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Hazard Analysis and Critical Control Point HACCP System

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الخلاصة

HACCP هي طريقة منهجية لتحديد وتقييم ومراقبة مخاطر السلامة. تم تعريفها من مخاطر مثل البيولوجية، العوامل الكيميائية، أو العمليات التي هي إلى حد معقول من المحتمل أن تسبب المرض أو الإصابة إذا لم يتم السيطرة عليها. في صناعة المستحضرات الصيدلانية، وهذه قد تشمل تصنيع بعض المضادات الحيوية والهرمونات والمواد السامة للخلايا أو غيرها من المستحضرات الصيدلانية النشطة للغاية

HACCP is a systematic method for the identification, assessment and control of safety hazards. Such hazards are defined as biological, chemical, or physical agents or operations that are reasonably likely to cause illness or injury if not controlled. In the manufacture of pharmaceuticals, these may include the

manufacture of certain antibiotics, hormones, cytotoxic substances or other highly active pharmaceuticals, together with operations such as fluid-bed drying and granulation, which are examples of hazard unit operations. HACCP plans are focused on hazards, the overall objective being to ensure that pharmaceuticals are safe for use.(1)

The use of inflammable solvents (solutions) and certain laboratory operations may constitute hazards.The following elements of the HACCP methodology are integral parts of the validation master file:

— development of a flow diagram of the process;

— verification of the flow diagram on site.

In addition, HACCP will extend this concept to include an analysis of the critical quality variables as well as the assessment of hazards affecting the safety of workers and environmental pollution hazards directly related to the concerned.(2)

Definitions

The following definitions may have different meanings in other contexts.

control (verb) : The taking of all necessary actions to ensure and maintain compliance with the criteria established in the HACCP plan.

control (noun) :The state where in correct procedures are being followed and criteria are being met.

control measure: Any action and activity that can be used to prevent or eliminate a pharmaceutical quality hazard or reduce it to an acceptable level.

critical control point (CCP): A step at which control can be applied and is essential to prevent or eliminate a pharmaceutical quality hazard or reduce it to an acceptable level.

critical limit: A criterion which separates acceptability from unacceptability.

flow diagram: A systematic representation of the sequence of steps or operations used in the production, control and distribution of a particular pharmaceutical.(3)

HACCP plan: A document prepared in accordance with the principles of HACCP to ensure the control of hazards which are significant for pharmaceutical quality in the production and supply chain.

Hazard: Any circumstance in the production, control and distribution of a pharmaceutical which can cause an adverse health effect.

hazard analysis: The process of collecting and evaluating information on hazards which should be addressed in the HACCP plan.

Monitor: The act of conducting a planned sequence of observations or measurements of control parameters to assess whether a CCP is under control.(4)

Pharmaceuticals: All products related to pharmacy, including starting materials, finished dosage forms, and biological and other specific products.(4)

Validation: The collection and evaluation of data, beginning at the process development stage and continuing through the production phase, which ensure that the manufacturing processes — including equipment, buildings, personnel and materials — are capable of

achieving the intended results on a consistent and continuous basis. Validation is the establishment of documented evidence that a system does what it is supposed to do.

Verification: The application of methods, procedures, tests and other evaluations, in addition to monitoring, to determine compliance with the HACCP plan.(4)

Principles

Any system based principle that regulate the system and HACCP system also based on seven principles.

The seven principles are:

1. Conduct a hazard analysis.

2. Determine the critical control points (CCPs).

3. Establish target levels and critical limit(s).

4. Establish a system to monitor the CCPs.

5. Establish the corrective action to be taken when monitoring indicates that a

particular CCP is not under control.

6. Establish procedures to verify that the HACCP system is working effectively.

7. Establish documentation concerning all procedures and keep records.(5)

Guidelines for the application of the HACCP system

The following guidelines will be found useful in applying the HACCP system:

• Before HACCP is applied to any sector, that sector should be operating in accordance with the principles of good practices.

• Management commitment is necessary if an effective HACCP system is to be implemented.

• HACCP should be applied to each specific operation separately.

• CCPs identified in any given example in any reference document may not be the only ones identified for a specific application or may be of a different nature.

• The HACCP application should be reviewed and necessary changes made when any modification is made in the product or process, or in any step.

• It is important, when applying HACCP, to take into account the nature and size of the operation.(6)

• There should be a HACCP plan. The format of such plans may vary, but they should preferably be specific to a particular product, process or operation. Generic HACCP plans can serve as useful guides in the development of product and process HACCP plans; however, it is essential that the unique conditions within each facility are considered during the development of all components of the HACCP plan.(7)

Training and education

As HACCP is a relatively new concept in the pharmaceutical industry, training of personnel in industry, government and universities in HACCP principles and applications is essential for its effective implementation.

In developing specific training to support a HACCP plan, working instructions and procedures should be drawn up which define the tasks of the operating personnel to be stationed at each critical

control point. Specific training should be provided in the tasks of employees monitoring each CCP.(8)

Opportunities should be provided for the joint training of industrial staff and the control authorities to encourage and maintain a continuous dialogue and create a climate of understanding in the practical application of HACCP.

The success of a HACCP system depends on educating and training management and employees in the importance of their role in producing safe pharmaceuticals.

Information should also be provided on the control of hazards at all stages of production and supply.

Employees must understand what HACCP is, learn the skills necessary to make it function properly, and must also be given the materials and equipment necessary to control the CCPs.(8)

Application

The application of HACCP principles consists of the following 12 stages, as identified in the logic sequence for application of HACCP.

1- Assemble a HACCP team

The pharmaceutical manufacturer should assure that product-specific knowledge and expertise are available for the development of an effective HACCP plan. This may be best accomplished by assembling a multidisciplinary team. Team members should therefore represent all the relevant disciplines, such as research and development, production, quality control, quality assurance, microbiology, engineering and distribution or others as applicable.Team members should have specific knowledge and expertise regarding the product and process.(9)Team members should be able to:

(a) conduct a hazard analysis;

(b) identify potential hazards;

(c) identify hazards which should be controlled;

(d) recommend controls and critical limits;

(e) devise procedures for monitoring

(f) recommend appropriate corrective action where deviations occur;

(g) verify the HACCP plan.(10)

2- Describe the product and process

A full description of the product and the process should be drawn up, including relevant quality information such as the composition, physical/chemical properties, structure, pH, temperatures, method of cleaning, drying, screening, mixing, blending, packaging, and the storage conditions. The method of distribution and transport should also be described. (10)

3-Identify the intended use

The intended use should be based on the expected uses of the product by the end user or consumer. In specific cases, vulnerable population groups, e.g. geriatric patients, infants and immunocompromised patients, may have to be considered.(11)

4-Construct a flow diagram

The flow diagram should be constructed by the HACCP team, and should cover all operations and decisions in a process.

When applying HACCP to a given operation, the steps preceding and following that operation should also be considered. A block-type diagram may be sufficiently descriptive.

5-On-site confirmation of flow diagram

The HACCP team should confirm the processing operation against the flow diagram during all stages and hours of operation.

6- List all potential hazards associated with each step

conduct a hazard analysis, and consider any measures to control identified hazards (Principle 1) When hazard analysis is conducted, safety concerns must be distinguished from quality concerns.

The HACCP team should list all the hazards that may be reasonably expected to occur at each step from production, testing and distribution up to the point of use.(11)

It should then conduct a hazard analysis to identify for the HACCP plan which hazards are of such a nature that their elimination or reduction to acceptable levels is essential.

6- List all potential hazards associated with each step

In the hazard analysis, the following should be included wherever possible:

— the probable occurrence of hazards and the severity of their adverse health

effects

— the qualitative and/or quantitative evaluation of the presence of hazards;
— the production or persistence in drugs of toxins, chemicals or physical agents

During the second stage, a hazard evaluation should be conducted, i.e. the severity of the potential hazards and the probability of their occurrence should be estimated.

The team should then decide which potential hazards should be addressed in the HACCP plan, and what control measures, if any, exist that can be applied for each hazard. More than one control measure may be required to control a specific hazard(s) and more than one hazard may be controlled by a specified control measure.(12)

Potential hazards in relation to at least the following should be considered:

— physical characteristics and composition of the product;

— processing procedures;

— microbial limits, where applicable;

— equipment;

— packaging;

— sanitation and hygiene;

— personnel;

— risk of explosions;

7-Determine critical control points (Principle 2)

A CCP in the HACCP system can be more easily determined by the use of a decision-tree, which facilitates a logical approach. The way that a decision-tree is used will depend on the operation concerned, e.g. production, packing, reprocessing, storage, distribution.

If a hazard has been identified at a step where control is necessary for safety, and no control measure exists at that step, or any other, the product or process should be modified at that step, or at an earlier or later stage, to include such a control measure. (14)

8-Establish critical limits for each CCP (Principle 3)

Critical limits must be specified and verified, if possible, for each critical control point. More than one critical limit may sometimes be elaborated at a particular step.

The criteria used often include measurements of temperature, time, moisture level, pH, and sensory parameters, such as visual appearance and texture. Critical limits should be scientifically based.

9 -Establish a monitoring system for each CCP (Principle 4)

Monitoring is the scheduled measurement or observation of a CCP relative to its critical limits. Monitoring should be recorded.

The monitoring procedures used must be able to detect loss of control at the CCP, and this information should ideally be available in time to make adjustments to ensure control of the process and prevent violations of the critical limits.

Where possible, process adjustments should be made when the monitoring results indicate a trend towards loss of control at a CCP.(14)

10-Establish corrective actions (Principle 5)

Specific corrective actions should be developed for each CCP in the HACCP

system in order to deal with deviations when they occur. These actions should ensure that the CCP is brought under control. Corrective actions should include at least the following:

(a) determination and correction of the cause of non-compliance;

(b) determination of the disposition of the non-compliant product;

(c) recording of the corrective actions that have been taken.(15)

11- Establish verification procedures (Principle 6)

Verification and auditing methods, procedures and tests, including random sampling and analysis, can be used to determine whether the HACCP system is working correctly.

Examples of verification activities include:

— review of the HACCP system and its records;

— review of deviations and product dispositions;

— confirmation that CCPs are kept under control.

12- Establish documentation and record keeping (Principle 7)

Efficient and accurate documentation and record keeping are essential to the

application of a HACCP system and should be appropriate to the nature and size

of the operation.

Examples of activities for which documentation is required include:

— hazard analysis;

— CCP determination;

— HACCP plan;

— critical limit determination.

Examples of activities for which records are required include:

— CCP monitoring activities;

— process steps;

— associated hazards;

— critical limits;

— verification procedures and schedule;

— deviations;

— associated corrective actions;

— modifications to the HACCP system.(16)

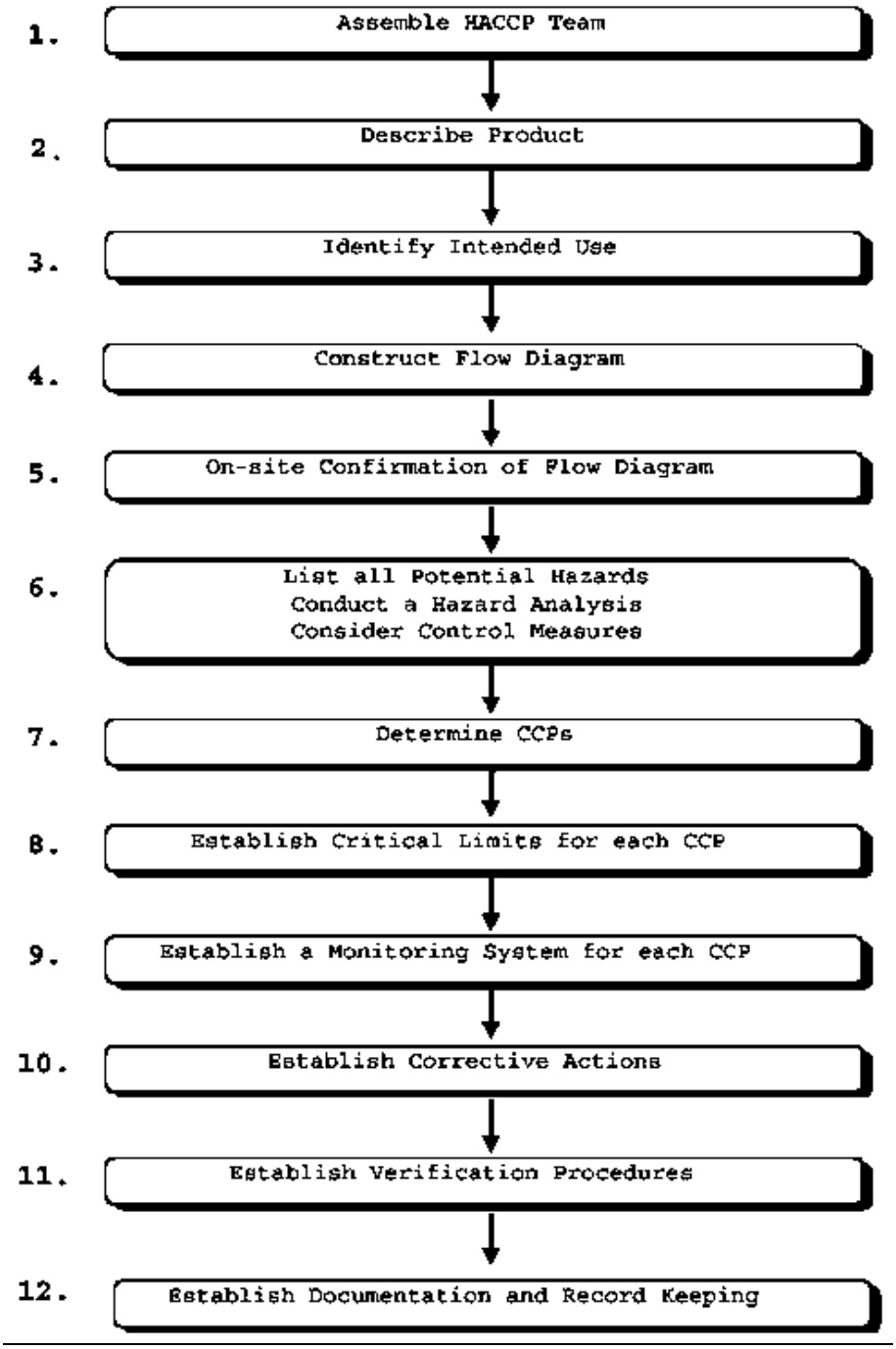
1. Describe Product

2. Diagram Process Flow

3. List

Step	Hazard(s)	Control Measure(s)	CCPs	Critical Limit(s)	Monitoring Procedure(s)	Corrective Action(s)	Record(s)

4. Verification


1.
Assemble HACCP Team
2.
Describe Product
3.
Identify Intended Use
4.
Construct Flow Diagram
5.
On-site Confirmation of Flow Diagram
6.
List all Potential Hazards
Conduct a Hazard Analysis
Consider Control Measures
7.
Determine CCPs
8.
Establish Critical Limits for each CCP
9.
Establish a Monitoring System for each CCP
10.
Establish Corrective Actions
11.
Establish Verification Procedures
12.
Establish Documentation and Record Keeping

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