Post Market Surveillance and Vigilance in Japan

Medical Device Safety Division,
Office of Safety I
Overview of Adverse Event Reporting

1. Reporting an event
   - Healthcare professionals / facilities
   - MAH (Marketing Authorization Holders)
     In 15 or 30 days (depending on seriousness and predictivity)

2. Investigation

3. Investigation

4. Adverse event report
   - PMDA

Manufacturer
Definition of Adverse Event

**Adverse event means unfavorable or harmful.**

1. Breakage, Malfunction, Poor Operating Performance, etc.

2. Defective Products

3. Problem with device specifications

4. Health Hazard related to use of the device

5. Inadequate Information on Package Inserts (IFU)

*Decided to be a cause of operational errors*

*Regardless of occurrence of health hazards*

*Regardless of occurrence of product problems*
Information included in Adverse Event Reporting

**Event description**
- What happened to the device
- What happened to the patient
- How the patient was treated after the event occurred

**Technical information**
- How the device was used
- Maintenance records
- Experience of the user
- Opinion of the user

**Patient information**
- Age, gender, weight
- Background
- Complications
- Medication/Treatments
- Clinical examination value
- Condition
- Patient outcome

**Device quality**
- Specification/Durability
- Manufacturing records

**Cause analysis**
- Device analysis results
- Simulation experiments
- Occurrence of similar events (trends)
- MAH’s conclusions

**Safety measures (as necessary)**
- Taken measures & Future plans
- Recall, Repair
- Written in package inserts/IFU
- Field safety notice
- Device modification
- Improvement of Training program

Information included in Adverse Event Reporting
Malfunction, failure, breakage, leak, fault, etc. of a medical device

<table>
<thead>
<tr>
<th>Possibility of Health Damage</th>
<th>Description in the package insert/IFU</th>
<th>Report’s due date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious Unknown (unanticipated)</td>
<td></td>
<td>30 days</td>
</tr>
<tr>
<td>Serious Known (anticipated)</td>
<td></td>
<td>15 days (Uncomprehended elevation of the incidence rate of AE)</td>
</tr>
<tr>
<td>Non-Serious Unknown</td>
<td></td>
<td>Annual reports</td>
</tr>
<tr>
<td>Non-Serious Known</td>
<td></td>
<td>—</td>
</tr>
</tbody>
</table>
### Adverse Event Report (2) - Foreign Case

- Malfunction, failure, breakage, leak, fault, etc. of a medical device

<table>
<thead>
<tr>
<th>Possibility of Health Damage</th>
<th>Description in the package insert/IFU</th>
<th>Report’s due date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious</td>
<td>Unknown (unanticipated)</td>
<td>30 days</td>
</tr>
<tr>
<td></td>
<td>Known (anticipated)</td>
<td>15 days (Uncomprehended elevation of the incidence rate of AE)</td>
</tr>
<tr>
<td>Non-Serious</td>
<td>Unknown</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Known</td>
<td>—</td>
</tr>
</tbody>
</table>
### Adverse Event Report (3) - Domestic Case

- **Health damage**
  (in case relation with the medical device cannot be denied)

<table>
<thead>
<tr>
<th>Health Damage</th>
<th>Description in the package insert/IFU</th>
<th>Report’s due date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serious</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>Known/Unknown</td>
<td>15 days</td>
</tr>
<tr>
<td>Except death</td>
<td>Unknown</td>
<td>15 days</td>
</tr>
<tr>
<td></td>
<td>Known</td>
<td>15 days (Uncomprehended elevation of the incidence rate of AE)</td>
</tr>
<tr>
<td><strong>Non-Serious</strong></td>
<td>Unknown</td>
<td>30 days (Except reports shown above)</td>
</tr>
<tr>
<td></td>
<td>Known</td>
<td>Annual report</td>
</tr>
</tbody>
</table>

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**Health Damage**:
- Death: Known/Unknown (15 days)
- Except death: Unknown (15 days)

**Report’s due date**:
- Known: 15 days (Uncomprehended elevation of the incidence rate of AE)
- Unknown: 30 days (Except reports shown above)
- Annual report

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**Notes**:
- Health damage
- Description in the package insert/IFU
- Report’s due date
<table>
<thead>
<tr>
<th>Health Damage</th>
<th>Description in the package insert/IFU</th>
<th>Report’s due date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serious</strong> Death</td>
<td>Unknown</td>
<td>15 days</td>
</tr>
<tr>
<td></td>
<td>Known</td>
<td>15 days (Uncomprehended elevation of the incidence rate of AE)</td>
</tr>
<tr>
<td></td>
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<td>Unknown</td>
<td>15 days</td>
</tr>
<tr>
<td></td>
<td>Known</td>
<td>15 days</td>
</tr>
<tr>
<td>Non-Serious</td>
<td>Unknown</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Known</td>
<td>—</td>
</tr>
</tbody>
</table>
### Other Reports

#### Adverse Infection Report

<table>
<thead>
<tr>
<th>Health Damage</th>
<th>Description in the package insert/IFU</th>
<th>Report's due date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Domestic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious</td>
<td>Unknown</td>
<td>15 days</td>
</tr>
<tr>
<td></td>
<td>Known</td>
<td>15 days</td>
</tr>
<tr>
<td>Non serious</td>
<td>Unknown</td>
<td>15 days</td>
</tr>
<tr>
<td></td>
<td>Known</td>
<td>—</td>
</tr>
<tr>
<td><strong>Foreign</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious</td>
<td>Unknown</td>
<td>15 days</td>
</tr>
<tr>
<td></td>
<td>Known</td>
<td>15 days</td>
</tr>
<tr>
<td>Non serious</td>
<td>Unknown</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Known</td>
<td>—</td>
</tr>
</tbody>
</table>

- **Study report**: Submitted within 30 days
- **Foreign Field Safety Corrective Action (FSCA) Report**: Submitted within 15 days
Overview of Adverse Event Reporting

1. Reporting an event

Healthcare professionals / facilities

2. Investigation

3. Investigation

MAH (Marketing Authorization Holders)

4. Adverse event report

5. Share information, Cooperation

Within 15 or 30 days (depending on seriousness and predictivity)

6. Consideration of safety measures

Manufacturer

Ministry of Health, Labour and Welfare (MHLW)
Collecting information

Manufacturer → MAH

Collecting information

Regulatory Agencies
- ANSM
- FDA
- BfArM
- MHRA
- EMA
- TGA

FSCA Report (within 15 days)

- Detailed information about the action taken in foreign countries
- Actions taken in Japan (recall, repair, provision of information, etc.)
Current Status

- Adverse Event Reporting is voluntary.
- Cases without adverse event is not reported.

Issues

- Certain information gathering is needed to take appropriate safety measures.
- Denominator of patient exposure in medical devices of interest is unknown.
Registry is:
A system constructed to manage patient data centrally and feedback its analysis to healthcare providers. (based on IMDRF Registry Working)

Information of all products of interest
Add registration in database to conditions for approval.

Information of all patients exposure
Add registration in database to conditions for use.

Database

Central management
Registry makes it possible to:

- Survey Long Period Use-Result.
- Calculate accurate incidence of Adverse Events.
- Conduct thorough monitoring and safety measures to medical devices which were approved under few clinical data.
Information gathering system of J-MACS

Hospital

Register adverse events

Database

E-mail

Information of adverse events

MAH

Adverse Event Report

(1) Death (in 15 days)
(2) Device malfunction (in 30 days)
(3) Infection (in 30 days)
(4) Nerve disorder (in 30 days)
(5) Massive bleeding (in 30 days)
(6) Other adverse event (periodic report)

Definitions of adverse events are harmonized not to cause differences in criteria in each hospital.
Disconnection of Transdermal Cable occurred frequently in Post-Market. The disconnection is a serious adverse event, because it causes an error on pump function.

http://duraheart.terumo.co.jp/medical/index.html
Bend Stress caused disconnection.

Improvement of the cable made 23 times stronger than the old model.

Application of Registry Data

- Registries
  - Hospital A
  - Hospital B
  - Hospital C
  - Clinical Record
  - Database
  - Patient Data

Application of Registry Data
- Marketing authorization
  - Re-examination
  - Historical control
- Publication
- Guidelines
Summary

- Post-Market safety measures are to restore unbalanced risk-benefit balance to a former condition.

- Safety measures are taken based on domestic and foreign safety information such as adverse event report, FSCA report, etc. reported by MAH.

- Registry makes it possible to take more appropriate and rational safety measures through more complete information gathering.

- Registry data is expected to apply not only to safety measures but also to reviews, studies, development of guidelines, etc.
Thank you for your attention!