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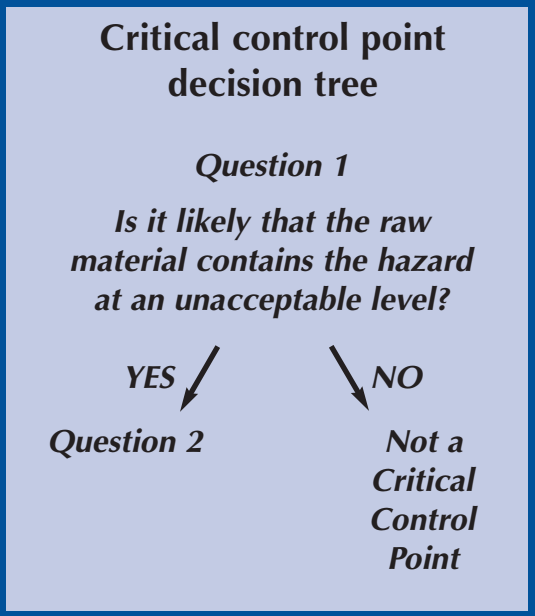

A SIMPLE GUIDE TO UNDERSTANDING AND APPLYING

THE HAZARD ANALYSIS CRITICAL CONTROL POINT CONCEPT

Third edition

ILSI
International Life Sciences INSTITUTE

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ILSI Europe

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CONTENTS

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FOREWORD

The Hazard Analysis Critical Control Point (HACCP) concept was developed in the early 1970s as a system to assure food safety. The basic principles underlying the concept were not new, but its introduction signalled a shift in emphasis from end-product testing to preventive control of critical aspects of the food chain from "farm to fork". HACCP is based on the recognition that manufacturers are responsible for determining the critical aspects of producing safe foods. It helps food manufacturers to improve the efficiency of control by providing a disciplined, systematic approach to the procedures for assuring food safety. It offers food inspectors the opportunity to obtain a more complete and accurate picture of a process and its control measures for an extended period of time. As such, it plays an important role in facilitating the international trade in food as governed by the WTO/SPS agreement.

The HACCP concept has been further developed, particularly during the five years before the first edition of this monograph was published in 1991. During these years, many texts on the subject were published, but there still remained gaps in the literature. After reviewing the available publications, ILSI Europe concluded at that time that:

- the description and definitions used in various texts lacked consistency
- there was no simple "how to do it" guide for users
- there was no explanatory summary text which could be used by decision-makers in industry and government who wished to learn about the concept.

The first edition of this monograph was written to address these points. It has been widely distributed and used for various purposes. It has been translated into German, Russian, Indonesian and other languages. Since then, the Codex Alimentarius published the document "Hazard Analysis and Critical Control Point (HACCP) System and Guidelines for its Application". This document has served as a reference text, and the second edition of the monograph was revised to reflect the Codex terminology. The contents were kept as in the first edition; changes were mainly made in the paragraphs dealing with Hazard Analysis.

In this third edition, the quantitative aspects of HACCP have been given more importance in relation to the concept of validation of HACCP elements as well as regarding the concept of Food Safety Objectives (FSO) currently discussed by the Codex Alimentarius. The original text was updated where necessary.

The first two sections, "What is HACCP?" and "The Benefits of HACCP", can be read along with the example given as an executive summary. The following sections on HACCP can serve as a concise "user's guide". For those who require a more thorough understanding of the system, the Appendix provides detailed explanations. The purpose of this monograph is to assist in understanding and applying the HACCP concept. We stress, however, that no text can substitute for practical experience, and we hope that this revised document will give those who want to use HACCP the necessary guidance.

List of acronyms

ADI:	acceptable daily intake
ALARA:	as low as reasonably achievable
CCP:	critical control point
CFU:	colony forming unit
FSO:	food safety objective
GMP:	good manufacturing practice
GHP:	good hygienic practice
HACCP:	hazard analysis critical control point
MRA:	microbiological risk assessment
MRL:	maximum residue limit
PO:	performance objective
SLDB:	small and less developed business
SPS:	sanitary and phyto-sanitary
12D:	decimal reduction value of 12 (12 log reduction)

WHAT IS HACCP?

The Hazard Analysis Critical Control Point (HACCP) concept permits a systematic approach to the identification of hazards and an assessment of the likelihood of their occurrence during the manufacture, distribution and use of a food product, and defines measures for their control. The resulting HACCP plan can be integrated in a more general Quality and Safety assurance plan. In its simplest form, HACCP consists of seven principles (summarised in Box 1):

- Identification of hazards and assessment of their severity and probability of occurrence (hazard analysis)
- Determination of critical control points required to control identified hazards
- Specification of critical limits that assure that an operation is under control at a particular critical control point
- Establishment and implementation of monitoring systems
- Execution of corrective actions when critical limits are not met
- Verification of the system
- Record keeping.

In the HACCP framework, the term **hazard** refers to any agent in, or condition of, food that is unacceptable because it has the potential to cause an adverse health effect. Examples of hazards are pathogenic micro-organisms and/or their toxins, chemicals such as carcinogens and allergens and physical objects such as stones, bones etc. that may injure the consumer.

Conditions conductive to hazards may be any of the following:

- the unacceptable presence of a biological, chemical or physical contaminant in raw materials, in semi-finished products, or in a production line environment
- the unacceptable potential for growth or survival of microorganisms and the unacceptable potential for generation of undesirable chemicals (e.g. nitrosamines) in semi-finished products, or in a production line environment
- the unacceptable (re)contamination of semi-finished or finished products with microorganisms, chemicals, or foreign material.

Hazard analysis is the procedure used to identify significant potential hazards and conditions leading to their presence in food. It evaluates the likelihood of the hazard being present and the severity of an adverse health effect when it occurs in order to determine if it is significant for food safety. When significant hazards and conditions leading to their presence in foods are identified, measures for their control have to be established.

A **critical control point** (CCP) is a raw material, location, practice, formulation or process where measures can be

BOX 1

The seven principles of HACCP according to Codex Alimentarius

Principle 1: Conduct a hazard analysis

Principle 2: Determine Critical Control Points (CCPs)

Principle 3: Establish critical limit(s)

Principle 4: Establish a system to monitor control of a CCP

Principle 5: Establish the corrective action to be taken when monitoring indicates that a particular CCP is not under control

Principle 6: Establish procedures for verification to confirm that the HACCP system is working effectively

Principle 7: Establish documentation concerning all procedures and records appropriate to these principles and their application

applied to prevent or minimise the likelihood of the presence of hazards at unacceptable levels. (Note that the term control as used here means "to have/to bring under control," and should not be confused with testing, checking or verification).

Application of Good Manufacturing Practices (GMP) – including Good Hygienic Practices (GHP) – is necessary to ensure that safe products are produced by keeping many elements of food production under control. They are sometimes referred to as "prerequisites to HACCP". For example, in the USA, the expression "prerequisite programs" is used in this context. Nevertheless, specific aspects of GMP are essential for food safety and have to be singled out as "critical" control points (CCPs). Clearly, when at a certain point in a food processing or preparation line a potentially severe hazard has a high probability of occurrence, specific control measures are necessary, and such a point is called a CCP.

Critical limits are values or characteristics of a physical, chemical, or biological nature that mark the line between acceptability and unacceptability for whatever is being measured. They indicate when acceptable (controlled) situations become unacceptable (out of control) with respect to the safety of the final product.

Monitoring is checking the conformity of the control at a CCP. It involves systematic observation, measurement, recording and evaluation. Recording the temperature during pasteurisation of milk is an example.

Corrective actions need to be taken when monitoring indicates loss of control. Corrective actions should ensure that unsafe products do not reach the consumer and should prevent, as far as possible, reoccurrence of the event.

Verification is performed to check whether the system is correctly implemented and achieving its objectives.

Record keeping ensures that information resulting from the HACCP study and implementation (for example monitoring files) of the resulting HACCP plan is available for verification, review, inspection, auditing or other purposes.

APPLICATION OF HACCP: THE EXAMPLE OF MILK

The principles of HACCP can be illustrated by taking the example of bringing milk from the dairy farm to the consumer. Among the hazards to consider is the presence of certain pathogens in the raw milk (for instance, *Salmonella*, *Campylobacter* and *Mycobacterium bovis*). It is an unacceptable event if the consumer becomes ill due to ingesting hazardous levels of these microorganisms. Hazard analysis is used to estimate the likelihood that the milk contains undesirable bacteria in levels (numbers) that may cause illness. In most cases, the analysis will show that consuming raw milk may be hazardous, and it will identify pasteurisation at the dairy plant as a specific control measure to make the milk safe.

Pasteurisation is thus identified as a CCP to control the hazards mentioned. It involves heating the milk, but there is a fine balance to be achieved: the heating must be sufficient to control the level of bacteria but not so extreme as to make the flavour unacceptable. In practice, milk is pasteurised in the dairy by heating it, for instance, to 71.7°C for 15 seconds. These can be the critical limits used to ensure the elimination (or in more precise terminology: reduction to an acceptable level) of a hazard. These limits can be monitored in the dairy by measuring the temperature and flow rate of the milk. If a deviation from the required time and temperature should occur, corrective actions, such as repasteurisation of the milk and adjustment of the processing conditions, should be taken. The safety of the milk can be verified by reviewing processing records to ensure critical limits have been met and, if necessary, microbiological analysis.

THE BENEFITS OF HACCP

Many commercial processes involve multiple stages from raw material production or acquisition through to the final product. A properly completed and implemented HACCP study identifies and controls the factors directly affecting the safety of a product. This allows the food producer to target technical resources efficiently. Identifying and monitoring CCPs is a more cost-effective and a more reliable method of assuring safety than the traditional inspection and end-product testing. The records and documentation provide excellent evidence that "all reasonable precautions" were taken and "due diligence" was exercised in order to prevent problems, evidence which may be necessary in case of legal action.

A HACCP study will not result, in all cases, in the elimination of all hazards but will assist in determining how best to minimise the remaining hazards. It is then up to the management to use that information correctly.

Moreover, HACCP can improve the relationship between food producers and food inspectors. In the past, conflicts have arisen, often over trivial matters, which have taken their attention away from more important issues. If control procedures follow clearly established rules, inspectors can have greater confidence in food producers. In addition, the availability of data collected throughout the process and over time greatly facilitates the task of the inspectors by providing them with a more complete and accurate picture of the total operation than they would be able to obtain from a single inspection. Governments are also better able to accept the responsibility taken by industry, because they can understand why and how controls are made. This has been recognised for instance by the Codex Alimentarius and the European Union. Because the application of the HACCP principles is recommended by the Codex Alimentarius, its use has been introduced all over the world. It is currently mandatory for all foods in the countries of the EU and for several products in the USA.

HOW TO PERFORM A HACCP STUDY

The start of any HACCP study is the collection and evaluation of data concerning the raw materials, the formulation of the product, the processing, storage, distribution, sales, preparation and use conditions (Table 1). This is essential for each HACCP study, even if it is performed in small or less developed businesses (SLDBs). In large, complicated or very sophisticated businesses, a multidisciplinary team is necessary to ensure that informed unbiased assessments are made. Each team member should have been trained in HACCP and have a working knowledge of the process/product under study. A typical HACCP team consists of a manager or supervisor responsible for the process under study, an engineer, a Quality Assurance Manager and, very often, a microbiologist. This team will be the core group; other experts can be called in as required. A team leader should be appointed to guide the discussions, and a secretary to record the decisions. The conclusions reached by the team can be summarised on a HACCP data sheet (see Table 2).

Application of the seven principles of HACCP as mentioned in Box 1 is essential for the production of safe foods. Thus, SLDBs should at least apply these, but they may take advantage of the use of so called generic HACCP plans developed for such enterprises for specific products or product groups. Such plans contain typical Critical Control Points, associated critical limits and monitoring procedures that will, when appropriately implemented, assure the safety of the commodity produced or prepared. Such generic HACCP plans should be used for guidance only; in most cases the appropriateness should be confirmed by an expert, who may also suggest changes to better suit the particular situation. This concise monograph will

TABLE 1

Examples of technical data that may be required for a HACCP study

1. Epidemiological and legal data on microbial pathogens, toxins and chemicals

- Incidence of foodborne illness (especially if related to similar product)
- Results of surveillance programmes and sentinel studies
- Legal microbiological food safety criteria and Maximum Residue Limits

2. Food Safety data

- Likely presence of microbiological and chemical hazards in raw materials (see category 1 above)
- Growth rates of pathogens in food products
- Death rates of pathogens under a range of conditions
- Fate of chemicals and toxins during processing, storage, distribution and use

3. Raw material, intermediate and final product data

- Formulation
- Acidity (pH)
- Water activity (a_w)
- Packaging materials
- Product structure
- Processing conditions
- Storage and distribution conditions
- Shelf life
- Consumer use instructions, package labelling, including code dating practices

4. Processing data

- Number and sequence of all processing stages including storage
- Range of product time/temperature conditions
- Handling of rework (recycled material from the manufacturing process)
- High/low risk area separation
- Flow conditions (for liquids)
- Presence of void spaces in processing equipment
- Efficacy of cleaning and disinfecting

TABLE 2

HACCP data sheet *(Data in Table are presented as examples only)*

Point of control (Raw Material or Process Step)	Hazards or Conditions leading to hazards	Control Measures	CCP Parameters	Critical Limits	Target Values	Monitoring	Corrective Actions
Egg product (ingredient in mayonnaise)	*Salmonella*	Supplier's quality assurance (QA)	"Absence" of *Salmonella* in eggs	Negative in 5 random samples of 25 g	No target value	Supplier certification with shipping records, supplier audits, microbiological testing	Rejection of suspected lots
Incoming raw milk	Mycotoxins	Farmer's education, feed supplier's QA	Aflatoxin M	Less than 0.1 ppb	No target value	Testing	Reinforcement of prevention programmes
Pasteuriser (in milk plant)	*Salmonella*, *Listeria*, *Campylobacter* etc.	Correct design and operation of the pasteuriser	Temperature and time of pasteurisation	Not less than 71.7 °C for 15 seconds	73 °C for 15 seconds	Temperature/flow rate recording; record of plant sensor calibration and diversion system operation	Repasteurisation
Chlorination of can cooling water	Recontamination with pathogenic microbes	Automatic dosing	Free available chlorine	1 ppm after cooling	1–3 ppm	Continuous chlorine monitor	Doser adjustment (blocking of batch and investigation)

describe HACCP and how it should be developed and implemented in more complex situations.

The following seven activities describe how a HACCP study should be performed according to the seven principles mentioned in Box 1.

Activity 1: Identification of Hazards and Control Measures

Defining the scope

The potential food safety concerns of the study, including the types of microorganisms, chemicals and foreign materials of concern must be defined. It is important to limit the extent of each HACCP study in order to keep it manageable. Each study should examine specific pathogens, chemicals and physical contaminants that may affect the safety of a particular product or group of products. In this way, it can be precisely defined for which hazards controls have to be established.

For example, the scope of four different studies might be:

- *Listeria* and *Salmonella* species, which are infectious pathogens, as potential hazards in soft cheese
- allergens in residues of other products in shared processing lines
- pesticides as contaminants in raw materials and in the line environment, and
- foreign material in finished products.

Often, several studies are needed to establish a complete HACCP plan.

Describing the product's characteristics, processing and expected use

When starting a HACCP study, the team must examine the food product's characteristics, the processes that are actually applied and its expected use by the consumer. Important areas to consider are:

- *formulation:* the raw materials and ingredients to be used and the parameters which may influence the product's safety or stability
- *processing:* the process parameters and conditions which affect or may create the hazards
- *packaging:* protection against contamination with chemicals or (re)contamination and growth of microorganisms (permeability, integrity, tamper protection are relevant aspects)
- *storage/handling:* the time and temperature conditions and handling in distribution centres, retail outlets and kitchens
- *customer practices:* use by the consumers, caterers or professional cooks (cooking, reheating, thawing, reconstitution, storage, re-use), and
- *target groups:* the end user (infants, adults, the elderly, immuno-compromised or sick people).

All of these factors must be taken into account to determine the probability of the presence of unacceptable levels of hazards at the moment of consumption if they are insufficiently controlled.

Producing a flow diagram

The next task is to produce a process flow diagram to serve as a guide for the study. The diagram should describe all the raw materials and the processing and packaging steps. It should include the data needed for microbiological, chemical and physical hazard analysis; for example, information on the likelihood of contamination with chemicals and foreign materials, as well as microorganisms and their toxins. Data are needed on time and temperature throughout the process and distribution, as well as on acidity (pH) and water activity (a_w) conditions, hygienic design, equipment characteristics, intermediate storage conditions and instructions for consumer use (Table 1). The team should confirm the flow diagram by examination at the production site of all stages of the manufacturing process, e.g. inspecting processing lines and storage facilities.

Determination of significant hazards

First, a complete list of hazards that could potentially be of concern is drawn up. Then, to identify significant hazards, a number of questions, such as those in the decision tree of Figure 1, have to be answered for each hazard that could be of concern at each food production step. One of the first questions would be: is it probable that the potential hazard is present in the raw material? When the answer is NO, this potential hazard in this raw material is of no concern (indicated with "no hazard" in Figure 1). This is also the case when the hazard under study is not likely to be in the line or its environment. Equally, if the hazard may be present, but the product itself will not be contaminated, it is not a significant hazard. However, if contamination was possible, further questions would have to be considered at each process step. For instance is the presence at an unacceptable level probable or is survival, persistence or increase possible that leads to an unacceptable level of the hazard? Again the potential hazard does not need to be addressed in the HACCP plan at this step if the answer is NO. When the answer is YES, the next question would be: is the reduction, if any, at a later step adequate to reduce the hazard to the acceptable level? If YES, the potential hazard is not further considered at this step (but the reduction step becomes a CCP). If the answer is NO, a significant hazard has been identified, for which control measures have to be established.

The concept of acceptable levels

For many agents of a biological or chemical nature, a potential hazard is not always a significant hazard with regard to the safety of the food. Many chemicals may only have an effect when ingested in a "high dose", ADIs and MRLs have been established for these. Even for certain potential carcinogens tolerable/acceptable levels have been set; often the "as low as reasonably achievable" (ALARA) concept is used in practice when no limits have been established. For microorganisms the concept of acceptable levels is less applied, but here also the ALARA concept is practised; different levels are accepted as tolerable for different pathogens, mainly depending on the severity of the potential health impact. For instance, it is widely accepted that pathogens such as *B. cereus* and *C. perfringens* cause only illness when present at high levels in a food (about 10^5-10^6 CFU/g). For *L. monocytogenes* many countries apply an acceptable level of <100 CFU/g at the moment of consumption. A similar reasoning may apply to physical hazards.

The concept of acceptable levels is crucial for HACCP, as is clear from the definitions of control measures and CCP. It is also inherent to the definition of hazard: the potential to cause an adverse health effect. Whether it is causing harm will, amongst other factors, depend on the level.

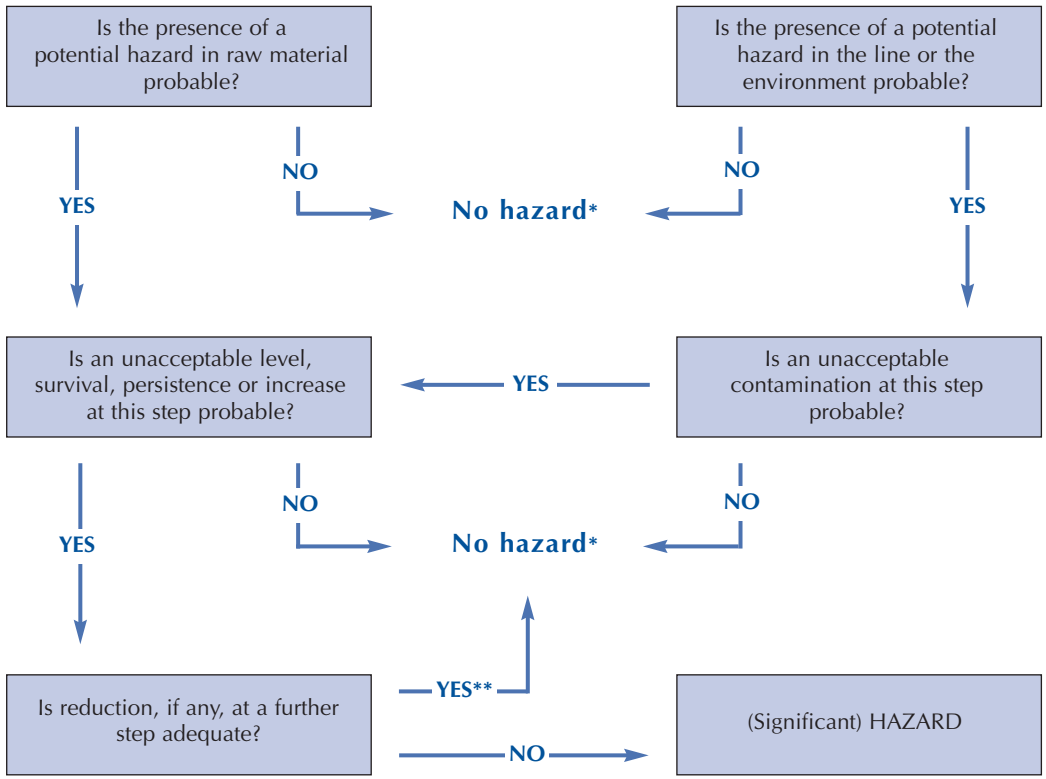
Consideration of control measures

Hazards can be controlled in many ways. Heating can kill micro-organisms and their growth can be prevented or limited by low or high temperatures, low water activity, by preservatives, etc. Residues of veterinary drugs and pesticides can often be controlled by keeping a certain time between application and slaughter, milking or harvest which would reduce the residue to an acceptable level. Strict separation between raw materials and processed foods is a control measure that prevents or limits cross-contamination with pathogens. Cross-contamination in processing lines with allergens can be eliminated through appropriate validated cleaning procedures and/or sensitive consumers can be informed by appropriate labelling. Visual inspection, sieving, metal detectors etc. may be effective in controlling physical hazards. The various options for control measures have to be considered for each significant hazard.

FIGURE 1

Hazard determination

Questions to be answered for each potential hazard at each step



* Not a hazard to be controlled at this step.
** Reduction step thus becomes a CCP.

Activity 2: Determination of Critical Control Points

Once the significant hazards have been identified and control measures considered, the study team must determine the Critical Control Points (CCPs). The team should examine the entire process, and ask for each identified hazard, at each step, questions such as:

- can the hazard be introduced into the product via the raw material under study? If this is the case, is it likely to be at, remain at, or increase to, unacceptable levels?
- is the formulation/composition of the raw material/ product critical to the safety of the product?
- does the process under study make the final product safe by reducing the hazard to an acceptable level, or by keeping it from increasing to dangerous levels?
- at this step, can the hazard be introduced into the product from the processing line or the environment, and if so, is it likely to be at, remain at, or increase to, unacceptable levels?

The decision tree in Figure 2 can be helpful to identify CCPs. Questions 1 and 2 in Figure 2 apply to the raw materials, and questions 3 to 6 apply to the process stages. The appendix outlines the reasoning behind the questions. Clearly, some of the questions are similar to the ones used to identify the significant hazards because of the conceptual link between hazards and CCPs. Hazard determination emphasises identification of hazardous agents which may reach the consumer when not properly controlled; during the determination of CCPs, the emphasis is on the identification of the sources of, or conditions leading to, the hazards, and on the measures to control them.

At each process step, the team should consider the possible consequence of a deviation from the "normal" GMP procedure, whether such a consequence could be unacceptable with regard to food safety, and the probability that it will occur. Moreover, the team must consider what happens to the product later on, to determine whether the process step is critical. A large amount of technical data may be needed for making decisions (Table 1). If the analysis suggests that it is not possible to control the hazard at a certain step, and that the hazard will not be reduced to an acceptable level later, the process (or product) should be modified to eliminate the point.

A CCP may be a raw material, formulation, location, practice or process stage, but it must be specific, for example:

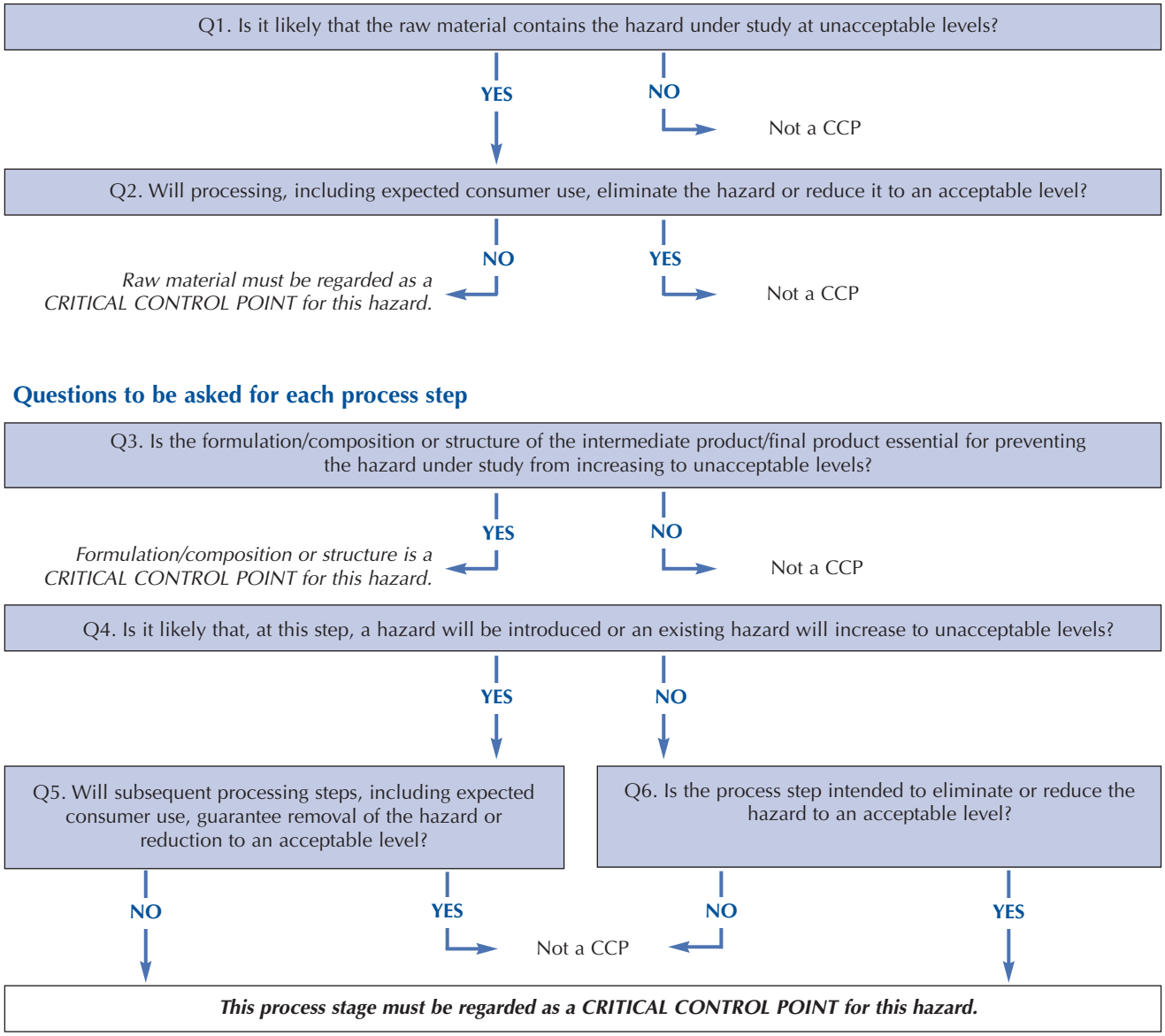
- a raw material with regard to the "absence" of specified contaminants
- acidification of a food to a specified pH
- drying a food under conditions that prevent pathogen increase
- the chlorination step of can cooling water, or
- a product pasteurisation step.

Activity 3: Specification of Critical Limits

The team must define the critical limits that assure that a hazard is under control. The critical limit is the value that separates acceptability from unacceptability for each CCP. They are the maximum values that should never be exceeded. In order to assure this, target values may be established. They take into consideration the variability of control measures. By making these target values more stringent they ensure that critical limits are always met. This can be seen in Table 2, which illustrates how a HACCP data sheet might be compiled. These target values are the process parameters necessary to achieve the required performance criteria that need to be validated (see sections "Validation" and "Quantitative aspects" for further information on validation).

FIGURE 2

Critical control point decision tree



Activity 4: Establishment of a Monitoring System

A monitoring system must be established, to ensure that each CCP is always under control, that is, that the critical limits or target values are met. This is illustrated in Table 2, which identifies the CCPs (what must be controlled and where control is achieved) and describes the associated control procedures (how the hazard will be controlled). Monitoring methods should be rapid to be effective. Physical/ chemical tests and observations are preferred, even for microbiological purposes, because microbiological methods tend to be time consuming. Ideally, they should allow adjustments to be made before the situation becomes unacceptable. In practice this means that the frequency of monitoring is linked to the volume of a product that is produced between two monitoring measurements. If a monitoring result shows that an unacceptable deviation occurred (i.e. the critical limit was exceeded), the product should not reach the consumer. The amount of product to be rejected, reworked or further investigated depends on the time passed since the last monitoring result showed that the situation was under control. Full records must be kept of all monitoring data for management, audits, trend analysis and scrutiny by inspectors.

Activity 5: Establishment of Corrective Actions

When critical limits are not met, the "out of control" situation should be rectified immediately and appropriate follow-up actions taken. Such actions should be planned and described during the HACCP study. From Table 2 two examples are taken, chlorination of cooling water and pasteurisation of milk. At the CCP where the chlorine level of the cooling water is critical, a concentration of less than 1 ppm should lead to an immediate adjustment of the chlorine dosing. If chlorine is absent, the batch should not be released until further examination has demonstrated that the product is safe. At pasteurisation, a temperature drop below 71.7°C should result in repasteurisation (via a flow diversion valve), adjustment of the heating equipment and an examination of the pasteurisation operation to find out why it happened. Once the cause of the problem has been identified, further corrective actions should be taken to prevent it from happening again.

Monitoring data should be examined systematically to identify the points where controls should be improved or where other modifications are needed. In this way, the system can adapt to changes by constant fine-tuning.

Activity 6: Verification of the System

Verification is a very important element of HACCP and should always be included. It is intended to provide additional information to reassure the producer (and the inspector) that application of HACCP results in the production of safe foods. It comprises two distinct activities, i.e. demonstrating conformity with the HACCP plan (are we doing what we planned to do?) and data gathering (did we meet our objectives, can things be improved?). It includes activities such as inspections and audits as well as the use of classical microbiological and chemical contaminant tests to confirm that the control measures operate as designed. Samples examined by inspection services and reviews of customer complaints can in certain cases also provide insight into the proper design and implementation of the system. Verification is different from monitoring. The gathered data may indicate, for instance, that certain things were overlooked in the HACCP plan or that the monitoring procedure is not good enough to assess the level of control. It may also be that the quantity of product that is kept on hold for further investigation, to determine release or no release, is too large, indicating that the frequency of monitoring should

be increased. It may provide information that, in practice, the product is used in a manner other than was foreseen during the HACCP study. As a consequence, changes in the HACCP plan need to be made. Verification is an ongoing activity, some aspects, e.g. environmental and product sample testing, may be specified in the HACCP plan, others may be done whenever there is a need.

Certification is a specific form of verification. It is performed by independent third parties; it deals with checking that a certain HACCP system, as described in a "HACCP standard", was applied. An auditor from a certification body will report on the business' performance in relation to the standard, but will normally not provide a judgement concerning the product's safety.

Activity 7: Record Keeping

Record keeping is an essential element of HACCP. This ensures that information gathered during the installation, modification and operation of the system would be readily accessible to everyone involved in the process as well as to outside auditors. It also helps to ensure the long-term continuity of the system. Records should include explanations of how the CCPs have been defined, descriptions of control procedures and modifications to the system, monitoring and verification data, a file of deviations from normal practice and corrective actions.

VALIDATION

Before the HACCP plan can be finalised and implemented essential elements need to be validated. Evidence must be obtained that the control measures indeed achieve what was intended. For example, does the heat treatment carried out to render a canned product safe achieve the 12 decimal reduction (12D)[1] of *C. botulinum* spores as required? Is the description on the label for preparing a frozen meal in a microwave oven sufficient for the purpose? Does the formulation of the product keep growth of the hazard under control?

In simple terms, validation means: does the evidence show the hazard(s) will be controlled? This is different from verification where the question is: were the things done correctly? Validation is in principle carried out before control measures or changes in control measures are implemented and as such it is putting the proverb "look before you leap" into practice.

1. The effect of a heat treatment is often given as a D-value (decimal reduction value), the 10-fold or 1-log reduction in number of micro-organisms.

QUANTITATIVE ASPECTS

HACCP involves a number of quantitative considerations

HACCP is quantitative by nature, and in its simplest form descriptors are used to determine the probability/likelihood that something may happen. Such descriptors are, for instance, found in the hazard determination tree: is the presence of a potential hazard in a raw material probable? The same question could be worded as: is presence possible or likely? Using these three different descriptors, often different answers will be obtained. For example, the presence of *Salmonella* in sugar is possible, but normally not likely. Examination of raw materials may provide numerical values that can be used to decide whether presence will be possible, probable or likely.

Another example deals with the selection of significant hazards from the list of potential hazards. This selection is based on the likelihood of their occurrence in the final product at levels that are unacceptable. Thus, judgements have to be made and decisions have to be taken based on quantitative considerations.

When determining CCPs, for example, the seriousness of a deviation from the normal Good Manufacturing Practices has to be estimated. If the deviation would have little or no impact on a product's safety, the process step would remain to be covered by GMP. However, if the deviation would have a major impact on the product's safety, the process or handling would become a CCP. Inherent to this decision is that the magnitude of this impact is related to the size or the seriousness of the deviation. Furthermore, at each CCP, the critical limits that have to be established are of a quantitative nature.

However, at present, the implementation of a truly quantitative approach to HACCP in relation to defined food safety goals is difficult because the indication of what is acceptable and what is not with regard to the safety of a food is not specified in most regulations or guidance documents. This hampers the clear definition of the level of control that is needed to ensure that the appropriate level of protection of the consumers is achieved.

In practice, a "benchmarking" approach often provides a useful indication of product safety. Most foods that have been processed to assure safety have an excellent record. Thus the level of a hazard obtained with GMP and HACCP can, based on the epidemiological evidence, be considered to be acceptable without expressing explicitly in quantitative terms what this level is. New products or changes in raw materials, processes, formulation, commercialisation, preparation and use, can be evaluated using such a benchmarking approach.

Recently, the concept of Food Safety Objectives (FSOs) has been introduced to provide a more formal guidance on the level of control necessary.

Food Safety Objectives

A Food Safety Objective (FSO) is a statement of the maximum frequency and/or concentration of a microbiological hazard in a food at the time of consumption that provides the appropriate level of protection.

Although the FSO concept is relatively new and is still evolving, it offers a practical means to convert public health goals into quantitative values that can be used by regulatory authorities and by food producers and manufacturers to manage food safety all along the food chain.

FSOs are established according to a participative, interactive and transparent process involving the regulatory authorities, the industry at large, the consumers and other interested parties. The limits indicated in an FSO reflect the best available scientific information, as well as technical and societal considerations from other sources. In particular, it should be evidenced that FSOs can be met by adequate GMP and HACCP systems.

As an example, an FSO could be expressed as: "the level of *Listeria monocytogenes* in ready-to-eat foods must not exceed 100 CFU/g at the time the foods are consumed".

FSOs can be used by health authorities to communicate clearly to producers/manufacturers what is expected of foods produced in properly managed processes. The FSOs form the basis on which these authorities can establish standards and guidelines. These should form the basis of assessments whether an operation is producing safe foods, i.e. whether the food does not exceed, under normal conditions of commercialisation and use, the established FSO.

The food industry at large (primary food producers, processors, retailers, caterers etc.) can use FSOs as a basis to manage food safety throughout the food production chain. This is done by translating the FSOs into a set of quantitatively stated requirements that would assist in the appropriate design of products, processes and control measures, i.e. compliance with the appropriate level of protection as expressed through the FSOs, while providing for flexibility of operation. FSOs also provide the necessary basis for validation.

Numerical calculations in HACCP

An FSO (or a benchmark) indicates the maximum level of a hazard at the time of consumption that should not be exceeded. In order to achieve this, it is necessary to consider the possible initial level of a hazard in a (semi-) raw product from primary production, and how this level may change (potential for growth, inactivation and recontamination) during the different steps in production, distribution, storage, preparation and final use of a product.

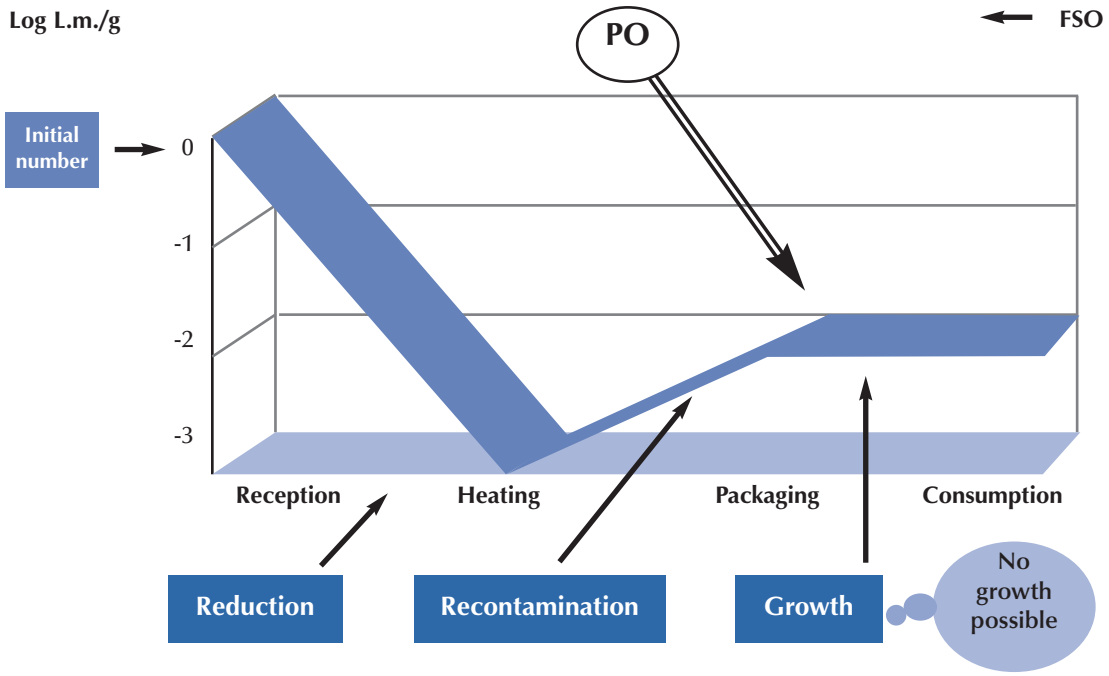
The hazard level which is acceptable at a specified step earlier in the food chain (which is called Performance Objective, PO) can be established using FSO as a guide. Knowing the contamination level at the start of a particular step, the effect (for example in terms of number of decimal reductions of a given pathogen) required in order to meet the acceptable level at the end of the step can be determined. One or more control measures may need to be applied at one or more steps in the food chain, or within a given process, in order to achieve this effect. The required effect of the control measure(s) that need to be applied (for example in terms of number of decimal reductions of a given pathogen) in order to meet the acceptable level can than be determined. Within the framework of HACCP, the determined effect of the control measure is used as a guide to establish the critical limits at the relevant CCPs.

For example, if an FSO for *Listeria monocytogenes* in a ready-to-eat product that does not support growth of this pathogen were to be set at 100 CFU *L. monocytogenes*/g at the moment of consumption, the acceptable level (PO) at the moment of commercialisation should be the same or targeted lower. An example is given in Figure 3. It is assumed that:

a) the initial number is around 1 CFU/g of the raw material;

FIGURE 3

L. monocytogenes in a product not permitting its multiplication



This figure represents the fate of *Listeria monocytogenes* in a ready to eat shelf-stable food. The initial level of the pathogen in the raw material is around 1 CFU/g and a heat treatment is applied which achieves a 3-decimal reduction. Unfortunately, recontamination of the product cannot be prevented, but does not reach a level of more than 1 *L. monocytogenes*/100g of product which is set as the Performance Objective. The condition of the product does not allow multiplication of *Listeria* during commercialisation and use, therefore the situation described is consistent with an FSO of 100 *Listeria monocytogenes*/g

b) the heat treatment achieves a 3-decimal reduction;

c) recontamination of the product cannot be prevented, but does not reach a level of more than 1 CFU/100g of product when GHP is effectively applied, and

d) the formulation of the product does not allow multiplication of *Listeria* during commercialisation and use.

In this situation the PO could be set at 1 CFU of *L. monocytogenes*/100g to restrict the recontamination as much as possible. Clearly, with this PO, the FSO will not be exceeded. When such calculations are made, the critical limits needed to achieve the required acceptable levels can be determined and validated.

Validation of numerical values

The expression of the result of control measures in quantitative terms greatly facilitates their validation, i.e. obtaining evidence that they are effective. In principle all requirements that have been set to assure that a safe product is obtained should be validated. For example, if the initial number of *Listeria monocytogenes* in a raw product should be less than 1 CFU/gram, this must be validated. If the re-contamination of a product with *Listeria monocytogenes* should be less than 1 CFU/100 gram, this must be validated. If the maximum increase of *Listeria monocytogenes* in a certain product that supports growth should be no more than a factor of 1000 before the food is eaten, this should be validated.

Data providing evidence on the performance of control measures can be found in historical data, scientific literature, codes of GMP, generic HACCP plans, growth models, small scale tests, etc. but it must be made sure that these are pertinent for the specific product and manufacturing or preparation conditions. Experimental studies such as challenge and storage tests may need to be carried out to obtain this pertinent information.

BOX 2

HACCP and Microbiological Risk Assessment (MRA)

Microbial growth and inactivation models and computer simulations of the fate of pathogens in the food chain are also applied in the framework of Microbiological Risk Assessment (MRA). MRA is a procedure used by regulatory authorities to understand the likelihood of adverse effects as a consequence of the consumption of a certain pathogen/food combination.

There are many similarities between an MRA and the hazard analysis part of a HACCP study. Both procedures identify hazards, study where and how they appear in the food chain, what the effect of potential control measures will be and determine the seriousness of potential health effects.

The result of an MRA is primarily utilised by public authorities to decide whether the estimated risk would be acceptable or, if not, what would be the best options for its management. It is also one of the scientific bases that the public authorities would consider when establishing FSOs. In this way, MRA may be indirectly linked with HACCP: outcomes of MRA and/or FSOs can be used to target the control measures at CCPs in a HACCP study. However, MRA is not needed to conduct a HACCP study.

Recently, much progress has been made in applying microbial modelling and computer simulation techniques to quantify the behaviour of microbial hazards associated with certain specific process steps used in the food industry (see also Box 2). When properly validated, these techniques are of value in the development of numerical calculations for validation of control measures and the effectiveness of HACCP plans.

WHEN TO IMPLEMENT A HACCP PLAN

Ideally, a HACCP study should be carried out as part of product and process development, so that potential hazards can be "designed out" at the earliest stage. In any case, a HACCP study results in a HACCP plan that should be correctly implemented to ensure that the appropriate control measures are put in place before products are put on the market.

A HACCP plan is the result of a HACCP study carried out for a specific product at a specific production site and is thus to be used for that product only. So-called generic or model HACCP plans can be used, however, to give guidance to the study team. After industrialisation or scaling up of the processing line, the HACCP study should be reviewed and the HACCP plan complemented when necessary. The study should consider all the differences in conditions between the pilot plant and factory.

For products currently manufactured without a HACCP plan, a HACCP study should best be carried out according to the guidelines described in this document. This ensures that no critical point has been overlooked, that appropriate control measures have been identified and implemented and that the required monitoring procedures and record-keeping systems have been put in place.

A HACCP study should be carried out again prior to implementing any significant changes in, for example, raw materials and packaging materials, production line layout, product formulation or product use. Evidently, the existing HACCP plan should be updated to reflect the findings of the new study.

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APPENDIX

IDENTIFICATION OF CRITICAL CONTROL POINTS USING FIGURE 2

Raw materials

To determine whether any of the raw materials (including ingredients, water, packaging material and processing aids) used in the final product are critical and should be controlled by a CCP, the study team should answer Q1 (and, if necessary, Q2) for each raw material used.

Q1. Is it likely that the raw material will contain the hazard under study at unacceptable levels?

The study team should answer this question in the light of epidemiological information, public databases, previous supplier performance and other information related to the safety aspects of the product. If the team is confident that the answer is no, the raw material will not be controlled by a Critical Control Point. If the team answers yes, move to Q2. If the members of the team are not sure of the answer, they should assume a yes response and move to Q2.

Q2. Will processing, including expected consumer use, eliminate the hazard or reduce it to an acceptable level?

The study team assumes that a significant hazard is present in the raw material and examines the manufacturing process sequentially using the flow diagram and examination of the production line to determine whether any of the steps (including consumer use) will remove the hazard or reduce it to a safe level. If the answer to this question is yes, the raw material is not critical, but the process step where the hazard is controlled is a CCP. If the answer is no, the raw material must be regarded as critical.

Process stages

To determine whether a particular formulation, process stage, location, practice or procedure is a CCP, the study team should answer Q3, Q4, and either Q5 or Q6, for each process stage.

Q3. Is the formulation/composition or structure of the intermediate product / final product essential for preventing the hazard under study from increasing to unacceptable levels?

The study team should use the appropriate technical data (for example, pH, water activity (a_w), temperature, levels and types of preservatives, water droplet size) to answer this question at each process stage. If, for example, the pH is critical to limit the growth of *C. botulinum* in a pasteurised product, the answer is yes, and the acidification becomes a CCP. If the answer is no, the acidification step is not a CCP.

Q4. Is it likely that, at this step, a hazard will be introduced or that an existing hazard will increase to unacceptable levels?

The study team should use the flow diagram and data from examination of the production line to determine whether the immediate processing environment (such as people, equipment, walls, floors, drains, raw materials) could contain the hazard under study and contaminate the product. The team must consider the possibility that, even if no single process step allows the hazard to increase to unacceptable levels, it may happen over several steps. In this case, an entire series of process steps can be considered a CCP.

The team should in this context consider the following points:

1. Is the process step carried out in an environment likely to contain the hazard?
2. Is product packaging essential for the prevention of contamination at this step?
3. Is cross contamination from another product/raw material possible?
4. Is (re)contamination from personnel possible?
5. Are there any void spaces in the equipment where the product can accumulate and stagnate, causing the hazard to increase?
6. Are time/temperature conditions of the in-process product such that the hazard could increase?

Note that technical data on product formulation will be needed to deal with points 5 and 6.

If the answer to Q4 is yes for any process step or group of process steps, the study team should ask Q5 for the same process step(s). If the answer to Q4 is no, the study team should move to Q6 for the same process step.

Q5. Will subsequent processing steps, including expected consumer use, guarantee the removal of the hazard or reduction to an acceptable level?

If the answer to Q5 is yes, the process step(s) is not critical and the study team should ask Q3 for the next process step. If the answer to Q5 is no, the process step(s) is a CCP. In this situation, the study team must define clearly what is critical: the actual process, the location or a practice or procedure associated with the process step(s).

Q6. Is this process step intended to eliminate the hazard or reduce the hazard to an acceptable level?

The study team should answer this question for each process step in the light of the flow diagram and line examination. This question will identify those processing steps that are specifically intended to render products microbiologically safe (for example, pasteurisation, retorting or cooking) or to remove physical hazards (for example, metal detection, sieving etc.).

If, after answering no to Q4, the team also answers no to Q6, the process step is not critical and the study team should ask Q3 for the next process step. If the answer to Q6 is yes, the process step is a CCP.

GLOSSARY

Control (verb): To take all necessary actions to ensure and maintain compliance with criteria established in the HACCP plan.

Control (noun): The state wherein correct procedures are being followed and criteria are being met.

Control measures: Any action and activity that can be used to prevent or eliminate a food safety hazard or reduce it to an acceptable level.

Corrective Action: Any action to be taken when the results of monitoring at the CCP indicate a loss of control.

Critical Control Point (CCP): A step at which control can be applied [and is essential] to prevent or eliminate a food safety hazard or reduce it to an acceptable level.

Critical limit: A criterion which separates acceptability from unacceptability.

Food safety: Assurance that food will not cause harm to the consumer when it is prepared and/or eaten according to its intended use.

Food Safety Objective (FSO): The maximum frequency and/or concentration of a hazard in a food at the time of consumption that provides or contributes to the appropriate level of health protection.

HACCP: A system, which identifies, evaluates, and controls hazards that are significant for food safety.

HACCP plan: A document prepared in accordance with the principles of HACCP to ensure control of hazards that are significant for food safety in the segment of the food chain under consideration.

Hazard: A biological, chemical or physical agent in, or condition of, food with the potential to cause an adverse health effect.

Hazard analysis: The process of collecting and evaluating information on hazards and conditions leading to their presence to decide which are significant for food safety and therefore 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.

Performance Objective (PO): The maximum frequency and/or concentration of a hazard in a food at a specified step in the food chain before the time of consumption that provides or contributes to an FSO or an appropriate level of health protection, as applicable.

Risk: A function of the probability of an adverse health effect and the severity of that effect, consequential to a hazard in food.

Risk Assessment (Codex Alimentarius): A scientifically based process consisting of the following steps: (i) hazard identification, (ii) hazard characterisation, (iii) exposure assessment and (iv) risk characterisation.

Step: A point, procedure, operation or stage in the food chain including raw materials, from primary production to final consumption.

Validation: Obtaining evidence that the elements of the HACCP plan are effective.

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

FURTHER READING

More details about the applications of HACCP may be found in the following publications.

Codex Alimentarius Commission (1997). Hazard Analysis and Critical Control Point (HACCP) system and Guidelines for its Application. Annex to CAC/RCP 1-1969, Rev. 3, FAO, Rome.

Campden and Chorleywood Food and Drink Research Association (1992). HACCP: A practical guide. Technical Manual No.38. Campden Food and Drink Research Association, Chipping Campden, Gloucestershire, England.

ILSI Europe (2004). Food Safety Objectives: Role in Microbiological Food Safety Management. Mike Stringer (Author). ILSI Europe Report Series. International Life Sciences Institute. Brussels. ISBN 1-57881-175-9.

ILSI Europe (2001). Principles of risk assessment of food and drinking water related to human health. Diane Benford (Author). ILSI Europe Concise Monograph Series. International Life Sciences Institute. Brussels. ISBN 1-57881-124-4.

ILSI Europe (1999). Validation and verification of HACCP. ILSI Europe Report Series. International Life Sciences Institute. Brussels. ISBN 1-57881-060-4.

ILSI Europe (1999). Food safety management tools. J.L. Jouve, M.F. Stringer and A.C. Baird-Parker (authors). ILSI Europe Report Series. International Life Sciences Institute. Brussels

International Commission on Microbiological Specifications for Foods (2002). Microorganisms in Foods. Book 7. Microbiological Testing in Food Safety Management. Kluwer Academic/Plenum, NY.

International Association of Milk, Food and Environmental Sanitarians, Inc. (1991). Procedures to implement the Hazard Analysis Critical Control Point system. International Association of Milk, Food and Environmental Sanitarians, Inc., Ames, lowa, USA.

International Commission on Microbiological Specifications for Foods (1988). Application of the hazard analysis critical control point (HACCP) system to ensure microbiological safety and quality. Microorganisms in Foods 4. London, Blackwell Scientific Publications.

Mayes, T. and Mortimore, S. (2002). Making the most of HACCP. Woodhead Publishing Limited, Cambridge, UK.

Mortimore, S. and Wallace, C. (1994). HACCP: A practical approach. Chapman & Hall, London SE1 8HN, UK.

US National Advisory Committee on Microbiological Criteria for Foods (1998). Hazard Analysis and Critical Control Point Principles and Application Guidelines. *Journal of Food Protection*, **61**, 1246-1259.

Relevant internet addresses

http://europe.ilsi.org

http://www.ilsi.org

http://www.who.int/foodsafety

http://www.who.int/foodsafety/publications/fs_management/haccp_teachers/en/

http://www.icd-online.org/an/html/courseshaccp.html

http://www.fao.org/es/esn

http://www.codexalimentarius.net

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