HOW APPLYING THE PRINCIPLES OF HACCP CAN MAKE YOU A BETTER AUDITOR

by Bob Pietrowski

Whenever I carry out an audit, I come away with two nagging questions in my head – "Did I give enough time and attention to those things which are most important?" and "Did I really communicate my concerns effectively to the auditees and are they motivated to make improvements and act on my recommendations?". Any audit is by definition a sampling exercise – we cannot see everything and challenge everything because we simply don't have the time. We must use that precious time to focus on those things that really matter. In short, we must apply the principles of RISK ASSESSMENT, and apply them to all facets of the audit...

- The planning of the audit
- The allocation of time and attention to the various activities to be audited
- The assessment of the severity of observations
- The way we communicate that severity to the auditee

There are numerous risk assessment procedures that can be used by the auditor to ensure that he/she concentrates on those activities which are most important to assure product quality and safety. Perhaps the most commonly used is Failure Mode Effect Analysis (FMEA), whereby potential hazards (things that can go wrong) are identified and the RISK associated with them is quantified by analysing and giving a score to…

- The SEVERITY of the hazard
- The probability of OCCURRENCE of the hazard
- The probability of DETECTION of the hazard should it occur

By multiplying together the scores for severity, occurrence and detection (or perhaps more correctly, non-detection) we can obtain an overall score for the risk

associated with the hazard and this can then be used to rank risks associated with any activity. We can use this risk ranking to determine how much time and effort we should spend when auditing this activity and assessing whether the risks, as we see them, are under adequate control. FMEA is a very useful risk assessment tool, but when auditing I prefer a derivative of FMEA called Hazard Analysis and Critical Control Points (HACCP).

WHAT IS HACCP?

HACCP has its origins in the food industry. It was developed in the 1960s by the Pillsbury food company, in collaboration with the US Army and NASA as part of a project to develop foods for the American space programme, and in particular to minimise the microbiological risks associated with those foods – no-one wants to suffer from food poisoning in a space suit! HACCP proved to be a great success and has become the process of choice for the assessment and control of microbiological risks in the food industry. But don't be fooled into thinking that HACCP is only useful for assessing microbiological risk and is applicable only to foods. I and many others have used the principles

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of HACCP to assess diverse risks in the pharmaceutical and biotech industries – and it works!

In its simplest form, HACCP involves a series of 7 linked steps…

1. Definition of the **product** and the **process**
2. Identification of **potential hazards** and **potential control measures**
3. Determination of **critical control points** (CCPs)
4. Establishment of **critical limits** for each CCP
5. Establishment of a **monitoring system** for each CCP
6. Implementation of a **corrective action plan** to re-establish control when necessary
7. Establishment of **verification procedures** to demonstrate compliance

It is the identification of so-called critical control points (CCPs) and all the steps that follow on from there which make HACCP such a unique and valuable tool, both in terms of controlling risk and as an aid to auditing.

Let us look at each of the 7 steps in a little more detail:

DEFINITION OF THE PRODUCT AND THE PROCESS

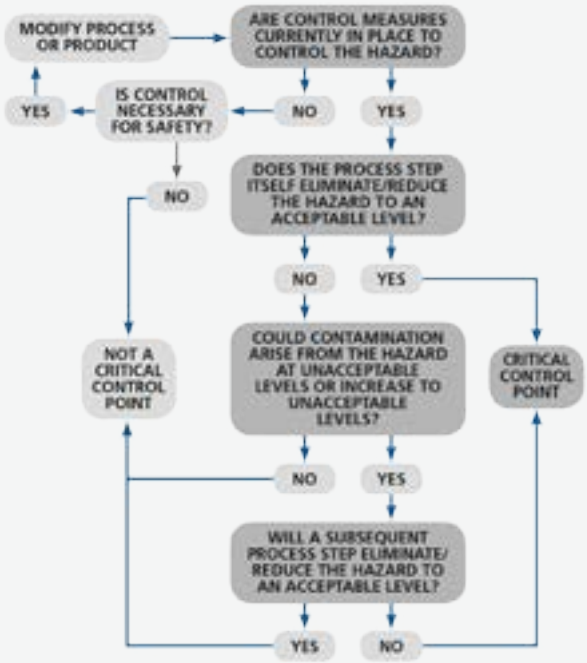
The first and most important step in any risk assessment exercise is ensuring that you really understand the product and the process. The product should be understood in terms of what it is, how it is used and, in particular, its critical quality attributes – those attributes which are essential to the safety and performance of the product. Similarly, it is essential to understand the overall process – all the steps, all the inputs, all the outputs, all the controls, etc. This can best be achieved by formally mapping out the full process. Identification of Potential Hazards and Potential Control.

MEASURES

We can now analyse the whole process and identify those steps which potentially constitute a hazard to achieving the key quality attributes. What we are doing is asking, "What could possibly go wrong and what measures are in place, if any, to stop it going wrong or alert us to the fact if it does go wrong?" This approach allows us to identify the critical control points in the process.

DETERMINATION OF CCPS

This can be done by using a decision tree as shown in the table below:



Once we have identified those critical steps in the process which must be under excellent control if product safety and quality are to be assured, we can go on to the other critically important steps aimed at achieving and demonstrating control.

ESTABLISHMENT OF CRITICAL LIMITS

For each CCP, a critical limit (or limits) must be established. The limit should be discriminatory – it should distinguish between what is acceptable and what is not. It may therefore be an accept/reject limit or an alert/action limit.

ESTABLISHMENT OF A CCP MONITORING SYSTEM

The establishment of an effective monitoring scheme for each CCP is an essential part of risk management by HACCP. The monitoring system must…

> Be able to detect loss of control

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- Provide timely information that permits corrective action to be taken, preferably before product rejection becomes the only option

Things which will influence the effectiveness of the monitoring system include…

- Monitoring frequency
- Sampling points
- Sample size
- Sensitivity of the analytical method

ESTABLISHMENT OF A CORRECTIVE ACTION PLAN

If monitoring data indicate a loss of control, appropriate action must be taken to regain control. This action should be, wherever possible, pre-agreed and committed to an official procedure and should include the following…

- What action is to be taken and when
- Who is to act
- How the effectiveness of the action is to be verified

ESTABLISHMENT OF VERIFICATION PROCEDURES TO DEMONSTRATE COMPLIANCE

Verification procedures may include…

- Trend analysis of data
- Review of deviations, batch rejections, etc, looking especially for repeat occurrences
- Periodic Quality Reviews

USING HACCP PRINCIPLES TO PERFORM BETTER AUDITS

The simple, 7-stage approach of HACCP can be invaluable to the auditor. Applied properly, it can ensure that the auditor…

- Concentrates time and effort on the most important issues (the CCPs)
- Asks the right questions to determine whether the CCPs are under adequate control
- Communicates his/her concerns and the reasons for those concerns
- Makes appropriate recommendations for corrective action

Thus, HACCP principles can bring structure, focus, objectivity and efficiency to any audit. For example…

Planning the Audit – Understanding the Product and the Process and Identifying the CCPs

This is a critical step which is often performed poorly. The auditor must understand the product and the process before he/she can carry out an effective audit. Remember…

IF YOU FAIL TO PLAN, YOU PLAN TO FAIL

HACCP demands that you take the time to really understand the product, in particular the critical quality attributes. It is these which will drive the audit and allow the auditor to focus on risk.

For a sterile injectable product, the critical quality attributes will include…

- Sterility
- Apyrogenicity
- Correct dose
- Container integrity

For a tablet product, they will include…

- Content uniformity
- Weight
- Dissolution

and many more.

By analysing the process and identifying the steps which are critical to achieving those quality attributes, the auditor can identify the CCPs for each attribute. He/she can then allocate time to ensure that each CCP is adequately audited. Furthermore, the auditor can explain the rationale of the audit to the auditee – where he/she intends to spend time, and why.

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CONDUCTING THE AUDIT

During the audit itself, the auditor should challenge each CCP and attempt to get answers to the following questions…

- Does the auditee recognise this as an area of risk (and hence a CCP)?
- Has the auditee attempted to 'design out' the risk?
- Have appropriate limits been set for this CCP?
- Does the auditee monitor at this point and, if so, is the monitoring programme sufficient – in terms of frequency, number of samples, sample size, means of analysis and communication of results – to exert control?
- Is the system capable of identifying loss of control or movement towards loss of control?
- Is there a clear, effective corrective action plan in place to regain control?
- Are there systems in place to demonstrate and confirm the adequacy of all these control measures through trend analysis of data, follow-up on corrective actions, change control, periodic review of deviations and other performance indicators?

COMMUNICATING CONCERNS

It is not enough simply to identify problems and concerns during an audit. The auditee must understand and share the auditor's concerns, otherwise they may not be sufficiently motivated to rectify the problem. Failure to communicate the reasons for concerns is perhaps the most common cause of inadequate follow-up to audits. The structured approach to identification of critical control points and the objective criteria by which the effectiveness of control measures can be judged provide the auditor with an excellent means of discussing concerns and can enable the auditor and auditee to find a common basis for understanding and agreement.

RECOMMENDATIONS FOR CORRECTIVE ACTIONS

Once there is clear understanding of the vulnerability and its scale, the task of making recommendations for corrective action becomes much simpler and more objective. What is more, the auditee will be better motivated to develop effective, permanent fixes for the problem.

IN SUMMARY

HACCP represents an excellent way of ensuring that the auditor focuses time and attention on those things that are really important and provides a structured, objective means of challenging the effectiveness of control measures. It is thus a really useful means of assessing risk and of communicating that risk to others. Although developed to address microbiological risk, it is easily adapted to suit any situation. I use it all the time and I strongly recommend that you try it!

For more information, contact **pharmamail@nsf.org** or visit **www.nsfpharmabiotech.org**

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