

Safety and Setting Standards

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In this issue of the ACRP *Monitor*, three articles have been selected as the basis for a Home Study test that contains 30 questions. For your convenience, the articles and questions are provided in print as well as online (members only) in the form of a PDF (requires Adobe Reader and text file). This activity is anticipated to take three hours.

Answers must be submitted using the electronic answer form online (members only, \$32). Those who answer 70% of the questions correctly will receive an electronic statement of credit by e-mail within 24 hours. Those who do not pass can retake the test for no additional fee.

Hardware/Software Requirements: Home Study tests require version 4.x browsers or higher from Internet Explorer, Mozilla Firefox, or Safari. A browser that can run Adobe Flash 9.0 is required to view the digital edition of *The Monitor*, and Adobe Acrobat is required to view PDFs of the Home Study test.

The **April 2011 *Monitor* Home Study** is based on the following three articles in this issue:

- 1. The New FDA Final Rule on IND Safety Reporting: Implications for Clinical Development Programs**
Sally Van Doren, PharmD, President and Chief Executive Officer, BioSoteria, Inc. | James Buchanan, PharmD, Senior Vice President for Pharmacovigilance and Risk Management, BioSoteria, Inc., and faculty member at University of California, San Francisco, School of Pharmacy and Berkeley Extension, and Touro College of Pharmacy
- 2. The Changing European Regulation: Starting with Postmarketing Pharmacovigilance**
Irene Fermont, MD, MSc, Vice President for Pharmacovigilance and Risk Management, Advanced Drug Development Services (ADDS) | Evelyne Lacabaratz, MSc, Safety Officer, ADDS | Caroline Pastor, MSc, Pharmacovigilance Operations Manager, ADDS | Michel Levy, MD, MSc, IEP INSEAD, President and Chief Executive Officer, ADDS | Aurore Andre, MA, MBA, Strategic and International Business Manager, ADDS
- 3. Integrated Case Management to Improve the Quality of Spontaneous Adverse Drug Reaction Reports**
Carole DeRoche, President, DDN Medical Affairs

HOME STUDY LEARNING OBJECTIVES

At the conclusion of this course, participants should be able to:

1. identify what types of safety data need to be reported to the FDA and under what conditions and timeframe during the conduct of an Investigational New Drug (IND) clinical trial.
2. discuss the European Regulation changes and identify impacts on postmarketing pharmacovigilance.
3. describe the importance of spontaneous ADR reports, explain their limitations, and list potential advantages of integrated case management to improve their quality.

This test expires on APRIL 30, 2012

(original release date: 04/01/2011)

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The Association of Clinical Research Professionals (ACRP) is an approved provider of medical, nursing, and clinical research continuing education credits.



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The Association of Clinical Research Professionals (ACRP) provides 3.0 contact hours for the completion of this educational activity. These contact hours can be used to meet the certifications maintenance requirement. (ACRP-2011-HMS-004)



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QUESTIONS 1–10 The New FDA Final Rule on IND Safety Reporting: Implications for Clinical Development Programs

1 The sponsor is required to expeditiously report any findings that suggest a significant risk in humans exposed to the drug arising from:

1. epidemiological studies.
2. market penetration studies.
3. any clinical studies being conducted.
4. pooled analyses of multiple clinical studies.

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

2 For significant risks arising from epidemiological studies, the 15-day reporting clock begins the day that the:

- A. principal investigator learns of the adverse event.
- B. clinical study report in which the finding is identified is finalized.
- C. safety department completes its review of the data.
- D. sponsor determines a finding suggests a significant risk in humans.

3 A clinically important increase in the rate of a serious suspected adverse reaction (SSAR) is subject to expedited reporting when it exceeds the rate listed in the:

1. protocol.
2. investigator's brochure.
3. clinical study report.
4. product labeling.

- A. 1 and 2 only
B. 1 and 4 only
C. 2 and 3 only
D. 3 and 4 only

4 An event can be determined to be "serious" based on assessment by the:

1. subject.
2. investigator.
3. sponsor.
4. caregiver.

- A. 1 and 2 only
B. 1 and 4 only
C. 2 and 3 only
D. 3 and 4 only

5 Sponsors of bioavailability and bioequivalence studies are:

- A. exempt from reporting serious adverse events to FDA.
- B. required to report all serious adverse events to FDA if the study is conducted under an IND.
- C. required to report all serious adverse events to FDA if the study is conducted outside the U.S. without an IND.
- D. required to report only suspected unexpected serious adverse reactions to FDA.

6 Adverse event expectedness is based on the section of the reference safety information (e.g., investigator's brochure) that lists:

- A. adverse events for which a causal relationship with the study drug is suspected or confirmed.
- B. all adverse events having been observed in clinical trials with the study drug.
- C. adverse events having been observed in products in the same drug class but not observed with the sponsor study drug.
- D. the events associated with the underlying disease under study.

7 For all IND safety reports from blinded studies, the study sponsor should:

- A. keep treatment assignment blinded for FDA submission but unblinded for IRBs and ethics committees.
- B. keep treatment assignment blinded for FDA submission.
- C. unblind subject treatment assignment prior to FDA submission unless an alternative reporting format is approved by FDA in advance.
- D. unblind subject treatment assignment and report even if subject was assigned placebo.

8 IND safety reports can be submitted to FDA using:

1. MedWatch Form 3500A for U.S. cases.
2. narrative format for U.S. cases.
3. CIOMS I Form for U.S. cases.
4. CIOMS I Form for non-U.S. cases.

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

9 Specific disease-related events that are study endpoints (e.g., mortality and major morbidity):

- A. must always be reported by the investigator as serious adverse events, regardless of causality and expectedness.
- B. can be written into the protocol as excluded from expedited safety reporting even if the event is unexpected and related to the study drug.
- C. can be considered expected for determination of expectedness of adverse events.
- D. can be written into the protocol as excluded from expedited safety reporting.

10 IND annual reports:

- A. can be submitted to FDA in the Developmental Safety Update Report (DSUR) format, but this is not mandated by FDA.
- B. should be submitted quarterly for the first year after IND submission, then annually thereafter.
- C. are mandated by FDA to be submitted in the DSUR format starting in the year 2012.
- D. should be submitted annually for the first two years after IND submission, then every three years thereafter.

QUESTIONS 11–20 The Changing European Regulation: Starting with Postmarketing Pharmacovigilance

11 According to WHO, pharmacovigilance (PV) activities include:

1. detection of adverse effects.
2. assessment of adverse effects.
3. identification of postmarketing issues only.
4. prevention of adverse effects.

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

12 The EU launched a review of PV regulation because of the:

1. growing number of EU Member States.
2. need to collaborate with the U.S. and follow FDA regulation.
3. new classes of products with complex safety profiles.
4. harmonization of local EU regulation.

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

13 New responsibilities of EU PV include:

1. swift exchange of safety issues between Member States.
2. each Member State keeps its own database.
3. developing a quality system to ensure compliance.
4. maintaining private inspection reports without dissemination to EMA.

- A. 1 and 2 only
B. 1 and 3 only
C. 2 and 4 only
D. 3 and 4 only

CORRECTIONS

Corrections to Home Studies can be found on the ACRP website and are incorporated directly into the online test.

14 PRAC is best described as a:

1. committee working with sponsors on PV quality compliance.
 2. consortium of PV health professionals and patients from each Member State.
 3. unique, centralized European body in charge of PV and risk assessment.
 4. group whose decisions apply equally across all Member States.
- A. 1 and 2 only
B. 1 and 3 only
C. 2 and 4 only
D. 3 and 4 only

15 The Periodic Safety Update Report (PSUR) will be:

1. submitted via EudraVigilance.
 2. assessed by PRAC only.
 3. reviewed by each Member State separately.
 4. harmonized in reference to the first commercialization in Europe.
- A. 1 and 2 only
B. 1 and 3 only
C. 2 and 4 only
D. 3 and 4 only

16 Actions to increase transparency include:

1. developing a safety web portal in all EU languages on EudraVigilance.
 2. diffusing simplified reports for the public.
 3. publishing PRAC meeting minutes.
 4. identifying products withdrawn from market with black symbol.
- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

17 Adverse reactions (post-marketing) are to be immediately reported for all

1. adverse reactions within or outside EU.
 2. nonserious and serious cases within EU.
 3. serious cases in countries outside EU.
 4. nonserious cases outside EU.
- A. 1 and 3 only
B. 1 and 4 only
C. 2 and 3 only
D. 2 and 4 only

18 Changes to simplify adverse reaction reporting include:

1. healthcare professionals and patients report directly on EU web portal.
 2. forms for patient use made easier.
 3. patient reporting done only electronically.
 4. reporting medication errors and off-label uses in the same way.
- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

19 A risk management system requires:

1. development of risk management plan only for “old products.”
 2. proactive surveillance with risk minimization activities.
 3. post-authorization studies on safety and efficacy.
 4. PSUR for postmarketing data only.
- A. 1 and 2 only
B. 1 and 3 only
C. 2 and 3 only
D. 3 and 4 only

20 Which keywords can be used to describe this new regulation and directive?

1. Reporting reduction
 2. Harmonization
 3. Transparency
 4. Benefit/risk assessment
- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

QUESTIONS 21–30 Integrated Case Management to Improve the Quality of Spontaneous Adverse Drug Reaction Reports

21 Spontaneous adverse drug reaction reports:

1. received by manufacturers and distributors must be documented.
 2. are accepted as basis for postapproval drug safety surveillance.
 3. have been decreasing over the past decade due to better safety surveillance.
 4. provide information about rare and unknown adverse drug reactions.
- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

22 In 2009, the total number of spontaneous adverse drug reaction (ADR) reports from healthcare professionals and consumers to FDA was approximately:

- A. 300,000.
B. 400,000.
C. 500,000.
D. 600,000.

23 Since 2000, the number of reports to FDA for serious, unexpected ADRs has increased by:

- A. 118%.
B. 248%.
C. 262%.
D. 300%.

24 Healthcare professionals are more likely to report:

- A. all ADRs that they observe.
B. nonserious and unknown ADRs.
C. nonserious and known ADRs.
D. serious ADRs.

25 Major concerns regarding ADR reports from consumers include:

- A. the ability to identify and describe the ADR.
B. the knowledge to determine the drug related to the ADR.
C. considering all ADRs to be serious events.
D. providing too much extraneous information about the ADR.

26 One major limitation of spontaneous ADR reports is that:

- A. too many ADRs are reported to manufacturers.
B. regulators do not consider spontaneous ADR reports important.
C. the data reported are often of poor quality.
D. the number of ADR reports increases each year.

27 Data collected on initial contact with reporter include:

1. patient demographics, suspected drug dosage, and ADR description.
 2. medical history and concomitant medications.
 3. consumer request for permission to contact HCP.
 4. description of side effects experienced with other drugs.
- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

28 Spontaneous reports of ADRs are:

- A. always reported specifically as an ADR.
B. rarely submitted by the prescribing HCP.
C. often embedded within an MI and/or PQC.
D. seldom made for serious ADRs.

29 One example of an ADR that may require investigation as a PQC by the manufacturer is:

- A. lack of drug effect.
B. drug administration error.
C. overdose.
D. angina pectoris.

30 Advantages of integrated case management may include:

1. higher quality ADR data from the reporter.
 2. lengthy complex case reconciliation processes.
 3. reduction in IT redundancy and costs.
 4. lower staff productivity, flexibility, and satisfaction.
- A. 1 and 2 only
B. 1 and 3 only
C. 2 and 4 only
D. 3 and 4 only