

Vigilance



Post Marketing Surveillance defined, Annexes II, IV, V, and VI Section 3, and Annex VII, Section 4

- “systematic procedure to review experience gained from devices in the post-production phase **including the provisions referred to in Annex X***, and to implement appropriate means to apply any necessary corrective action.” “...obligation for the manufacturer to notify the competent authorities of the following incidents immediately on learning of them:
 - (i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;
 - (ii) any technical or medical reason connected with the characteristics or performance of a device for the reasons referred to in subparagraph (i) above leading to a systematic recall of devices of the same type by the manufacturer.”
- ***Directive 2007/47/EC**



Post Marketing Surveillance defined, Annexes III Section 5

- “systematic procedure to review experience gained from devices in the post-production phase , and to implement appropriate means to apply any necessary corrective action.”
“...notify the competent authorities of the following incidents immediately on learning of them:
- (i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient or user or other persons or to a serious deterioration in his or their state of health;
- (ii) any technical or medical reason connected with the characteristics or performance of a device for the reasons referred to in subparagraph (i) leading to a systematic recall of devices of the same type by the manufacturer.”



Incident? Reportable?

- Glass particles are found in a contact lens vial.
- An infusion pump is designed with an alarm. The infusion pump stops due to a malfunction of the pump, but fails to give the appropriate alarm. There is no patient injury.
- Batch of out of specification blood glucose test strips are released by the manufacturer. A patient uses the strips according to the manufacturer's instructions, but the readings provide incorrect values leading to incorrect insulin dosage, hypoglycemic shock, and hospitalization.



Incident? Reportable?

- X-ray vascular system during patient examination, the C arm uncontrolled motion. The patient was hit by the image intensifier and the patient's nose broken. The system was installed, maintained, and used according to the manufacturer's instructions.
- Stability tests of a CRP test, the internal QC found that after several months of storage, the test yielded false increased values with neonatal samples. This could lead to a wrong diagnosis of the existence of inflammatory illness and wrong treatment of the patient.



The MEDDEV addressing Vigilance has been adopted!

- MEDDEV 2-12.1 rev 5 (April 2007) replaces rev 4 issued in 2001
- Clarifies reporting requirements and enacts more stringent timeline requirements, inter-CA communication
- Discusses content of the European database (EUDAMED)
- In force as of January 1, 2008



Interesting Features of MEDDEV 2-12.1 Rev 5

- 56 pages - biggest MEDDEV to date
- Complicated, multi-interpretative, but closer to MDR & GHTF than Rev 4
- FIELD SAFETY CORRECTIVE ACTION (FSCA), FIELD SAFETY NOTICE (FSN), USE ERROR and ABNORMAL USE are new concepts introduced in this revision
- RECALL and ADVISORY NOTICE terms deleted
- EUDAMED makes its introduction



Organization of MEDDEV 2.12.1 Rev 5

- Table of Contents
- Section 3, SCOPE
- Section 4, DEFINITIONS
- Sections 5-9, Role and responsibilities of stakeholder groups: Manufacturers, National Competent Authority, Notified Bodies, the Commission, and Users.
- Annexes 1-9



Section 4, DEFINITIONS (4.1-4.21)

- ✓ Abnormal Use (4.1):" Act or omission of an act by the OPERATOR or USER of a MEDICAL DEVICE as a result of conduct which is beyond any means of risk control by the MANUFACTURER. "

Abnormal use is **not reportable** under this MEDDEV (5.1.5.3)



Definitions, continued

- ✓ Field Safety Corrective Action (4.6) includes Recall, Retrofit, etc.
- ✓ Field Safety Notice (4.7) Dear Doctor Letter, etc.
- ✓ Immediately (4.9) "...without any delay that could not be justified. "
- ✓ Indirect Harm (4.11)



Definitions, continued

- ✓ Periodic Summary Reporting (4.16)
- ✓ Serious Public Health Threat (4.17)
- ✓ Trend Reporting (4.18)
- ✓ Unanticipated (4.19) “A deterioration in state of health is considered UNANTICIPATED if the condition leading to the event was not considered in a risk analysis.”



Definitions, Continued

- ✓ Use Error(4.20) “Act or omission of an act, that has a different result to that intended by the MANUFACTURER or expected by the OPERATOR of the MEDICAL DEVICE. ”

User error reporting is mandated, if it led to death or serious deterioration in health (5.1.5.1)



Event or Incident, both or none?

- The term “Near Incident” is deleted, “Events” and “Incidents” are introduced.
- All Incidents **are** Events, but **not all Events are Incidents!**
- Events may be malfunction, mislabeling or labeling deficiency, degradation, etc.
- Whether an “event” is an “incident”, must be determined quickly (5.1.1)



Criteria A-C (5.1.1, Criteria for Incidents to be reported by Manufacturers to Competent Authorities)

- A. An event has occurred
 - B. The manufacturer's device is suspected to be a contributory cause of the INCIDENT
 - C. The event led, or might have led, to... death or a serious deterioration in health
- Any event which meets criteria A-C in 5.1.1 is considered an Incident and must be reported!



A. An event has occurred

- Malfunction or deterioration
- False positive or false negative
- Unanticipated adverse reaction or side effect
- Interactions with other substances or products
- Degradation/destruction of the device
- Inappropriate therapy
- Inaccuracy labeling



B. The manufacturer's device is suspected to be a contributory cause of the INCIDENT

- Health care professionals' opinions
- Manufacturer's preliminary assessment
- Evidence of other INCIDENTS
- Other evidence



C. The event led, or might have led, to one of the following outcomes:

- Death of a patient, USER or other person
- Serious deterioration in state of health of a patient, USER or other person

Examples of Serious deterioration state of health: life-threatening illness, permanent impairment body function, condition necessitates medical intervention, indirect harm, fetal distress.



New Timelines

- Under Rev 5, if an Event is an Incident, it should be reported “immediately”
- Supposedly one has time to investigate **IF** reporting is justified, however.....
- Not every Event can be assessed for reportability immediately.
- Report to National Competent Authority in the country of occurrence of the INCIDENT, unless specified differently



Reporting timeline differences between old MEDDEV and the Directive

- Rev 4 requires Incidents to be reported within 10 (Incident) or 30 (Near Incident) days
- National laws vary from 2, 5, 10, 15 and 30 days, or “as soon as possible” (France)
- All were somewhat incorrect since MDD states one needs to report “immediately.”
- See Annex II (3.1) , IV (3), V (3.1)
- **MEDDEV 2.12-1 rev 5 harmonizes this**



5.1.7, Timescale of Initial reporting of an Incident

- Serious public health threat: IMMEDIATELY, but not later than 2 calendar days
- Death or UNANTICIPATED serious deterioration in state of health: IMMEDIATELY, not later than 10 calendar days
- Others: IMMEDIATELY, not later than 30 calendar days



INCIDENT REPORT (5.1.6, Annex 3)

- Report submitter: manufacturer, Authorized Representative, other.
- One form for initial, follow-up, and final.
- Electronic submission is encouraged.
- May include statement that report is “made by the manufacturer without prejudice and does not imply any admission of liability for the INCIDENT or its consequences.”



Field Safety Corrective Action (5.4.4)

- In MEDDEV Rev 5, FSCA is synonymous with recall or withdrawal!
- Recall Notice is now replaced by the Field Safety Corrective Action (FSCA) report , FSCA Report Form is available in Annex 4
- If recall is ordered **outside** the EU, but product **is** sold in EU, the FSCA should be reported to the CA as a FSCA report
- Detailed notification process with defined list of recipients and contents – Annex 4



Field Safety Corrective Action (4.6)

- Action taken by a manufacturer
- Reduce risk of death or serious deterioration in the state of health
- Already placed on the market



- Through PMS or vigilance a manufacturer becomes aware of a limited number of reports of misuse of the device, serious clinical consequences were addressed in labeling and IFU. Manufacturer decides to send letter to all users reminding them of the correct use of the device but no changes to labeling or IFU are necessary.
- An IVD for detecting bacterial antigen in CSF is found to cross react with another bacterium which causes meningitis. This could result in the wrong antibiotics being administered.



- An IVD is shipped with a reagent missing. Users cannot run the test without it. The manufacturer exchanges distributed product for complete test kits.
- Manufacturer of a syringe pump identified small risk that pumps within a range of SN may not alarm if the syringe plunger clamp was left open, putting patients risk for over or under infusion. Manufacturer issued instructions on detecting and correcting the problem and checking the 'clamp open' detection mechanism during routine maintenance was added to the service manual.



Field Safety Notice (FSN) (5.4.4.2)

- Rev 5 “recommends” a FSN be submitted to the appropriate CA **48 hours prior** to release for comment
- Provides solution to sending it to only one country (wait and see....)
- Guideline spells out content of the FSN in Annex 5!



Exemptions from Reporting (5.1.3-5.1.5.3)

- Common & well-documented incidents (5.1.2.2)
- Deficient device prior to its use (5.1.3.1)
- Event caused by patient conditions (5.1.3.2)
- Service-life or shelf-life exceeded (5.1.3.3)



Exemptions from Reporting, continued

- Protection against fault functioned correctly (5.1.3.4)
- Negligible likelihood of occurrence of death or serious deterioration of state of health (5.1.3.6)
- Expected and foreseeable side effects (5.1.3.5)



Medical Device Expected and Foreseeable Side Effects

- Old rules exempted “side effects” from reporting
- Some manufacturers created long list of “side effects” so they would not have to report anything
- **Side effects now reportable** under certain conditions (still not obvious, but closer to MDR) (5.1.3.5)



Access to the Device and Analysis (5.3.2)

- Not taken for granted by the MEDDEV
- If manufacturer wants to perform destructive analysis, NCA should be pre-notified! Wait for 10 days following submission of Initial Incident Report
- Seems very cumbersome and in fact, may be counterproductive



Exemptions from Reporting, continued

IN SUMMARY: **always report** unless the event is known to the CA(s). Evidence has to be collected in case of doubt to support the decision not to report.



Responsibilities of the Manufacturer

- Manufacturer must notify relevant CA about Incident and FSCA
- Responsible for investigating incident and taking necessary corrective action
- Mfr must keep AR, CA, NB & Distributor informed of Incidents & FSCAs (3.3.1) as appropriate
- Where applicable, mfr must keep NB informed of post-production phase issues potentially impacting the Certification
- Specific obligations for discontinued or custom-made products



Responsibilities of the Authorized Representative

- AR or manufacturer shall notify relevant national CA of Incident and FSCA (3.1.1)
- May be designated as suitable contact point for purposes related to medical devices vigilance (5.1)
- May be notified by manufacturer of incidents and FSCA (5.1, 3.1.1)
- May report incidents (5.1.6)



Responsibilities of the Competent Authorities

- Detailed in section 6
- The CA should perform Risk Evaluation to allow definition of corrective actions
- Monitoring of corrective actions (6.2.3)
- Coordination between CAs (6.3)
- Dissemination of information between CAs (6.3.5)



Responsibilities of the Distributor

- Agreed practice and procedure between manufacturer and distributor
- Investigation or evaluation of incidents
- How and what information should be recorded
- How different parties are advised of the incident
- What testing or evaluation conducted
- Circulation of FSN



Competent Authority Guidances

- UK MHRA Directives Bulletin no. 3 Guidance on the operation of the EU vigilance system in the UK
- Irish Medicines Board GUIDANCE NOTE 7 - THE VIGILANCE SYSTEM FOR MEDICAL DEVICES, SUR-G0002-1, 1 November 2007
- Irish Medicines Board GUIDANCE NOTE 8 - FIELD SAFETY CORRECTIVE ACTIONS FOR MEDICAL DEVICES AND *IN-VITRO* DIAGNOSTIC MEDICAL DEVICES, SUR-G0001-1, 1 November 2007
- Irish Medicines Board GUIDANCE NOTE 13 - INCIDENT REPORTING FOR GENERAL MEDICAL DEVICES AND ACTIVE IMPLANTABLE MEDICAL DEVICES, SUR-G0003-1, 1 November 2007



Competent Authority Guidances

- Irish Medicines Board GUIDANCE NOTE 18 - INCIDENT REPORTING FOR GENERAL MEDICAL DEVICES AND ACTIVE IMPLANTABLE MEDICAL DEVICES, SUR-G0003-1, 1 November 2007
- Irish Medicines Board GUIDE TO ADVERSE INCIDENT REPORTING FOR *INVITRO* DIAGNOSTIC MEDICAL DEVICES, SUR-G0004-1, Guidance Note 18, 1 November 2007



- <http://www.mhra.gov.uk/Publications/Regulatoryguidance/Devices/DirectivesBulletins/CON2033888>
- http://www.imb.ie/images/uploaded/documents/GN07_SUR-G0002_TheVigilanceSystemForMedicalDevices.pdf
- http://www.imb.ie/images/uploaded/documents/GN08_SUR-G0001_FSCAForMedicalDevices&IVDs.pdf
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