GHTF

Study Group 2 (SG2)

GHTF

Overview of SG2

Presentation Topics: Overview

- Who We Are
- Terms of Reference
- Aim
- Achievements
- Vision
- Document Map

SG2 – Who We Are

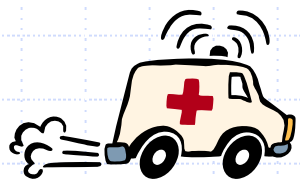
- 14 members
- Half industry half regulators
- Representing 3 regions
  - Europe
  - North America
  - Asia/Pacific

SG2 Terms of Reference

- Examine the requirements for the reporting of medical device adverse incidents involving medical devices,
- Recommend ways to harmonize:
  - Reporting requirements of medical device adverse events
  - Post-market surveillance
  - Other forms of vigilance
- Promote dissemination of relevant information

Aim of GHTF SG2

- Improve protection of public health and safety of patients, users and others
- Evaluate reports and disseminate information which may reduce the likelihood of or prevent repetition of adverse events
- Define post market medical device reporting and surveillance requirements and guidelines on an international basis



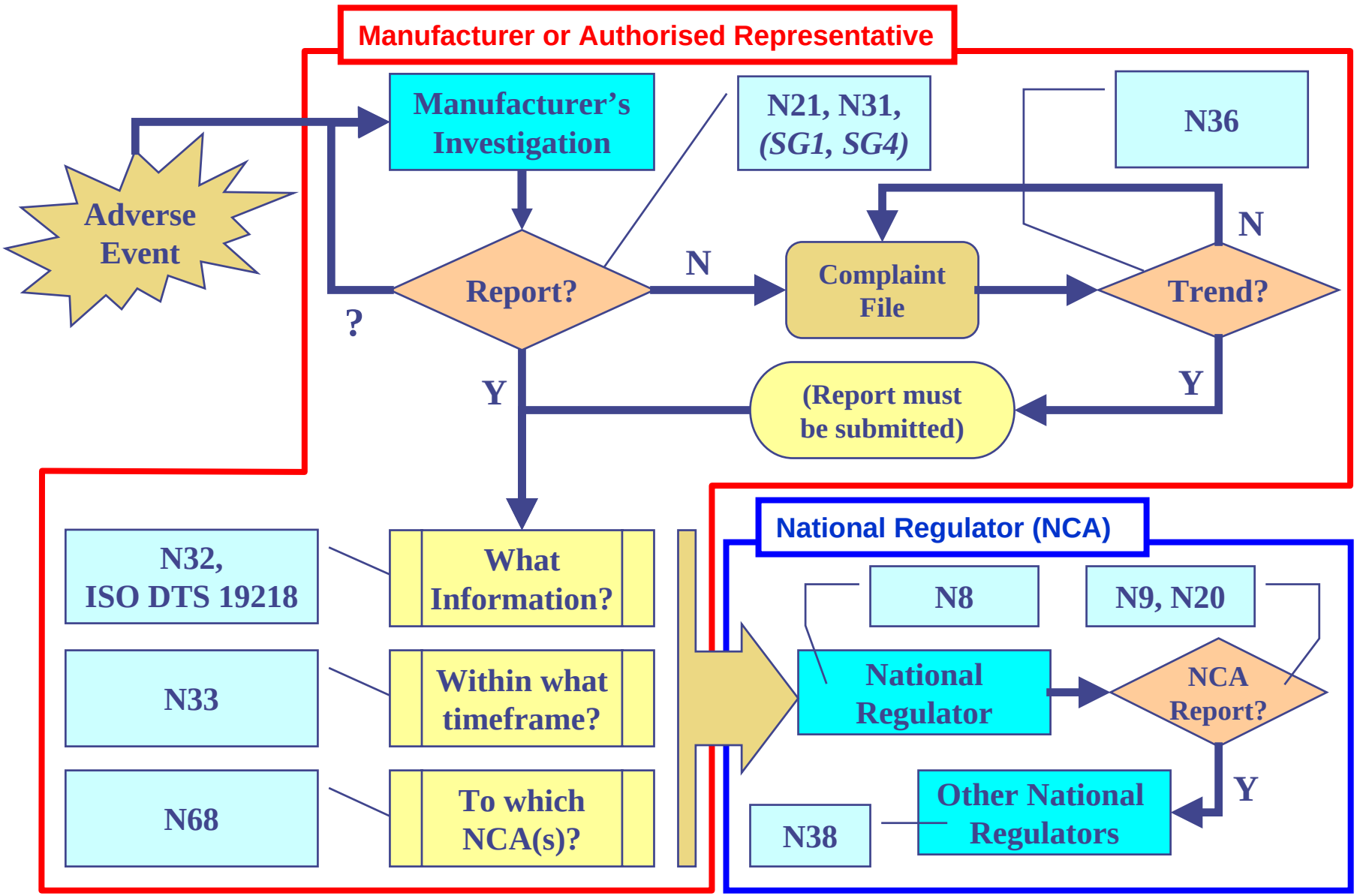
SG2 Achievements

- Compared participating countries regulatory systems to determine a baseline for harmonization
- Developed guidance for manufacturer reporting of adverse events
- Developed an international system for exchange of high risk reports between competent authorities
- Ten Final Documents on Website

SG2 Vision

- Globally harmonized medical device adverse event reporting, vigilance, and post-market surveillance process

“Map” of SG2 Guidance



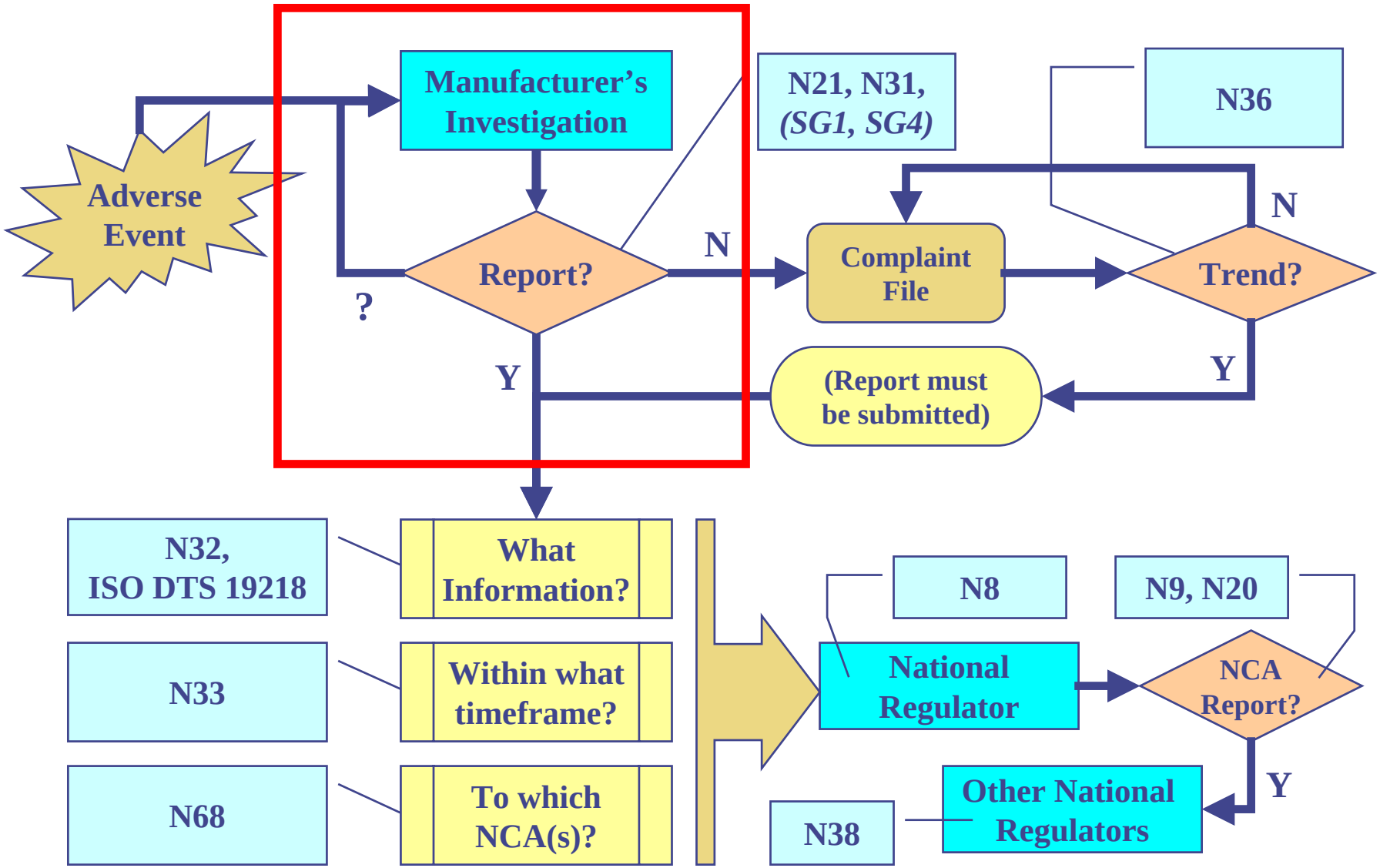
SG2 Publications

- **Vigilance (Adverse Event reporting by manufacturers to NCAs)**
  - SG2-N8R4: Guidance on How to Handle Information Concerning Vigilance Reporting Related to Medical Devices
  - SG2-N21R8: Adverse Event Reporting Guidance for the Medical Device Manufacturer or its Authorized Representative
  - SG2/N31R8: Proposal for Reporting of Use Errors with Medical Devices by their Manufacturer or Authorized Representative
  - SG2/N32R5: Universal Data Set for Manufacturer Adverse Event Reports
  - SG2-N36R7: Manufacturer's Trend Reporting of Adverse
  - SG2-N33R11: Timing of Adverse Event Reports
  - SG2-N68R3: Who Should Adverse Event Reports be Sent To?

SG2 Publications (cont'd)

- **National Competent Authority Reports (Vigilance Exchange)**
  - SG2-N9R11: Global Medical Device Competent Authority Report
  - SG2-N20R10: National Competent Authority Report Exchange Criteria
  - SG2-N38R14 Application Requirements for Participation in the GHTF National Competent Authority Report Exchange Program.
- **Information**
  - SG2-N6R3: Comparison of the Device Adverse Reporting Systems in USA, Europe, Canada, Australia & Japan
  - SG2-N16R5: SG2 Charge & Mission Statement

Adverse Event Reporting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Other National Regulators

Presentation Topics: AE Reporting

- Adverse Event Reporting Guidance (N21)
- Use Error (N31)
- AE Trend Reporting (N36)
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- To Whom to Report (N68)
- Report Data Set (N32)

AE Reporting Guidance

The objective of adverse event (AE) reporting and subsequent evaluations is to improve protection of the health and safety of patients, users and others by disseminating information which may:

- reduce the likelihood of adverse events, or
- prevent repetition of adverse events, or
- alleviate consequences of such repetition.

AE Reporting Guidance

The term "manufacturer" means

- the manufacturer,
- its authorized representative or
- any other person who is responsible for placing the device on the market

AE Reporting Guidance

The existing regulatory requirements of the participating countries involved in SG2 require medical device manufacturers to notify National Competent Authorities (NCAs) of certain adverse events.

AE Reporting Guidance

- The guidance document represents a global model, which provides guidance on the type of adverse events associated with medical devices that should be reported by manufacturers to a NCA.
- It is based on the regulatory requirements existing in the participating member countries.

AE Reporting Guidance

- The guidance is not identical to current regulatory requirements.
- The document provides a future model towards which existing systems should converge.
- The principles laid down in the document should be considered in the development or amendment of regulatory systems in the participating countries or other countries.

AE Reporting Guidance

- Some NCAs also encourage reporting of adverse events by users.
- The guidance document does not include requirements for user reporting.
- It is recommended that NCAs promptly inform the pertinent manufacturers about reports received directly from users.

AE Reporting Guidance

- The act of reporting to a NCA is not considered an admission of manufacturer, user, or patient liability.
- Submission of a report does not represent a conclusion by the manufacturer that the information is complete or confirmed.
- A report is also not a conclusion that the medical device caused or contributed to the adverse event.
- It is recommended that reports carry a disclaimer.

AE Reporting Guidance

- Any event which meets three basic reporting criteria is considered as an adverse event and should be reported to the relevant NCA.
- Under specified conditions some types of events are exempt from reporting.

AE Reporting Guidance

- Basic reporting criteria:

1) An event must have occurred.

  - Malfunction or deterioration
  - Inadequate design or manufacture
  - Inaccuracy in labeling
  - Significant public health concern
  - Other information from testing or literature

AE Reporting Guidance

- Basic reporting criteria:

2) The manufacturer's device is associated with the event.

  - Opinion from healthcare professional
  - Previous similar events
  - Other information available to the manufacturer

AE Reporting Guidance

- Basic reporting criteria:

3) The event led to one of the following:

  - Death of a patient, user or other person or
  - Serious injury of a patient, user or other person
  - No death or serious injury, but event might lead to death or serious injury if the event recurs

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AE Reporting Guidance

Serious injury is defined as:

- Life threatening illness or injury.
- Permanent impairment of a body function or permanent damage to a body structure.
- A condition requiring medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

AE Reporting Guidance

- The term “permanent” means irreversible impairment or damage to a body structure or function, excluding minor impairment or damage.

- Medical intervention is not in itself a serious injury. It is the reason that motivated the medical intervention that should be used to assess whether an event should be reported.

AE Reporting Guidance

- Reporting may be exempted if any one of a set of exemption rules is applicable.
- However if a NCA requires reporting a specific type of event due to a significant public health concern, the exemption is no longer applicable.
- Similarly those adverse events which are subject to an exemption become reportable to the NCA if a change in trend (usually an increase in frequency) or pattern is identified.

AE Reporting Guidance

- Exemption Rules

Whenever any one of the following exemption rules is met, the adverse event does not need to be reported to a NCA by the manufacturer.

AE Reporting Guidance

- Exemption Rules

1) Deficiency of a new device found by the user prior to its use.

   Regardless of the existence of provisions in the instruction for use provided by the manufacturer, deficiencies of devices that would normally be detected by the user and where no serious injury has occurred, do not need to be reported.

AE Reporting Guidance

- Exemption Rules

1) Deficiency of a new device found by the user prior to its use.

   Example

   User performs an inflation test prior to inserting the balloon catheter in the patient as required in the instructions for use accompanying the device. Malfunction on inflation is identified. Another balloon is used. Patient is not injured.

AE Reporting Guidance

- Exemption Rules

2) Adverse event caused by patient conditions.

When the manufacturer has information that the root cause of the adverse event is due to a patient's condition, the event does not need to be reported. These conditions could be preexisting or occurring during device use.

AE Reporting Guidance

- Exemption Rules

2) Adverse event caused by patient conditions.

Example-

Orthopedic surgeon implants a hip joint and warns against sports-related use. Patient chooses to go water skiing and subsequently requires premature replacement due to not following directions.

AE Reporting Guidance

- Exemption Rules

3) Service life of the medical device.

When the only cause for the adverse event was that the device was used beyond its service life as specified by the manufacturer and the failure mode is not unusual, the adverse event does not need to be reported.

AE Reporting Guidance

- Exemption Rules

3) Service life of the medical device.

Example

Loss of sensing after a pacemaker has reached end of life. Elective replacement indicator has shown up in due time according to device specification. Surgical explantation of pacemaker required.

AE Reporting Guidance

- Exemption Rules

4) Protection against a fault functioned correctly.

Adverse events which did not lead to serious injury or death, because a design safety backup feature protected against a fault becoming a hazard (in accordance with relevant standards or documented design inputs), do not need to be reported.

AE Reporting Guidance

- Exemption Rules

4) Protection against a fault functioned correctly.

Example-

An infusion pump stops, due to a malfunction, but gives an appropriate alarm (e.g. in compliance with relevant standards) and there was no injury to the patient.

AE Reporting Guidance

- Exemption Rules

5) Remote likelihood of occurrence of death or serious injury.

Adverse events which could lead, but have not yet led, to death or serious injury, but have a remote likelihood of causing death or serious injury, and which have been established and documented as acceptable after risk assessment do not need to be reported.

AE Reporting Guidance

- Exemption Rules

5) Remote likelihood of occurrence of death or serious injury.

Example-

Manufacturer of pacemaker released on the market identified a software bug and determined that the likelihood of occurrence of a serious injury with a particular setting is remote. No patients experienced adverse health effects.

AE Reporting Guidance

- Exemption Rules

6) Expected and foreseeable side effects.

Side effects which are clearly identified in the manufacturer's labeling or are clinically well known as being foreseeable and having a certain functional or numerical predictability when the device was used as intended need not be reported.

AE Reporting Guidance

- Exemption Rules

6) Expected and foreseeable side effects.

Example-

Placement of central line catheter results in anxiety reaction and shortness of breath. Both reactions are known and labeled side effects.

AE Reporting Guidance

- Exemption Rules

7) Adverse events described in an advisory notice

AE's that occur after a manufacturer has issued an advisory notice need not be reported individually if specified in the notice. Advisory notices include removals from the market, corrective actions, and product recalls. The manufacturer should provide a summary report, the content and frequency of which should be agreed with the relevant NCA.

AE Reporting Guidance

- Exemption Rules

7) Adverse events described in an advisory notice.

Example-

Manufacturer issued an advisory notice and recall of a coronary stent that migrated due to inadequate inflation of an attached balloon mechanism. Subsequent examples of stent migration were summarized in quarterly recall reports and individual events did not have to be reported.

AE Reporting Guidance

- Exemption Rules

8) Reporting exemptions granted by NCA.

Common and well-documented events may be exempted by a NCA from reporting or changed to periodic reporting upon request by the manufacturer.

Presentation Topics: AE Reporting

- Adverse Event Reporting Guidance (N21)
- Use Error (N31)
- AE Trend Reporting (N36)
- Reporting Timeframes (N33)
- To Whom to Report (N68)
- Report Data Set (N32)

Use Error

- Use Error:

  Act, or omission of an act, that has a different result to that intended by the manufacturer or expected by the operator.
  - **Note -** Use error includes slips, lapses, mistakes and reasonably foreseeable misuse.

Examples:

- Despite proper instruction and proper design according to manufacturers analysis operator presses wrong button
- Operator enters incorrect sequence and fails to initiate an action such as infusion

Use Error

- Abnormal Use:

  Act, or omission of an act by the operator or user of a medical device as a result of conduct that is beyond any reasonable means of risk control by the manufacturer.

Examples:

- Failure to conduct device checks prior to each use as defined by the manufacturer.
- Continued use of a medical device beyond the manufacturers defined planned maintenance interval as a result of user's failure to arrange for maintenance

Use Error

Note - Foreseeable misuse that is warned against in the instructions for use is considered abnormal use if all other reasonable means of risk control have been exhausted.

Use Error - Reportability

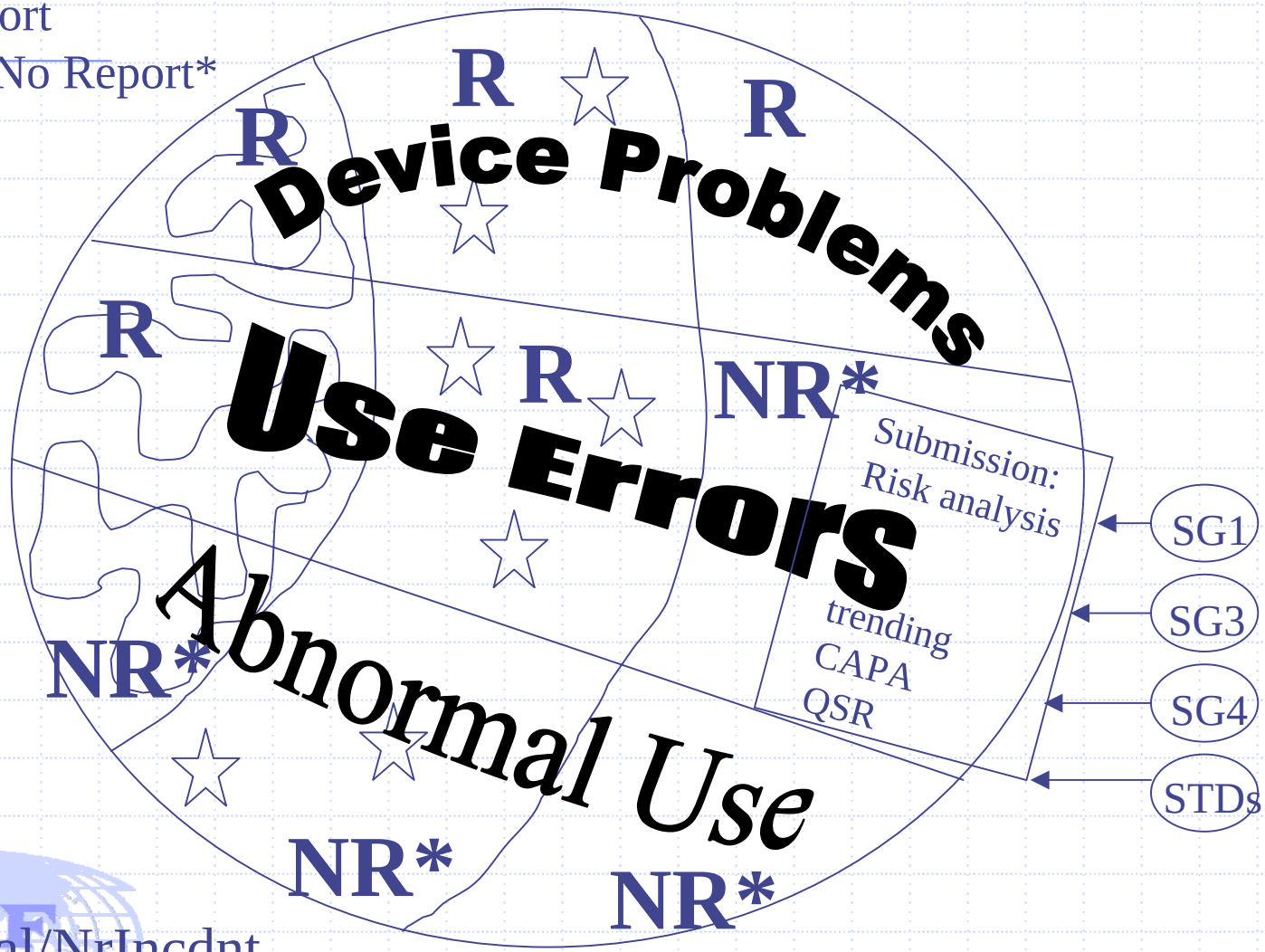
- Use errors related to medical devices which did not result in death or serious injury or serious public health concerns, need not be reported by the manufacturer to the national competent authorities.
- Use errors become reportable by the manufacturer to the national competent authorities when a manufacturer:
  - Notes a change in trend that can potentially lead to death or serious injury of public health concern.
  - Initiates corrective action to prevent death or serious injury or serious public health concern.

Use Error - Reportability

- Abnormal use need not to be reported by the manufacturer to the national competent authority under adverse event reporting procedure. Abnormal use should be handled by the healthcare facility and appropriate regulatory authorities.
- If manufacturers become aware of instances of abnormal use, they may bring this to the attention or other appropriate organizations and healthcare facility personnel.

The Universe of Device Associated Adverse Events

R=Report
NR*= No Report*



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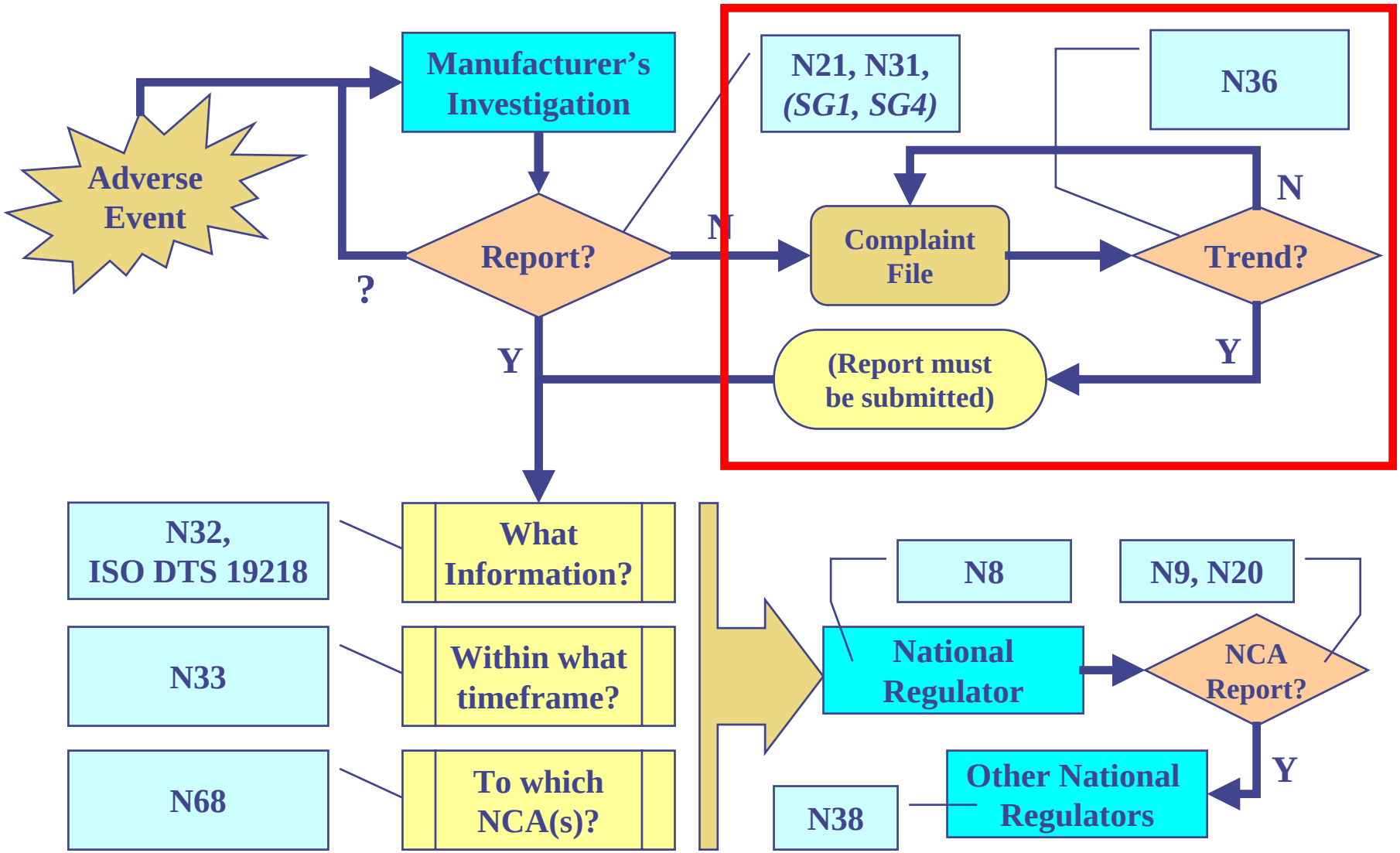
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AE Trend Reporting

- Adverse events specifically exempted from reporting become reportable if there is a change in trend (usually an increase in frequency) or pattern is identified.
- The SG2 document on trend reporting describes the criteria for identifying a significant increase in the rate of adverse events.
- Not a handbook of statistical techniques
- Provides guidance to assist manufacturers to perform trending.

AE Trend Reporting

- Quality management system standards include requirements for trending product complaints including those considered AEs.
- The same methods can be used for trending complaints and trending AEs.
- Trending of complaints may lead to a corrective and preventive action.
- Trending of AEs may lead to a report to a NCA.

AE Trend Reporting

Basic trending parameters

$$i = n/d \text{ where}$$

i represents a trend data point

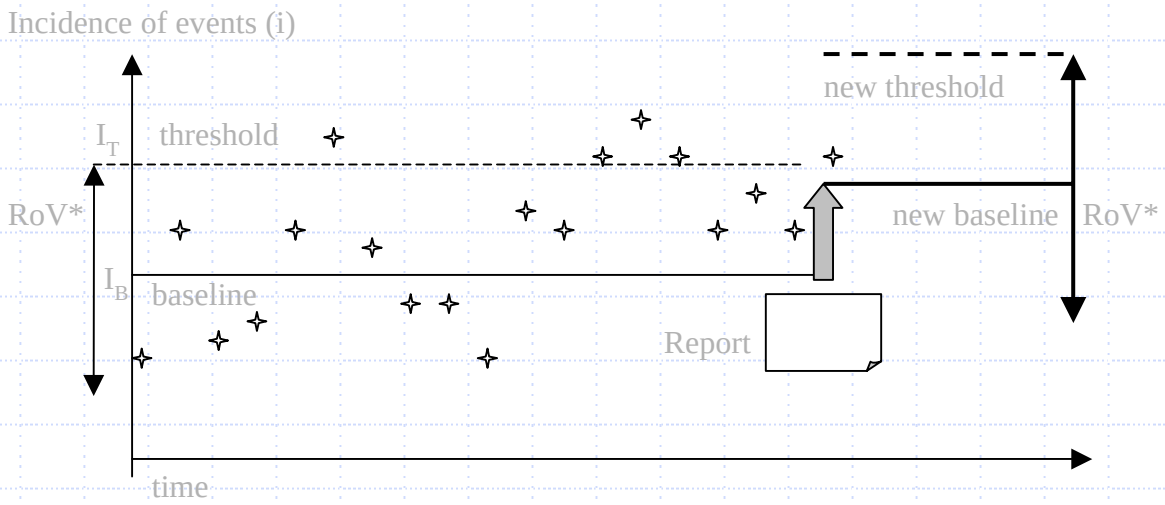
n is the number of events in a given time interval

d is the product volume (by clinicians, patients, etc.) in the market during that time interval

i is the observed incidence expressed as a percent.

AE Trend Reporting

- Example of an upward shift in trend



* normal Range of Variance

AE Trend Reporting

- Base Line I_B
  - The base line is the expected or normal rate of incidence of an event expressed as a percent of the products in use.
  - Base line values can be established through the use of tools and methods such as risk analysis, reliability models, or historical data.

AE Trend Reporting

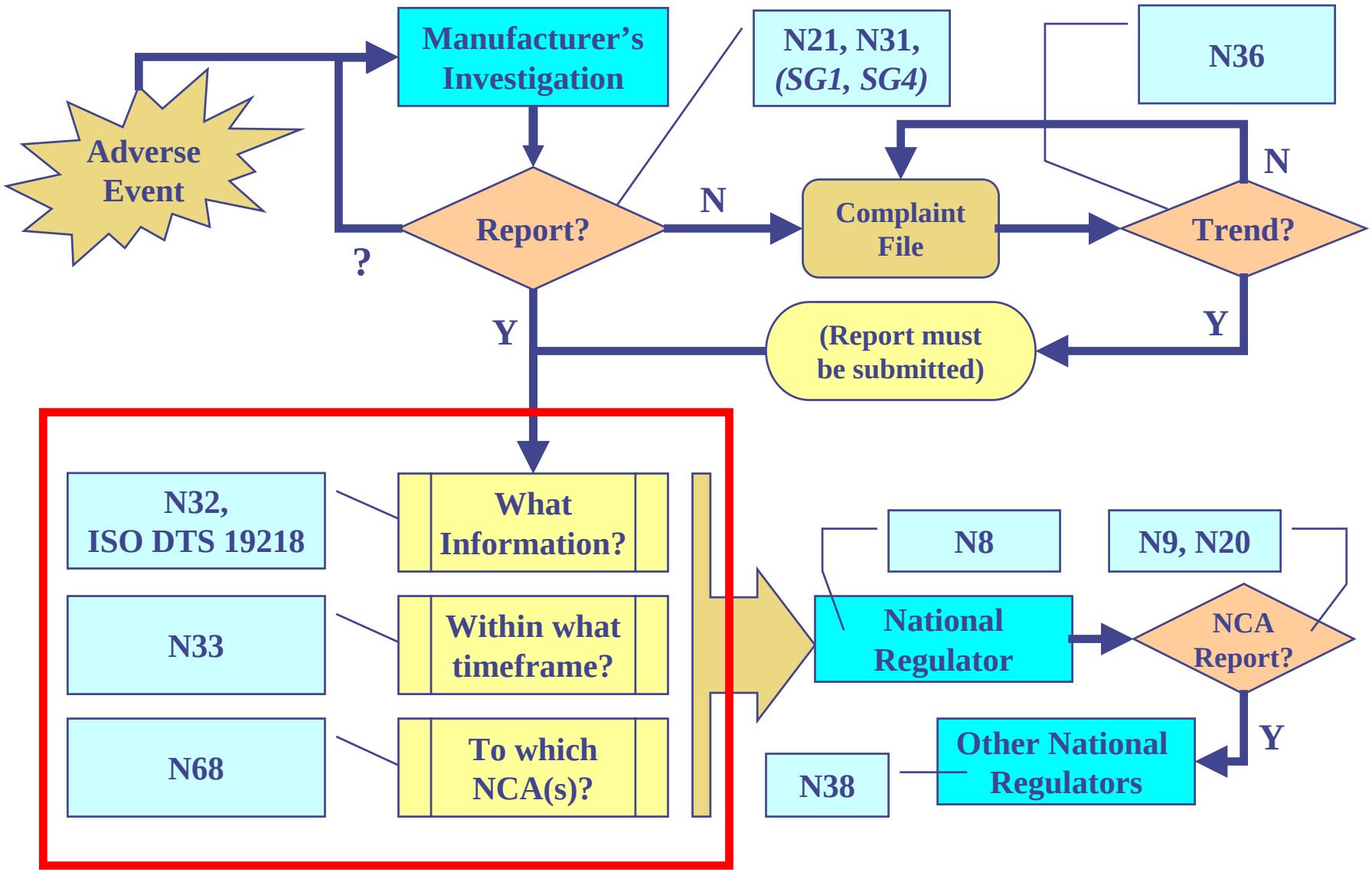
- Threshold I_T
  - The threshold, expressed as a percent of products in use, is the incidence rate which is above the expected or normal variation in rate.
  - Threshold values may be established from the expected or measured variation in incidence rate.
  - Threshold values will be different depending on the product category.

AE Trend Reporting

- Time interval
  - The time interval should be long enough to gather sufficient data for the analysis.
  - The time interval should be short enough to facilitate timely corrective action.
  - For higher volume products a typical time interval may be 1 month.

AE Trend Reporting

- Significant increase in observed incidence
  - a rapid and continuous increase in (i) over a limited number of time intervals for high volume products (e.g. over 1 - 3 months)
  - a slow and continuous increase in (i) over a larger number of time intervals for low volume products (e.g. over 3 - 6 months)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Reporting Timeframes

- Adverse events that result in unanticipated death or unanticipated serious injury or represent a serious public health threat must be reported immediately by the manufacturer.
- All other reportable events must be reported as soon as possible by the manufacturer, but not later than 30-elapsed calendar days following the date of awareness of the event.

Reporting Timeframes

- **Immediately:** For purposes of adverse event reporting, immediately means as soon as possible, but not later than 10 elapsed calendar days following the date of awareness of the event.
- **Serious public heath threat:** Any event type, which results in imminent risk of death, serious injury, or serious illness that may require prompt remedial action.

Reporting Timeframes

- **Unanticipated:** A death or serious injury is considered unanticipated if the condition leading to the event was not considered in a risk analysis performed during the design and development phase of the device. There must be documented evidence in the design file that such analysis was used to reduce the risk to an acceptable level.

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To Whom to Report

- At present, some jurisdictions (USA, Japan) require that all adverse events, regardless of where in the world they occurred, must be reported to them. This means that manufacturers must often submit more than one report to separate regulatory authorities about the same event.
- SG2 considered several options that might resolve this situation, including the establishment of a global database for submission of adverse event reports.

To Whom to Report

- In lieu of creating a guidance document, it was decided to provide this status document which provides a reference for the medical device manufacturer regarding where adverse events should be sent by listing the current national requirements of the five GHTF founding members, as well as the legal reference to those requirements.
- This document provides a useful summary but manufacturers refer to national requirements in relation to this matter.

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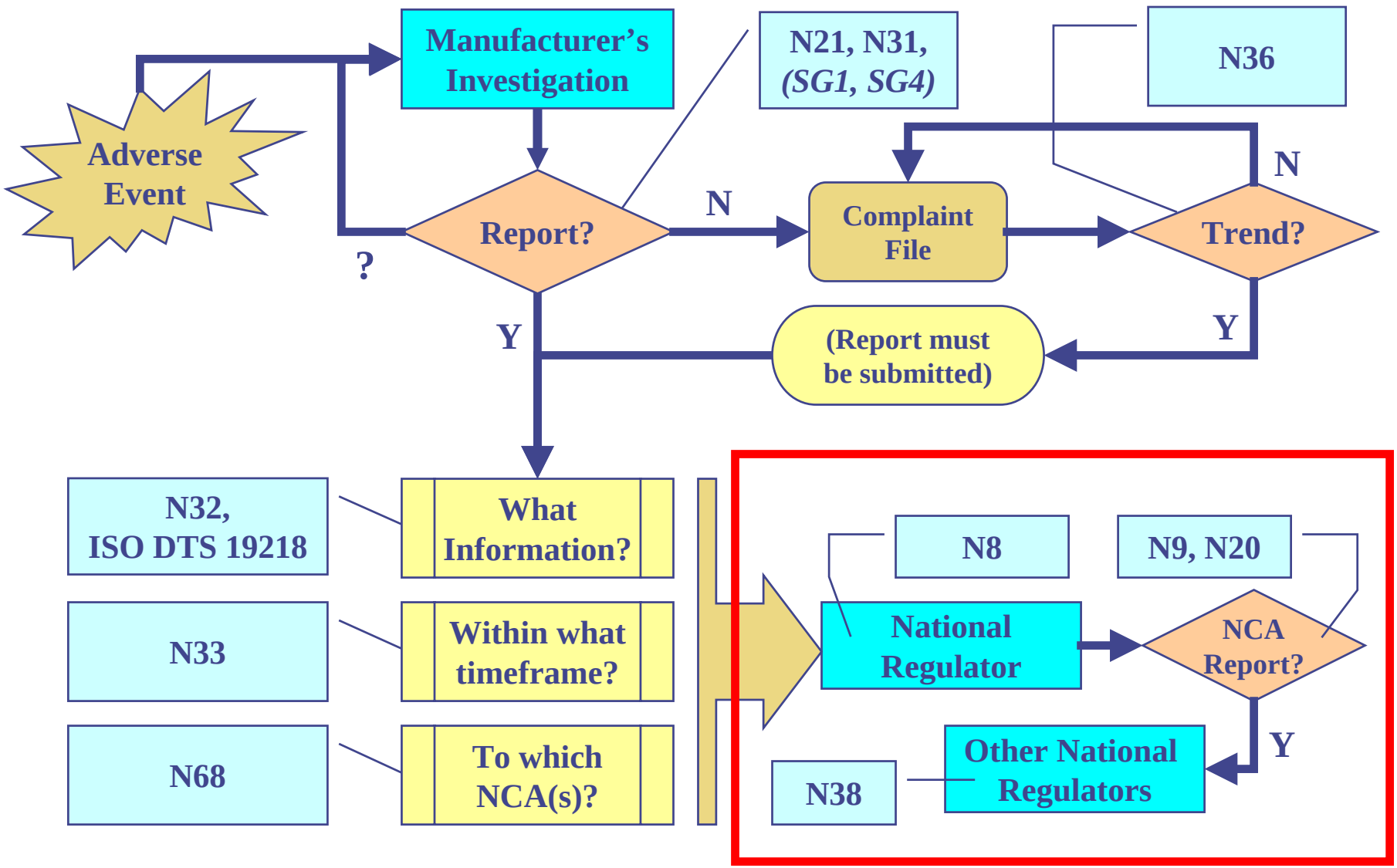
Report Data Set

- **Event information:** Dates, Reporter details, Healthcare facility details, Patient details, Event type and description, Notified CA's, Resolution description
- **Device Information:** Manufacturer, Generic device group, Disposition, Results of analysis, Corrective action taken.
- **Other:** Comments, Notified Body details, CAs notified of Corrective action

NCAR: N9, N20, N38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Presentation Summary

- National Competent Authority Report
- N20 - Medical Devices: Post Market Surveillance: National Competent Authority Report Exchange Criteria
- N9 - Global Medical Device Competent Authority Report
- N38 - Application Requirements for Participation in the GHTF National Competent Authority Report Exchange Program

N 20 - Exchange Criteria

- Criteria / method for exchange of info between competent authorities
- High concern or public health threat
- Criteria such as;
  - Seriousness
  - Unexpectedness
  - Vulnerability of population
  - Class I recall
  - Notifications to public by NCA

N9 – Report Form

- Form and guidance for exchange between competent authorities

GLOBAL MEDICAL DEVICES COMPETENT AUTHORITY REPORT

Form N9R11

This form should be used for the exchange of information between National Competent Authorities only

1. Is this report confidential? Yes [ ] No [ ]

Reference and Reporter Data

2. NCA report ref. no.:	3. Local NCA reference no.:	4. Related NCA report nos.: (if any)
5. Manufacturer Ref/Recall no.:	6. Sent by: (Name and Organization)	7. Contact person: (if different from 6)
8. Tel:	9. Fax:	10. E-mail:

Device Data

11. Generic name/ kind of device:			20. CAB/Notified Body no.:
12. Nomenclature id:	13. No.:		
14. Trade Name and Model:			21a. Device approval status:
15. Software version:			
16. Serial no.:	17. Lot/batch no.:		b. Risk Class:
18. Manufacturer: Country: Full Address: Contact: Tel: Fax: E-mail:	19. Authorized rep (if different from 18): Country: Full Address: Contact: Tel: Fax: E-mail:		22. Action taken: [ ] None [ ] Recall [ ] Safeguard Clause [ ] Other (specify)

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Event Data

23a. Background information and reason for this report:

23b. Is the investigation of the report complete?: *[ ] Yes [ ] No*

24a. Conclusions:

24b. NCA of _____ is willing to take the lead and co-ordinate the investigation

25a. Recommendation to receivers of this report:

25b. Device known to be in the market in:

25c. Device also marketed as (trade name):

Report Distribution

26. This report is being distributed to the NCAR Secretariat for further distribution to NCAR participants.

This report is also being distributed to:

[ ] EEA states, EC, ESA, and EFTA

[ ] The following targeted NCAs:

[ ] The manufacturer / authorized rep.:

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N38 – Participation in NCAR exchange

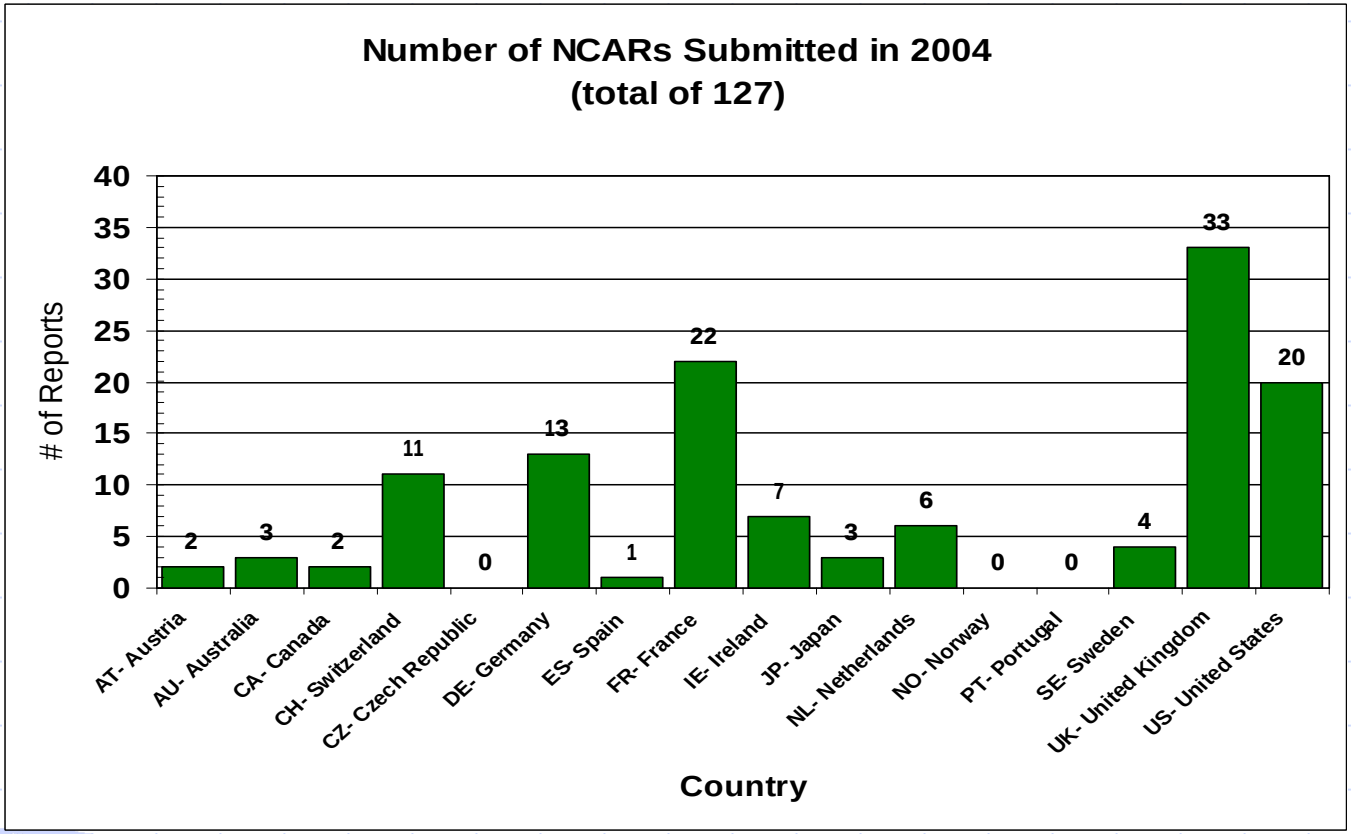
- Guideline for participation in NCAR exchange
- Full and Associate participants to NCAR exchange
- Training, commitments, confidentiality

N38 Summary

Participant Level	Associate	Full
Type of Information Sought	Public	Confidential
Prerequisites		
Possible Admin Charge	Yes	Yes
Working Reporting System	No	Yes
Training *	Yes	Yes
A Commitment to:		
Confidentiality	No	Yes
Full Participation	No	Yes
Single Contact Point	Yes	Yes
Must be NCA	No	Yes

* Training on N9 and 20 for Associate and Full training for Full Participant

Summary Statistics for NCAR Exchange



GHTF

Case Study: Implementation of SG2 Guidance in Australia

GHTF SG2 N21R8

Section	Description	Status
1.1-1.3	Definition of reportable event	Implemented in the law S41FN, S41MP, examples and plain English definition in TGA Guidance 11
Reporting Exemption Rules		
2.1	Deficiency of a New Device Found by the User Prior to its Use	Implemented, but TGA Guidance says "always instead of "normally".
2.2	Adverse Event Caused by Patient Conditions	Implemented in TGA Guidance
2.3	Service Life of the Medical Device	Implemented in TGA Guidance
2.4	Protection Against a Fault Functioned Correctly	Implemented in TGA Guidance
2.5	Remote Likelihood of Occurrence of Death or Serious Injury	Implemented in TGA Guidance
2.6	Expected and Foreseeable Side Effects	Implemented in TGA Guidance
2.7	Adverse Events Described in an Advisory Notice	Implemented in TGA Guidance
2.8	Reporting Exemptions Granted by NCA	Implemented in TGA Guidance

Other Documents

Doc #	Description	Status
N31	Use Error	Not implemented, user errors are reportable in Australia - this is explicit
N32	Universal Dataset	Implemented in TGA Guidance, minor local variations: ARTG#, ARTG Manufacturer#
N33	Timing for Adverse Event Reports	Implemented in the Medical Devices Regulations: Difference - "Immediate Reports" in 2 calendar days. "Death and Serious Injury Reports" in 10 Calendar Days
N36	Trending of Adverse Event Reports	Implemented, trending mentioned in TGA Guidance
NCA Reporting		
N9	NCAR Form	In Use
N20	NCAR Exchange Criteria	In Use, Full Participation