Emergency Plan To Deal With Absenteeism

Contents

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Objective

This emergency plan is prepared to provide guidelines to ensure uninterrupted supply of medically necessary drug products (MNPs) to patients during emergencies, natural or man-made. Such emergencies often lead to restriction in movement of manpower and material, thus resulting in higher absenteeism and operational disruption in manufacturing facilities producing drug products, APIs and components. This emergency plan details out measures to tackle such operational challenges.

Background

In todays globalized pharmaceutical supply chain, any regional or national emergency has the potential to disrupt operations across the world. Such emergencies may relate to natural calamities, wars, or as a recent example, pandemic outbreaks such as COVID-19.

Such emergencies often lead to severe restrictions in movement of people and goods. In situations like these, it becomes even more imperative to ensure supply of drugs to patients, while managing the shortage of manpower and material in pharmaceutical manufacturing units.

An emergency plan to deal with such situations, therefore should ensure that

- Manufacturing units are prepared to continue operations during emergency
- There is no disruptions in supply chain of medically necessary products
- Special precautions are taken in the facilities to ensure the safety and quality of the products
- Appropriate measures are taken for safety of employees and their families
- Activities are planned to proactively educate and motivate employees regarding their responsibilities

The plan outlined in this document focuses specifically on tackling employee absenteeism at a single site and/or at network level for multi-facility companies engaged in manufacturing of MNPs. Consideration shall be given to cross utilization of staff & skill set matrix of other facilities of the companies in order to avoid MNP shortage.

Critical elements to be ensured during emergency

The following elements should be ensured before implementing the revised plan for continuation of operations in emergency situation:

- The drug product and components must be of standard quality, safe for use, and effective
- The product should meet minimum standard of identity, strength, quality and purity
- Any changes implemented to deal with emergency are approved by quality unit prior to execution
- Changes which may have impact on product quality must be carried out only after thorough quality risk assessment. All changes should be documented prior to implementation
- Appropriate documentation of all such activities to be maintained within GMP system
- Training to be provided to relevant personnel on revised processes to ensure seamless execution
- Notification to be provided to regulatory agencies of implementation of emergency plan and deactivation once normalcy is regained

Emergency Plan and execution

1. Identification of Medically Necessary Products (MNPs)

List of the products manufactured at each manufacturing site shall be evaluated to Identify medically necessary products. Such products shall include, but not be limited to

- Products used for treatment of patients arising out of ongoing emergency
- Products required for regular maintenance of chronic medical conditions such as diabetes, asthma, cardiovascular diseases, neurological, psychotropic or Psychiatric disorders, etc.
- Products required for treating acute conditions like infections (antibiotics, antibacterial and anti-viral)
- Products required for pre and post-operative care
- Lifesaving drugs like anti-cancer drugs
- Vaccines
- Products which are in shortage in market or products for which the company has the maximum market share or is the sole supplier

2. Measures to minimize absenteeism at the manufacturing site

An assessment shall be done to understand level of absenteeism in different functions (including critical roles), to understand impact on regular operations. Need to establish minimum number of employees in manufacturing & quality control & support functions like warehouse, engineering, quality assurance, human resources, administration etc.to run the operation.

Reasons for absenteeism shall also be identified, which may include but are not limited to

- Disruption of public transportation
- Blockades of roads
- Blockades& containment in certain areas
- Restriction of movement across the state borders
- Curfew in the area for entire or partial timings
- Sickness / injury / death

Appropriate mitigation steps to minimize the impact of situations mentioned above include

- Increase the inventory of MNPs, components & other ingredients
- Alternate supplies for components, ingredients as well as alternate sources for transportation & distribution need to be located
- Providing company transportation for employees
- Obtaining government approval for operating manufacturing facilities under emergency situations
- Providing accommodation within or near the premises
- Alteration of working hours to suit curfew periods & other restrictions of time.
- Providing additional safety measures to employees to overcome dangers arising out of emergency
- Using employees from other sites where MNPs are not manufactured
- Enabling work from home for people who are not required to come to site
- Cross functional training to personnel to ensure adequate competency build up for reassigning responsibility

3. Plan for operating with reduced number of people

To continue operation with high absenteeism, following steps shall be taken

Activities not related to actual manufacturing and release of products may deferred, such as

- Periodic data trending (EM, complaints, incidences, utility monitoring
- APQR (Annual Product Quality Review)
- Retention sample evaluation
- Continued process verification
- Periodic re-qualification of non-critical equipment
- Self-Inspection, internal audit, periodic audit trail review
- Vendor audits (desktop audit based on paper document should be considered)
- Deferring investigation closure of minor deviation, complaints, change controls etc.
- Not requiring second person verification for less critical steps (though self-check of work recommended)
- Continual improvement plan

Reduction of activities directly related to manufacturing or testing, based on comprehensive risk assessment.

A list of potential activities which can be discontinued, deferred or carried out at reduced frequency, without impacting quality of the products, shall be prepared encompassing various functions like manufacturing, quality control, quality assurance, engineering services, warehouse, etc.

Any such reduced activity should be reviewed and approved by Quality Unit, and documented through deviation / change management / QMS, as applicable at the site. The Quality Unit shall assess the execution of the plan and relevant outcome prior to release of a product / lot in market.

Following are examples of such activities which can be reduced without impacting the quality of the products in various operations at the manufacturing sites

3.1. Warehouse operations

- The frequency of monitoring conditions in the warehouse can be reduced based on available controls like automated data logging, alarm systems, etc., provided the past trends provide assurance that conditions are being maintained as per requirements

- Frequency of testing of material scheduled for re-testing (after completion of re-test period) can be deferred based on risk assessment.
- Cleaning frequency in the non-essential areas can be reduced (except in the areas like sampling rooms and dispensing rooms where the materials get exposed)

3.2. Manufacturing operations

- Manufacturing of drug products in sequence till packing in campaign basis without waiting for in-process test results, in the cases where process validation & trend of past results show that robustness is established
- The frequency of monitoring of temperature / RH / pressure differential in the manufacturing areas can be reduced, provided past trends show high assurance that conditions are maintained within limits
- Elimination of dual check where automated controls such as data acquisition, barcode scanning, equipment generated printouts, etc. are available
- Reduction in frequency of in-process checks where automatic controls are available
- Reduction in frequency of challenge tests where past history shows low probability of failure
- Deferring scheduled preventive maintenance and requalification of equipment (including critical equipment), wherein past history supports continued operational status of equipment
- Deferring annual medical checkup but ensuring monitoring of health regularly

3.3. Quality control activities

NOTE: No reduced testing is applicable to finished product testing. Finished product to be released only after full testing. Some of the testing activities can be reduced or skipped based on risk assessment and past trends.

- **Testing of incoming material**

Where the performance of drug product is known to be dependent on-specific tests performed on raw materials, continue to perform such tests despite reduced testing protocol

Other test parameters can be omitted or frequency of testing can be reduced (e.g. one out of ten lots), or can be referred from the vendor's COA based on risk assessment which may include but not limited to

a) At least one identification test shall be performed
b) Trend data of the test results of previous analysis
c) Failure rate of the material
d) Vendor reliability is established e.g. previous audit outcome and vendor qualification
e) Single product manufacturer or material manufactured in dedicated facility

Packaging material can be released based on COA & critical tests which are predefined.

- **In-process chemical tests in drug product**

Reduction of in-process tests such as blend analysis, blend uniformity test in drug product, and in-process dissolution testing can be considered based on risk assessment. Some of the factors which can be considered are as follows

a) Trend data evaluation
b) Evaluation of previous failures
c) Evaluation of the criticality of the manufacturing process
d) Concentration of API in the formulation
e) Availability of tests in final product such as content uniformity test

- **In-process chemical test in API (Drug Substance)**

Reduction / elimination of reaction monitoring and intermediate testing can be considered based on

a) Trend data evaluation
b) Evaluation of previous failures including OOT results
c) Reaction process and degradation pathway
d) Evaluation of forced degradation study and development data
e) Process control on next stages e.g. purging of any specific impurity in the next stage
f) Control in finished product

- **Stability study**

Elimination of testing or skipping some tests of intermittent stations (other than terminal time points) during long term stability study of commercial product / lots can be considered based on stability trend data. Testing at critical time points like 12 month, 24 month and 36 months shall be continued.

- **Microbial testing of raw materials and non-sterile finished products**

Elimination or reduction of frequency of microbial testing of raw materials and non-sterile products may be considered based on evaluation of manufacturing process, excipients used, past trends, water activity, etc. Microbial testing can be eliminated or frequency can be reduced during stability testing. Microbial testing of raw material can be waived off if finished goods are checked for microbial load.

- **Monitoring of utilities**
  a. For Purified water and WFI systems
     i. Microbial monitoring frequency / sampling points may be reduced based on the past trends, design of system, presence of controls like continuous ozonation, etc.
     ii. Chemical testing if applicable can be eliminated based on online monitoring of TOC and conductivity.

  b. Reduction / elimination of potable water testing based on trend data and seasonal variation.

  c. Reduction in frequency of environmental monitoring in non-sterile manufacturing may be considered based on design and control of manufacturing environment (e.g. terminal HEPA filter in HVAC system), trend data evaluation, maintenance of area / equipment. In case of sterile product manufacturing, reduced monitoring may be considered in non-critical areas (other than Grade A and B) based design of equipment / area (e.g. isolator-based system or conventional line with barrier mechanism)

3.4. Quality assurance activities

a. Parametric release for shipment may be considered for sterile products (without awaiting results of sterility test) based on the trend data of microbial monitoring, design of area / equipment and maintenance, online particulate matter evaluation, and media fill history to confirm sterility assurance level in

the lots. Release for final distribution in such cases to be done only after the final release which includes sterility testing.

b. Deferred media fill simulation based on past performance of media fills, failure rate evaluation, design and performance of equipment/ line/ area, maintenance of area / equipment, excursion in microbial count, extent of human intervention, training of personnel etc.

3.5. Engineering services / plant maintenance

- **Preventive maintenance (PM)**

Scheduled PM may be deferred and the equipment / instrument continued to used based on risk assessment e.g. evaluation of equipment / instrument performance e.g. breakdowns, calibration failures, frequency of replacement of critical parts etc.

In many of the cases PM is carried out by external agencies. Since during such emergencies, the service engineers from these agencies/ manufacturers may not be available at the site, the parameters feasible to be carried out at site can be performed on site by trained site personnel, if required on-line help remotely can be taken from service engineers.

- **Calibration of plant gauges and instruments**

Scheduled calibration of equipment / instrument can also be deferred based on risk assessment and past trends of failures.

For any failure however reported during PM and calibration carried out later, immediate impact assessment on product performance (manufactured, tested and released) needs to be carried out.

- **Filter cleaning / replacement**

Frequency of cleaning / replacement of filters in HVAC and other utility systems may be considered for reduction based on the risk assessment and past trends of data like pressure differentials. type/nature of product etc.

- **Monitoring of operating parameters for utility systems**

Frequency for monitoring of parameters like pressure differentials, temperatures, humidity, flow rates, burning hours, etc. can be reduced based on the risk assessment, availability of data acquisition systems and the past trends.

4. Dealing with material shortages

Emergency situations may result in material shortages due to larger impact at location of the supplier's facility, transportation problems, and resource constraints at supplier's end. To deal with such issues, use of alternate vendors / suppliers with reduced supplier qualification process may be considered. Past history of such suppliers with supplying material to other manufacturers, audits conducted by regulatory agencies, and other customers, etc. can be considered for vendor qualification.

5. Activation / Deactivation of emergency plan

Emergency plan shall be activated when conditions mentioned earlier like war, pandemic, natural calamity etc. occur in the area resulting in disruption of normal operation and high absenteeism of people.

Deactivation of emergency plan shall be considered once prevailing conditions normalize and government-imposed restrictions are eased-off and accordingly, regulatory authorities should be communicated.

Summary of Key Guidelines

- All steps required for protection of employees and the work place safety shall be implemented.
- Reduction in activities related to manufacturing a specific batch shall be considered only after all other efforts addressing activities not connected with manufacturing a specific batch, do not yield the desired outcome.
- All changes shall be done following change control process and after doing risk assessment.
- Wherever required, appropriate training shall be provided to personnel involved in execution of the plan.
- Regulatory agencies of relevant countries shall be intimated following appropriate procedure defined by the agency if any.
- After return of normalcy, the emergency plan shall be deactivated and normal operations shall be resumed. All the activities which were deferred due to emergency plan shall be completed within reasonable period after resumption to normalcy.
- After resuming normal activities, regulatory agencies shall be again informed about deactivation of emergency plan. Include all information related to manufacturing facility affected, date of the plan implemented, contact information for site responsible person etc.

Reference

1. Reference Guideline: FDA Guidance for Industry “Planning for the effects of High Absenteeism to Ensure Availability of Medically Necessary Drug Products “March 2011.