactions with patients who may be anxious and reluctant to share information with a person that they do not know.

Nurses are also trained during their clinical experience to communicate with a wide variety of health care providers consequently serving as patient advocates and liaisons between the patient and health care provider. These skills are also readily transferable to interviewing health care providers who are reporting an adverse event during the initial contact as well as initiating follow-up interactions with health care providers.

Contact center agents must also learn the regulations and procedures required for definition, documentation, processing and reporting of AEs and PCs. The combination of comprehensive interviewing of the reporter, excellent communication skills with both patients and health

care providers and a thorough understanding of AEs and PCs provides an ideal CC-Agent. These individuals are not only capable of uncovering an embedded AE or PC during the initial contact but, at the same time, they obtain all available information required for processing the reported events during the initial call. As a result, the need for follow up with either patients or health care providers is minimized and efficiency of case processing improved. While nurses are not the only health care professionals who can serve as CC-Agents, their unique combination of skills makes them ideal candidates for these positions.

### Case Processing Procedures

Procedures should also be designed to ensure data quality, review each case for an embedded AE or PC, and maximize processing efficiency. Documentation of all available case information for each AE and/or PC during the initial call by one CC-Agent minimizes loss of information due to transfer of calls. Likewise, if the caller is transferred to a different agent for each type of report, the repetition of information increases the potential for discrepancies. Data capture in one electronic system that can be accessed by each group responsible for processing different types of cases further reduces the potential for error. Documentation of all available data for the entire case during the initial call minimizes the need for follow up, minimizes inconvenience to the reporter and improves efficiency of case processing.

Following receipt, documentation and data entry of case information, each case should be reviewed for an embedded AE or PC report. Peer review of case data including the AE and/or PC narrative is one very effective way to accomplish this and minimize the potential of overlooking the embedded event.

This review should be timely in order to accommodate the strict reporting requirements for both AEs and Alert PCs required by the regulations. Training opportunities exist for the entire CC-Agent staff when the embedded AE or PC is not identified during documentation but is subsequently identified through peer review.

### Table 3 - Strategies to Uncover Embedded Adverse Events Conclusion

#### Contact Center Agents

- Clinical experience interviewing patients
- Experience communicating with health care professionals
- Regulatory training for AE and product complaint reporting

#### Case Processing

- All case information received and documented by one CC-Agent
- Data captured in one electronic system accessible by all groups
- Timely peer review of case data for embedded AE and/or PC

Adverse event and product complaint reports are often embedded within a case contact initially placed for a different reason. Since reports of both AEs and PCs are related to the safe use of pharmaceutical products, it is critical that embedded AEs and PCs be uncovered, documented and processed in a timely way so that regulatory reporting obligations are met. An experienced, well trained contact center staff and processing procedures designed to uncover

these event are necessary to assure compliance with the regulations.

### References

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