IMDRF International Medical Device Regulators Forum

FINAL DOCUMENT

International Medical Device Regulators Forum

Title: Medical Devices: Post Market Surveillance: National Competent Authority Report (NCAR) Pilot Plan; Implementing Material

Authoring Group: NCAR Working Group

Date: 2 October 2015

Toshiyoshi Tominaga, IMDRF Chair

IMDRF International Medical Device Regulators Forum

IMDRF National Competent Authority Report (NCAR) Exchange Program

IMDRF/NCAR WG (PD1) N14

Introduction

- Background
- The IMDRF Exchange Program
    - Participation
    - Exchange Criteria
    - Confidentiality
    - NCAR Exchange Program Secretariat

PART I

Background

Objective of the Working Group

To review the GHTF NCAR Exchange Program and to advise on opportunities for improvement.

Action and Progress

- Members of the GHTF NCAR program were surveyed for the strengths and weaknesses of the GHTF system.

- Review of survey results and a plan for addressing issues was presented to the MC.

- A draft of a guideline outlining a new exchange was developed and presented to the Management Committee. IMDRF/NCAR WG (PD1) N14.

Action and Progress

- The N14 Document was subject to external consultation before being endorsed by the Management Committee (IMDRF 7 Tokyo March 2015).
- Implementation materials were developed.
- Training is ongoing.
- The GHTF NCAR Exchange Program ceases operation on September 30th 2015.
- Pilot Phase October 2015 – March 2016.
- Full implementation April 2016.

PART II

The New IMDRF NCAR Exchange Program

Participation

Participation in the IMDRF NCAR Exchange Program is limited to the IMDRF Management Committee (MC) Regulators.

Australia	**Europe**
Brazil	**Japan**
Canada	**Russia**
China	**United States of America**

Participation

European participation in the exchange will include those European Member States who have:

- Undergone the appropriate training; and
- Implemented appropriate confidentiality agreements.

Participation

Non-IMDRF Management Committee Regulators that are currently involved in the existing GHTF Exchange **will not be eligible** for participation in the IMDRF NCAR Exchange Program.

How to Join the IMDRF NCAR Exchange Program

What **Management Committee Members that participated in the GHTF** NCAR Exchange have to do to join the new exchange?

Participants will be **required** to:

1. assure that appropriate confidentiality arrangements are negotiated; and
2. receive the appropriate training.

Before joining the IMDRF NCAR Exchange Program.

How to Join the IMDRF NCAR Exchange Program

How can **Management Committee members not previously involved in the GHTF** NCAR Exchange join the new exchange?

IMDRF MC Regulators not previously involved in the Program **must**

- inform the IMDRF MC of their wish to do so by providing a written request
- and meet all criteria for participation.

Training for Participants

Training will include:

- Review of the implementation materials which outline the key elements of the exchange:
  - Definitions
  - The Exchange Criteria
  - The Exchange Format
  - Confidentiality
- Regional training / mentoring to become familiar with the implementation materials.

PART III

NCAR Exchange Criteria

Information can be found in document IMDRF/NCAR WG/N14 Final:2015 at http://www.imdrf.org/documents/documents.asp

The Current Exchange Criteria when using the NCAR Form

(Annex 1 of the N14 document)

- A NCAR is used to send information that another regulator may not already be aware of.

- One or more of the following three criteria must be used to determine whether it is appropriate to send information using a NCAR.

1. EVENTS LEADING OR HIGHLY LIKELY TO LEAD TO UNANTICIPATED SERIOUS PUBLIC HEALTH THREAT

1a) Unanticipated due to the following:

- The issue has not arisen before;
- An increase in the frequency of this issue;
- Change to the situation in which its occurring; and/or
- A change in the outcome of the issue

AND

1b) Serious Public Health Threat – on its own may not mean a NCAR is necessary (for example where the impacted batch or device is supplied to one hospital or health jurisdiction)

Seriousness is determined by:

- Technical or clinical assessment by the competent authority;
- The actual or potential impact to patients or others;
- Difficulty in recognizing the issues and how to prevent or mitigate them.

NCARs should not be used for advising of single incidents, unless those incidents have a clear implication for public health.

Serious Public Health Threat

- Any event type which results in imminent risk of death, serious injury or serious illness that requires prompt medical action.
- A serious injury is either:
  - A life threatening illness or injury,
  - A permanent impairment of a body function or permanent damage to a body structure,
  - A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

Examples of “Unanticipated Serious Public Health Threat”

- Reports of a serious eye infection potentially causing permanent damage to sight.
- The reports are for the same type of eye lubricant drops.
- Results of testing reveals that the eye drops have the same bacteria.
- Further investigation finds that the sterilization process was not checked and the handling procedures were not followed.
- The manufacturer makes large batches of this eye drop and has distributed the batch globally.

Unanticipated Serious Public Health Threat

- Reports of serious injuries and a death within 6 months of receiving a breast implant.
- Symptoms indicate that the patient is being poisoned by a substance used in the manufacture of silicone.
- The NCA conducts an unannounced inspection of a manufacturer of breast implants.
- The NCA finds that the implants are being manufactured with gel that has toxic properties.
- The manufacturer's paperwork and the NCA's investigation indicates that the gel has been used in only five batches.

- The NCA sends a notification to countries supplied with the five batches to alert them to this issue.

Unanticipated Serious Public Health Threat

- A heart valve with new antibacterial properties on the sewing cuff has been in the market for 2 years.
- Reports, sent to the NCA, of thrombosis have now risen above the expected rate. The number of serious injuries and deaths is also above equivalent device rates.
- The heart valves have been promoted widely and they have been supplied in many countries.
- The NCA's investigation indicates that the new antibacterial used in its manufacture may be the cause of the adverse events.

- The NCA decides to suspend supply to continue investigating.
- However, the NCA notifies other NCAs of the results of the investigation and action to date.

2. OBSERVATIONS FROM NATIONAL TREND ANALYSIS

A trend noticed by a NCA is circulated to other participating NCAs when:

- Increase in frequency of adverse events is
  - significantly higher than the manufacturer expected frequency; or
  - significantly higher than the frequency observed with similar devices

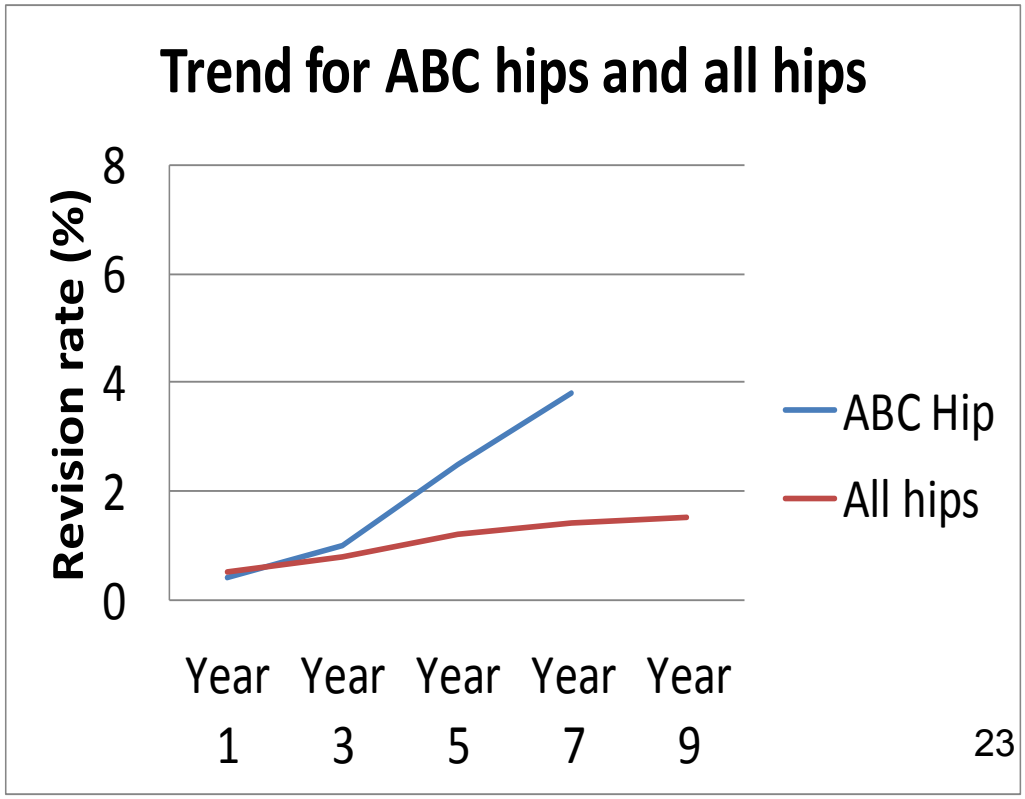
AND

- The adverse events are likely or highly likely to lead to a serious public health threat.

Example of National Trend Analysis

NCA informs other agencies about a hip prosthesis that is having a higher than average revision rate.

- Analysis of information is that the implant is being revised due to metal sensitivity.
- Revision rate becomes significant and is increasing rapidly after 3 years of implantation.
- Country of origin of NCAR is also taking action to prevent further use.



3. REQUEST AND/OR SHARING OF INFORMATION

A NCA may request and/or share information on:

- An event or events;
- An increase in seriousness or frequency;
- Issues found with a manufacturer's Post-Market Surveillance (PMS) / Quality Management System (QMS); or
- Regulatory status changes of a device(s).

The information may be about a specific device or class/group of devices.

Requests for information may relate to:

- Experience with the device;
- Actions undertaken;
- Opinion and/or advice.

Sharing information should relate to whether:

- The consequences are likely to lead or have already led to serious public health threat; and
- Whether other jurisdictions could be impacted.

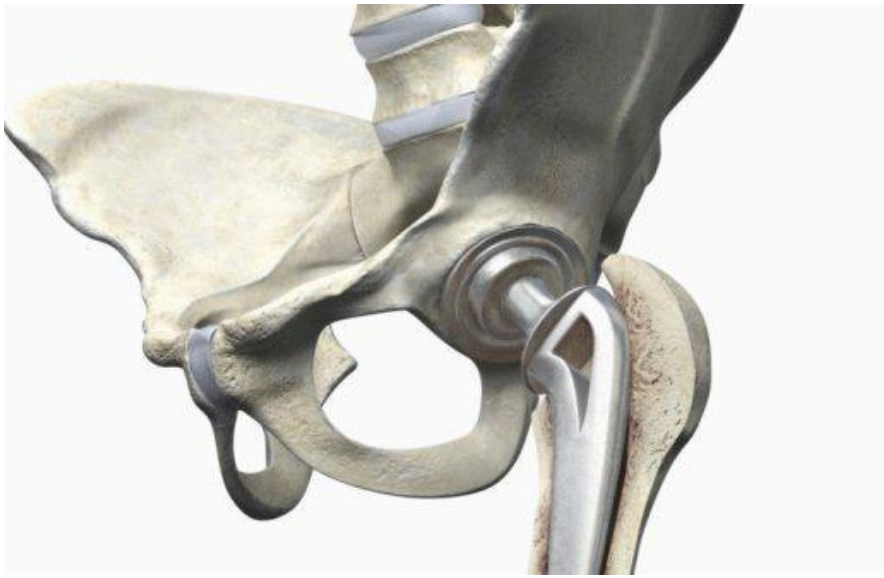
Example of Sharing Information

- Information is being shared about an adverse event and the solution in case action is required elsewhere.
- A death was associated with the failure of a physiological monitor to alarm when a patient on telemetry hook-up had an irregular heart beat.
- Investigation revealed that the monitor's alarms would not be triggered if it was not able to detect a rhythm from the telemetry unit when the telemetry unit was more than 3 meters away. The monitor was interpreting interference or absent transmission as though no patient was connected.

- The outcome of the investigation was that the frequency used between the monitor and telemetry unit be switched to another frequency which was appropriate for telemetry use.

Example of Requesting Information

- A NCA has had reports of problems with a particular hip replacement.
- There are a number of issues with a particular model.
- The NCA isn't sure if there is an issue with the implant or an issue more locally.
- As the investigation is ongoing the requesting NCA has indicated that the request is confidential.
- The NCA sends out an NCAR requesting information from other NCAs that it has a confidentiality agreement with about any adverse events, complaints or other information that will assist in its investigation.



Critical Issues

In the case where a Critical Issue of Significant Public Health Threat exists and the NCA enforces measures on the affected manufacturer, it is envisaged that such actions should be communicated via the NCAR Secretariat to all participants of the NCAR Exchange program.

Example of Critical Issue
Haemodialysis

- An investigation into the deaths of a number of patient in several haemodialysis units revealed that the dialyser used on these patients was not manufactured according to correct procedures.
- The filaments in the dialyser were made using a material that had not been certified for use in this manner and the leachate was toxic when exposed to blood.
- The manufacturing records indicated that the dialysers were sold to only one hospital however, the deaths were from several hospitals that were not associated with the hospital in the manufacturer's records.
- The NCA immediately shut down the manufacturing site and sent a NCAR to all member countries to alert them to the issue.
- As the manufacturer could not provide sufficient information about the supply of the dialysers the NCA advised that they had ceased use of all dialysers and issued a Field Safety Correction Action (Recall) notice from this manufacturer until the investigation was completed and solutions approved.

Example of Critical Issue
Pacemaker

- Analysis of information, including adverse event reports and an inspection of a manufacturing site by a NCA indicates that there is a problem with pacemaker software in all batches of implantable pacemakers manufactured before a certain time period.
- The software is not detecting when the battery has depleted and triggering an alarm.
- The consequence for pacemaker dependent patients could be death.
- The NCA notifies all NCAs as the issue is widespread.

PART IV

Confidentiality

- IMDRF Management Committee Regulators who wish to participate in the NCAR Exchange Program must ensure that they have a confidentiality agreement in place :
  - with as many **other participants** in the exchange as possible / appropriate **and**
  - with the **NCAR Secretariat**.

"Confidential"

- NCARs identified as "Confidential" by the author of the NCAR may only be shared with NCAR exchange program members with whom the authoring NCA has confidentiality arrangements.

"Confidential"

- NCARs identified as "Confidential" by the authoring NCA are circulated **by the authoring NCA** to participants of the NCAR Exchange Program with whom they have confidentiality agreements.

- A copy of the NCAR is also sent to the NCAR Secretariat for recording purposes.

“Non-Confidential"

- NCARs identified as "Non-Confidential" by the author of the NCAR may be shared with all NCAR exchange program members.

“Non-Confidential"

- NCARs identified as "Non-Confidential" by the authoring NCA are circulated **by the NCAR Secretariat** to all participants of the NCAR Exchange Program.
- The NCAR Secretariat confirms that the correct sequential references and attachments have been provided prior to circulating the NCAR. Content is not edited.

"Confidential" / " Non-Confidential"

- This is decided by the authoring NCA on a case by case basis.
- No defined criteria – dependant on the authoring country's classification of confidential information.
- The more information shared in the exchange the more valuable the exchange.

PART V

NCAR Secretariat

- The organization which **facilitates** and **monitors** the exchange of NCARs between reporting National Competent Authorities (NCAs) and other NCAR participants in accordance with this guidance.

- The NCAR Secretariat is the recipient and repository of all NCARs.

Role of the NCAR Secretariat

- To facilitate and monitor the exchange of NCARs between reporting NCAs and other NCAR exchange program participants in accordance with guidance IMDRF/NCAR WG (PD1) /N14.
- To maintain a repository of all NCARs communicated through the NCAR Exchange Program.

Role of the NCAR Secretariat

- To monitor the quality and consistency of the NCAR Exchange Program by ensuring that the exchange criteria are appropriately applied and the correct documentation and nomenclature are used.
- To validate and circulate non-confidential NCARs in line with the provisions of guidance IMDRF/NCAR WG (PD1) /N14. The content of a NCAR **will not** be edited by the NCAR Secretariat.

Role of the NCAR Secretariat

- To generate statistical analysis / reports regarding participation in the NCAR Exchange Program on a periodic basis (a minimum of bi-annually) for the IMDRF MC.
- To support training in relation to the NCAR Exchange Program.
- To organise a bi-annual teleconference with the participants of the exchange to review the operation of the exchange and resolve any issues identified.

Role of the NCAR Secretariat

- To maintain a repository of training materials.
- To maintain a repository of the information exchanged through the NCAR Exchange Program.
- To maintain a list of participants in the NCAR Exchange Program.

Role of the NCAR Secretariat

- The NCAR Secretariat has no decision-making or policy-making powers.

- The NCAR Secretariat does not assess or propose action on the NCARs as this is the responsibility of the author of the NCAR and/or the recipients of the NCAR.