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Review Article

Handling of Deviation Control in Pharmaceutical Industry: A Review

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Abstract

Deviation: Deviation can be defined as any activity/ event which is in the form of noncompliance from designed standard. Deviation happened in pharmaceutical industries on day to day basis during performing the routine activities.

Various Regulatory health authorizes has defined procedure to address the occurred deviation during the operational activities to understand the impact of deviation on the quality of the products.

Regulation are in place as per the ICH norms to handled the unavoidable circumstances by recording the deviation occurred and thereafter to address the same considering the impact of the same on quality, efficacy and safety of the drug products.

Details below are on deviation controls and its handling methodology to address the issue accordingly.

Planned Deviation: Planned deviation can be defined as activity/ event which is planned in advance/ priory to perform differently against the standard.

Incident/ Unplanned Deviation: An incident can be defined as unplanned or uncontrolled activity/ event in the form of non-compliance from designed standard.

Correction: Repair, rework or adjustment and related to the disposition detected discrepancy/ nonconformance.

Corrective Action: Action taken to rectify or correct a specific deviation or undesirable situation is known as corrective action.

Preventive Action: Action taken to eliminate the cause of deviation or undesirable situation to prevent the future occurrence of similar instances is known as preventive action.

Keywords: Deviation, Deviation Control

Introduction

No deviation is permitted to the laid down procedure. However, in case the deviation has been found unavoidable, the same must be immediately brought to the notice of Quality Assurance.[1,2]

In case deviation found unavoidable, planned deviation to be raised for approved procedure, whereas, when there is observation which is non-compliance to the standard procedure/ manufacturing instruction/ analytical instruction or any other laid down standard procedure, incident/ unplanned deviation to be raised. Deviation shall be logged in deviation log.[1,2]

Planned deviation is defined as activity/ event which is planned in advance to perform differently against the standard. Deviation is been initiated by the initiator department before performing the activity.[1,3,4]

Incidents/ unplanned deviation are occurrences/ errors during execution of an activity which may or may not have impact on the quality, purity and strength of a drug product.[1,3,4]

Concerned person/ department who notice the incident immediately raise incident form with the brief description of incident happened/ noticed.[4,11]

The initiator should mention the allocated deviation

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number at the respective process step/ document/ where the deviation has taken or incident has occurred.[4,11]

Mention the Deviation related to the release of batch in the Certificate of Conformance copy issued, as applicable.[4, 11]

Methods

Procedure for Handling of Planned Deviation

Definition: Planned deviation is a deviation, which is opted knowingly for temporary period to avoid ineluctable situation without impacting the quality and safety of the drug product.[5]

- Planned Deviation: write the standard and the proposed deviation details with the respective document name, document number and respective step number wherever applicable along with the reason/ justification and the supporting data.[6,7]
- The initiating department Head/ Designee shall provide the appropriate CAPA and shall document the same in planned deviation. Shall also assess whether the procedure proposed in deviation is affecting the other batches/ material.
- Forward the signed deviation form to the concerned department and to QA for logging the deviation, after logging deviation QA shall assess the impact of deviation on other parameters.
- During impact assessment study, QA shall analyze impact of proposed procedure on various aspects like process, product, stability, regulatory, validation, training, specification, standard test procedure, batch document, SOP, maintenance, cleaning/ Passivation or any other related parameter.
- Initiator department should forward the deviation form to the respective department (s) head for comment (s).
- QA Head reviews details of deviation, corrective action plan and comments for the raised deviation. Based on the findings of adequate justification and corrective action QA Head decide on approving or not approving of deviation.
- In case of non-approval of deviation, deviation stand as closed and no action is required further. Close the deviation before release of the batch in case of specific batch related deviation. Closure of deviation shall cover the completion of all the actions proposed in corrective action.
- Based on the nature of the planned deviation, appropriate impact assessment summary reports shall be attached, if required. Attach supporting document reference number/ copy of the document confirming closure of action plan for closure of deviation.
- All the actions proposed in the deviation shall be closed within 30 days from the date of initiation of the deviation. If any actions are pending from the proposed deviation even after completion of 30days, deviation extension form shall be taken by the concerned departments.
- The deviation extension form with appropriate justification by concerned department Head shall be approved by Head QA. Maximum two extensions shall be allowed from the initial target date with proper justification. If any actions are not closed even after completion of second extension target date, the further monitoring shall be carried out through CAPA procedure.
- Closure of deviation for completion of correction/ corrective action shall be evaluated by QA. Based on satisfactory completion of actions proposed for approval of deviation QA shall dispose the respective deviation.

Procedure for Handling of Incident/ Unplanned Deviation

Definition: Uncontrolled consequence in the form of non-compliance within the defined system or procedure at any stage of operation (manufacturing, packaging, testing, holding and storage) of drug product is called as unplanned deviation[5]

- Incident/ unplanned deviation: Occurrence of the incident shall be brought to the notice of the concerned department head and QA immediately.[6,7]
- QA should log the incident and assign the number. Immediate corrective action to be taken, Investigation on the incident occurred to be carried out by the Concerned department head. Investigation details shall identify the other batches and products possibly affecting the quality and safety of the drug product based on the nature of incident.
- Investigation details shall find out the root causes(s) leading to incident happened. Based on the investigation and evaluation concerned department head shall take corrective and preventive action and shall document in incident form.
- Corrective and Preventive action drawn shall address the cause (s) of the incident. It shall be ensured by department head that if any incident is associated with a batch then the immediate corrective action must be completed before release of the batch.
- After satisfactory review of details, QA Head shall approve the incident. In case of non-approval of the incident by the QA Head, the batch in question shall not be processed further and the recommendation of the QA Head shall be followed.
- Where there is failure of a batch due to incident then it shall be investigated separately as per Investigation of Failure procedure.
- The incident/ unplanned deviation shall be closed within 30 days from the date of initiation of the incident with appropriate summary reports and submit to QA for closure. If the actions are pending even after completion of 30days, deviation extension form shall be taken by the concerned departments and same

shall be approved by Head QA.

- Maximum two extensions shall be allowed from the initial target date with proper justification. If any actions are not closed even after completion of second extension target date, further monitoring shall be carried out through CAPA procedure

Assignment of Deviation Number

Deviation log shall be maintained by QA department covering details like:

- Sr. No.
- Product/ Material Name
- Batch No.
- Department
- Issued by/ Date
- Received By/ Date
- Planned/ Unplanned (Incident)
- Details of deviation
- Closed on
- Remarks

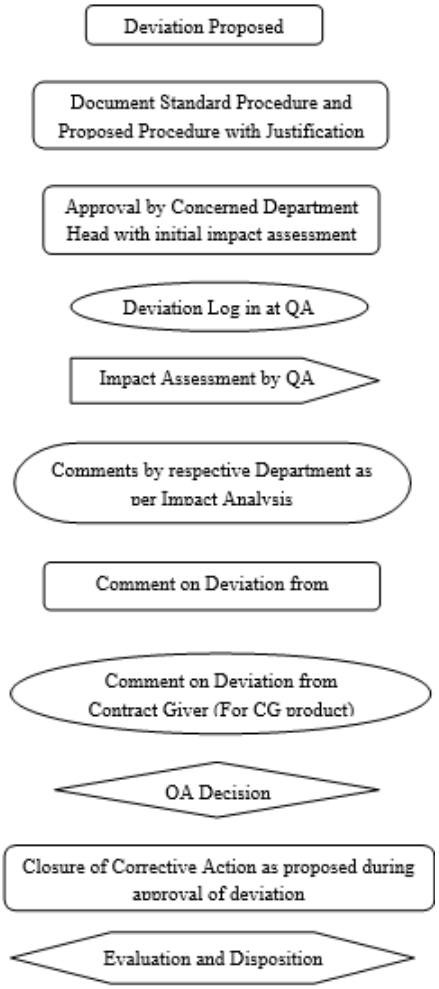

Figure 1.Flow sheet of handling planned deviation

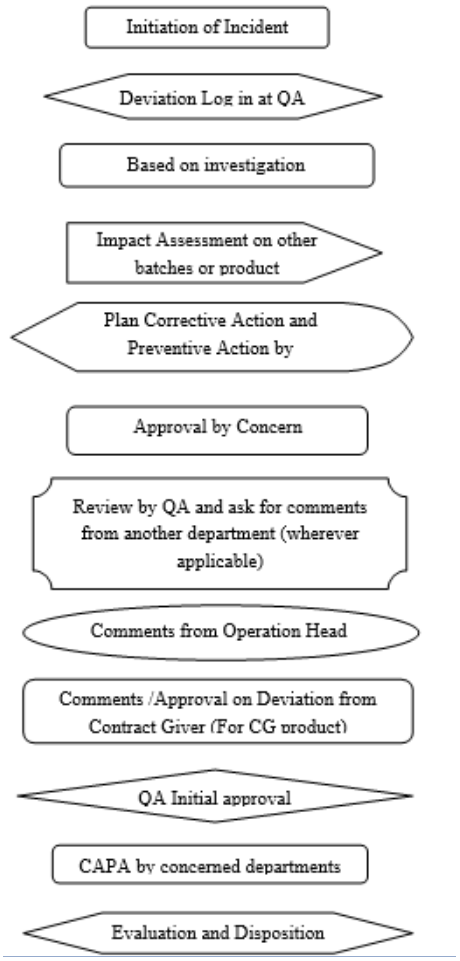

Figure 2.Flow sheet of handling incident/ unplanned deviation

Results

Table 1.Monthly deviation details (Year 2017)

Months	Departments						Total
	Production	Warehouse	QA	QC	RND	Engineering	
January	4	5	2	3	0	0	14
February	5	8	2	9	0	0	24
March	3	6	1	10	0	0	20
April	3	4	1	7	4	0	19
May	5	6	1	9	3	0	24
June	2	7	0	3	1	1	14
July	4	5	1	4	0	1	15

August	10	4	2	6	3	0	25
September	4	3	0	7	1	0	15
October	10	8	0	11	0	0	29
November	3	3	0	18	1	0	25
December	4	7	0	6	1	0	18
Total	57	66	10	93	14	2	242

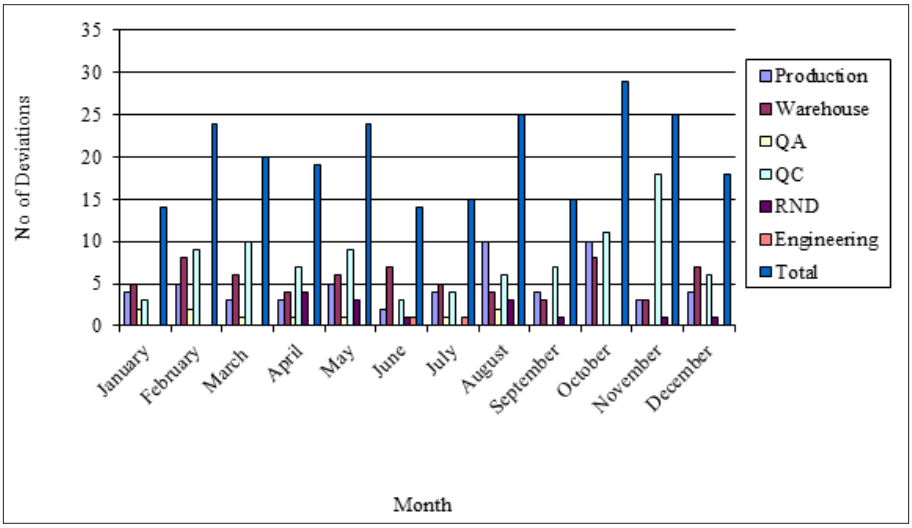

Figure 3.Graphical representation on monthly deviation details

Discussion

Classification of Deviations

The deviation shall be classified in to two categories. Deviations as major or minor based on the severity of the deviation occurred/ planned.[8,9]

Minor Deviations: When the deviation does not affect any quality attribute, a critical process parameter, or an equipment or instrument critical for process or control, it would be categorized as Minor.

- Possible examples of minor deviations are given below:
- Skip of FEFO (first expired-first out) principle in raw material handling
- Balance out of tolerance used to determine gross weight of raw materials upon reception
- Pressure differential out of established limits in class D washing area
- Inadequately trained personnel to perform warehouse cleaning activities
- Raw materials received in a damaged container
- Manometer readings in the sampling booth are crossed the action limits
- During packing activity, the Pharma code sensor not working

Major Deviations: When the deviation affects a quality attribute, a critical process parameter, an equipment or instrument critical for process or control, of which the impact to patients (or personnel/ environment) is unlikely, the deviation is categorized as Major.

Possible examples of major deviations are given below:

- Use of unapproved reference standard to test an API or drug product
- Production started without line clearance
- Filter integrity test has been carried out using equipment with no documented installation qualification completed
- Untrained personnel responsible for segregating the approved and rejected raw material in the warehouse
- Expired or rejected API component used
- Physician Sample wrongly printed with price
- Manufacturing instructions were not followed
- Wrong batch details were printed
- SOP`s or method of analysis not followed during analysis
- Spillage of materials in the floor
- Breakdown of any machine during processing
- mix-up of two batches

Review of Deviations /Incidents

- On start of every month QA shall review the status of deviation and shall follow up with respective department for closure of deviation. Review the Deviation log by QA at every quarter.
- During Review following shall be considered total number of deviations occurred during the quarter, cumulative deviations for the year, number of deviations as planned and incident, number of major and minor deviations, and common area/ nature of deviations and status of CAPA.

- Review Product related deviations in the Annual Product review of every product to assess the impact of these deviations on the trend of the parameters evaluated during Annual Product Review and on any other quality parameters.

Responsibility

- Initiator department/ Observer shall be responsible for initiating, reporting and completing the deviation form, furnish the justification, comply with the corrective and preventive action recommendations and movement of deviation/ incident log out of QA department.
- Concerned department head shall be responsible for investigation drawing and implementing corrective and preventive action.
- Quality Assurance shall be responsible to logging; evaluating, identifying impact of the deviation and disposing of deviation.
- R&D Head, Operation Head shall be responsible for the review of the deviation and to give necessary corrective and preventive action.
- Quality Assurance Head/ Designee shall be responsible for approval/ rejection of the deviation and ensuring that corrective and preventive actions are implemented effectively.

Conclusion

- All this deviation handled during this period was initiated, investigated, closed along with the appropriate CAPA in-line with deviation handling procedure.
- Total number of deviations (planned & unplanned) recorded in the year 2017 is 242. Number of deviations recorded in QC is more during this period followed by Production department.
- Based on the overall review of the deviations, we have noted that most of the deviations logged are related to manufacturing process, packaging, labeling, documentation, testing, equipment, facility related during this year.
- We have noted that, few tests like particle size analysis, X-ray diffraction, etc. needs to be outsource from external testing laboratories due to non-availability of in-house testing facilities and hence due to number of such samples were recorded for testing was more, number of deviations was recorded more.

Conflict of Interest: None

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Annexure 1

Planned Deviation Form

Section 1: (Logging)			
Deviation Number: (To be Allotted by QA)		Date of Report	
Initiator Department			
Section 2: (Details of Deviation)			
Document/ Material/ Product/ Method/ Others (Specify):			
Document No./ AR No./ Item Code No./ Batch No./ Others (Specify):			
Standard Procedure			
Deviation Planned			
Reason/ Justification for Deviation			
Other Batches Affected with this Deviation	YES NO	If Yes, Batch No	
Initiator Sign/ Date		Concerned Department Head/ Designee: Sign/ Date	
Section 3: Impact Analysis By QA			
Comments from other departments are required (if yes specify the name of department)	Impacted/ Concerned Dept(s)	Action Required (To be filled by Concerned Department Head/ Designee)	Sign Of The Concerned Dept Head/ Designee
• Process			
• Product			
• Stability			
• Regulatory			
• Validation			
• Training			
• Material Raw/ Packing			
• MFR/ MPR/ BMR/ BPR			
• SOP			
• Maintenance			
• Cleaning/ Passivation			
• Other(S)			
Comments from Plant Manger (Sign/ Date)			
Comments from Contract Giver (Sign/ Date)			
Section 4: (Approval)			
Comments from QA Head/ Designee: (Sign/ Date)			
	Deviation Allowed	Deviation Not Allowed	
To be closed on or before			
Section 5: (Closure)			
Status of Corrective Action (Concerned Department Head Sign/ Date)			
Evaluation and Disposition			
Done by QA In charge (Sign/ Date):		Approved By: QA Head / Designee (Sign/ Date):	

Annexure 2

Unplanned/ Incident Form

Section 1: (Logging)			
Deviation Number: (To be Allotted by QA)		Date of Report	
Initiator Department		Date of Occurrence	
Section 2: (Details of Incident)			
Document/ Material/ Product/ Method/ Others (Specify):			
Document No./ AR No./ Item Code No./ Batch No./ Others (Specify):			
Brief Description of Incident Occurred			
Immediate Correction Done			
Investigation details			
Identified Cause (s)			
Other Batches Affected with this Deviation	YES NO	If Yes, Batch No	
Corrective & Preventive Action			
Initiator Sign/ Date		Concerned Department Head/Designee: Sign/ Date	
Section 3: (Evaluation by QA)			
Comments from Other Department are required (if Yes) Specify the name of department	Department	Comments by Dept. Head and Sign	
Comments from Plant Manger (Sign/ Date)			
Comments from Contract Giver (Sign/ Date)			
Section 4: (Approval)			
Comments from QA Head/ Designee: (Sign/ Date)			
Section 5: (Closure)			
Status of Corrective Action and Preventive Action (Concerned Department Head Sign/ Date)			
Evaluation and Disposition			
Done by QA In charge (Sign/ Date):		Approved By: QA Head/ Designee Sign/ Date):	