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GHTF SG2 Guidance:

Reporting of Medical Device Adverse Events

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Post-Market Surveillance

- Post-Market Surveillance is the collection of information on the quality, safety or performance of Medical Devices after they have been placed in the market.
- A balanced Post-Market Surveillance system will contain an appropriate mix of proactive and reactive activities.

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Post-Market Vigilance

- (Post-Market) Vigilance is the reporting and investigation of medical device adverse events and incidents. Both the manufacturer and the Regulatory Authority play major roles.

- By its very nature, Vigilance is a REACTIVE activity *(the manufacturer or authority receive reports and REACT to them)* - this is not intended to be a derogatory statement

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A Pictorial view of PMS

Post-Market Surveillance Information is used for:

- **Injury prevention**
- **Development of standards**
- **Regulatory refinement**
- **Product improvement**

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SG2 Guidance
Adverse Event Reporting by Manufacturers

- 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?

GHTF SG2 N54R8

SG2 Guidance

Report Handling & NCAR Program

- SG2-N8R4: Guidance on How to Handle Information Concerning Vigilance Reporting Related to Medical Devices
- 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.

GHTF SG2 N79R8

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SG2 Guidance
Other documents & guidance

- SG2-N6R3: Comparison of the Device Adverse Reporting Systems in USA, Europe, Canada, Australia & Japan
- SG2-N16R5: SG2 Charge & Mission Statement
- SG2-N12R4: Précis
- SG2-N47R4: Review of Current Requirements Regarding Post-market Surveillance
- SG2-N57R8: Content of Field Safety Notice
- SG2-N61R6: PMS Harmonisation Chart

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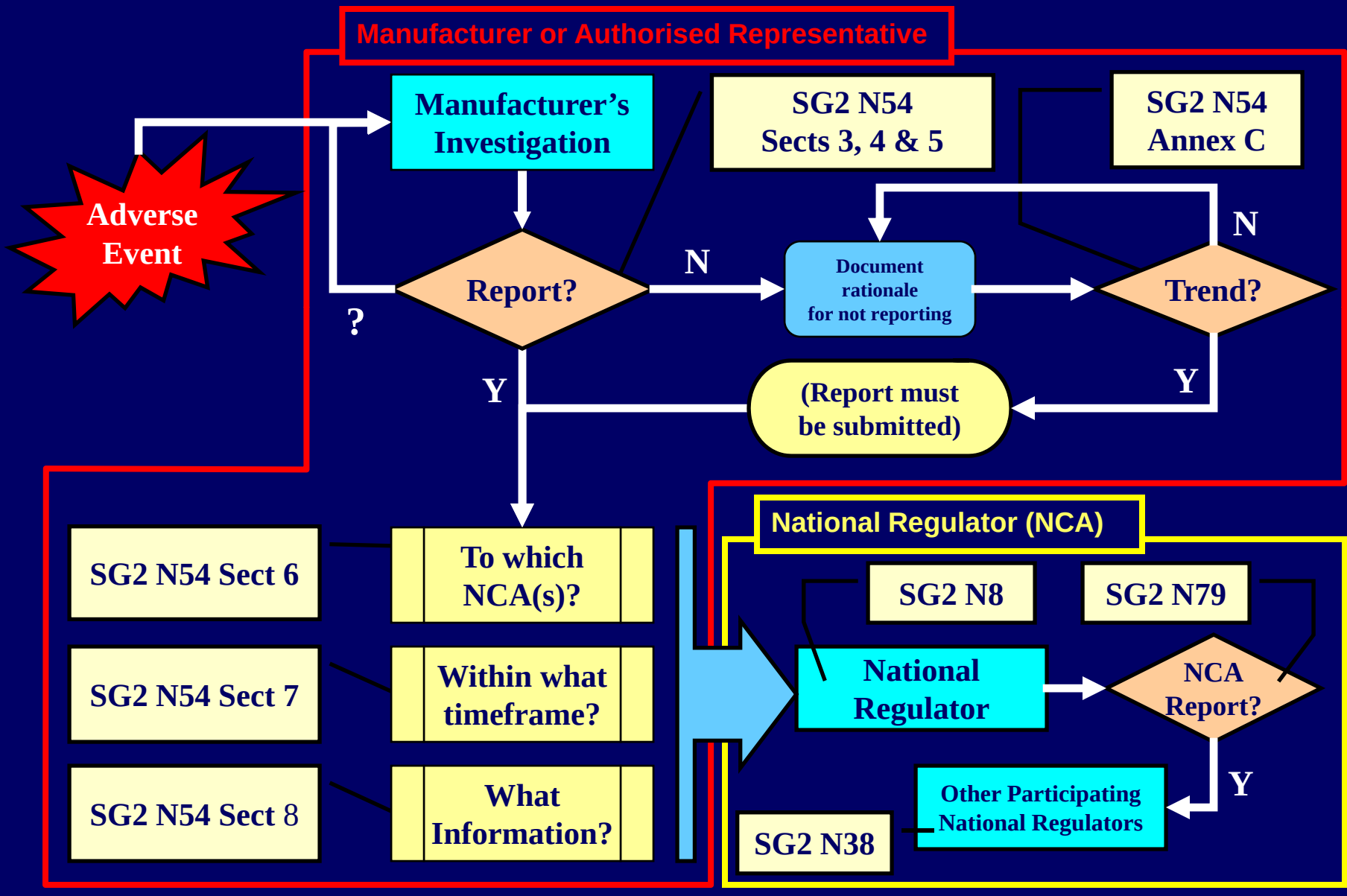
Map of SG2 Guidance on AE Reporting



GHTF SG2 N54 :

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Annexes :

- A. Universal data set
- B. Timing of AE report
- C. Trends
- D. Use error

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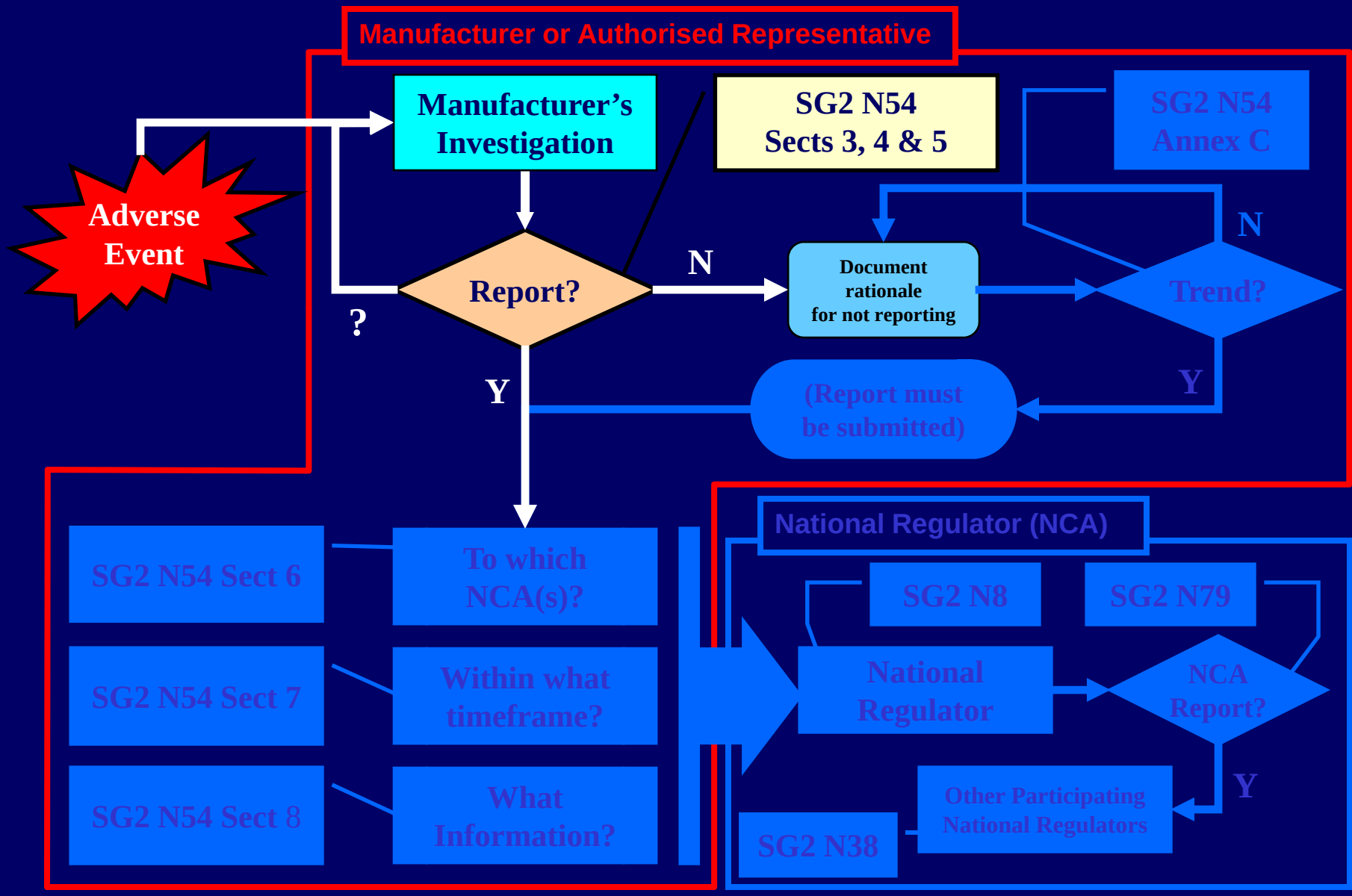
Reporting Criteria and Exemptions



GHTF N54 Section 3.0
Three Basic Reporting Criteria

- An EVENT must have occurred

AND

- The manufacturers device was ASSOCIATED with the event

AND

- The event led to the death or SERIOUS INJURY of a patient user or other person, OR might lead to death or serious injury if the event re-occurs

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EVENT

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

ASSOCIATION (WITH THE DEVICE)

- When the association with the device is difficult to establish, the manufacturer must rely on:
  - Opinion from healthcare professional
  - Previous similar events
  - Other information available to the manufacturer
- If there is any doubt, assume that the device was associated with the event.

SERIOUS INJURY

- Life threatening illness or injury
- Permanent (irreversible) 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

GHTF N54 Section 4.1- 4.8
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

Exemption Rule 1

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

   Deficiencies of devices that would always be detected by the user and where no serious injury has occurred, do not need to be reported

Exemption Rule 1 Example

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

Exemption Rule 2

2) Adverse event caused by patient conditions

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

Exemption Rule 2 Example

2) Adverse event caused by patient conditions

Example-
Revision of an orthopedic implant due to loosening caused by the patient developing osteoporosis

Exemption Rule 3

3) Service life or shelf 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

Exemption Rule 3 Example

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

Exemption Rule 4

4) Malfunction protection operated correctly

Adverse events which did not lead to serious injury or death, because a design feature protected against a malfunction becoming a hazard, do not need to be reported

Exemption Rule 4 Example

4) Malfunction protection operated correctly

Example-

After a malfunction of an infusion pump it gives an appropriate alarm and stops (in compliance with relevant standards). There was no injury to the patient

Exemption Rule 5

5) Negligible 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

Exemption Rule 5 Example

5) Negligible 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 negligible. No patients experienced adverse health effects

Exemption Rule 6

6) Expected and foreseeable side effects which meet <u>all</u> the following criteria :

- Clearly identify in the manufacturers labeling
- Clinically well known and having a certain qualitative and quantitative predictability when used & performed as intended
- Documented in the device master record, with risk assessment prior to occurrence
- Clinically acceptable in terms of patient benefit are not reportable

Exemption Rule 6 Example

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

Exemption Rule 7

7) Adverse events described in an advisory notice

AEs 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

Exemption Rule 7 Example

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

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Exemption Rule 8

8) Reporting exemptions granted by NCA

Upon request by the manufacturer and agreement by NCA common and well-documented events may be exempted from reporting or changed to periodic summary reporting

GHTF N54 Section 4
Other considerations

- If a NCA requires reporting a specific type of event due to a significant public health concern, the exemptions are no longer applicable
- 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

GHTF N54 Section 5 & Annex D
Use Errors

- Use Error: Section 5 (N54) + appendix D

  Act, or omission of an act, that has a different result to that intended by the manufacturer or expected by the operator

  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

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GHTF N54 Section 5 & Annex D
Abnormal Use

- 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-

  – Use of a medical device in installation prior to completing all initial performance checks as specified 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

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Use Errors & Abnormal Use

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 result in death or serious injury or serious public health threat should be reported by the manufacturer to the National Competent Authority

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.

Abnormal Use - 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

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The Universe of Device Associated Adverse Events

R=Report
NR*= No Report*

= Death
= Serious Injury
= Malfunction /No Incident

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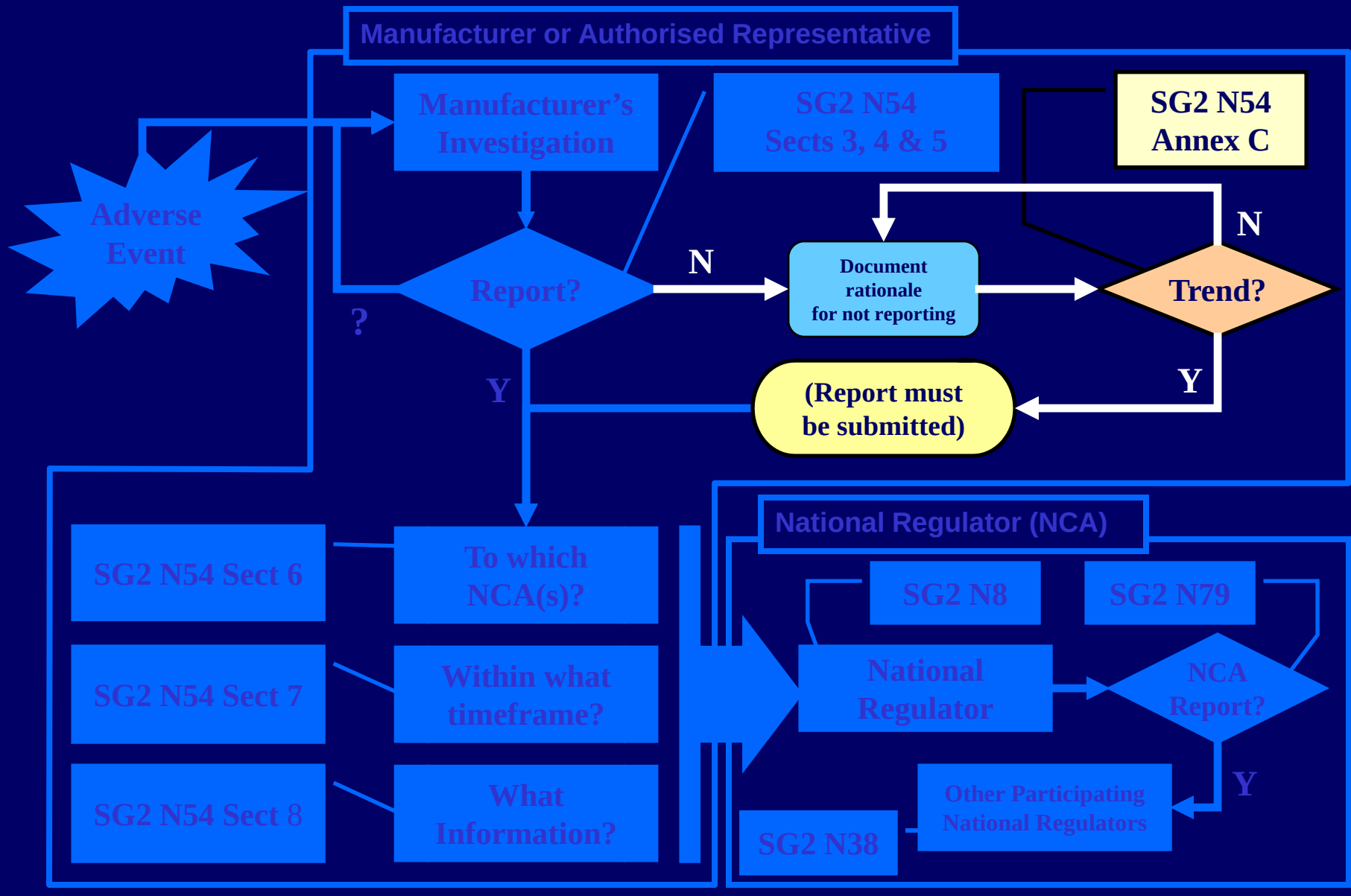
Trends

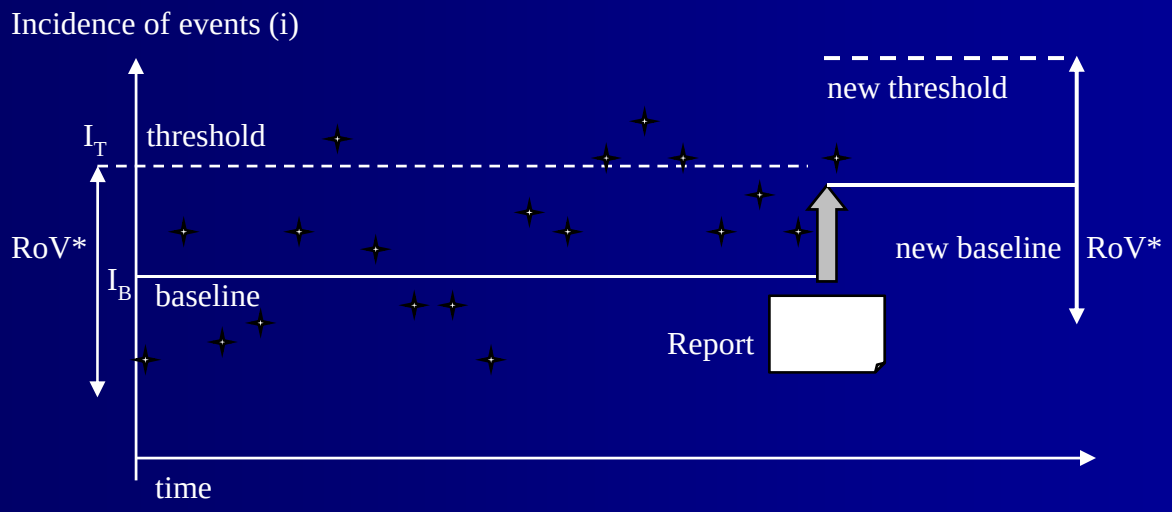

Manufacturer or Authorised Representative
Manufacturer's Investigation
SG2 N54 Sects 3, 4 & 5
SG2 N54 Annex C
Adverse Event
Report?
?
N
Document rationale for not reporting
Trend?
N
Y
Y
(Report must be submitted)
National Regulator (NCA)
SG2 N54 Sect 6
To which NCA(s)?
SG2 N54 Sect 7
Within what timeframe?
SG2 N54 Sect 8
What Information?
SG2 N8
SG2 N79
National Regulator
NCA Report?
Y
Other Participating National Regulators
SG2 N38

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

- Example of an upward shift in trend



* normal Range of Variance

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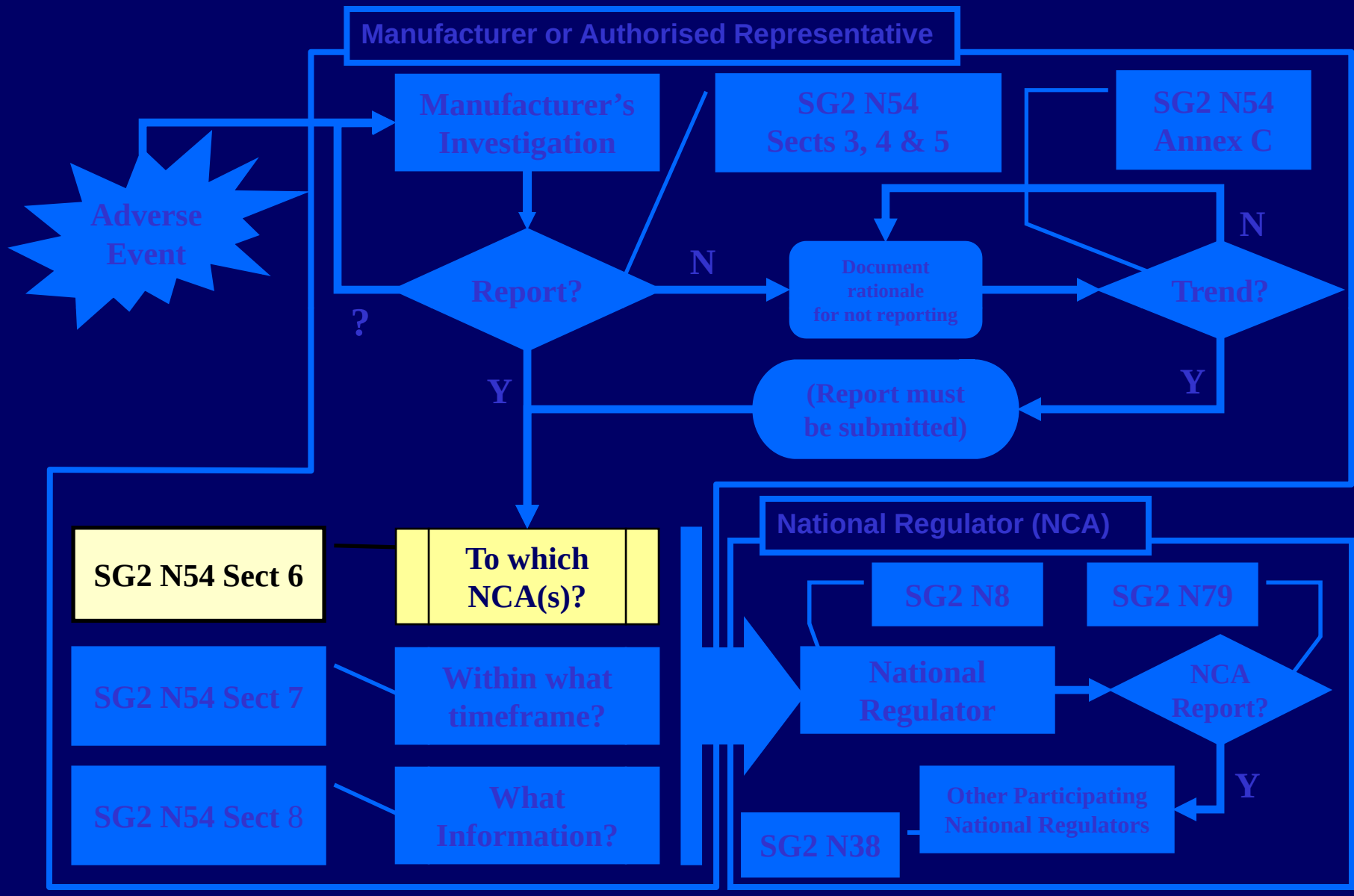
To Which NCAs to Report?



GHTF N54 Section 6
To Whom to Report

- Adverse Events must be reported to a National Competent Authority (NCA) according to applicable requirements in each jurisdiction. NCAs should provide a contact point to manufacturer from reporting
- SG2 considered several options that might resolve this situation, including the establishment of a global database for submission of adverse event reports

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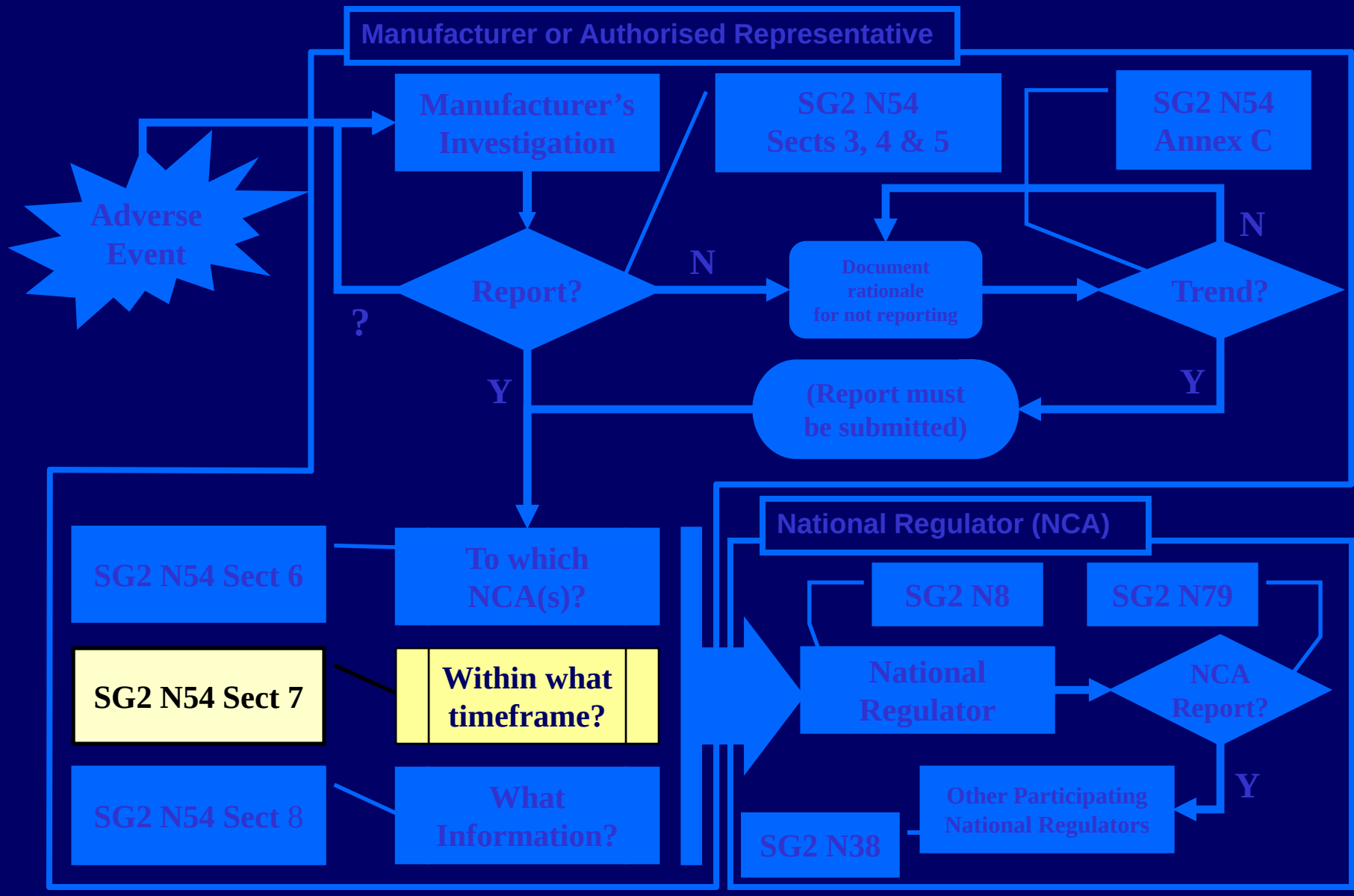
Within What Timeframe?



GHTF N54 Section 7 & Annex B

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

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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

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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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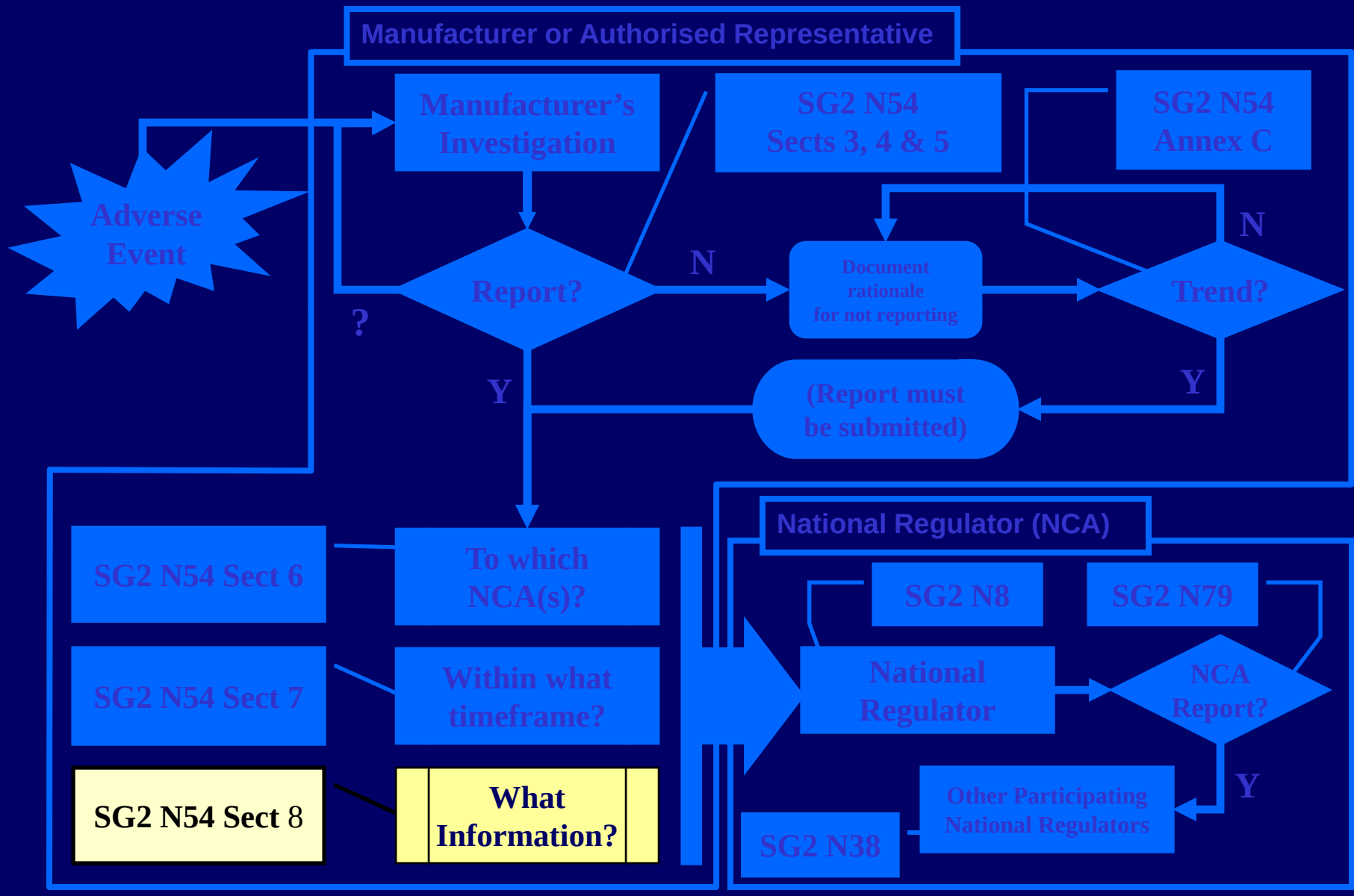
What Information (Dataset)?



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