DECODING PHARMA

QUALITY ASSURANCE DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Event Reporting and Investigation	**Effective Date:**
Supersedes: Nil	**Review Date:**
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1. **Purpose:** To define procedure for event reporting and investigation.

2. **Scope:** This SOP is applicable to all events which can affect the Safety, Identity, Strength, Purity and/or Quality of the product which can be,
   - 2.1 Facility related.
   - 2.2 Utility/Service related.
   - 2.3 Storage related.
   - 2.4 Production related or occurred during processing.
   - 2.5 Raw/Packaging material sampling, testing or release related as per recommendation.
   - 2.6 In-process and finished product sampling testing related.
   - 2.7 Distribution related.
   - 2.8 Confirmed failures out of repeat analysis and out of specification investigations.
   - 2.9 Unplanned deviations from approved procedures e.g. Standard operating procedure, protocol, BMR etc., without prior authorization and documentation.
   - 2.10 Breakdown.
   - 2.11 Any accident having impact of SISPQ of the product.
   - 2.12 Any other.

   Note: 1. Events related to equipment or machine breakdown shall be handled through breakdown maintenance system. Due to breakdown if product can be impacted then event shall be raised.
   2. This procedure is not applicable for manufacturing and analysis of trial batches, method development and method transfer activities.

3. **References, Attachments & Annexures:**

   3.1 **References:**
   - 3.1.1 SOP of Corrective/Preventive actions recommendations.
   - 3.1.2 SOP of Planned Modification.
   - 3.1.3 SOP of Change Control.
   - 3.1.4 SOP of Break down Maintenance Procedure
   - 3.1.5 SOP of Risk Management
   - 3.1.6 SOP of OOS

   3.2 **Attachments:**
   - 3.2.1 **Attachment 1:** Format for Event report.
   - 3.2.2 **Attachment 2:** Format for event report register.
   - 3.2.3 **Attachment 3:** Format for investigation report register.
   - 3.2.4 **Attachment 4:** Format for investigation report.
   - 3.2.5 **Attachment 5:** Cause and effect (fish bone) diagram for event and incident investigation.
   - 3.2.6 **Attachment 6:** Flow chart for event reporting and investigation
   - 3.2.7 **Attachment 7:** Human Error: A Quality System Based Strategic Approach.
   - 3.2.8 **Attachment 8:** Format for target date extension of Event/Investigation report.
   - 3.2.9 **Attachment 9:** Repetitive Event Trending and CAPA effectiveness evaluation.

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3.3 **Annexure** : NA

4. **Responsibilities:**

4.1 **Concerned Person:**

4.1.1 To report event to a supervisor or department head and/or Quality Assurance at the earliest.
4.1.2 To report event & investigation to a supervisor or department head.
4.1.3 To document and review the event
4.1.4 To provide feedback if required during investigation.
4.1.5 To investigate the event/incident.
4.1.6 To evaluate the impact on quality of the product.
4.1.7 To prepare the event and investigation report.
4.1.8 To provide all relevant supporting data to initiate corrective and preventive action recommended and complete it.
4.1.9 To apply for target date extension.

4.2 **Concerned Department Supervisor :**

4.2.1 To carryout investigation.
4.2.2 To prepare event and investigation report.

4.3 **Concerned Department Head:**

4.3.1 To ensure that event is reported to QA as early as possible from the notice.
4.3.2 To assign responsibility to concerned person to review and document the event and it's investigation, if required.
4.3.3 To provide guideline for event review and investigation.
4.3.4 To review and approve the event & investigation report.
4.3.5 To evaluate the impact on quality of the product.
4.3.6 To review the event and investigation report.
4.3.7 To ensure completion of all corrective action / preventive action (CAPA) recommended.
4.3.8 To ensure that all QA and CQ observations are complied.
4.3.9 To review target date extension form of event/investigation report.

4.4 **Quality Assurance:**

4.4.1 To register event and assign a sequential number to each event.
4.4.2 To evaluate impact on quality of the product and to allow the process to continue to the next phase of manufacturing, packing or release for distribution, if no impact is evident.
4.4.3 To assist in investigation.
4.4.4 To review event and investigation report.
4.4.5 To review the justification submitted in event report prior to investigation with respect to potential product or process impact in order to allow the process to continue to the next phase of manufacturing, packing or release for distribution, if no product / process impact is evident.

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4.4.6 To allot a sequential number to each investigation based on event report recommendation.
4.4.7 To maintain event report and investigation report registers.
4.4.8 To monitor the recommended CAPA and implementation through relevant SOP.
4.4.9 To monitor the event reporting and investigation as per procedure and time lines defined in the guideline.
4.4.10 To close the event and investigation report.
4.4.11 To categorize the event for criticality level.

4.5 **QA Head:**
4.5.1 To monitor the activity as per SOP.
4.5.2 To review and approve event & investigation report wherever required.
4.5.3 To recommend requirement of event notification to factory management.
4.5.4 To inform the Qualified person in case of EU and other countries as applicable in case of incidence.
4.5.5 To review event criticality as defined by QA.
4.5.6 To review target date extension form.

4.6 **Corporate Quality:**
4.6.1 To select event/investigation reports randomly for review and provide comments.
4.6.2 To suggest action based on notification received.

4.7 **Quality Head:**
4.7.1 To approve target date extension form of event/investigation report.
4.7.2 To review and approve event/investigation report when required.
4.7.3 To approve rational for continuation of related activity in case of event.

4.8 **Factory Head:**
4.8.1 To review and approve event and investigation report when required.

5. **Distribution:**
5.1 Quality Assurance
5.2 Production
5.3 Engineering
5.4 Warehouse
5.5 Quality Control
5.6 Personnel & Administration
5.7 Management Information System

6. **Definitions of Terms:**
6.1 **Event :**
6.1.1 Any unforeseen event.
6.1.2 Deviations from approved protocols or standard operating procedures without prior authorization and documentation.

6.1.3 Any variance from established specification or requirements stated in quality system document, which includes but not limited to SOP (Standard Operating Procedure), BMR (Batch Manufacturing Record), PO (Packing Order), that would affect the safety, identity, strength, purity and/or quality of the product.

6.1.4 Activity or the operation performed in excess of that defined in a BMR, SOP or other approved documents (BMR may allow adjustment of machine, pH, however on excessive number of adjustment is an event).

6.2 **Investigation**

6.2.1 General process of information or data gathering, analysis & checking possible causes to find out cause.

6.3 **Repetitive events / equipment breakdowns:**

6.3.1 Same event occurring in same product more than once. e.g. Less yield in same product batches or different product batches processed on same machine/equipment.

6.3.2 Same equipment failure/process parameter out of limit occurring in same equipment more than once. e.g. temperature out of limit during coating process.

6.3.3 The same equipment failure/process parameter out of limit occurring in different equipment/machine due to a common utility problem. e.g. cooling zone temperature out of limit in different tunnels.

6.4 **Corrective action:**

6.4.1 The term "correction" usually refers to the repair, rework or adjustment made to the product as part of the disposition of an existing nonconformity.

6.4.2 A corrective action is action taken to eliminate the causes of an existing non-conformity, defect or other undesirable situation in order to prevent recurrence.

Note: There can be more than one cause for a non-conformity. Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence.

In ISO and other guidance three terms are used to explain CAPA. i.e. Correction, Corrective action and Preventive action. But for easy understanding only two terms are used in below examples.

6.5 **Preventive action:** A preventive action is an action taken to eliminate the cause of a potential non-conformity, defect or other undesirable situation in order to prevent its occurrence.

Note: There can be more than one cause for a potential nonconformity.

Preventive action is taken to prevent occurrence whereas corrective action is taken to prevent recurrence.

6.5.1 **Examples of Corrective action and Preventive action:**

6.5.1.1 **Event:** Punch breakage while compression of drum no. 5.

6.5.1.1.1 **Cause identified:** Wear and tear on prolonged usage of the punches.

6.5.1.1.2 **Corrective actions:** 1) Passed the compressed tablets of drum number 5 through metal detector. 2) Replaced the broken punch with new punch set. 3) Destroyed the punch set.

6.5.1.1.3 **Preventive action:**1) To restrict the use of the tool set upto compression of X million tablets.

6.5.1.2 **Event :** After drying, yield of lubricated granules found approximately X kg less.

6.5.1.2.1 **Cause identified**: Particle flow sensor of FBD was switched off. The operator was not aware of the importance of the sensor.

6.5.1.2.2 **Corrective actions:** 1) Qty of lubricants reduced proportionately before lubrication. 2) Training given to the concerned.

6.5.1.2.3 **Preventive action:** The particle flow sensor shall be put on during the drying operation and shall be ensured by the supervisor and shall be made as a part of FBD checklist.

6.6 **Root Cause:** The specific reason for the failure or event. It can be confirmed root cause where the reason for failure or event is known or a probable root cause where the root cause is suspected to be reason for failure or event and need to be ascertained by further investigation or experimentation/trials/proven hypothesis.

6.7 **Abbreviation:**

6.7.1 **CAPA:** Corrective and preventive actions
6.7.2 **BMR:** Batch manufacturing record.
6.7.3 **SISPQ:** Safety, Identity, Strength, Purity and Quality.
6.7.4 **FDA:** Food and drugs administration.
6.7.5 **EIR:** Event investigation report.
6.7.6 **ISO:** International organization for standardization.
6.7.7 **CDER:** Center for drug evaluation and research.
6.7.8 **QA**: Quality Assurance
6.7.9 **SOP**: Standard Operating Procedure
6.7.10 **MIS**: Management information System
6.7.11 **OOS**: Out of Specification.

7. Procedure:

7.1 Event reporting, investigation and closing:

7.1.1 Reporting of events:

7.1.1.1 All events must be reported immediately to responsible supervisor or department head. QA department shall clarify in case if there is any question or doubt whether any observation is an event or not.

7.1.1.2 In case the event has occurred during sampling, dispensing, manufacturing or packaging of the material /batch, the material or batch shall be immediately kept on QA Hold. This will help to ensure that batch is not released for distribution prior to closure of the event.

7.1.1.3 Event shall be initiated in following circumstances:

7.1.1.3.1 Processing deviation that have affected or potentially could affect SISPQ of product.
7.1.1.3.2 A general system failure to follow procedure.
7.1.1.3.3 An action limit is exceeded.
7.1.1.3.4 A value is outside the processing parameters.
7.1.1.3.5 At the discretion of QA department, when there are excessive minor errors and/or recording errors. Errors that are found and corrected by manufacturing; however, are repetitive.
7.1.1.3.6 When documents are reviewed reviewer may ask to raise an event investigation report based on the information (or lack of required information) recorded in the documents.
7.1.1.3.7 Based on QA's recommendation in breakdown maintenance memo in case of equipment/machine or related utility breakdown while product processing which may impact SISPQ of product/associated batch(es).

7.1.1.4 A single event report may be used for more than one lot if the date of event or date of reporting of event is same.
7.1.1.5 Event report shall not be issued for minor events such as unjustified cross out, write over. The same can be documented in history sheet of BMR.
7.1.1.6 Events that are identified/noticed by concerned department, which do not have potential impact on product or process and the same is documented with corrective actions taken do not require filing of an event report e.g. spillage of raw material.
7.1.1.7 This procedure is not applicable in case of event in method development, analysis for trial and study purpose.

7.1.2 **Event Report Preparation :**

7.1.2.1 The person identifying the event shall fill the event report (Refer Attachment – 1) and forward to department head/QA.
7.1.2.2 The event report shall be filled as per the following guideline.
7.1.2.3 **Event Report No.**

7.1.2.3.1 QA shall allocate event report number as per below procedure and enter the details in Attachment-2.
7.1.2.3.2 Event report number shall be allocated as per following system.
7.1.2.3.3 It shall be in the format of "**EIR-X-YY/NNN**".

Where, **EIR** is for Event Report, **X** refers to department code (Refer Table – 1)
"YY" shall refer to year of event. Last 2 digit of year (19 for 2019 and 20 for 2020 and so on.)
"NNN" refers to serial no. of event in the particular department.
Every year, 3 digit serial number shall start from 001 and shall run continuously irrespective of the change in department code.

e.g. First event of 2022 in QA department shall be EIR-QA-1/001, second event of 2022 in QC department shall be EIR-QC-22/002.

Table – 1

DEPARTMENT	CODE
Quality Assurance	QA
Quality Control	QC
Warehouse	WH
Production	PRD
Engineering	ENG
Personnel	PER
Information Technology	IT

7.1.2.4 **Date of event:** Mention date on which event occurred.

7.1.2.5 **Reported by/Date:** Mention name of individual by whom event is reported and date on which event was reported. (It shall be date of observation)

7.1.2.6 **Department:** Mention name of department in which event has happened.

7.1.2.7 **Documented by/Date:** Mention name of supervisor who drafted & documented the event along with date of starting of documentation.

7.1.2.8 **Product/Material/System details:** Mention name of Product/Material/System if the event is related to it. Otherwise mention not applicable (N/A).

7.1.2.9 **Batch/Document/Equipment no. :** Mention Batch no./A. R. No./Reference Document no./Equipment no. if the event is related to it. Otherwise mention N/A.

7.1.2.10 **Event description:** Mention detail description of the event which shall include, When (date and time), Where (location/area/room no.), with What (material/product, B. No./A. R. No./equipment/machine), by Whom (person involved if any) and How (event/malfunction seen) the event seen/happened/noticed. Also include impact on product if affected due to event.

7.1.3 **Following questions can be asked to formulate an event.**

7.1.3.1 **Identity**

7.1.3.1.1 What is the unit with the malfunction?

7.1.3.1.2 What is the malfunction?

7.1.3.2 **Location**

7.1.3.2.1 Where is the malfunction seen?

7.1.3.3 **Timing**

7.1.3.3.1 When was the malfunction seen?

7.1.3.3.2 When has it been seen since?

7.1.3.4 **Magnitude**

7.1.3.4.1 What is the extent of the malfunction?

7.1.3.4.2 How many units are affected?

7.1.3.4.3 How much of any one unit is affected?

7.1.3.5 **Brief event review**

7.1.3.5.1 Event review/preliminary investigation shall be done to find out the cause of the event which shall include following. (Refer : Attachment-5)

7.1.3.5.2 The review findings/outcome and conclusion shall be mentioned in brief instead of only specifying like “satisfactory”/“OK”/“within limit”.

7.1.3.6 **Discussion with concern person**

7.1.3.6.1 Interview of the employee who witnessed the event should be performed as soon as possible to know the exact details of the event.

7.1.3.7 **Document review:** Review following documents depending on the event and include findings.

7.1.3.7.1 Batch manufacturing record.

7.1.3.7.2 Batch packing record.

7.1.3.7.3 Standard operating procedure.

7.1.3.7.4 Stability data

7.1.3.7.5 Cleaning and usage record of equipment/tools/machines.

7.1.3.7.6 Sensitization/Sterilization/depyrogenation record.

7.1.3.7.7 Environment monitoring record.

7.1.3.7.8 Raw/packaging/IP & FP sampling/analytical records.

7.1.3.8 **Equipment/Machine review**

7.1.3.8.1 Preventive maintenance or breakdown history of the machine.

7.1.3.8.2 Review of cleaning and usage log.

7.1.3.8.3 Operating parameters (whether within qualified range)

7.1.3.8.4 Calibration or qualification record.

7.1.3.8.5 Standard operating procedure.

7.1.3.9 **Manpower review**

7.1.3.9.1 Review of training record.

7.1.3.9.2 Review of job responsibility.

7.1.3.9.3 Human Error: A Quality System Based Strategic Approach (Attachment-7) as explained below shall be followed.

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Error	Corrective Action	Preventive Action
Knowledge Based	• Proceduralize requirements • Train Employee	• Review Department Training Program • Close Gaps
Lapse Based	• Counsel Employee (Verbal, Written, Disciplinary)	• GMP training
Cognitive Based	• Match Employee to Abilities	• Evaluate Knowledge Assessment Effectiveness
Value Based	• Counsel Employee (Verbal, Written, Disciplinary)	• GMP training
Skill Based	• Match Employee to Abilities	• Evaluate Knowledge Assessment Effectiveness
Time Pressure	• Increase staffing • Reassign duties • Create or Update Plans (Planning)	• Conduct process FMEA
Inadequate Equipment	• Increase Inspection & Checks • Equipment Lock Out / Tag Out • Re qualify / Re validate after fixing or replacing Equipment	• Evaluate adequacy of Qualification / Validation Resources and Procedures. • Close Gaps
Fatigue	• Increase Staffing • Plant layout study • Reassign Duties	• Flow chart Processing • Conduct Process FMEA • Evaluate Resources Lading • Close Gaps
Inexperience	• Match Employee to Abilities	• Evaluate Knowledge Assessment Effectiveness
Design & Construction Deficiencies	• Increase Inspection & Checks • Equipment Lock Out / Tag Out • Re qualify / Re validate after fixing or replacing Equipment	• Evaluate adequacy of Qualification / Validation Resources and Procedures. • Close Gaps
Unworkable Procedures	• Revise Procedure • Conduct Training to new revision	• Flow chart Processing • Conduct Process FMEA • Update procedure • Conduct Training

7.1.3.10 **Material review**

7.1.3.10.1 Raw material, packaging material, in-process, finish product specification, test procedure and analytical report.

7.1.3.10.2 Vendor qualification.

7.1.3.10.3 Material stock record.

7.1.3.10.4 Storage Conditions

7.1.3.11 **Other**

7.1.3.11.1 Include any other parameters depending on the nature of the event.

7.1.4 **Root cause (assignable/probable)**

7.1.4.1 A clear description of identified/probable root cause of event shall be recorded based on review findings.

7.1.4.2 If no root cause or probable root cause is identified then it shall be mentioned that assignable root cause not identified.

7.1.4.3 If root cause identified then check whether event is repetitive.

7.1.5 **Impact analysis:** Impact analysis on risk based approach to be studied & documented on product batch/es, system, machine etc. as applicable.

7.1.5.1 If there is no impact on quality of the product: Release the batch/es.

7.1.5.2 If there is impact on quality of the product: Extrapolate the impact to affected batches of same or other products.

7.1.5.3 If there is impact on other batches: Allot Investigation No. to the event and carry out investigation. If the there is no impact on other batches: Release the affected batches.

7.1.6 **Corrective Actions (Prerequisite for Batch Release)**

7.1.6.1 Include the corrective actions to be taken as a prerequisite for the batch release.

7.1.7 **Other Corrective and Preventive Actions taken/recommended**

7.1.7.1 Include Corrective and Preventive actions if any. Corrective actions and Preventive actions which need a long term action plan shall be monitored through corrective action request (CAPA). Reference CAPA number shall be recorded in the event report.

7.1.8 **Root cause identification/Repetitive event/Impact on other batches (including marketed batches if required):**

7.1.8.1 Evaluation on root cause identification, repetitive event and impact on other batches shall be included as “X” by concerned department in consultation with QA.

7.1.8.2 To identify the repetitive event, last one year trend of event (from the date of the event) shall be checked. For example if the event occurred on 15th June 2021, event history of June 2020 to June 2021 shall be checked.

If event is repetitive	Record repetitive event number and raise investigation number.
If event is not repetitive	Do impact analysis.

7.1.9 **Event Level**

7.1.9.1 Events shall be categorized based on the criticality of the levels of events i.e. Level 1, Level 2 & Level 3. The event criticality level shall be decided by QA personnel. Levels of events can be defined as below :

7.1.9.2 The criticality level can be decided based on nature of event, identified root cause and impact on other lots / batches.

7.1.9.3 **Level 1:** No impact on quality of product. e.g. Material spillage/ documentation / recording / calculation errors etc.

7.1.9.4 **Level 2:** No significant impact on quality of product and failure of QA system e.g. Utility fluctuation, out of specified range, equipment breakdown, process parameters not achieved, failure in in-process checks by production, yield out of limit etc.

7.1.9.5 **Level 3:** Significant impact on product or unknown root cause or repetitive event after implementation of CAPA. Significant unknown root cause covers investigation and CAPA. Monitoring of CAPA on yearly basis. e.g. Failing in IP/FP specifications (OOS results), product mix-up, cross contamination, accountability is out of limit etc.

7.1.10 **Batch disposition**

7.1.10.1 Decision on event batch/es & other batches disposition whether released or rejected shall be included by QA based on event evaluation.

7.1.10.2 This decision shall be “decision in principle” based on impact of event on the batch and list corrective and preventive actions.

7.1.10.3 Actual batch disposition shall be done once all corrective actions identified as pre-requisite for batch release are completed.

7.1.11 **Investigation Number :** Assign a investigation number in following conditions :

7.1.11.1 The root cause of event is not identified and a detailed investigation is to be carried out to identify the root cause.

7.1.11.2 The event is of repetitive nature hence need an detailed investigation so that elaborate CAPA can be defined.

7.1.11.3 There is an impact on other batches and the impact need to be investigated and evaluated in detail.

7.1.11.4 In case of confirm OOS results where laboratory errors are ruled out.

7.1.11.5 The Investigation number shall be assigned as per **X-YY/NNN** format and record the details in Attachment-3.
Where **X** refers to Department Code,
Department code shall be used as per mentioned in the Table-1 given under point number 7.1.2.3 (for Event Report numbering).

YY refers to year. Last 2 digit of year shall be 21 for 2021, 23 for 2023 and so on.
"NNN" refers to serial no. of event which runs continuously irrespective of the change in department code.
Every year 3 digit serial number shall start from 001.
e.g. First Investigation report of 2021 in QC department shall be numbered as QC-21/001, Second Investigation report of 2021 in Production department shall be numbered as PRD-21/002.

7.1.12 If Investigation is not required mention NA for Investigation number, allotted by, investigation completion date, responsible person.

7.1.13 A list of events shall be sent to CQ on weekly basis for their reference and notification purpose. CQ shall select events based on criticality.

7.1.14 The chosen event reports shall be send to CQ either in draft form or signed one depending on 15 days time line. CQ shall review the events. CQ comments shall be updated in final print out of event if the report was forwarded in draft form or through an addendum to event report if the event was forwarded after approval.

7.1.15 **Prepared by**

7.1.15.1 The person who has prepared the event report shall sign the same with date.

7.1.16 **Reviewed by**

7.1.16.1 Section head, QA and Concern department Head shall review the report and sign the same with date.

7.1.17 **Approved by**

7.1.17.1 QA Head shall review and approve the report signing the same and placing the date.

7.1.18 **Notification to Factory Management**

7.1.18.1 QA Head shall recommend requirement of event notification to factory management based on level of event and nature of criticality.

7.1.18.2 The event report based on QA Head's recommendation shall be sent to Factory Management for approval in case of following, but not limited to

7.1.18.2.1 For level 3 events

7.1.18.2.2 If event triggers an investigation

7.1.18.2.3 If QA head feels that the event report needs review and approval of Factory management.

7.1.18.2.4 Mention NA if event is of Level – 1 or 2 and QA Head decides that Notification to Factory Management is not required.

7.1.18.3 The event report shall be returned back to concerned department for taking approval of Factory management.

7.1.19 The event/investigation details shall be entered in the register as per Attachment-2 and Attachment-3 respectively and the register shall be updated.

7.1.20 A photocopy of approved event/investigation report shall be filed in respective Batch Records.

7.1.21 **Batch Disposition**

7.1.21.1 Once corrective actions identified as pre-requisite for batch release have been completed, QA shall verify the same and release the batch for further processing.

7.1.22 **Closure of Event Report**

7.1.22.1 All event report shall be closed once the batch disposition is done. CAPA shall be issued for tracking the rest of the Corrective and Preventive actions which are not completed.

7.1.23 **Time line**

7.1.23.1 All event report shall be signed off within 15 working days from the date of reporting of event or before batch release whichever is earlier. However, concerned department can obtain an extension for due date to complete event investigation from QA Head.

7.1.23.2 To get extension Attachment no.8 shall be filled by concerned department. It shall be reviewed by Concerned Department Head, QA head and shall be approved by Quality Head.

7.2 **Investigation Report preparation:** Investigation report shall be prepared as per guideline given below. (Refer investigation report format as Attachment-4).

7.2.1 **Investigation Report No.**

7.2.1.1 Mention investigation report number referring event report register or event report. Make entry of issuance in the register as per Attachment-3.

7.2.2 **Reference Event Report No.**

7.2.2.1 Mention reference event report number referring investigation report register or event report.

7.2.3 **Event Level**

7.2.3.1 Mention event level referring event report.

7.2.4 **Date of Event**

7.2.4.1 Mention the date on which event occurred.

7.2.4.2 Product/Material/System Name, Batch/Document/Equipment No. & Event description: Details shall be reproduced from event report.

7.2.5 **Investigation details**

7.2.5.1 Documents can be reviewed for the investigation of event based on it's nature.

7.2.5.2 Cause and effect diagram given in Attachment-5 which can be referred for investigation and to identify causal factors.

7.2.5.3 History (whether such incidences happened in past) shall be reviewed.

7.2.5.4 Following documents but not limited to shall be reviewed (as required):

7.2.5.4.1 Manufacturing documents.

7.2.5.4.2 Cleaning documents.

7.2.5.4.3 Environment monitoring records.

7.2.5.4.4 Sequential logs of equipments/machines.

7.2.5.4.5 Qualification/calibration records of equipments/machines.

7.2.5.4.6 Preventive/breakdown maintenance records of equipments/ machines.
7.2.5.4.7 Relevant SOPs.
7.2.5.4.8 Relevant specification/test procedures/sampling procedure.
7.2.5.4.9 Stability data.
7.2.5.4.10 Training documents of concerned persons.
7.2.5.4.11 Trend of process/quality parameters of the product/equipment/ material used. (comparison of event batch with other batches).

7.2.5.5 The investigation report shall also address review of additional testing/trial data as appropriate and risk assessment.

7.2.6 **Root cause**

7.2.6.1 A clear description of identified and / or probable root cause of event shall be recorded based on investigation. If no root cause is identified, it shall be mentioned that assignable root cause not identified.

7.2.6.2 Examples of some of the root causes are given below for guidance purpose.

Causes for production related events can be	• Reason for equipment malfunctioning • Working process not defined properly • Reason for Utility failure • Lack of communication • Lack of knowledge of working personnel • Reason for environment variability (Temperature, Humidity) • Use of unqualified / uncalibrated / machine / equipment.
Causes for storage related events can be	• Material lost due to improper storage • Not knowing the storage conditions • Storage conditions not followed properly • Spillage during storage • Human error in handling • Dispensing error
Causes for facility related events can be	• Inadequate facility: Congested, Dirty, cracking, drainage, uncontrolled environment etc. • Inadequate Equipment: Not meeting range, non-calibrated, not precise etc. • Inadequate Man-power: Insufficient, un-trained, un-educated, inexperienced etc.
Other causes include	• Vendor Change • Wrong Specification • Improper sampling technique • Improper supervision

7.2.7 **Impact analysis**

7.2.7.1 Include the impact on product batch/es due to the action taken. Summary of impact analysis on other products/batches/marketed batches/product quality/ sterility assurance/system/environment as applicable shall be referred as a part of risk analysis.

7.2.7.2 If impact analysis reveals that there is impact on marketed products then requirement of notification to regulatory bodies eg. Field Alert Report shall be evaluated.

Note : In case of event if investigation is required and parallely activity related to event is required to be continued (eg.: production of batches) , separate rational for continuation of activity shall be given which shall be approved by quality head.

7.2.7.3 In investigation if impact on process validation is concluded then adequacy and suitability of process validation shall be evaluated. If required revalidation shall be done.

7.2.7.4 If in the same drug product again event is observed and impact on process validation is concluded then redevelopment shall be initiated and further commercial manufacturing of the drug product shall be hold.

7.2.8 **Corrective Actions (pre-requisite for Batch Release)**

7.2.8.1 Include the immediate corrective actions taken to correct machine/system/ batch. Identify the CA which are pre-requisite for batch release.

7.2.9 **Other corrective and Preventive actions (taken/recommended)**

7.2.9.1 Include preventive actions if any

7.2.9.2 Preventive actions shall be monitored through corrective action request (CAPA). Reference CAPA number shall be recorded in the investigation report.

7.2.10 **Information to third party required (if required) given by / Date**

7.2.10.1 If information to third party is required then information given by name and date on which information has been given to third party shall be mentioned in this column.

7.2.11 **Recommendation for batch disposition**

7.2.11.1 Investigation team shall mentioned their recommendation for disposition of batch based on investigation findings.

7.2.11.2 Final decision on disposition of event batch/es & other batches disposition shall be decided by QA Head based on event evaluation.

7.2.11.3 This decision shall be only decision in principle based on impact of event on the batch and list corrective and preventive actions.

7.2.11.4 Actual batch disposition batch shall be done once all corrective actions identified as pre-requisite for batch release are completed.

7.2.12 **Conclusion**

7.2.12.1 Final conclusion shall be mentioned based on investigation findings.

7.2.13 A list of events shall be sent to CQ on weekly basis for their reference and notification purpose. CQ shall choose the no. of events required for their review from the list given.

7.2.14 The chosen event reports along with investigation reports wherever applicable shall be sent to CQ either in draft form or signed one depending on 30 days time line. CQ shall review the reports. CQ comments shall be updated in final print out of report or through an addendum to event report.

7.3 **Investigation time-lines and closing**

7.3.1 The investigation of an event can be initiated parallel to process of event documentation.

7.3.2 The concerned department shall complete the report within 30 calendar days from date of event reporting.

Note : QA will ensure the closure of the investigation before final release of the batch.

7.3.3 To get extension Attachment-8 shall be filled by concern department. It shall be reviewed by Concern Department Head, QA head and shall be approved by Quality Head.

7.3.4 All event investigation report shall be closed once the batch disposition is done. CAPA shall be issued for tracking the rest of the corrective and preventive actions which are not completed.

7.4 **Review and approval of investigation report :**

7.4.1 Thus prepared investigation report shall be circulated for reviewed by concerned Department Head, Production Head and QA Head.

7.4.2 The concerned department shall forward the investigation report to Factory Head and Quality Head for review and approval.

7.5 **Final disposition of batch and closure of investigation :**

7.5.1 It shall be filled by QA Executive or designee with date.

7.6 **Archival of event and investigation reports :**

7.6.1 Event report and investigation report shall be attached together and shall be archived in the QA department.

7.6.2 Copy of closed CAPA shall be attached with respective event or investigation report wherever needed.

7.6.3 If an Attachment is prepared to address the comments of any internal or external reviewer, the same shall also be archived.

7.7 **Periodic review of events**

7.7.1 Event trend shall be evaluated on quarterly basis based on the criticality of the event levels for identification and correction of reoccurring / repetitive events as well as for effectiveness of CAPA (Corrective Actions and Preventive Actions) to reduce/prevent repetitive events.

7.7.2 Product wise and root cause type-wise trending of repetitive events with respect to CAPA shall be done as per Attachment-9 after the end of each quarter.

7.7.3 Root cause type shall be defined as below

7.7.3.1 Equipment related

7.7.3.2 Human related
7.7.3.3 Material related
7.7.3.4 Process related

7.7.4 Based on quarterly review umbrella investigation to be prepared for repetitive nature of event and investigation.

7.7.5 Based on umbrella investigation requirement of further CAPA shall be identified.

7.8 **Management notification :**

7.8.1 Critical events shall be immediately notified to management (CQ).

7.8.2 If for any event, CAPA is taken and before closure of the same, another similar event occurs then notification to management (CQ) shall be sent and decision to release the batch(s) shall be taken on case by case basis based on impact on SISPQ.

7.9 **Addendum report :**

7.9.1 Event/investigation reports can be re-opened for further investigation under circumstances as listed below. An addendum report shall be prepared for further updation.

7.9.1.1 If the document is found to be deficient on further review.
7.9.1.2 If the CAPA suggested in report on implementation are found to be inadequate to avoid events from repetition.
7.9.1.3 If any auditor/reviewer finds event/investigation report deficient or inadequate.

DECODING PHARMA

QUALITY ASSURANCE DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Event Reporting and Investigation	**Effective Date:**
Supersedes: Nil	**Review Date:**
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Attachment – 1
Event Report

Report No.:_____

Date of Event:		**Reported By:**		**Reported Date :**	
Department:		**Documented By:**		**Documented Date:**	
Product / Material / System Details:				**Batch / Document / Equipment no. :**	

Event Description :

Target date for investigation completion:	Revised target date (if investigation not completed in time):

Investigation Team:			
Subject Expert:	(Name)	(Designation)	(Sign & Date)
Department Head:	(Name)	(Designation)	(Sign & Date)

QA representative:	(Name)	(Designation)	(Sign & Date)
Other member as suggested by QA Head:	(Name)	(Designation)	(Sign & Date)

Brief Review
Discussion with concerned person :

DECODING PHARMA

QUALITY ASSURANCE DEPARTMENT

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Brief Review			
Document review:			
Equipment review:			
Manpower review:			
Material review:			
Others:			
Root cause (Assignable ☐ /Probable ☐):			
Impact analysis:			
Corrective Actions (pre-requisite for Batch Release) :			
Other Corrective Actions & Preventive actions : **CAPA no.**			
Root cause identified : **Yes** ☐ / **No** ☐	Repetitive event : **Yes** ☐ / **No** ☐	Impact on other batches : **Yes** ☐ / **No** ☐	Event Level :_____ (To be filled by QA)
Batch disposition:	**To Be Released** ☐	**To Be Rejected** ☐	**Refer Investigation** ☐
In case root cause not identified or repetitive event or/there is impact on other batches, assign investigation number to investigate it further.			
Investigation Number		**Alloted by/Date:**	
Investigation completion date *(within 30 days from date of event reporting)*		**Responsible Person**	
Remarks of Approver (if any):			

DECODING PHARMA

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Brief Review				
Signatures				
Prepared By / Date	**Reviewed by / Date Section In-charge**	**Reviewed by / Date Department Head**	**Reviewed by / Date Quality Assurance**	**Approved by/ Date QA Head**

Notification to factory management to be given in case of an event is level 3, triggers investigation or as decided by approver of the event.
Notification to Factory Management required Yes ☐ / No ☐

(Factory Head)	:	**(Quality Head)**	:

Final Batch Disposition :

QA Executive (or Designee) / Date

Closure of Event Report :

QA Executive (or Designee) / Date

DECODING PHARMA

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Attachment – 2
Event Report Register

S.No.	Event Report No.	Date of reporting	Product/ material/ equipment/ instrument/ system name	Doc. No./B. No./ Equipment No./Instrument No.	Event description	Target Date of Completion	Root cause identified/not identified	Event level	CAPA No.	Status (Open/Closed)	Investigation No.	Remarks	Sign

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Attachment – 3
Investigation Report Register

S.No.	Investigation No.	Product/ material/ equipment/ instrument/ system name	Doc. No./B. No. /Equipment No./ Instrument No.	Investigation description	Ref. Event Report No.	Target date for completion	Responsible person	Status (Open/Closed)	CAPA No.	Remarks	Sign

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Attachment – 4
Investigation Report

Investigation Report No.:	**Date of Event**	
Reference Event Report No.		
Event Level		
Product/Material/System Name:		
Batch/Document/Equipment no.:		
Investigation Description:		
Investigation details:		
Root cause		
Impact analysis		
Corrective Actions (Pre-requisite for batch release)	**CAPA no.**	
Preventive actions taken/recommended	**CAPA no.**	
Information to third party required (if required) given by/Date		

DECODING PHARMA

QUALITY ASSURANCE DEPARTMENT

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Recommendation for batch disposition:	
Conclusion	

Remarks of Approver		
Prepared By **Sign & Date:**	**Reviewed by** **(Section In-charge):**	**Reviewed by** **(Quality Assurance):**
Reviewed by **(Department Head):**	**Reviewed by** **(QA Head):**	
Approved by **(Factory Head):**	**Approved by** **(Quality Head):**	
Final Disposition of Batch		**QA Executive (or Designee)/Date**
Closure of Investigation		**QA Executive (or Designee)/Date**
***Note: Content of investigation report can be changed according to the nature of event.**		

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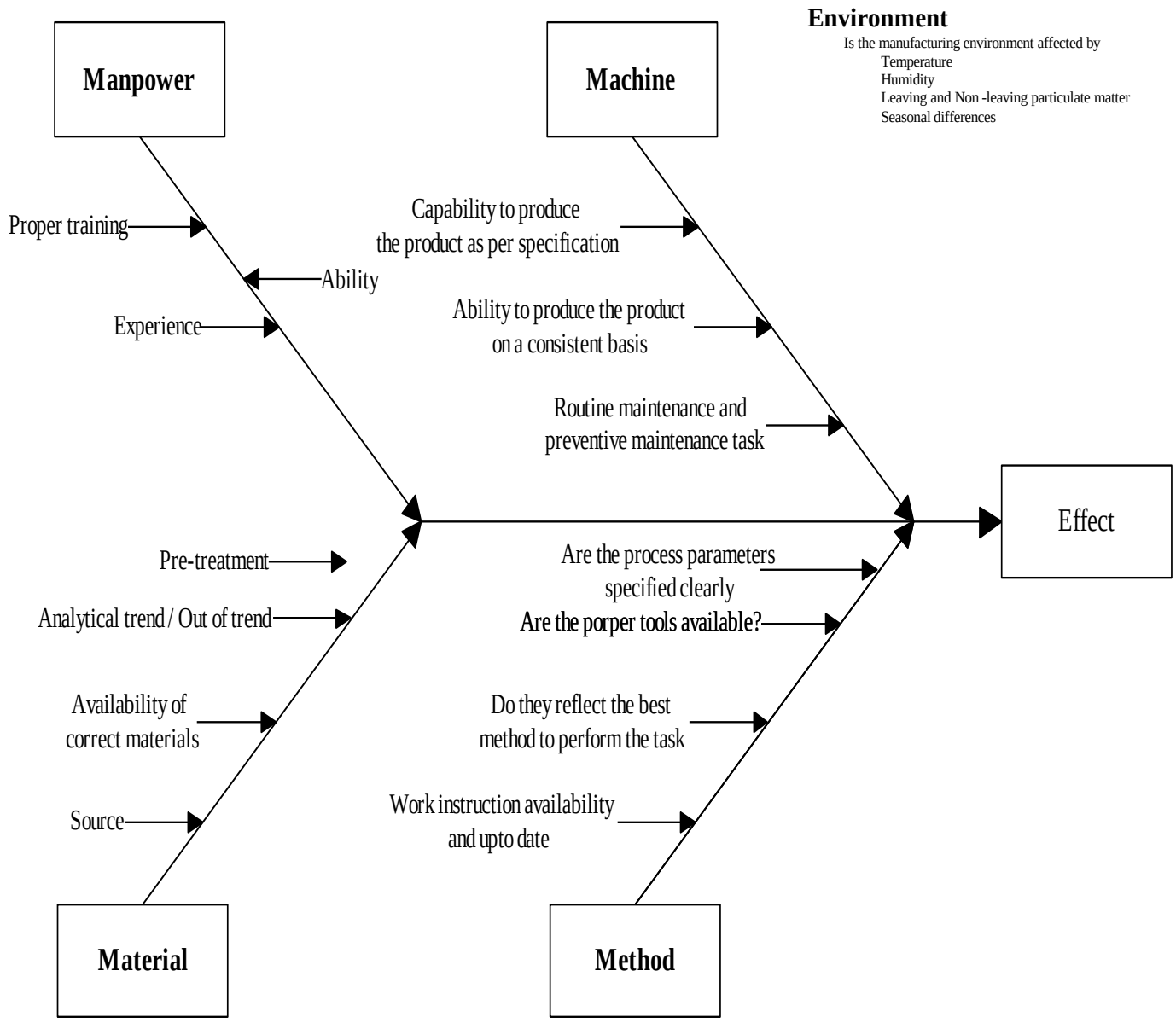
Attachment-5

Cause and effect (Fish bone) diagram for event/Incident investigation



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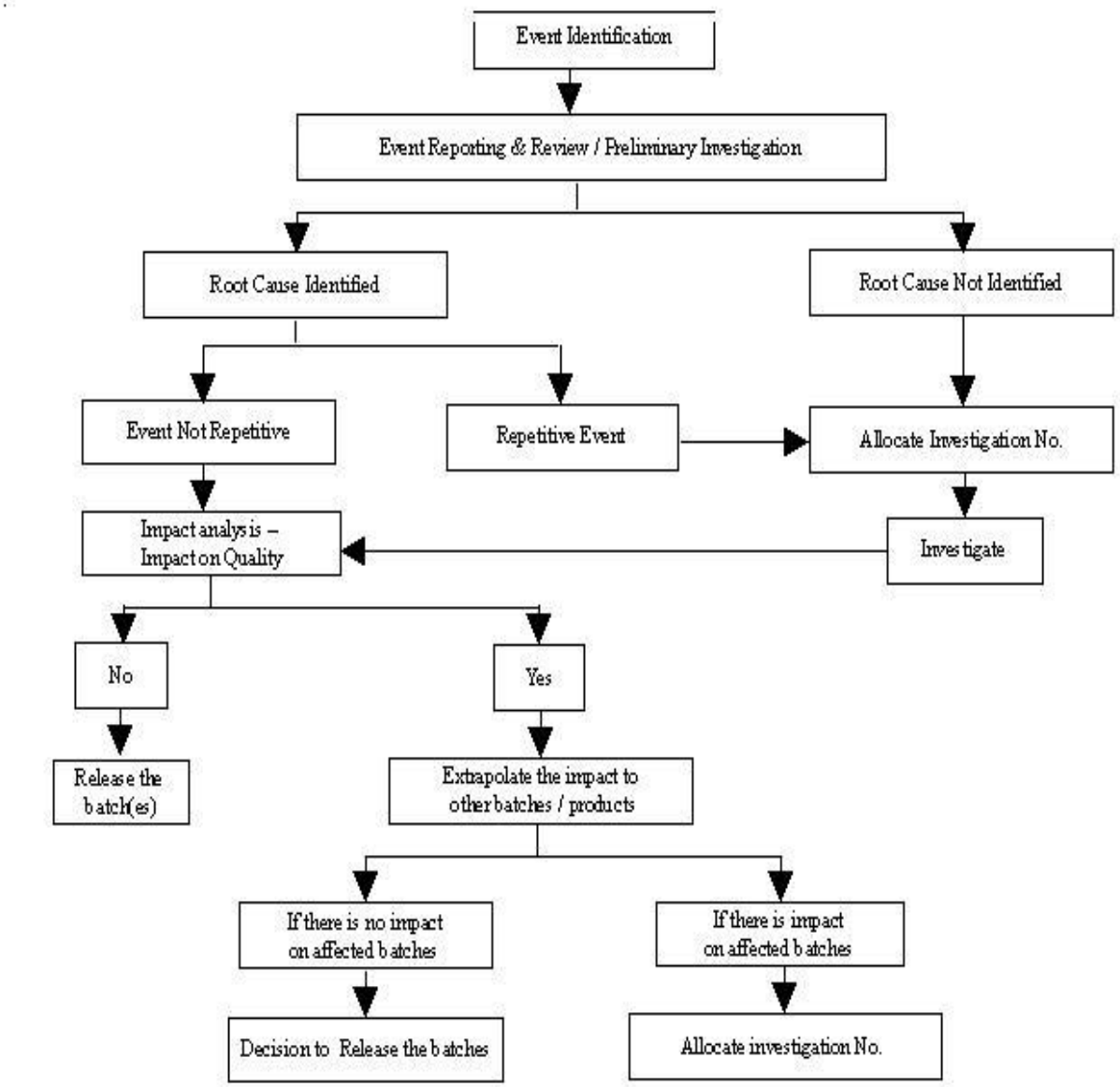
Attachment-6
Flow chart for event reporting and investigation



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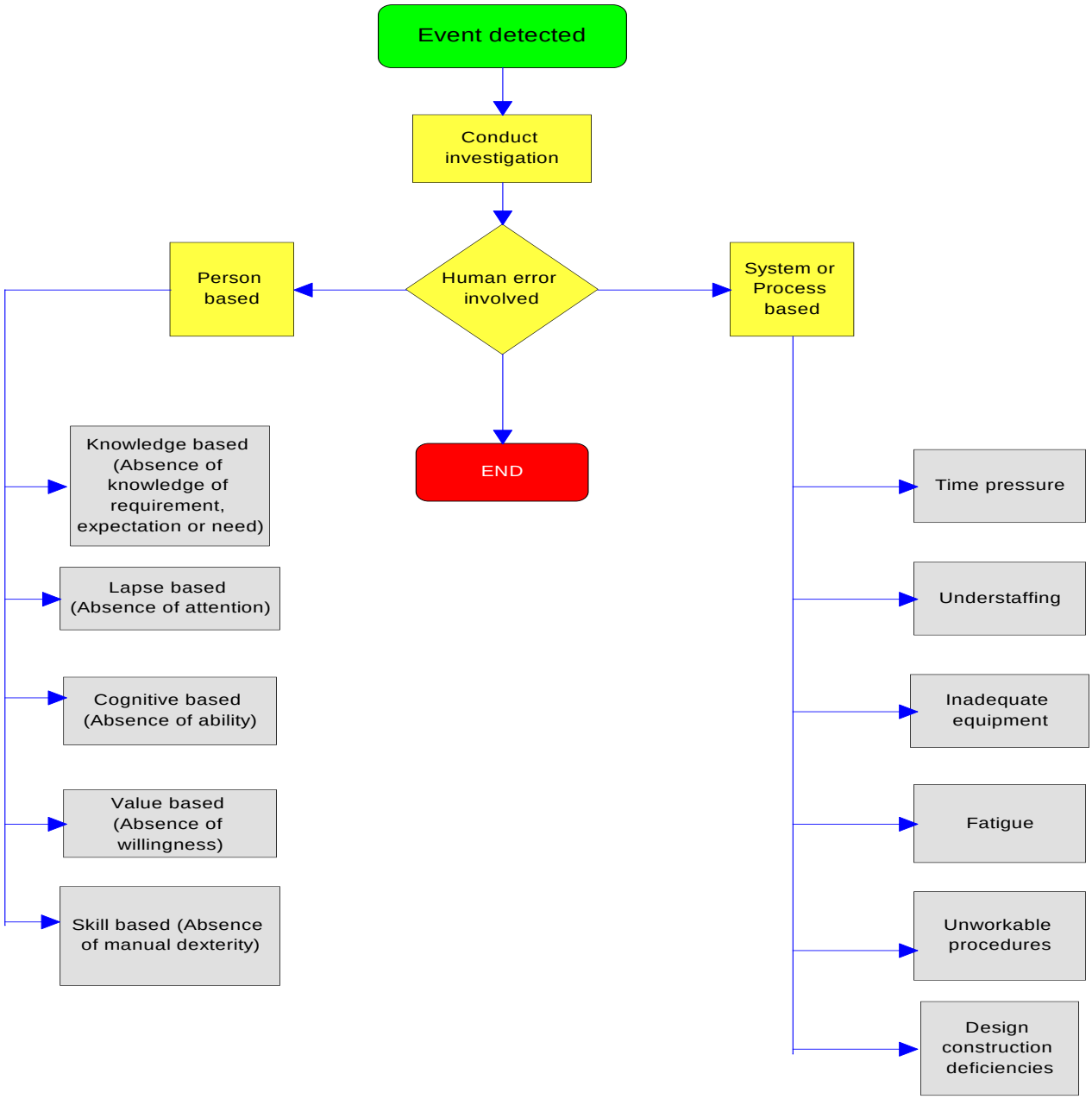
Attachment-7

Flow Chart for Human Error: A Quality System Based Strategic Approach



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Attachment 8
Format for target date extension of Event/Investigation report

Event Report No.: _____ Investigation report No. : _____

Initial Target Completion date: _____

Current status of Investigation:

Pending activities for Investigation:

Reason for delay:

Justification for Delay

Revised target Date:

Prepared by: Reviewed by Department Head Reviewed by QA

Approved by Quality Head

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Attachment 9
Repetitive Event Trending and CAPA effectiveness evaluation

Date of Event	Event No.	Event Level	Product name	B. No.	Event details	Root cause type	Action taken	CAPA	Remarks
								Review of Qtr-2 **Review of Qtr-3** **Review of Qtr-4**	
								Review of Qtr-2 **Review of Qtr-3** **Review of Qtr-4**	
								Review of Qtr-2 **Review of Qtr-3** **Review of Qtr-4**	

8. **History:**

Version No.		Effective Date	