Adverse Event Terminology and Coding Working Group

Sept 2017

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H. Ishikawa

Office of Standards and Guidelines Development
Pharmaceuticals and Medical Devices Agency
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Recent Meetings

• Apr 5th, 2017
  16th Teleconference
• June 13th – 16th, 2017
  4th Face to Face meeting in Ispra, Italy
• July 6th, 2017
  17th Teleconference

Coming Meetings

• Oct 11th, 2017
  18th Teleconference
• Nov 28th – Dec 1st, 2017
  5th Face to Face meeting in Moscow, Russia
What was the problem at device level?

Which components were involved

What were the probable causes of the problem

Cause Investigation (Annex B-D)

What adverse events happened at patient level

Patient Problem (Annex E)

Medical Device Problem (Annex A)

Component (Annex F)
Title: IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes

Main Body: published on April 10th in 2017

revised with the addition of Annexes B, C and D, and presented to MC as proposed final document (Edition 2)

Annex A (Medical Device Problem):
published with mapping on April 10th in 2017

Annex B – D (Cause Investigation):
presented to MC as proposed final document

Annex E (Patient Problem): under discussion

Annex F (Component): to be discussed after Annex E takes shape
Annex B-D: Cause Investigation Terms and Codes

- Based on FDA terms and ISO terms
- Consist of IMDRF codes, terms and definitions
- 3 annexes

Annex B: Type of Investigation (1 level)
(e.g., Testing of Actual/Suspected Device, Testing of Device from Same Lot/Batch, Trend Analysis)

Annex C: Investigation Findings (3 levels)
(e.g., Biological Problem Identified, Cytotoxicity Problem Identified, Microbial Contamination)

Annex D: Investigation Conclusion (2 levels)
(e.g., Cause Traced to Device Design, Cause Traced to Manufacturing, Quality Control Deficiency)
### Annex B: Type of Investigation

**Note:** Select as many terms as necessary/appropriate to characterise the investigation

**Device (bold):** For the purpose of this Annex B, a **device** means a medical device including accessories and components.

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testing of Actual / Suspected Device</td>
<td>The investigation employed relevant empirical testing of the actual <strong>device</strong> suspected in the reported adverse event in order to establish their functional and other properties and to identify possible causes for the adverse event. Relevant testing would typically be based on test methods used for evaluating safety and performance as described in the latest relevant standards.</td>
<td>B01</td>
</tr>
<tr>
<td>Testing of Device from Same Lot/ Batch Retained by Manufacturer</td>
<td>The investigation employed relevant empirical testing of the <strong>device</strong> of the same lot or batch than that of the suspected <strong>device</strong> in the reported adverse event in order to support the identification of possible causes for the adverse event. Testing was performed using the <strong>device</strong> retained by the manufacturer (i.e., was not shipped). Relevant testing would typically be based on test methods used for evaluating safety and performance as described in the latest relevant standards.</td>
<td>B02</td>
</tr>
<tr>
<td>Testing of Device from Same Lot/ Batch Returned from User</td>
<td>The investigation employed relevant empirical testing of the <strong>device</strong> of the same lot or batch than that of the suspected <strong>device</strong> in the reported adverse event in order to support the identification of possible causes for the adverse event. The <strong>device</strong> was returned from the user. Relevant testing would typically be based on test methods used for evaluating safety and performance as described in the latest relevant standards.</td>
<td>B03</td>
</tr>
<tr>
<td>Testing of Device from Other Lot/ Batch Retained by Manufacturer</td>
<td>The investigation employed relevant empirical testing of the <strong>device</strong> of another lot or batch than that of the suspected <strong>device</strong> in the reported adverse event in order to support the identification of possible causes for the adverse event. This includes <strong>devices</strong> without a lot/batch designation. Testing was performed using the <strong>device</strong> retained by the manufacturer (i.e., was not shipped). Relevant testing would typically be based on test methods used for evaluating safety and performance as described in the latest relevant standards.</td>
<td>B04</td>
</tr>
</tbody>
</table>
Annex C: Investigation Findings

### Annex C Investigation Findings ("what were the findings?")

**Device (bold):** For the purpose of this Annex C, a *device* means a medical device including accessories and components.

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biological Problem Identified</td>
<td>Problems relating to, caused by or affecting biological processes or living organisms.</td>
<td>C01</td>
</tr>
<tr>
<td>Biocompatibility Problem Identified</td>
<td>The device causes cellular or tissue responses that elicit an undesirable local or systemic effect in the recipient or beneficiary of that therapy. (See ISO 10993)</td>
<td>C0101</td>
</tr>
<tr>
<td>Biological Contamination</td>
<td>The undesirable presence of living organisms such as bacteria, fungi, or viruses or their products (enzymes or toxins).</td>
<td>C0102</td>
</tr>
<tr>
<td>Endotoxin Contamination</td>
<td>The undesirable presence of toxins associated with certain bacteria (e.g. gram negative bacteria).</td>
<td>C010201</td>
</tr>
<tr>
<td>Microbial Contamination</td>
<td>The undesirable presence of microorganisms or microbes such as bacteria and fungi (yeasts and molds).</td>
<td>C010202</td>
</tr>
<tr>
<td>Material or Material Leachate Pyrogenic Problem</td>
<td>The undesirable presence of pyrogens or fever-producing organisms caused by materials that permeate through the device.</td>
<td>C0103</td>
</tr>
<tr>
<td>Cytotoxicity Problem Identified</td>
<td>The device was found to have an undesirable level of toxicity to living cells.</td>
<td>C0104</td>
</tr>
<tr>
<td>Genotoxicity Problem Identified</td>
<td>The device’s ability to cause</td>
<td>C0105</td>
</tr>
<tr>
<td>Carcinogenic</td>
<td>The device’s ability to trigger</td>
<td>C010501</td>
</tr>
</tbody>
</table>
## Annex D: Investigation Conclusion

### Annex D: Investigation Conclusion ("why did the incident/adverse event occur?")

**Device (bold):** For the purpose of this Annex D, a **device** means a medical device including accessories and components.

<table>
<thead>
<tr>
<th>Level 1</th>
<th>Term</th>
<th>Definition</th>
<th>Code</th>
<th>Level 2</th>
<th>Term</th>
<th>Definition</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cause Traced to Device Design</td>
<td>Problems traced to the design specifications (e.g. in the requirements, testing processes, hazard analysis, implementation strategy).</td>
<td>D01</td>
<td></td>
<td>Design Inadequate for Purpose</td>
<td>Problems traced to design/design features of the device that do not support or interfere with the intended purpose of the device.</td>
<td>D0101</td>
</tr>
<tr>
<td></td>
<td>Human Factors Engineering - Device Difficult to Operate</td>
<td>Problems traced to inappropriate and/or inadequate assessment and engineering design of the device to accommodate how or where the device will be used.</td>
<td>D0102</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Human Factors Engineering - Device Difficult to Assemble</td>
<td>Problems traced to inadequate design of the component parts and/or assembly steps resulting in the device not being able to be assembled correctly.</td>
<td>D0103</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Human Factors Engineering - Device Difficult to Reprocess</td>
<td>Problems traced to inadequate design of the reprocessing steps and/or the device resulting in the device remaining unclean.</td>
<td>D0104</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Missing or Inadequate Safety Measures</td>
<td>Problems traced to inadequate design or complete lack of safety measures leading to device malfunction or unintended properties of the device including possible hazards for persons using the device.</td>
<td>D0105</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Design Change Validation Inadequate</td>
<td>Problems traced to inadequate or lack of validation of design changes of the device leading to malfunction or unintended properties of the device including possible hazards for persons using the device.</td>
<td>D0106</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cause Traced to Component Failure</td>
<td>Expected or random component failure without any design or manufacturing issue.</td>
<td>D02</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cause Traced to Manufacturing</td>
<td>A defect in the processes or systems used in the</td>
<td>D03</td>
<td>Manufacturing Deficiency</td>
<td>Problems traced to manufacturing process</td>
<td>D0301</td>
<td></td>
</tr>
</tbody>
</table>
Annex E: Patient Problem

- Based on FDA terms and refers to MedDRA
- Consists of IMDRF codes, terms and definitions
- JRC contributed the results of their own research on “the patient problem nomenclatures” at F2F in Ispra, and now organizing the structure of Annex E with mapping to MedDRA terms
- Communicating with MedDRA, SNOMED and ICD closely
Thank you!