

Reporting Adverse Events and Market Research

AE Reporting by MR – A New Responsibility?

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Adverse Events Are Increasingly Important

- Today, we live in an environment where the focus on the safety of a drug sometimes seems to generate more interest than its benefits
- There is increased attention to the safety of medications in both the pre- and post-marketing phases
- Compulsory reporting of adverse events applies to market research vendors who are agents of the manufacturers

AEs are a Serious Medical Problem

- Annual deaths in UK: 20,000; in US: 100,000 estimated
- Adverse Drug Reactions are the 4th leading cause of death in US, ahead of pulmonary disease, diabetes, AIDs, accidents and automobile deaths
- 6,000 to 8,000 patients hospitalized *daily* in the UK because of ADRs
- Why so many?
 - Two-thirds of doctor visits result in prescriptions
 - ADRs increase exponentially with four or more medications
 - OTC and herbal medicines are significant contributors to ADR risk

AEs Present Serious Legal and Financial Problems Too

- Product issues
 - Vioxx withdrawn voluntarily; Bextra at FDA request
 - Accutane and malformation and suicides
 - Crestor and muscle damage; Lipobay/Baychol withdrawn
 - Rezulin, Redux, Raplon, Lotronex
- Litigation costs
 - One drug withdrawal has resulted in
 - \$1 billion jury award for a single product-related death
 - \$5 billion class action settlement
 - \$17 million set aside for litigation reserves
- Ethical image of pharmaceutical manufacturers is compromised in minds of consumers

What are Current Standards for Reporting AEs?

- The two main pillars of pharmacovigilance are
 - Voluntary reporting (from health professionals and consumers in some places)
 - Mandatory reporting from manufacturers and distributors of pharmaceutical products

Legal Obligation

- Under European and UK Regulations/Legislation, any company that markets a drug must have a system in place to collect and evaluate all information about Adverse Events which can be rapidly evaluated
- There are very strict timelines for reporting Adverse Events to the Regulatory Authorities. The Clinical/Drug Safety Department at each Pharmaceutical Company is tasked with assessing, databasing, following up and reporting such events within this strict timeline.
- If the company does not comply with the regulatory requirements, the Regulatory Authorities may impose penalties. This may be in the form of a warning or a formal caution. However, the Authorities also have the power to take criminal proceedings against the responsible Drug Safety Officer which can result in imprisonment.

Definitions

- Serious AEs* include:
 - Death
 - Life-threatening
 - Hospitalization – initial or prolonged
 - Disability
 - Congenital anomaly
 - Required intervention to prevent permanent damage/impairment

* For further definitions of AEs see MedRA (the Medical Dictionary for Regulatory Activities); also the WHO-ART (WHO) and COSTART (FDA) but MedRA is replacing them

Expanding Definition of Adverse Event

- In spirit of 'risk-sharing' some pharmaceutical companies (based on legal and regulatory staff advice) want reports from market research on **anything** that might even be construed as an adverse event
- “Untoward medical occurrence in a patient administered a pharmaceutical product that does not necessarily have a causal relationship with treatment. An adverse event (experience) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product”
- This includes lack of efficacy and already known side-effects

Components of an AE report

- A safety report is not complete unless it contains these four data elements:
 - An identifiable patient(s)
 - How specific?
 - An identifiable reporter
 - Can we identify respondent?
 - A suspect drug or biological product
 - An adverse event
 - Is the report about an AE - adverse event or an ADR - adverse drug reaction?
 - labeled AE or only non-labeled/non-expected AE?

Evolution of Responsibility in AE Reporting

- Increasing concerns from pharmaceutical manufacturers and from regulatory agencies
- Expanded definition of comprehensiveness in reporting by pharmacovigilance departments
- Responsibilities of pharmacos extend to all employees and all persons acting as “agents” of the pharmacos



No clear *common* path for Market Research professionals YET

The Industry Reaction

We need to report because . . .

The law clearly mandates the industry to report adverse events; and vendors, when contracted by the industry, become an extension of the pharmaceutical company for whom they are working.

**(Head of Market Research,
Industry)**

New contract language . . .

Provider shall not initiate or participate in any communication with the FDA concerning AEs unless required by law or requested to do so by the Company . . . (possible contract language)

Supplier and employees of Supplier shall report all Adverse Drug Experiences related to company products . . . within 24 hours of receipt of such Adverse Drug Experience using the attached form . . . (possible contract language)

But there are concerns . . .

My personal opinion is that reporting adverse events that may come up via marketing research is potentially a violation of respondent confidentiality. It further would create so much additional work on the part of vendors that some studies may become too expensive to conduct.

I personally feel that it would be both highly inappropriate and harmful to create that precedent. Researchers are not clinicians, nor are they all medically knowledgeable enough to accurately collect and report that kind of information to the FDA, or even back to the hiring company. There is a formal channel for reporting those kinds of events through pharmacists and physicians, and creating an informal approach through market research channels is wrong-headed and ill-advised (not to mention a bad idea!)

Clarifying Chaos
*What Do Professional
Organizations Say?*

Yes, we should . . .

ESOMAR and EphMRA language

When a marketing research project includes the actual usage by a respondent of active substance or any other medication or medical application which might cause an allergenic or other undesirable effect it must be carried out according to GCP (Good Clinical Practice) guidelines.

- How clear is this language?
 - It does not specify who is the one who administers the substance (the researcher?)
 - However, language can be interpreted as including a market research situation in where a researcher does not administer a drug but asks the respondent – patient or MD – about actual use of a medication

National Associations differ:

US

CASRO language

Research Company shall be deemed to have fully complied with the adverse drug effects reporting requirement of the Agreement if it uses reasonable commercial efforts to suggest to survey respondents who may have experienced an adverse drug effect to report same to their physicians, to the manufacturer of the drug with which such event is associated or to the FDA.

Research Company shall have no liability with respect to any failure to report or misreporting of any adverse event.

- The view of CASRO's Pharma Taskforce is that market research companies cannot really assume responsibility or liability for adverse event reporting because vendors are not equipped to do it effectively
- The thrust is on encouraging respondents to report adverse events if they think they may have occurred

National Associations differ: Europe

“Adverse Events reporting would contradict to the professional principles and rules of market and social research which requires that anonymity must always be safeguarded and that any research activities must clearly be separated from any other activities....research agencies are obliged, as part of their general social responsibility –to remind the respondents (especially physicians) at the end of the interview on their duties regarding adverse event reporting”

“This is not for debate [should or shouldn't we report) . . . Pharma companies need to provide training to agencies and brief the full market research team on how to report” (recommendation made during Adverse Event Reporting presentation at the latest BHBIA meeting, April, 2006)

- German position similar to the one proposed by CASRO in US as expressed by Director General for the ADM and President of EFAMRO in a communication to EphMRA
- The UK, in contrast, BHBIA (British Health Care Business Intelligence Association) already debating guidelines on how to report and no longer on “should we report”

What are the concerns?

- A question of privacy and confidentiality
- A question of disrupting the natural flow of research/adding burden to the research
- A question of threatening the relationship of market researcher and respondent
- A question of “know-how”
- A question of liability and indemnity
- Will “Good Samaritan” law apply to us?
- What about secondary data?

*But while we are pondering how
to proceed . . .*

The train is speeding down the
track!



Join us at the AE
Workshops for further
discussion!