Association Internationale de la Savonnerie, de la Détergence et des Produits d'Entretien
International Association for Soaps, Detergents and Maintenance Products

GUIDELINES FOR THE SAFE HANDLING OF ENZYMES IN DETERGENT MANUFACTURING

Version 2 – September 2013

Complete report

Enzymes Occupational Exposure Working Group

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This guidance is an update based on the previous version of February 2002.

List of abreviations

ACGIH	American Conference of Governmental Industrial Hygienists
A.I.S.E.	International Association for Soaps, Detergents and Maintenance Products
AVG	Average
BOS	Behavioural Observation System
BTPS	Body Temperature and Pressure, Saturated
CIP	Cleaning in place
CPI	Cleaning Products Industry (UK)
CpK	Capability ratio
CV	Coefficient of variation
CVC	Central Vacuum Cleaning System
DMEL	Derived Minimal Effect Level
DNEL	Derived No-Effect Level
ELISA	Enzyme linked immuno-absorbent assay
FEV	Forced expiratory volume
FVC	Forced vital capacity
GLP	Good Laboratory Practise
GPIT	Guinea Pig Intratracheal Test
HEPA	High efficiency particle absorption which typically removes >99.995 % of particles
HSE	Health and Safety Executive (UK)
IBCs	Intermediate Bulk Containers
IgE	Immunoglobulin E
IUATLD	International Union Against Tuberculosis and Lung Disease
LOD	Level of Detection
MCA	Multi-cause analysis
Ng/m3	Nanogram per cubic metre
OEG	Occupational Exposure Guideline
PEFR	Peak expiratory flow rate
PIR	Problem investigation report
PPE	Personal Protective Equipment
PVC	Portable Vacuum Cleaner
RAST	Radioallergosorbent test
REACH	EU Regulation on Registration, Evaluation, Assessment and restriction of Chemicals, 1907/2006/EC
RPE	Respiratory Protective Equipment
SDA	Soap and Detergent Association (US)
SDIA	Soap and Detergent Industry Association (UK) now renamed CPI
STEL	Short Term Exposure Limit
TWA	Time Weighted Average
UCL	Upper Control Limit

Chapter 1 - Introduction

Enzymes are important constituents of modern detergent products. They are proteins which catalyse chemical reactions. They break down soils and stains and thus achieve improved washing performance. The major types of enzymes used are proteases (to remove proteinaceous stains), amylases (for starch removal), lipases (for fat removal) and cellulases (for general cleaning and to remove cotton fuzz).

Enzymes were first introduced into detergent washing powders in the mid-1960s. Unfortunately the potential adverse health effects of enzymes, particularly the induction of respiratory conditions including asthma and hay-fever, were not recognized at that time and the enzymes used were in a dusty form, resulting in significant exposure to workers handling them. Within a few years, reports were published indicating a high level of workers handling enzymes had developed respiratory symptoms. Recognition of these adverse effects led the detergent industry and enzyme manufacturers to take steps to reduce exposure. Major reductions in the dustiness of enzymes, achieved by granulation and changes of product form, the introduction of process and equipment control measures and safe-handling procedures to reduce exposure, and improved monitoring methods led to virtual elimination of occupational respiratory disease due to detergent enzymes. At the present time, such effects are only found when process or equipment controls are inadequate or when failure to comply with recommended safe practice occurs.

This document aims to provide guidance on the safe handling of enzymes. Whilst primarily aimed at the detergent industry, including both powder and liquid plants, the principles of the guidance are generally applicable to other enzyme-handling occupations. The document describes the **health hazards** of enzymes, the **management procedures** required to ensure adequate controls are introduced in the manufacturing site and complied with (including training and audit requirements), the **process and equipment design** features and **safe-handling procedures** which should be used to ensure exposure is kept to an acceptably low level and the principles and methods of **monitoring comply** with the standards set. Recommendations on **analytical methodology** and **health surveillance** procedures are also described. Following the recommendations of the document should minimize the risk of occupationally induced illness due to enzymes.

The document reflects the state of technology and scientific understanding of enzyme safety at the time of writing (2013). Thus the approaches described herein are considered the most appropriate available at the present time, but will be subject to change as technical advances (e.g. plant and equipment design, analytical methods) and scientific understanding (e.g. prediction of antigenic potential of different enzymes) improves.

The document addresses the use of enzymes in detergent manufacturing facilities within Europe. While the general advice is widely applicable, some of the guidance given may not be applicable to production sites in other parts of the world.
REACH regulation (Registration, Evaluation, Authorisation and Restriction of Chemicals, (EC) 1907/2006) requires demonstration of adequate control of risks for identified uses and exposure scenarios should be communicated to ensure implementation of risk managements through the supply chain.
"Recommendations on safe handling of enzymes" gain even more additional value in the light of REACH. The guidance supports both the enzyme manufacturers/importers as well as the detergent manufactures so that they can meet the REACH obligations managing the adequate control of risks of enzymes.

Chapter 2 - Health Hazards

Enzymes have a low order of toxicity. The main safety concern associated with enzymes is the potential induction of respiratory allergies, as recognized in the late 1960s among workers in detergent manufacturing plants handling non-encapsulated enzymes (1,2).

Liquid and powder detergents containing enzymes have now been produced and used safely by the consumer since the 1970s. Prior to enzyme encapsulation a few sporadic cases of respiratory sensitisation were observed in consumers in general (3). With the introduction of encapsulated enzymes, the incidence of adverse respiratory symptoms has virtually disappeared (4). Therefore, allergy to enzymes is to be considered an occupational hazard solely.

2.1. Allergy

Enzymes are proteins and may cause respiratory allergy similar to other well-known allergens like pollen, house dust mites and animal dander.

Development of respiratory allergy

When allergens such as enzymes are inhaled in the form of dust or aerosols they may give rise to the formation of specific antibodies. This process is called sensitisation and is a manifestation of the immune system responding to the foreign protein. People who are sensitised do not experience any adverse effects and sensitization does not predict the likelihood of respiratory symptoms occurring. A low number of sensitised individuals may be found in all enzyme handling facilities but past experience in facilities which handle enzymes safely shows that these low incidences are not associated with the presence of individuals with clinical symptoms (5).

Some sensitised people may upon a further exposure to the enzyme develop respiratory allergy with symptoms similar to those of asthma and hay-fever.

People who have an immunological response to a variety of common allergens, e.g. pollen, are defined as “atopics”. Some studies have shown that atopics may have an additional risk of developing allergies when exposed to enzymes (6). However, the impact of atopy is still under discussion. Although atopics may develop an allergy more easily than others, not all atopics will become sensitised to enzymes. Conversely, non-atopics can also develop allergic symptoms.
Smokers have an increased risk of becoming sensitised and developing allergy symptoms (7).

Symptoms of respiratory allergy

Allergies to enzymes may include the following symptoms:

- Itching and redness of the mucous membranes
- Watery eyes/nose
- Sneezing
- Nasal or sinus congestion
- Hoarseness or shortness of breath
- Coughing
- Tightness of the chest

The symptoms may develop during or after working hours, and will normally disappear within hours or a few days after exposure ceases.

Symptoms of ordinary cold or influenza may resemble those of enzyme allergy. However, if symptoms similar to a cold, coughing or shortness of breath appear more often than normal, especially during working days and more seldom or never during weekends or holidays, the symptoms should be evaluated by a physician.

Other forms of allergy

There is no scientific evidence that enzymes are skin sensitisers by skin contact or cause sensitisation by ingestion (8, 9, 10, 11, 12, 13).

2.2. Irritation

Enzyme preparations containing proteolytic enzymes are capable of causing eye and skin irritation. Other enzymes like lipases, cellulases and amylases are unlikely to cause irritation.

Irritation of the skin is most likely to appear on parts of the body where perspiration occurs, i.e. armpits, groin, hands and feet, or in areas where the skin is rubbed, such as by a face mask or collar. The irritation often appears as redness of the skin. When exposure ceases, the irritation disappears.

Irritation of the eyes occurs upon direct contact with the mucous membranes. To protect the mucous membranes against lesions, eyes need to be rinsed with water immediately in cases of direct contact with irritant enzymes.

Other components of a liquid or encapsulated enzyme may also contribute to skin and eye irritation.

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Chapter 3 - Setting of Occupational Exposure Guidelines for Enzymes within the Detergent Industry

Occupational Exposure Guidelines (OEGs) for enzymes are established in order to provide guidance on exposure levels which are not associated with clinical symptoms (although a limited degree of sensitisation may occur at these levels). It is not known what annual incidence of new sensitisations is associated with an exposure level which can induce clinical symptoms. However, typically, well-controlled facilities would not exceed an incidence of 3% new sensitisations amongst its workforce per annum (1). This represents a pragmatically acceptable upper limit, and one which is not associated with the generation of clinical symptoms, either in newly sensitized workers or in those that have been sensitized for some time (2).

Under new EU legislation (REACH), there is a requirement to define safe conditions of use for a substance for which human exposure is expected. This is based on setting a derived no-effect level (DNEL) for the substance. Where a DNEL cannot be established, e.g. for respiratory sensitizing substances, then a derived minimal effect level (DMEL) is recommended (3). For the bacterial and fungal enzymes a DMEL of 60 ng/m3 has been proposed and is used in the detergent industry.
This has been established by thorough retrospective review of occupational experience using validated employee medical surveillance data against exposure records generated over an extended period of time (2).

Application of adjustment factors to account for particular circumstances such as co-exposure with surfactants has limited sensitization induction, avoided any meaningful risk of the elicitation of symptoms with known enzymes and provided an appropriate level of security for new enzymes whose potency has not been fully characterised. For example, in a major part of the detergent industry, this has led to general use of occupational exposure limits 3-10 times lower than the 60 ng/m^3 starting point.

3.1. OEGs of currently used enzymes in detergent manufacturing

There is only one occupational exposure limit established by regulatory agencies for enzymes. This is for Subtilisins (proteolytic enzymes derived from Bacillus subtillis or related species). A limit of 60ng/m^3, based on at least one-hour sampling, was set by the ACGIH. This limit has been adopted by several countries, as shown in Appendix 3.1. The limit of 60 ng/m^3 was set on the basis of the predicted safe level for Subtilisin exposure following the recognition that significantly higher levels of exposure in the workplace induced clinical symptoms. In the UK, a revised occupational exposure limit of 40 ng/m^3 based on eight-hour sampling was set for Subtilisins in 2005 (6).

Decades of experience demonstrates that enzymes can be used safely by ensuring that the exposure is strictly limited. Occupationally, a DMEL of 60 ng/m^3 provides an excellent starting point for safety assessment, with experience showing that downward adjustment of this value to take account of particular circumstances ensures safe working practice.

Within the detergent industry it was recognized that co-exposure with surfactants may enhance the allergenic effect of the enzyme. The adjuvant effect of the detergent matrix on the antigenic potential of enzymes was demonstrated at high levels of detergents and enzymes in guinea pig studies (4,5). However, when comparing to the occupational

situation it is necessary to recognize the big difference in the exposures and exposure patterns (4).

In addition to the levels set for enzymes, an industry guidance value for the overall detergent dust levels is recommended as 1 mg/m^3 to avoid respiratory irritation from the detergent formulation.

3.2. Determination of OEGs for new enzymes

The introduction of new enzymes may require the setting of an OEG, since new enzymes may have a different allergenic potential than existing enzymes. This issue raises the question of the relative allergenicity of enzymes. Considerable effort has been expended, notably with animal models, to try to find ways to measure this. The usefulness and predictivity of animal models for enzymes as respiratory sensitizers has been described in the original version of these guidelines (A.I.S.E. 2002) and discussed recently in general for respiratory sensitizers (chemicals as well as proteins) (7). The animal models may have met with rather limited success, particularly in terms of their more general adoption, but they have served to show that while enzymes may vary in their relative allergenic potency, that variation seems to be within a fairly restricted window. The original enzyme allergens used and on which the current occupational exposure limits are set have turned out to be amongst the more potent substances tested to date, giving some confidence that in reality it is unlikely that enzymes of dramatically increased allergenic potency will arise. Indeed, it seems quite possible that newer materials, either by chance or more likely by design, will tend to be no more, or even less potent as respiratory allergens (2).

Enzyme manufacturers can give some advice on the OEGs they are using for new enzymes. These values may need lowering for use within the detergent industry, as the presence of surfactants may increase the antigenicity of some enzyme classes, as demonstrated in animal studies (4.5) and suggested by a comparison of sensitisation and clinical disease frequency rates in enzyme manufacture compared with detergent manufacture. Typically, detergent manufacturing plants use a level which is three to four times lower than that used in enzyme manufacturing plants. An alternative approach to setting OEGs is to consider the OEG(s) of existing enzymes and the degree of similarity between the new enzyme and existing enzymes (enzyme suppliers can provide this information).

3.3. Verification of OEGs

The introduction of a new enzyme into the work place should be followed up by a confirmation that the OEG is appropriate by evaluating the sensitisation incidence in potentially exposed workers. Initially it is recommended that immunological testing be performed at less than 12-monthly intervals (ref chapter 8) to provide an early indication of the validity of the OEG(s) used. Evidence of a higher than acceptable incidence (greater than 3% per year) (1) of sensitisation occurring - despite adherence to the OEG - would require a review of control and work procedures, and possibly a lowering of the OEG.

Chapter 3 - Appendix 1: Examples of Subtilisin exposure regulatory limits (2011 version).

These levels may be revised in the future.

The long established limit of 60 ng/m³ for pure Subtilisin as originally set by ACGIH has been adopted by the majority of countries as illustrated in the table below.

Country	**Value – ng/m³**	**Time Limit**
Argentina	60	Ceiling
Australia	60	"Peak Limitation"
Belgium	60	TWA
Canada[1]	60	Ceiling
China	15 30	TWA STEL Only applicable for the Detergent Industry (8)
Colombia	60	Ceiling
Denmark	60	Ceiling
Finland	15 60	TWA (8hour) STEL
Iceland	60	STEL
Indonesia	60	Ceiling (High vol. Sampling)
Ireland	60	TWA (8 hour), STEL (15 min.)
Israel	60	Ceiling
Italy	60	Ceiling
Malaysia	60	Ceiling
Mexico	60	Ceiling
New Zealand	60	Ceiling
Nicaragua	60	Ceiling
Norway	60	Ceiling
Peru	60	Ceiling (High flow sampling)
Portugal	60	Ceiling
Singapore	60	STEL (15 min.)
South Africa	60	Ceiling
Spain	60	STEL (15 min.)
Sweden	90 (3 glycine units/m³*)	Occupational Ceiling Limit
Sweden	30 (1glycine unit/m³*)	Occupational Level Limit**
Switzerland	60	STEL (15 min.)
UK	40	TWA based on eight-hour sampling
U.S. - Workplace - ACGIH	60	Ceiling (STEL)
U.S. - Federal, Workplace - NIOSH	60	60 minute average (STEL)
U.S. State - California	60	≥ 60 minute average (STEL)
Uruguay	60	Ceiling
Venezuela	60	TWA

[1] Including all 10 provinces and 3 territories

* 1 glycine unit is approximately equivalent to 30ng of pure Subtilisin

** "Occupational Level Limit" not defined in regulation

TWA: Time weighted average

STEL: Short term exposure limit

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Chapter 4 - Management and Supervision

The objective of these guidelines is to protect the health of the workforce exposed to enzymes. They apply not only to the manufacturing sites that companies operate themselves, but also to any other contractor or co-packer company working with enzymes or products which contain enzymes on behalf of the main producer. It is important that the guidelines are followed in order to care for, and to minimize risk to, employee health and comply with the requirements of EU legislation.

As with any other workplace activity, employers of those handling detergent enzymes have a responsibility to ensure that the health and safety of their employees is protected. This duty necessitates a full understanding of the potential risks that are present in the workplace and requires arrangements to be put into place to mitigate those risks. The duty of care of employers extends not only to direct employees (line operatives, maintenance staff, engineers, laboratory staff etc.) but also to contractors, agency staff, cleaners, visitors and others who may be affected by the activity in question.
Regulatory requirements are established by most countries to protect the health and safety of employees. Within the EU the requirements are increasingly stringent and designed to safeguard the rights of employees to work in a safe environment (national legislation stemming from the EC Framework Directive 89/391/EEC). Management is therefore under a strict legal duty to provide conditions of employment which do not endanger the health of workers.

While management shoulders a large proportion of the responsibility for safety in the workplace, others also have a significant part to play. For the enzyme safety program to be successful, employees need to participate fully. Training is essential for each employee to understand the potential hazards, how to use the control measures implemented and how their actions and activities at work influence or impact the control measures. Each individual employee is also under a legal duty to safeguard their own health, and that of others, by complying fully with safe working practices prescribed by the employer.

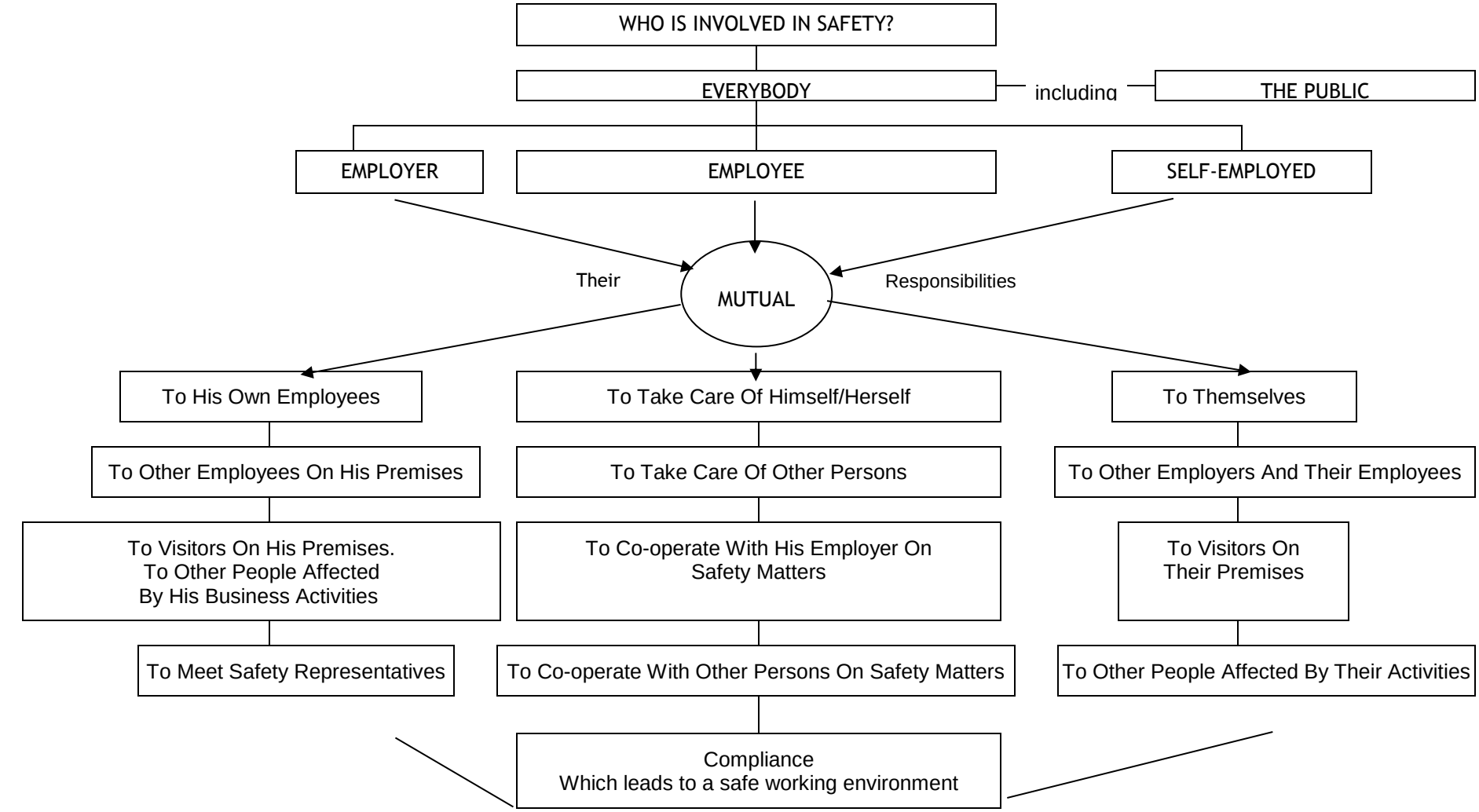
Accepted best practice is to conduct a risk assessment on every activity in order to determine what safeguards need to be put in place to ensure safety. Enzyme handling is no exception. The risk assessment should include both an operational and equipment related evaluation. The rest of this chapter provides a brief overview of risk assessment and some indications of risk management considerations when enzymes are used.

Figure 1 illustrates the inter-relationships in the management of safety.

THE EMPLOYER'S DUTY IS TO ENSURE THE HEALTH SAFETY & WELFARE FOR ALL HIS EMPLOYEES AT WORK
AND, IN PARTICULAR, TO PROVIDE AND MAINTAIN:

Safe Places of Work
Safe Systems of Work
Safe Equipment
Safe Use, Handling, Storage & Transport of Articles and substances
Healthy Working Environment
Welfare Facilities at Work
Information, Instruction, Training, Supervision
A Safety Policy

Figure 1



4.1. Risk Assessment

Use of risk assessment represents best practice and is a legal requirement in health and safety management in the EU.
The REACH regulation (1907/2006) requires that adequate control of risks be demonstrated for all identified uses of substances. Enzymes are classified as R42: "May cause sensitisation by inhalation" in accordance with the dangerous substances Directive (67/548/EEC) and respiratory sensitiser (cat1) H334: "May cause allergy or asthma symptoms or breathing difficulties if inhaled" in accordance with CLP regulation. Exposure scenarios (ESs) covering the identified uses supported by the Manufacturer/Importer have to be generated and communicated to downstream users, if the tonnage of the enzymes is equal to or more than 10 tons per year.
Risk is defined as a combination of the probability, or frequency, of occurrence of a defined hazard and the magnitude of the consequences of the occurrence. It is a function of the potential hazard of the activity or agent in question multiplied by the exposure to that activity or agent.

RISK = HAZARD x EXPOSURE

Hazard

A hazard is a property or situation that in particular circumstances could lead to harm. Only when the hazard of a material is fully understood can any risks be properly identified. In the case of detergent enzymes the hazards are identified in Chapter 2. They can be summarised as irritation of skin and mucous membranes and respiratory (but not skin) sensitisation. Sensitisation (the development of enzyme specific antibodies) is not in itself a disease since it can only be determined by immunological testing and has no adverse health consequences. The hazard to be controlled is the subsequent development of symptoms of allergy to enzymes, i.e. rhinitis, itching and watering eyes, shortness of breath and, ultimately, occupational asthma. Sensitisation is however, a pre-cursor of allergy symptoms and as such can be used to monitor individuals.

In a detergent powder factory, almost all ingredients are powders, and so airborne dusts are a potential hazard. With the exception of enzymes, other dusts would be considered nuisance dusts, causing simple physical irritation of the mucous membranes, rather than having any specific toxicity. Control of atmospheric dust levels generally, and an enzyme level in particular, is therefore important. Most industrial dusts contain particles of a wide range of sizes. In liquid plants the hazard is from aerosolisation of enzyme-containing liquid (droplets in the air) or dust from dried liquid.

Exposure

The extent of exposure to enzymes is determined by the way they are handled and the potential dust generation from process equipment. Frequency of contact and duration of contact are the key parameters in determination of exposure. Potential for enzyme exposure can be simply indicated by:

- Appearance of visible dust or dried liquid in the workplace
- Spillages of enzymes and enzyme containing powders and liquids
- Inadequate handling of empty enzyme packages and packaging for enzyme-containing powders
- Use of temporary fixes to equipment used for handling enzymes and enzyme containing powders

However, air sampling and monitoring can more accurately indicate potential levels of exposure since low levels which are invisible to the naked eye can cause health effects. (See Chapter 7).

Occupational Exposure Guidelines (OEG)

When workplace airborne levels are monitored, they should be compared to the appropriate OEG. Dusts without specific toxicity (nuisance dusts) have been allocated limits for exposure by expert bodies. For example, in the UK these are 10mg/m3 for total inhalable dusts and 4 mg/m3 for respirable dust (8-hour time weighted average). Subtilisins, (a type of proteolytic enzymes) have also been allocated a permissible exposure limit of 60ng/m3 by various regulatory authorities and advisory bodies and a workplace exposure limit of 40ng/m3 by UK. However, within the detergent industry a lower figure is frequently used (see chapter3). The purpose of such limits is:

- To indicate a level below which the health effects due to enzyme exposure should not be induced
- To allow comparison of actual airborne levels with maximum permissible levels
- To indicate the need for measures to control exposure if actual levels approach or exceed the limit values, and
- To check the efficiency of those control measures once in place

When comparing exposure to nationally agreed occupational exposure standards (see Appendix in Chapter 3) or our own industry occupational exposure guidelines, it should be noted that in most countries a time weighted average applies. Exposure standards are expressed as time weighted averages based on a short term 15 min or long term 8-hour reference period. For 8 hour exposure limits, if the shift length deviates from 8 hours, or where overtime lengthens the working day, permissible limits should be adjusted by multiplying time of exposure by length of exposure and dividing by the 8-hour reference period. An example of how to work out an 8-hour TWA is given below.

For example, a worker could be employed as follows:

Time	**Task**	**Exposure (ng/m3)**
2 hours	work in production facility	3
0,5	break	0
2	work in production facility	2.5
0,5	break	0
3	work in production facility	3.5
	included 15 min cleaning a spill	8

Such a pattern of exposure would be calculated as a time weighted average exposure of

$$\frac{(1 \times 0) + (2 \times 3) + (2 \times 2.5) + (2.75 \times 3.5) + (0.25 \times 8)}{8}$$

= 2.8 ng/m3 averaged over 8 hours

Initially, safety precautions would be needed until data are gathered to establish that control measures are effective and protective equipment is no longer needed.

In addition to checking average exposure over a shift, it is also important to identify and monitor tasks where there may be short term, higher levels of "peak" exposure that can also contribute to the development of enzyme-related allergies. Such exposure can occur in maintenance or spill situations. A 15 minute short term exposure limit (STEL) is applicable to such situations and in Europe this limit is also 60ng/m3.

Estimation of Risk

Each operation in which an employee (contractor, visitor etc) can come into contact with enzymes should be identified and evaluated for potential exposure (this is often done by breaking down the process into individual actions - task analysis). For example, a worker pouring out enzymes or cleaning a vessel used for containing enzymes would be considered as having a high probability of exposure while someone operating a closed system for dispensing would have negligible exposure. Each task can therefore be quickly assessed in terms of potential exposure to enzymes as "yes/no/maybe". Conclusions of no potential exposure would require verification while the risk of tasks with a yes or maybe answer would require further investigation and additional detailed information added to the assessment.

Similarly, the consequences of exposure should be considered in terms of their severity. Exposure to high levels of airborne enzyme may be considered to involve severe consequences (occupational asthma), while skin contact would result in mild consequences (possible skin irritation).

Combining the probability of harm resulting from exposure to the hazard and the consequences of exposure to that hazard allows prioritisation of activities into high, medium, low and negligible risks. Assessments are considered suitable and sufficient if the detail and expertise with which they are carried out are commensurate with the nature and degree of risk arising from the work and the complexity and variability of the process. In other words, the greater the potential risk involved, the greater the skill and experience required to ensure that an adequate risk assessment has been undertaken and appropriate controls introduced.

	Consequences			
	Severe	Moderate	Mild	Negligible
Probability				
High	high	high	medium/low	Near zero
Medium	high	medium	Low	Near zero
Low	high/medium	medium/low	Low	Near zero
Negligible	high/medium/low	medium/low	Low	Near zero

For the overall detergent dust levels, an OEG of 1 mg/m^3 is recommended to avoid respiratory irritation from the detergent formulation.

4.2. Risk Management

Having characterised and prioritised the risk involved in a given activity, it is then necessary to use the information generated to manage or control that risk. Those risks identified as high obviously require immediate attention and the greatest degree of control. Risks can be controlled using a well-accepted hierarchy of approaches. The options should be addressed starting at the top of the list. Personal protection is only acceptable in situations where the other options are not viable.

- Prevent exposure
    - Eliminate the hazard
    - Substitute the hazard by a less hazardous substance

- Control of exposure
    - Isolate the hazard to prevent exposure
    - Reduce exposure by engineering means
    - Reduce exposure by use of safe procedures and working practices
    - Reduce exposure by personal protection

Risk management also involves ensuring that the controls put in place to manage the risk are effective. This will involve inspection of engineering controls, monitoring of airborne levels of enzymes to confirm efficiency, auditing of procedural controls and observation of the behaviour of operatives involved in enzyme handling (see chapters 7, 9 and 11). The risk assessment will determine the frequency and extent of monitoring and procedures in the event of monitoring results exceeding pre-determined action levels.

Prevention of Exposure

The first step in the management of risks is to attempt to prevent exposure to the hazard. In the case of enzymes it is not possible to eliminate enzymes completely since they perform a unique and important role in detergent formulations.

Control of Exposure

In the hierarchy of control measures, where elimination is not possible, other means of reducing potential exposure must be employed (See chapter 5 for details). Again, results of the risk assessment will give guidance as to the level of control necessary.

Exposure can be controlled by isolation of the enzyme. Total enclosure of the process so that enzymes are never allowed to escape into the atmosphere is a form of isolation. While this route is preferred, it should be remembered that even in such cases, fully contained equipment has to be opened for cleaning and/or maintenance, and can occasionally break down, so other measures must also be in place for such eventualities.

Engineering controls such as provision of laminar flow booths, local exhaust ventilation, and equipment chosen or modified to prevent dust generation should all be used.

Procedural controls such as restricting access to areas where higher risk activities are carried out permit to work procedures, provision of good training and safer standard working practices and procedures can also significantly limit exposure. Such procedural controls must be actively managed and enforced to be effective.

Where enzymes are handled, there should be clear accountability in the plant organization for equipment performance for:

- Operator training and competency checks for all personnel working on or around enzyme handling equipment
- Standard operating procedures to deal with spills in a way that minimizes exposure
- Maintenance of local exhaust ventilation systems to the original system design

Personal protective equipment (PPE) has a role to play in the control of exposure but only in certain, well defined circumstances. PPE should never be used routinely as a substitute for other, more permanent control measures since this type of equipment can easily be misused, forgotten or damaged. It is also uncomfortable to wear for long periods. Circumstances in which PPE is acceptable are discussed in Chapter 5.

4.3. Management of Change

There should be a system in place to manage and track changes such as formulation, plant and equipment, processing, procedures and people. Change management procedures should ensure:

- Changes are reviewed and implemented by competent personnel
- Potential exposure issues are addressed in the initial review of the change
- Adequate funds are made available to complete all aspects of the change before start up
- Tests at start up after changes ensure that performance and control specifications are met

4.4. Risk Communication

Having completed a risk assessment, and established risk management measures, those potentially affected must be informed of the risks and measures taken to control them.

Such information is often provided in the form of training. Communications should aim to:

- Educate and inform of the potential hazards and risks
- Encourage safe attitude and behaviour
- Ensure that information is readily available
- Create trust and confidence
- Allow consultation

4.5. Monitoring

Having completed a risk assessment for a given task and established which controls are needed, it is then essential for management to ensure that those controls are working effectively and achieving the results expected.

- As with the determination of which control measures to use, the extent and frequency of monitoring those controls is determined by the risk assessment; the greater the risk, the greater the monitoring effort required. Objectives of monitoring are to look for trends in results that will:
- Confirm that existing controls are adequate
- Confirm that operational procedures are being complied with
- Confirm a good margin of safety when engineering or operational changes are introduced

- Indicate when control measures are deteriorating so that action can be taken to rectify deficiencies before there is a problem
- Reassure employees and others that working conditions are safe
- Indicate the scale of a problem in the event of a breakdown or other control failure and confirm when the issue has been brought under control

From a management perspective it is important to set limits for those items being monitored. Operational procedures are needed to ensure that deviations from predetermined acceptable levels are detected quickly and communicated to an appropriate person so that remedial action can be taken. Sampling of airborne dust and enzymes is an obvious example of monitoring, but there are other issues that also need to be covered.

Workplace airborne enzyme sampling is fully covered in Chapter 7. This is critical for safe handling of enzymes and it is imperative that it is managed well. Sampling includes environmental (general workplace) and personal dosimetry. A well-trained and experienced operator is essential for collecting the samples and for analysis. Similarly, expert knowledge is required to design an appropriate sampling strategy. Management input is needed to ensure that procedures are available to recognize when levels have exceeded predetermined limits and to control exposure, possibly by additional emergency means, until monitoring results show a return to normal working conditions.

Where engineering controls are used, monitoring is required to ensure that equipment is functioning properly. Regular documented checks (both routine and full checks against specified performance criteria) are needed for local exhaust ventilation and other equipment to confirm working order. In addition, regular planned maintenance should avoid equipment failure. More detail is given in Chapter 5.

Compliance with operational guidelines can be monitored. There are a variety of approaches available, one of which, Behavioural Observation System, is described in Chapter 6. General levels of tidiness and housekeeping can also be monitored, for example, by planned inspections designed to look for key hazards and problems areas.

Health surveillance is required whenever a task or operation involves health risks to the operator which are identifiable and measurable, and when the measurement gives direct benefit to the individual being measured. In the case of enzyme exposure, the risk is the development of sensitisation and respiratory symptoms. Sensitisation can be monitored by detecting the presence of enzyme specific antibodies, respiratory symptoms by medical checks and lung function tests. These are detailed in Chapter 8. Again, management input is required to make sure that procedures are developed to check employee health and to respond to adverse changes detected. Careful consideration should be given to provision of health surveillance for long term contractors and other frequent visitors to sites where exposure is possible.

When health surveillance or other forms of monitoring are undertaken, monitoring records should be kept for long periods. Local legislation may vary, but in principle, 30 years is considered a minimum period for record retention.

4.6. Training

All potentially exposed employees and contractors and other visitors to the site should have proper training in the operation and correct use of any procedure involving enzymes

or enzyme containing material. Employees should also be trained in the use of contingency measures so that they know immediately what to do in the event of spills or other incidents.

Such training should be provided as part of the induction programme for all new staff (including temporary staff and contractors) before they work with enzymes or in an area where there is potential for exposure to enzymes (i.e. where other people may be using enzymes, even intermittently). It should also form part of a rolling programme of retraining for all employees to prevent complacency and to ensure that new developments and information are passed on to all employees. All training should be documented and attendance at training sessions recorded. Training must be given in work instructions and operational procedures and compliance with these procedures monitored, especially when the employee is new to the job, or a new task is introduced.

4.7. Audit

Auditing is discussed more fully in Chapter 11. Auditing gives objective confirmation that all safeguards identified as necessary to ensure worker safety can be shown to be in place and effective.
From a management point of view the important elements to note are:

- As with controls and monitoring, the extent and frequency of the audit is proportional to the risks involved
- Auditing can be an internal function, undertaken regularly and reporting to senior management. However, it is advisable to have this function independent from the manufacturing structure and seen as impartial. Periodic external audits are also helpful in providing objectivity and a “new set of eyes” on familiar issues
- Audits should focus on the key issues identified as important in enzyme handling Management therefore has the responsibility of deciding on priorities and responding to audit feedback
- Auditing should include all aspects of the safe working programme, engineering records, analytical records and equipment and health surveillance
- Auditing is not just for auditing’s sake but to ensure that all the defined procedures are being carried out. Non-compliances should not just be recorded but action should be taken to rectify the issues identified as soon as possible

Chapter 5 - Control of exposure during the handling of enzymes and the manufacture of enzymatic detergents

To prevent the exposure of employees to enzymes during the manufacture of detergent products, there is a series of well-established engineering controls and operational procedures that have been developed over many years by the industry and which are now considered to be best practice. They are complementary elements, and each element should be in place if proper control is to be achieved.

The key strategies are:

- The prevention of enzyme dust formation by using plant designed to prevent or minimize damage to enzyme encapsulates during the manufacturing process
- The prevention of aerosol formation from liquids by using plant designed to prevent or minimize the formation of aerosols during the manufacturing process
- The containment at source of any dust or liquid aerosols that may be produced during handling and manufacture by using totally closed process equipment, or enclosed equipment maintained under negative pressure by ventilation control
- The avoidance of any routine or uncontrolled spillages of raw material, or intermediate and finished products containing enzymes, including from waste & packaging
- The clean / hygienic design of plant and equipment

The intent is to prevent operator exposure to enzymes and to detergent products containing enzymes, via inhalation.

Whilst dilution (or general) ventilation is essential to provide a wholesome working environment, and it may further reduce a low level of background airborne contaminants, it is not a suitable alternative to containment and control at source for hazardous materials such as enzymes. The role of dilution ventilation can be illustrated by reference to the "Hierarchy of Control", a defined series of steps that should be considered when approaching any situation where control of a hazard[1] is required.

In relation to airborne dust and enzymes, these are:

- Elimination (i.e. remove the hazard completely)
- Substitution (i.e. substitute the hazard for a lesser one)
- Isolation (i.e. totally isolate the hazard – 100%)
- Enclosure and Ventilation (i.e. enclose the hazard and contain it using ventilation)
- Local Exhaust Ventilation (i.e. direct ventilation control at the source)
- General or dilution Ventilation (i.e. in the workplace)
- Respiratory Protective Equipment. (i.e. control the inhalation of the airborne material)

In broader terms, and following the hierarchy, control of airborne enzyme centres around the following aspects:

[1] The term "Hazard" could refer to any chemical, physical or biological hazard and the generic Control Hierarchy can be applied to any of these, but here we have tailored the hierarchy for use with hazardous airborne materials.

- Enzyme Quality and Form (Substitution of dusty powders with low dust encapsulates)
- Enzyme Supply units (Isolation: packaging should directly connect with the process)
- Engineering Controls for Manufacture and Packing (Isolation, Enclosure and Ventilation)
- General Building / Plant Design via hygienic design principles
- Operational, Maintenance and Emergency Procedures
- Personal and Respiratory protection

Elimination, the first step of the control hierarchy, is impractical for enzymes, as they are a vital ingredient in detergent products, and as yet there is no real alternative for effective stain removal at low temperatures.

Primary control of exposure during normal manufacturing operations should always be achieved by physical containment, engineering and ventilation controls, and not by the use of respiratory protection.

Whilst the use of respiratory protection should always be considered as a last resort for primary control of exposure, its use still has a role even when operating to best practice. For example in cases where a secondary safeguard is required because a specific task may have a high potential risk of exposure, or in the event that emergency or maintenance situations arise.

The following sections highlight the principles of how best practice can be applied to the handling of enzymes, and the manufacture of biological detergents. The control measures are described in terms of the process steps and for ease of reference the flow-sheets in 5.1 describe the major process steps and the relevant sections for making powders and tablets and for liquids processes.

5.1. Enzymes Quality and Form

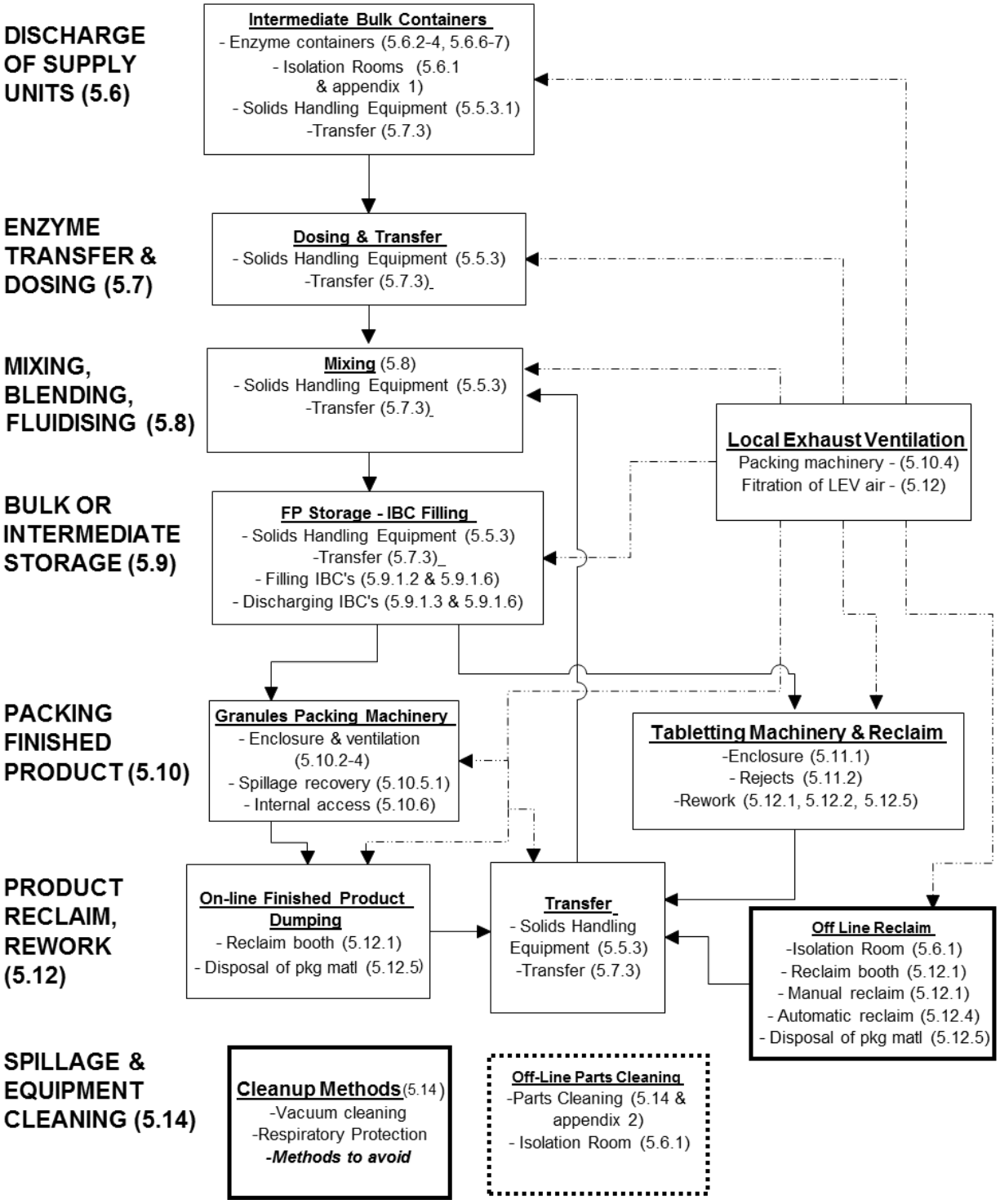
There are two main forms of enzyme products supplied for detergent manufacture:

- Enzyme encapsulates [solids], and
- Enzyme liquids / slurries

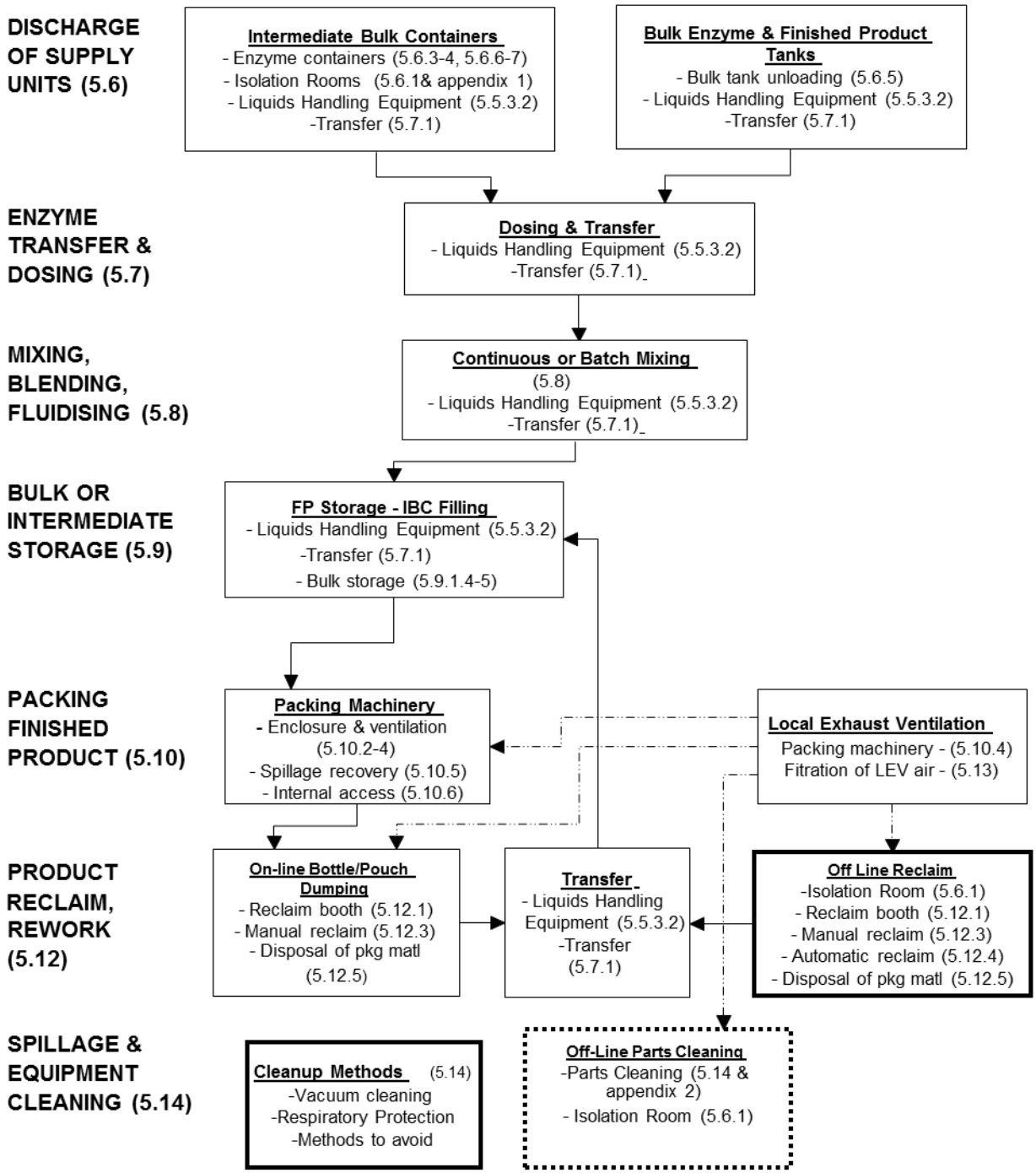
Encapsulated enzymes **must** be used for the manufacture of detergent powders or tablets. Powdered enzymes must not be used due to the higher risk of enzyme dust generation.

Encapsulated enzymes must meet a suitable quality standard with respect to the level of free enzyme dust present in the bulk material and/or the resistance of the encapsulate to damage within the process. This will be discussed in more detail in Chapter 10.
Enzymes in liquids or slurries are not encapsulated and thus there is a greater risk of exposure to airborne enzyme due to aerosolization, or to dust as a result of spillage drying out.

GRANULES & TABLETTING PROCESS STEPS - BY UNIT OPERATION (section reference no.)



LIQUID PROCESS STEPS - BY UNIT OPERATION (section reference number)



5.2. Supply Units

The choice of supply unit is often very strongly influenced by cost, size, availability, transport, the options for handling and discharge, and the disposal of the empty packaging.

When Big Bags[2] are selected as the appropriate supply unit, the disposable type Big Bags are the recommended option. Handling and disposal of Big Bags will be discussed in detail in the section 5.3.

Encapsulated enzymes may be supplied in:

- Returnable Heavy Duty Rubber/PVC Big-bags
- Disposable Big-bags with a removable polythene liner
- Disposable Big-bags with a fixed polythene liner
- Intermediate Bulk Containers (Rigid IBCs)
- Polythene Lined Cardboard Kegs
- Metal drums
- Plastic drums

Liquid Enzymes - or slurries - may be supplied in:

- Road Tankers
- Intermediate Bulk Containers (Rigid IBCs)
- Metal drums
- Plastic drums
- Batch size unit dose containers (5 – 25 litre)

Depending upon local availability, and the requirements for filling the supply units, not all of the above options will necessarily be available from every supplier. However the supply unit should match the discharge equipment at the factory to ensure that discharge is achieved safely. This is discussed in more detail in section 5.6.

Supply units that are purchased or delivered in error and cannot be safely discharged using the equipment available should not be used, and should be returned to the supplier.

5.3. Storage of Supply Units

Supply units must be stored to avoid damage to the packaging and/or the contents. If it is practical to do so, then supply units should be stored in an area dedicated for that purpose and protected from damage by physical barriers [walls / fencing / etc.].

Supply units should not be double stacked during transport or storage unless specifically designed to be so. Big bags of encapsulated enzymes must never be double stacked as this will crush the encapsulates and release enzyme dust.

As a minimum supply, units should be stored away from frequent traffic to minimize the risk of damage by vehicles / fork lift trucks. The storage location should be clearly signed with the appropriate hazard. Emergency procedures, spillage equipment, and personal

[2] Also referred to as FIBC's i.e Flexible Intermediate Bulk Containers

protective equipment must be stored locally and be immediately available to deal with spillages.

Only trained operators / emergency response teams should be called upon to deal with spillages / damaged supply units.

5.4. Disposal of Empty Supply Units

There are two options for dealing with empty supply units:

- Return to the supplier for disposal or re-use
- Disposal as waste

In either case contaminated packaging waste must be safely contained within another closure (e.g. a clean polythene bag, cardboard box, or palletised and stretch wrapped) to ensure safe handling at all downstream stages of the disposal operation.

Such preparation of packaging waste for disposal should be carried out under controlled conditions, e.g. in the isolated discharge area [5.6.1], by operators wearing suitable respiratory and personal protection. Guidance on respiratory and personal protection may be found in sections 5.15 and 5.16.

5.4.1. Return to the supplier

In some instances it may be possible to return some, or all, of the packaging to the supplier for either disposal, recycling, or re-use.

Packaging returned to the supplier should be in a safe condition, with no external contamination, and no risk of loss of integrity during the return trip.

Return for re-use is practical for:

- Returnable Heavy Duty Rubber/PVC Big-bags
- Intermediate Bulk Containers (IBCs)
- Metal drums
- Plastic drums

The decision to return packaging will depend upon the cost of transportation as compared with disposal.

Return to the supplier for disposal essentially applies to any type of supply unit, but this will need to be checked and agreed with the supplier in advance, and there may be a cost associated with this.

Before returning rigid IBC's [plastic / metal] to a supplier it is preferable to denaturate the residues left inside the containers by placing them outside and filling / washing with hot water at 80C. The rinse water should be maintained at 80C for 30 minutes to ensure enzyme denaturation prior to draining. A full risk assessment and documented procedure is required, and respiratory protection must be used as a safeguard during this activity.
For supply units that contain removable polythene liners, only the inner liner may need to be treated as contaminated waste, providing that the outer supply unit remains uncontaminated throughout use.

5.4.2. Direct Disposal

The chosen disposal route may depend upon local or national legislation, or availability of suitable incineration facilities or landfill areas, and of course cost.

The recommended options for direct disposal of flexible packaging as waste are as follows:

- Incineration as special waste
- Landfill as special waste

When disposing of contaminated packaging as "special waste" off site, it should be ensured that only licensed contractors and licensed disposal facilities are used. The factory should adhere to "Duty of Care" to ensure that contaminated waste is disposed of correctly, and according to contract (i.e. transferred using approved transport, to an agreed waste disposal facility, where it is handled accordingly).

5.5. Building and Plant Design Considerations

5.5.1 General Principles

Buildings and plant should be designed as far as is possible to provide an environment that is easy to maintain in terms of hygiene and which minimizes damage to encapsulates and spillage in powder plants or minimizes the generation of aerosols in liquid plants by avoiding spraying, splashing, or spillage.

Any areas where it is difficult to remove spillage, or settled dust, due to restricted access, or location, will act as a "reservoir" and provide a constant background of airborne dust and enzymes. During maintenance operations, refurbishment, etc this "reservoir" may also result in significant peak exposures, and/or personal contamination, when the dust is disturbed, or when periodic cleaning is attempted.

Therefore it is essential that clean design principles be used for buildings and restricted access areas are designed out of plant and equipment. The design should always facilitate cleaning with the use of a vacuum tool. The correct specification for vacuum cleaners is discussed in section 5.14.

Figure 2 shows an example of an isolated room, illustrating some clean design features.

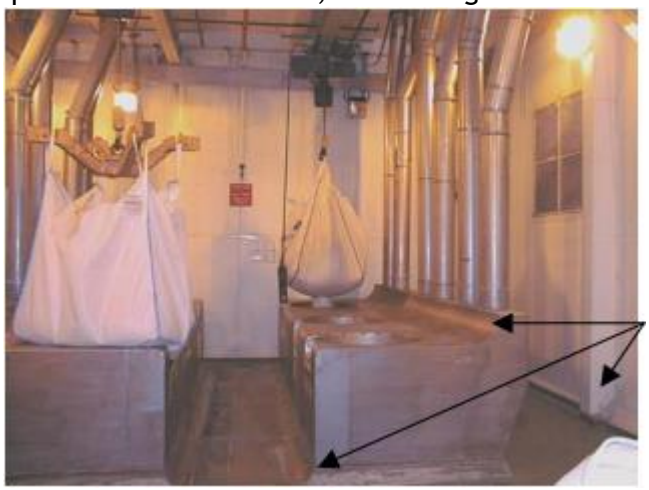


Figure 1: Isolated room showing clean design features

5.5.2. Buildings

Walls should be smooth, and sealed (e.g. painted), or clad in a smooth material that is easy to keep clean. Skirting (or baseboards) should be rounded. Fittings such as shelves, cupboards, etc., should be kept to a minimum and be positioned such that they can be easily cleaned. Old fittings and fixtures that are no longer necessary should be removed.

Ceilings should be smooth, and consideration given to access for periodic cleaning.

Floors and stairs should be smooth and easy to clean. They should be painted a dark colour to make spillage of powder or encapsulates easy to see. Open metal gridding should not be used as this is difficult to clean and allows spillage to percolate through to other levels.

Windows: complex window frames should be avoided, as these are difficult to keep clean.

Beams / girders / equipment supports / ductwork should be tubular shapes instead of boxed or I-Beams, with clean design [curved] column feet, and consideration given for access for periodic cleaning, and/or provision of specialist cleaning tools.

5.5.3. Equipment

Process equipment in powder plants should be designed to minimize damage, and wear and tear, on encapsulates. In general, equipment which has moving parts which could form traps or gaps should have those gaps large enough so that there are no points of shear to prevent the risk of encapsulate damage and dust generation.

Since enzyme liquids or slurries have a risk of dust generation from drying out and a greater potential for aerosolization, the process and packing equipment should be designed to control this additional risk by effective containment of liquids, i.e. no leaks, and by minimizing the chance of spraying and/or splashing of liquid.

The interface of employees with the manufacturing plant, and in particular with packing machinery, is the greatest potential source of personal exposure to dust and enzyme aerosols. These interfaces, or at least the frequency at which they need to occur, should be eliminated or reduced as follows:

Process and packing equipment design should eliminate external spillage and reduce liquid splashing by:

- Using “gentle” tangential transfer points, restricted drop heights, and avoiding splashing of liquids onto surfaces [including liquid surfaces]
- Designing efficient enclosures to contain any spillage and liquid splashes fully within the equipment
- Using internal spill pans/trays to collect and maintain spillage fully within the equipment with spillage removal designed in
- Designing access doors that can be opened without causing spillage to the floor [Sliding doors are best, hinged doors tend to pull air and airborne material out of an enclosure when the door is opened]
- Incorporating product reject positions within the enclosure
- Incorporating proper sampling points into plant and equipment
- Efficient machine set up to avoid frequent stoppages and manual interventions
- Use of CIP Technologies [Cleaning in Place]

In locations where spillage is evident, or routine, and not yet eliminated, this can be achieved by using external spill pans/trays to minimize the distance that products "fall" through the air, to keep the products off the floor, and contain them for subsequent cleaning by vacuum.

The design intent should be to eliminate or reduce spillage. Where it does occur, the objective should be to contain it, and remove it by an automated recovery system which will reduce the need for frequent cleaning of spillage as is found in filling machines. Alternatively the design of plant, equipment, or area, should ensure it is easy to clean with a vacuum tool. The specification for vacuum cleaners is discussed in section 5.14.
The integrity of the filter in any equipment with HEPA filtration must be ensured (see Appendix 3.

5.5.3.1 Powder Handling equipment

Belt Conveyors

Belt conveyors should be fully enclosed under ventilation control with a recommended inward velocity of 1m/s at all openings. "Lay on"guides and side skirts (see Figure 6) are used to direct and keep the powder in the centre of the belt and prevent loss of powder into the belt mechanism where damage to enzyme encapsulates may occur. Safe collection of spillage should be built into the design to reduce the need for routine entry for cleaning. Transfer points should also be fully enclosed and ventilated as above, to prevent damage to the encapsulate/finished product, the side of the transfer chutes should be sloped and the fall less than 3 metres in height.

Any provision for access should be locked off if not intended for use by unauthorised employees. Any doors or openings that are intended for routine access should be taken into consideration when specifying the level of ventilation control. Sufficient ventilation should be applied to ensure that the average inward air velocity meets the standard specified above when access doors are in the open position.

Storage Tanks, Silos, Hoppers

The vent pipes on any tanks, vessels or hoppers into which enzymes / enzyme products are discharged or collected must be controlled to prevent the release of dust into the workplace. This may be achieved by use of passive HEPA filtration on the displaced air if it is vented into the building, or by directing the vent pipe into the local exhaust ventilation system. In the event the latter option is chosen the vent pipe can be de-coupled from the ventilation system to prevent excess negative pressure developing within the vessel. Alternatively the vent may be exhausted externally without filtration at a location suitable to prevent re-entry of the exhaust back into the building. All dust control filters should be fitted with an automatic cleaning device for the filter medium.

Bucket Elevators

These are subject to the same control principles as belt conveyors. The speed of the conveyor should be selected to prevent spillage internally. Mechanisms should be fitted to prevent over filling and to remove residual material from buckets during emptying, and to safely contain any spillage that occurs internally such that it can be safely removed during cleaning and/or maintenance.

Valves

The use of valves to control the flow of encapsulates and finished products within chutes and ducting should be kept to a minimum as all valves operate with a 'Nip Point' which is a potential cause of enzyme break up. There are also areas within the valves where residual material can build up which might lead to a potential exposure during maintenance.

5.5.3.2 Liquid Handling /Transfer Equipment

Pipes

Rigid pipes should be leak free. Welded joints are preferred. Other options are compression joints and flanges. If flanges are used, these should be covered with a flange protector to prevent the development of sprays if the flange/seal fails. Flexible pipes for unloading should be robust enough to with stand abrasion and bending. Couplings for flexible discharge lines should be dry-break or cam-lock type to prevent spillage from pipe work that is disconnected.

Pumps

Preferred pumps for transfer and dosing are based on a leak free mechanical seal design i.e. magnet drive or sealed motor and pump combination. Pneumatic pumps are used but exhaust air must be vented outside the building away from any air intakes, or filtered through a HEPA filter prior to discharge. Isolation valves should be fitted to the feed and delivery side of the pump for spill free removal during maintenance.

Single diaphragm pumps used for liquid enzymes (or enzyme intermediates and products) should only be used if the exhaust air is vented to the outside (away from any intake air) as minor faults in this type of equipment can generate significant aerosol concentrations in the exhaust air. Some types of air driven multiple diaphragm pumps may be acceptable, as there is a far lower probability that multiple diaphragms could fail at the same time. The use of these should be backed up with regular maintenance to ensure reliability, and the use of a detection system to detect a faulty membrane. In addition there must be no likelihood that product could contaminate the compressed air exhaust. HEPA filters (see 5.13) may be used as a secondary protection on the air exhaust. An example of a suitable pump is a Sandpiper ST1-A with four membranes and leak detection.

Tank Vents

Displaced air from tanks/vessels that is vented back into the work place must be controlled by HEPA filtration. Air vented outside should be vented away from any intake air, and can be done so without filtration.

Valves

Valves should have leak free seals. Those connected to the pipe or pump with flanges should be covered with flange protectors to prevent the development of sprays if the flange/seal fails.

5.6. Discharge of Supply Units

Best practice when designing a safe discharge system for enzymes is to completely isolate the operator from the enzyme raw material. There should be no direct interface between the operator and the raw material. Supply units should be coupled and sealed directly to the discharge equipment to ensure this. The process should be undertaken in an area that can provide a high level of containment and control should a spillage, or release, occur. Finally all operators in the discharge area should be provided with, and wear, suitable respiratory and personal protective equipment as secondary protection, as in the event of a spillage or release of enzymes in this area, it is highly likely that a significant peak exposure will immediately occur. Personal and respiratory protection is discussed in detail in sections 5.15 and 5.16.

5.6.1. Isolation of Discharge Process

The best practice for discharge of supply units (with the exception of road tankers) is to locate the discharge equipment within a containment area, or booth, designed specifically for the handling of hazardous materials. The area should have a high air change rate to effect rapid dilution and removal of any airborne dust or aerosol in a direction away from the operator's breathing zone, and without allowing the dust or aerosol to settle. Turbulent airflow should be minimized to ensure effective control and removal of airborne contamination.

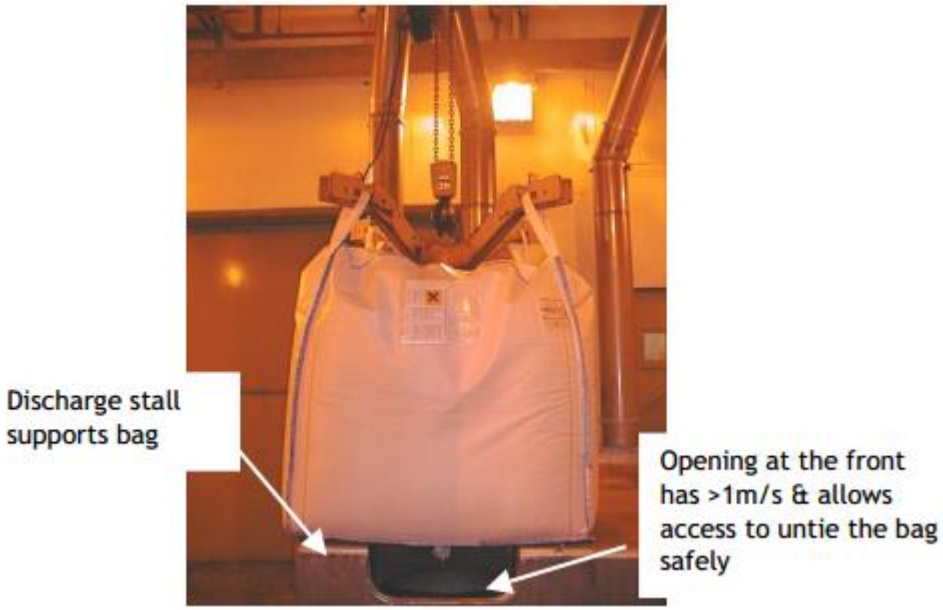


Figure 2 : Enzyme Bag Discharge

An example is the use of a laminar downflow booth [Appendix1]. These provide a high level of containment through the use of laminar downflow air, and a high rate of air change (800/hr) recirculated through high efficiency (HEPA) filtration.

Another example is the location of the discharge equipment within an enclosed room, or booth, that is maintained under negative pressure at all times, with an inward air velocity of $\geq$ 1.0 m/s at all gaps or openings that lead to the outside of the room or booth [for example gaps around doors of transfer pipework], and good air change rate (e.g.$\geq$ 10 air changes per hour). This will ensure that any airborne contamination is maintained within the room, or booth, but this system is less efficient than a laminar downflow booth at removal of airborne contamination or preventing dust or aerosol from settling out.

In either case local exhaust ventilation at the discharge point may be required to prevent the release of dust or aerosol if the supply unit is not directly coupled to the discharge equipment. This is discussed in more detail in the following sections.

Whichever system of discharge is in place, it should be ensured that empty supply units are externally clean (i.e. not contaminated with dust / enzyme) and / or contained before they are moved away from the isolated discharge area. Contaminated materials such as polythene liners, returnable Big-bags etc, should be handled as detailed in section 5.4.

5.6.2. Discharge of Big-bags

The primary mechanism for discharge of Big-bags is via gravity. Following this there are several options for transfer of enzyme encapsulates which will be discussed in section 5.7. The discharge of a Big-Bag is shown in Figure 2.

Single trip / disposable Big-bags with removable polythene liners.

For polythene lined Big-bags, safe discharge systems incorporating automated liner removal are an example of a best practice solution. These should be located within a controlled discharged area as discussed in 5.6.1.

The operation of an automated liner removal system should roll up the polythene liner onto a spool, which can then be manually removed in its rolled-up form, and placed directly into a larger polythene bag to await disposal.

If it is uncontaminated, the outer Big-bag should be manually folded flat and collated on a pallet, or in a large box, to await disposal or return / re-use.

Returnable Big-Bags with fixed polythene liners and disposable Big-bags

Returnable heavy-duty Big-bags and bags with fixed polythene liners should be discharged via a dump station located within a suitable discharge area (5.6.1) and controlled by additional local exhaust ventilation at the discharge point. The Big-bag outlet should "seal" to the dump station as tightly as possible to prevent the escape of dust, and to maximise the effect of the local exhaust ventilation.

A facility to deflate empty bags prior to removal should be installed to minimize operator exposure to the residual dust and enzymes that may be present on the inner surfaces of the Big-bag, and which may be expelled during deflation. This may be achieved by the attachment of a flexible vacuum hose connected to the vent port[3] of the Big-bag. Vacuum for deflation may be provided by a HEPA vacuum cleaner or by connection to the local exhaust ventilation system. Bags should be free from any external contamination before deflation and folding.

[3] A vent port should be included in the specification for the Big-bag

Bags should be folded during deflation to simplify handling, collation, and return to the supplier. Folded bags should be stored / collated in large polythene bags, or polythene lined cardboard crates, which can be sealed for return to the supplier.

Disposable Big-Bags with fixed polythene liners should be deflated in the same manner as returnable bags and then sealed in a large polythene bag ready for disposal.

5.6.3. Discharge of Intermediate Bulk Containers (Rigid)

This type of rigid IBC is more commonly used for liquids, but can also be used for encapsulated enzymes. Discharge of liquids is normally via direct connection of pipe work to the valve on the front of the IBC.

Liquids IBCs

Liquids IBCs may be discharged into a variety of holding tanks, hoppers, weighing vessels etc, or may be used to dose directly into a continuous process. In any event, the IBC should be coupled to the process using a dry-break or cam-lock type coupling to avoid any spillages during the coupling / de-coupling operation. The cap on the top of the IBC should either be vented, or should be loosened slightly to allow air to enter during the discharge operation. As air will be drawn into the IBC during discharge, and will not be expelled, there is no need to incorporate filtration into this vent. If the IBC can vent into the room, a cap incorporating a HEPA filter needs to be installed to prevent the release of aerosols.

The discharge areas - whether a downflow booth, or enclosed discharge room - should be provided with suitable secondary containment to contain gross spillage of enzymes in the event of a failure of the IBC, or associated pipework. This may be in the form of a physical barrier to maintain the spillage within the controlled area, or a closed drainage channel to prevent liquid leaving the controlled area and to safely direct the spillage to an intermediate holding tank incorporating suitable venting facilities to prevent the escape of aerosol.

Rigid IBC for Encapsulates

Encapsulates will not flow through the outlets of standard Liquids IBCs as they are designed primarily to hold liquids. Dense phase vacuum transfer via the top-filling hatch is the only real option to discharge these type of IBCs used in this way.

The lid on the top of the IBC should be removed only within the controlled discharge area. The vacuum lance may then be inserted into the contents.

Dense-phase vacuum transfer is discussed in section 5.7.2. Lean Phase vacuum transfer must never be used as this will severely damage the encapsulates.

Alternatively, rigid IBCs specifically for handling solids may be obtained. This type of IBC may be fitted with a conical base and locking system to allow a relatively dust-free discharge operation.

The main disadvantage of these types of systems is the cost of transporting this type of IBC back to the supplier.

5.6.4. Discharge of Kegs and Drums

Polythene-lined Cardboard Kegs

Cardboard kegs are often tipped by means of specialised fully contained keg tipping equipment, which normally incorporates a glove box through which the inner polythene liner may be opened, allowing the encapsulate to discharge into a hopper. Whilst this offers good control, it has the potential to generate high concentrations of airborne dust, so additional local exhaust ventilation should be fitted to the unit to ensure dust containment throughout the complete operation.

Best practice for the discharge of encapsulates from kegs is to avoid the tipping operation. One option is the use of dense phase vacuum transfer (5.7.2). The keg should be opened within the controlled discharge area; the liner untied and folded back, and the vacuum lance placed into the contents. The enzyme is then removed from the keg and transferred to the process by vacuum. However it should be stressed that the specification of equipment for the transfer of enzyme encapsulates by vacuum is critical to avoid damage and the release of enzymes. Lean phase vacuum transfer must never be used.

Once kegs are empty, there are two options for disposal:

Option 1: The inner liner should be vacuumed off using the vacuum lance or HEPA vacuum cleaners (5.14), to remove visible dust or any remaining encapsulate. The liner should then be carefully removed, rolled up and folded whilst under ventilation control, and placed into a secondary container (an empty keg or polythene bag) for disposal. Unless they are to be returned to the supplier, empty kegs should be crushed to prevent unauthorised re-use. Unless they are obviously contaminated, crushed cardboard kegs can be treated as normal waste.

Option 2: The liner is carefully folded back into the keg, and the keg is resealed, and disposed of as a single contaminated unit.

The **latter option** is the simplest in terms of operation, but requires an area in which to store complete kegs prior to disposal, and it also incurs a higher disposal cost as the complete unit is considered to be contaminated waste.

Metal or Plastic Drums for Liquids

As with rigid IBCs, drums should be discharged from within the controlled discharge area, using dry-break or cam-lock type couplings fitted to the threaded opening in the drum lid.

Once the first half of the dry-break coupling is fitted to the top of the drum, the drum will need to be positioned on its side in a purpose built cradle, which is slightly sloped forwards to ensure that the contents are emptied effectively. If a cam-lock coupling is used, a shut off valve will have to be fitted before the drum is positioned in the cradle.

Drums may then be discharged by gravity, or by the use of pumps.

The use of dip-pipes or “Drum pumps” is not recommended. These are prone to cause spillage and personal contamination on removal from the drum and during storage when not in use.

As with liquids IBCs, the controlled discharge area should be surrounded by secondary containment to contain gross spillages.

Metal or Plastic Drums for Encapsulates

These drums may be used as an alternative to cardboard kegs. They are often larger, more robust, weatherproof, do not need a liner and thus there is no flexible packaging for disposal.

Drums are often tipped by means of specialised tipping equipment. Whilst this offers good control, it has the potential to generate high concentrations of airborne dust if containment is poor, so tipping equipment should be fully contained and fitted with local exhaust ventilation to ensure control throughout the complete operation.

Best practice for the discharge of encapsulates from drums is to avoid the tipping operation. One option is the use of dense phase vacuum transfer (5.7.2). The drum should be opened within the controlled discharge area and the vacuum lance placed into the contents. The enzymes are then removed from the drum and transferred to the process by vacuum. However it should be stressed that the specification of equipment for the transfer of enzyme encapsulates by vacuum is critical to avoid damage and the release of enzymes.

5.6.5. Discharge of Road Tankers

Whilst it is relatively uncommon, road tankers may be used for the delivery of liquid enzymes. The same general principles of containment apply:

- The discharge bay and storage vessels should be surrounded by secondary containment to contain gross spillages
- Personal and respiratory protection should be worn when coupling / uncoupling the road tanker from the storage facility

Enzyme may be used direct from the road tanker left in situ, or transferred to on site bulk storage vessels, tanks. (see chapter 5.5.3.1 for ventilation of storage tanks)

5.6.6. Dispensing Enzymes into Batch-Sized Unit Containers

Where there is any interface between people and enzymes, there is a risk of exposure from the inhalation of dust and / or aerosol. Manual dispensing of enzymes carries a high risk of exposure, but in some instances it cannot be avoided, due to the small quantities required [e.g. in pilot plants] and / or the inherent accuracy of automated dosing systems when dealing with small quantities.

Manual dispensing of enzymes may be achieved safely but requires a high level of engineering control, along with a high quality of personal and respiratory protection.

The need for the following should be evaluated:

- An isolated dispensary for weighing out / repackaging enzymes as discussed in 5.6.1
- Suitable transfer containers as specified in 5.6.7
- Local exhaust ventilation at the dispensing station
- Direct coupling of the transfer container to the process
- Positive pressure respiratory protection as detailed in 5.15.2
- Protective overalls as detailed in 5.16
- Handling of spillage as detailed in 5.14

It is essential that the supply units from which enzymes are to be dispensed are suitable for the purpose, and are in a fixed position from which the contents can be dispensed safely. The operator should not dispense the contents of the supply unit by direct tipping / pouring, which could result in the spillage of the complete contents of the supply unit.

5.6.7. Discharge of Batch-Sized Unit Containers

In some instances, and in particular for the smaller volume operations, it is possible to obtain batch-sized unit doses of enzymes, pre-packed into relatively small manageable containers. Some alteration of the batch size may be necessary to allow such purpose-bought units to be used, either singly, or in multiples.

Alternatively, a bulk supply of enzyme may be pre-dispensed at the factory, prior to manual addition to the process from a suitable transfer container (see below). Routine dispensing of enzymes has a high potential for exposure to dust and / or aerosol and must only be carried out under effective ventilation control (5.6.6).

In many cases, an enzyme is manually dosed directly from these units into the process. It is important that this type of operation is carried out in accordance with the general principles applied to the discharge of supply units. Dosing from these units will be discussed further in section 5.7.

Whether the transfer container is obtained from the supplier, or from an "in-house" dispensary, it should fulfil the following requirements:

- Solid sided / rigid
- Translucent / transparent for visibility
- Strong enough to withstand foreseeable impacts, including being dropped
- Fixed lid that will not come off if the container is dropped
- Light enough when full to be manageable
- Fitted with "Dry break" or other closed couplings to ensure containment during discharge

Depending on the design, these can be used for both liquids and encapsulates.

5.7. Enzyme Transfer and Dosing

In plants where the process layout is relatively simple, transfer of both enzymes encapsulates and liquids may be achieved by gravity. In some plants a combination of gravity and powered systems may be required, and in others enzyme transfer may be solely by powered systems, such as conveyor belts, dense phase vacuum transfer, or pumps.

In any instance containment should be assured at all times. There must be no release of enzyme dust or aerosol.

Containment can be achieved by two means:

- Complete enclosure – a physically sealed / closed system
- Partial enclosure and ventilation control

When enzyme encapsulates are conveyed, transferred and dosed it is essential that the plant and equipment is designed to minimize any damage to the granules, thus maintaining their integrity.

Some types of transfer equipment can damage enzyme encapsulates by the application of crushing, shearing or abrasive forces. These includ screw conveyors, disk conveyors, brush conveyors, and drag conveyors. Their use is not recommended unless an evaluation has been made of the potential for encapsulate damage using a suitable analytical method (see Chapter 10), and the conveying equipment is proven not to cause significant physical damage.

Dosing of enzyme encapsulates should be undertaken at the latest possible point in the production process. This will minimize the amount of plant and equipment that will be contaminated with enzymes, and reduce the distance within the plant that enzymes will be conveyed, thus minimizing the potential for encapsulate damage, and the potential for exposure of maintenance operators.

Dosing should only be carried out using contained and controlled dosing systems. Manual dosing of enzymes should never be carried out by open tipping, or pouring, through the man way, or over the side, of any vessel. The potential for exposure to dust and aerosol, or for spillage and / or personal contamination, is too high using a manual method.

An example of liquid enzyme transfer pumps is shown in Figure 4.

Figure 3: Example of Enzyme Transfer Pump Sets

5.7.1. Dosing Of Liquid Enzyme

Continuous Manufacturing Plant

Continuous dosing plants bring together two or more metered streams of liquid and mix them together. Typically a continuous enzyme dosing facility brings together the product base and the enzyme. The enzymes may be pumped from a storage facility, or direct from a supply IBC.

Liquid enzyme should be the last raw material dosed into the product to minimize the enzyme contamination of the process equipment.

Liquids dosing plants are quite complex, often pressurised, and there are many points at which leaks may occur. Therefore it is recommended that the dosing plant is sited in a contained [authorised access] area under negative pressure to maintain an inward airflow of 1.0m/s, with a minimum of 3 to 4 air changes an hour.

Access to the dosing area should be restricted to authorised employees, wearing respiratory protection as secondary protection in the event that a failure has occurred. The area should be kept dry to aid the visual detection of loss of containment.

Batch Manufacturing Plants – Automated dosing

Liquid enzymes are added to a batch-mixing vessel containing the remainder of the product formulation. Typically, batch-mixing vessels have a man way that can be opened to either observe the product, or to take samples for analysis. It is at this point that there is a risk of exposure to enzyme aerosol from either the liquid enzyme, or the enzyme product. To avoid exposure the following should be in place:

- The mixing vessel should be under the control of exhaust ventilation to achieve a recommended air velocity across [or into] the man way of > 1.0 m/s
- Enzyme dosing and mixing should only take place with the man way in the closed position. Ideally dosing and mixing equipment should be interlocked with the man way
- Enzyme and reworked enzyme products should be added tangentially, or down the side of the mixer wall to reduce the potential for generating aerosol from splash filling

Ideally the mixing vessel should have no access points, or hatches, that can be opened during normal operation, and the vessel should be effectively sealed.

Batch Manufacturing Plants – Manually Operated Dosing Systems

Manual dosing of liquid enzymes should never be carried out by open pouring through the man way, or over the side, of any vessel. The potential for exposure to aerosol, from spillage or from personal contamination is too high to risk using this method.

Manually operated dosing should be achieved using closed transfer vessels, as described in 5.6.7. The transfer, or supply, container should be fitted with one half of a dry-break type coupling that connects securely with its corresponding half fixed in place on the mixing vessel. The dosing may be achieved manually by opening the valve once the dry-break coupling is assembled, or it may be remotely actuated by an automatic control system.

5.7.2. Transfer & Conveying of Enzyme Encapsulates

Enzyme encapsulates should only be transferred or conveyed using equipment that is proven to prevent or minimize damage to the granules as discussed in section 5.6.3. The requirements for belts and conveyors used to transfer encapsulates are also described in section 5.5.3.1. Alternatively, as described below, dense-phase vacuum transfer may be used.

Dense-Phase Vacuum Transfer

When enzyme encapsulates move, or flow, there is a potential for abrasion to occur which can, if significant, result in the degradation of the encapsulation and the release of enzymes. If movement, or flow, occurs at high velocity, both abrasion and impact damage will occur and enzymes dust will be released from the damaged encapsulates.

Traditional lean-phase (or dilute phase) pneumatic transfer **must never** be used for the conveying of enzyme encapsulates.

Lean Phase Pneumatic conveying

- Operates at high velocities (> 20m/s) resulting in severe abrasion and impact damage to enzyme encapsulates
- Has a low solid to air ratio, often 10:1 or less
- Conveys materials "in flight" thus increasing the potential for high velocity impacts
- Generally operates continuously allowing the build-up of velocity through momentum
- Operates at positive pressure resulting in a risk of loss of dust containment
- Will cause significant damage to encapsulated enzyme

Dense Phase Vacuum Transfer

Dense-phase vacuum transfer can be used safely to convey enzyme encapsulates in closed pipe systems providing that the correct equipment specifications are used.

Dense phase vacuum transfer:

- Operates at low velocities (2 – 10 m/s) thus minimizing abrasion and impact
- Has a high solids to air ratio, up to 50:1
- Conveys material in "slug flow" (i.e. with a short start/stop cycle) thus reducing impact damage and the build-up of velocity through momentum
- Operates under negative pressure thus ensuring containment in the event of minor system leaks [i.e. air always moves inwards at defective seals or minor faults]

Safe system design also relies on:

- Minimizing the number of bends required
- Using bends of the correct radius (10 x pipe diameter) – no sharp bends
- Using smooth and consistent materials of construction (Stainless steel) for pipework and bends. (Do not use flexible pipework to construct bends)
- Controlling the maximum vacuum available for conveying

Dense-phase vacuum transfer operates under negative pressure – any leaks, or poor joints in the pipework will not release dust; air will always be drawn into the system. It moves the maximum volume of solids, using the minimal amount of air, at a relatively low

velocity (2-10 m/s). Impact damage at bends is minimized by controlling the velocity using a "slug flow" process. This is generated using a short start/stop vacuum cycle and prevents the build-up of momentum and gently conveys encapsulates through the pipework.

This method of transfer can move the encapsulate over a relatively large vertical height (i.e. 15 m), and because it is closed pipe technology, it provides no physical transfer points or "pinch points" as with belts or other mechanical conveying systems. It also allows the transfer of enzymes to the process from ground level, which means less movement of supply units within the plant.

Validation

The use of any dense phase vacuum conveying equipment must be validated for the enzyme encapsulates in use to ensure that they remain within the quality specification for material received into the plant. This can be achieved by direct measurement of the "dustiness" of the enzyme encapsulate before and after conveying using the methodology described in Chapter 10. Many suppliers of vacuum conveying equipment offer test facilities to enable conveying trials to be undertaken. Under no circumstances should dense phase vacuum transfer be used without thorough validation.

It must also be stressed again that the use of higher velocities, or lean phase vacuum transfer systems will significantly damage, if not destroy, encapsulates and these types of systems must not be used.

5.7.3. Dosing of Enzyme Encapsulates

Dosing of encapsulated enzymes into the formulation should take place at the last possible point prior to mixing/blending to minimize the enzyme contamination of the manufacturing plant and equipment, and minimize the distance within the plant that enzymes travel; thus minimizing the potential for encapsulate damage from the process plant and equipment.

Dosing equipment is normally positioned beneath a small intermediate hopper, or buffer vessel containing encapsulate. This vessel should either be totally sealed or placed under ventilation control to prevent the release of dust, or if vented then the vent should be controlled by filtration as discussed in 5.5.3.

Some types of dosing equipment can damage enzyme encapsulates by the application of crushing, shearing or abrasive forces. This includes screw conveyors, and their use is not recommended unless analysis of particle break-up shows no increase in enzyme dustiness.

Automated dosing may be achieved using dosing belts (see 5.5.3), vibratory feeders or volumetric dosing.

Vibratory feeders

Vibratory feeders are generally small units, and are relatively easy to seal. However the flexible connections that are necessary to allow the vibratory action are prone to fracture, or to come loose, releasing dust to the working environment. Routine inspection and maintenance of flexible connections must be undertaken at a suitably identified frequency to ensure that this does not occur. It is recommended that this type of unit be maintained under negative pressure by the use of ventilation control, and that flexible connections are double walled.

The outlet of vibratory feeders should be secured to the downstream process equipment.

Volumetric Dosing

Volumetric dosing equipment is normally "in line" and as such is part of a closed process. It is normally unnecessary to add ventilation control, unless there is a risk of dust release.

Care must be taken if valves are used to control volumetric dosing units during filling and discharge as certain valve types will damage encapsulated enzymes [5.5.3.1].

Manually Operated Dosing Systems

Manual dosing of enzyme encapsulates should never be carried out by open pouring through the man way, or over the side, of any mixing vessel. The potential for exposure to airborne enzyme dust, for spillage, or personal contamination is too high to risk using this method.

Manually operated dosing should be achieved using closed transfer vessels, as described in 5. 7. The transfer or supply container should be fitted with one half of a dry-break type coupling that connects securely with its corresponding half fixed in place on the mixing vessel. The dosing may be achieved manually by opening the valve once the dry-break coupling is assembled, or it may be remotely actuated by an automatic control system.

5.8. Mixing / Blending / Fluidising

There are many options for mixing the post-dosed formulation ingredients to obtain the final product, including fluidising (powders), continuous drum mixers (powders), static mixers (powders and liquids), batch mixing vessels (powders and liquids) and continuous plants (liquids). When selecting mixers, the principle is to avoid "close nips" or tolerances which can cause crushing or shearing of powders. This can be assessed by using a test for encapsulate integrity (chapter 10).

Depending upon the manufacturer of the plant, there will be a large variation in the standard of enclosure, and containment. For some plants containment is implicit in the design, as with continuous dosing plants for liquids for example, but in others there may be a risk of dust and/or aerosol release, particularly at the loading transfer points. In all instances, transfer points should be enclosed as far as is practicable, and the containment assured by the application of ventilation control.

5.9. Bulk or Intermediate Storage

Following the mixing operation there are several possibilities for the storage and distribution of product, both powders and liquids:

- Bulk storage in silos or tanks, or other fixed vessels
- Intermediate storage in mobile tote bins or IBCs
- Storage in Big-bags (powders only)
- Supply direct to packing machinery

Bulk storage can apply to powders and/or liquids.

5.9.1. Intermediate Storage in Mobile Tote Bins / IBCs

Intermediate storage may apply to both powders and liquids, but it is more common for powders. It is often also used for the storage of reclaimed material from line rejects, out-of-specification product, or trade returns.

Approximately 1000kg of finished product may be stored in a movable bin that can then be discharged direct to the packing machinery, or back into the process. This type of bin is often used for the collation of powder from reject packs. Handling of line rejects / trade returns is discussed in greater detail in 5.12.

5.9.1.1. Filling of Intermediate Tote Bins (Powders)

Filling of intermediate tote bins should be without the release of dust or aerosol. Some commercially available designs for handling of powders incorporate "dust-tight" filling and discharge valves, to be used in dedicated filling and discharge equipment. This type of bin is recommended as best practice. There is however other variations in design and construction as follow:

- Rigid, smooth sided [metal / plastic] with lids and filling aperture
- Rigid, smooth sided, open topped with or without a lid
- Flexible sided [e.g. canvas] open topped buggies with or without a lid

The use of lids on intermediate storage containers is recommended to prevent enzyme dusts from being moved out of the top by room air currents in storage locations and during transport and to contain dust from the collapse of the powder pile in the bin during normal emptying operations.

The tote bins may be moved either by forklift truck, or manually if they are stable, and fitted with suitable wheels.

For bins with tops that open, the filling station should be fully enclosed and ventilated by a combination of local exhaust ventilation at the filling head, and enclosure ventilation to maintain the overall integrity of the filling operation. An inward air velocity of $\geq$ 1.0 m/s is recommended at any gaps or openings in the enclosure. Higher velocities may be needed for some filling operations to overcome high velocity displace air from rapid filling of the bin.

Ideally the filling head should seal to an aperture on the top of the tote bin to minimize dust generation and spillage. Rigid smooth-sided bins are less likely to accumulate dust and regenerate airborne dust during use than flexible sided bins.

The exterior sides of the bin should also be smooth to prevent any dust from building up on the outside of the bin, or external bracing struts, during successive filling operations.

5.9.1.2. Discharge of Mobile Tote Bins (Powders)

Discharge should be undertaken without the release of dust. The commercially available bin systems designed for dust-free materials handling are considered as best practice.

Many basic tote bin designs incorporate a flexible outlet, similar to the discharge trunk of

a Big-bag, which is located in the base of the bin. To discharge the tote bin, this flexible outlet is dropped into a"dump station", which is often no more than a hole in the floor. It is essential that dust control be undertaken at these locations. This can be via a combination of ensuring a good physical seal between the outlet and the "dump station", and the provision of local exhaust ventilation. Figure 4 shows an example of an intermediate storage container, illustrating the match between the discharge outlet and the dump station.

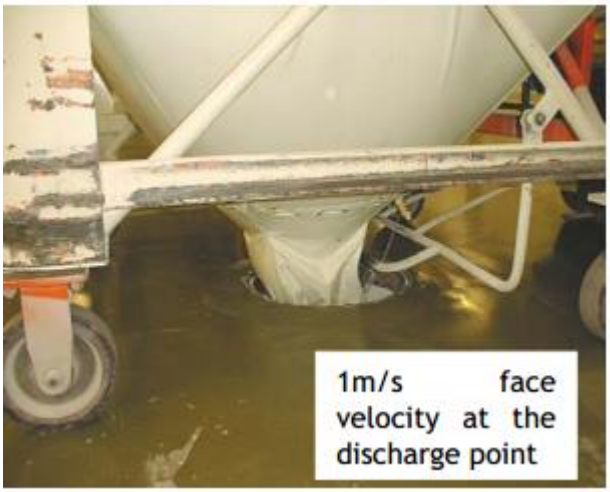


Figure 4: Intermediate Container Discharge

The manual release [untying] of the outlet carries a high risk of exposure to dust. Therefore remote systems should be used to prevent the need for any operators head/breathing zone to be close to the outlet as it is released and dropped onto the dump station. Lever, slide valve, or release pin systems located on, and operated from, the sides of the bins are acceptable. Rope ties which need to be manually unfastened beneath the tote bin are not acceptable since these necessitate the operator being very close to the outlet as it falls and discharges.

5.9.1.3. Filling of Intermediate Liquids IBCs

IBCs used for intermediate liquids handling are normally 1000-litre capacity. Aerosols will be generated during the filling operation as the liquid products "splash" against the bottom of the container, or onto the surface of the liquid in a partly filled container. This aerosol is displaced from the IBC along with air, as the IBC fills. IBCs should therefore be filled using closed systems that fully seal to the filling point. Moveable spill trays to catch any drips from the filling nozzle should be provided and cleaned immediately after use. Air vented from the IBC during filling should be filtered to remove aerosol, or discharged into a local ventilation system (see 5.6.3).

5.9.1.4. Discharge of Intermediate Liquids IBCs

IBCs should be discharged following the advice provided for liquid enzymes in section 5.6.3.

5.9.1.5. Big-bag Filling, discharge and Re-use of Big-bags

Big-bags are commonly used for the storage of finished powder, and supply of powder to packing machinery. Big-bags used for this purpose are often re-used within the factory without any attempt to wash or clean the bags. This leads to a significant build-up of dust within the bag, and on the exterior surface, which becomes a major source of operator exposure when the bags are handled during filling, discharge, and deflation.

Used Big-bags should be disposed of, or cleaned, at a frequency that is sufficient to prevent significant exposure to airborne dust as a result of their handling.

Big-bags should be regularly inspected to ensure that they do not present a significant risk during re-use as a result of their standard of cleanliness or physical condition. Damaged bags should be disposed of or properly repaired.

Big-bag filling should be undertaken using dedicated filling systems designed to prevent the release of dust. The filling inlet of the Big-bag should be sealed to the filling head by means of an inflatable bladder seal (see Figure 5). The use of clamps, or weighted neck rings, are seldom effective at producing a dust tight seal sufficient for enzyme containing products and are not recommended.

It should be ensured that Big bags are not externally contaminated with powder post-filling. Any such contamination should be removed by a vacuum cleaner before the bag is moved. This prevents inadvertent exposure and spillage.

Big-bag filling and handling should be undertaken within a controlled area as discussed in 5.6.1.

The recommended practice for the discharge of Big-bags is discussed in section 5.6.2.

Figure 5: Big-Bag Filling Head

5.9.2. Supply of product Direct to Packing Machinery

In many instances there are either no facilities for the intermediate storage of finished powder, or intermediate storage is not required. Direct feed to the packing machinery is typically undertaken by the use of one or more systems:

- Conveyor Belts
- Bucket Elevators
- Dense Phase Vacuum Transfer
- Closed Pipework (Liquids)

Packing machinery is normally supplied from a hopper, or vessel, located above the filling equipment. These vessels should be sealed, vented, or controlled as discussed in 5.5.3.

To avoid spillage from conveyor belts, powder should be accurately positioned onto the belt by the use of lay on guides and edge skirting, as in figure 6.

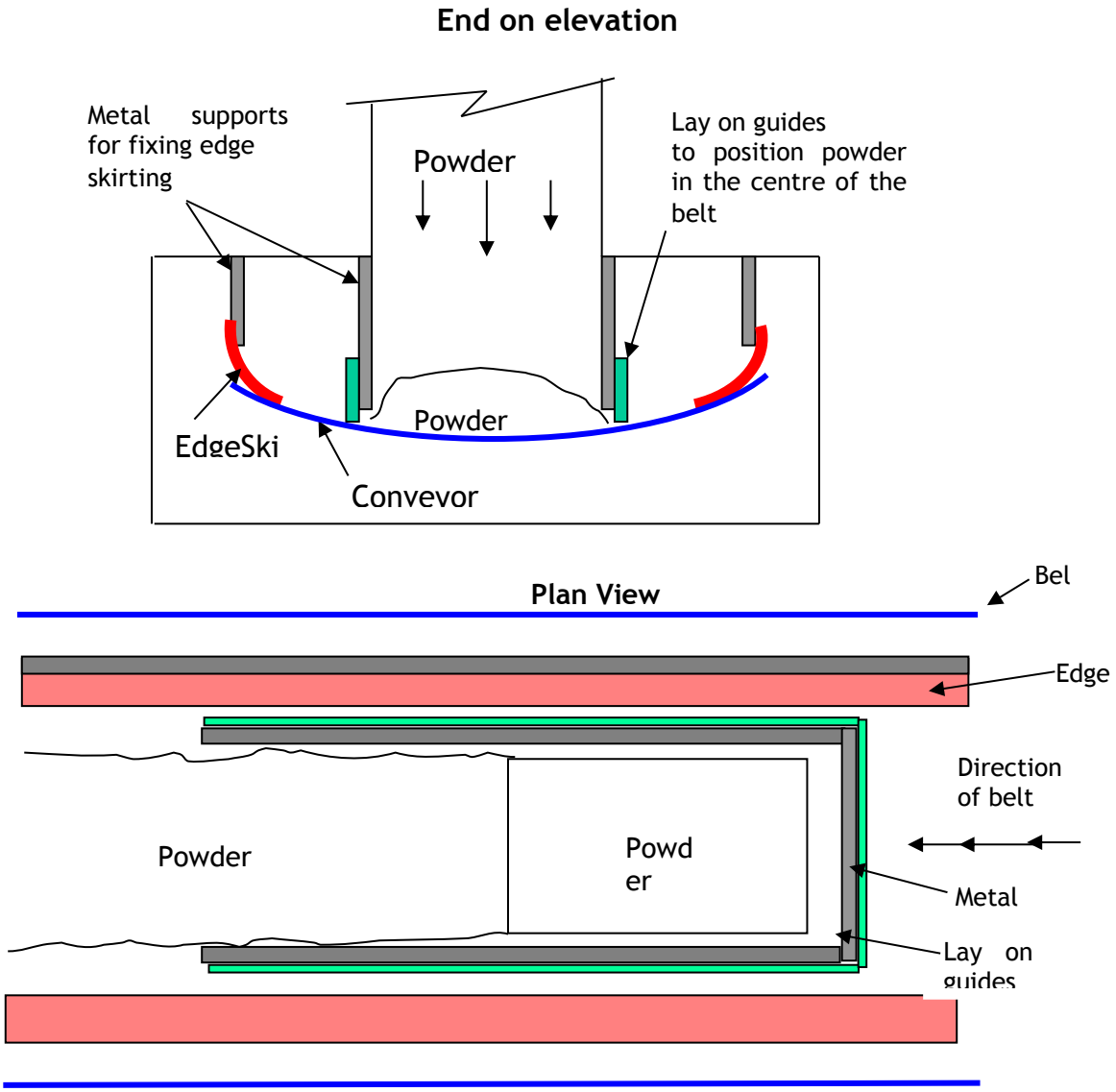


Figure 6: Lay on Guides and Edge Skirting

5.10. Packing of Finished Product

Packing involves the filling of containers with product, either by gravity, or by force (i.e. under pressure, or with the input of energy). Filling containers with powders or liquids by any means will result in the generation of dust and/or aerosol.

When powders are introduced into a container, the air inside the container is displaced through the bulk of the powder, and is expelled from the container. Dust is entrained in this displaced air. Good packing machine design can minimize exposures during filling operations through capture and containment of dusts and aerosols at source.

Liquid products produce aerosols when they "splash" against the bottom of the container, or onto the surface of the liquid in a partly filled container. This aerosol is displaced from the carton along with air, as the carton fills.

Manual packing of enzyme products (i.e. hand scooping of powder and dumping into a container) carries with it a very significant risk of exposure to dust and/or aerosols and should not be undertaken except under exceptional circumstances. Where it is undertaken, compulsory controls should be in place to limit potential exposure.

5.10.1. Packing Machine Design

Packing machine design is a critical component of a safe-handling programme because most exposures to enzymes are likely to occur from packing operations. Packing equipment design should minimize the need for internal access for maintenance and cleaning through improved mechanical reliability, the elimination of internal spillages and the use of automated spillage recovery systems.

The design intent should be to eliminate or reduce spillage, and where it does occur to contain it, and remove it by an automated recovery system. Alternatively design the plant, equipment, or area, to be easy to clean with a vacuum tool. Details of suitable vacuum cleaners may be found in section 5.13.

For some packing machines special [locally designed] vacuum tools may be required to reach inaccessible places and/or to carry out safe and effective cleaning.

Compressed air must never be used for cleaning of packing machinery.

5.10.2. Packing Machine Enclosures

Packing machines should be enclosed as much as is practicable. To maximise the effect of ventilation control, all major openings in the enclosure should be minimized, and all doors or other such access points should be fitted with effective seals. The face velocity at carton exit should be high enough to overcome the velocity of the air displaced from the enclosure by the motion of the containers on the conveyor belt leaving the enclosure.

For routine access points, sliding doors are better than hinged doors. The latter, when opened, can "pull" contaminated air out of the enclosure and into the working environment. Sliding doors do not have the same effect, and in comparison to hinged doors only need to be opened sufficiently to gain access. All doors and access points should be interlocked with the machine operation to prevent injury.

The operation of the packing machine should also be interlocked with the ventilation control to prevent the operation of the packing machine if the ventilation has failed, or it has dropped to a level where it cannot provide control.

The packing machine enclosure should contain:

- The filling head
- The addition of sundry items (scoops, cups, etc.)
- The capping or sealing equipment
- The carton rejects position
- The carton rejects bin

Separate enclosures may be used in locations where this equipment is comprised of stand-alone units, but the conveyors connecting the units should be enclosed up to the point where the sealed, check-weighed packs exit the packing machinery, and the connecting conveyors should be fitted with spill trays.

To ensure that the required make up air enters the packing machine enclosure uniformly when the doors are shut, and thus preventing any ventilation "dead spots" in which dust may settle, narrow intake slots or louvres may be positioned around the sides of the enclosure. Care should be taken that the air velocity through these slots also achieves the recommended air velocity, and that powder spillage inside the machine cannot escape through them.

In some instances, such as where the packing machinery has a complex shape, it may be advisable and easier to construct an enclosure around the complete machine. The sides of such an enclosure should be near enough to the machine so as not to make a walk-in room. If a walk in room is created, it may require the use of RPE, more ventilation and additional area to clean-up.

5.10.3. Packing Machine Ventilation

Sufficient extract ventilation should be provided to ensure that a recommended air velocity of $\geq$1.0 m/s is achieved at all gaps or openings in the structure, including any intake slots constructed to ensure a uniform airflow within the enclosure as discussed above (see Figure 7). At lower velocities than this it is found that, due to the turbulent flow of air into the openings of an enclosure, containment can be poor.

Several extraction points may be required on the enclosure to obtain a uniform airflow both into, and within, the enclosure.

By minimizing the size (area) of any openings, and ensuring the effective closure of doors etc, the volume of air required to maintain the recommended airflow can be considerably reduced.

The face velocity at the carton exit should be high enough to overcome the fanning action of the row of containers leaving the enclosure.

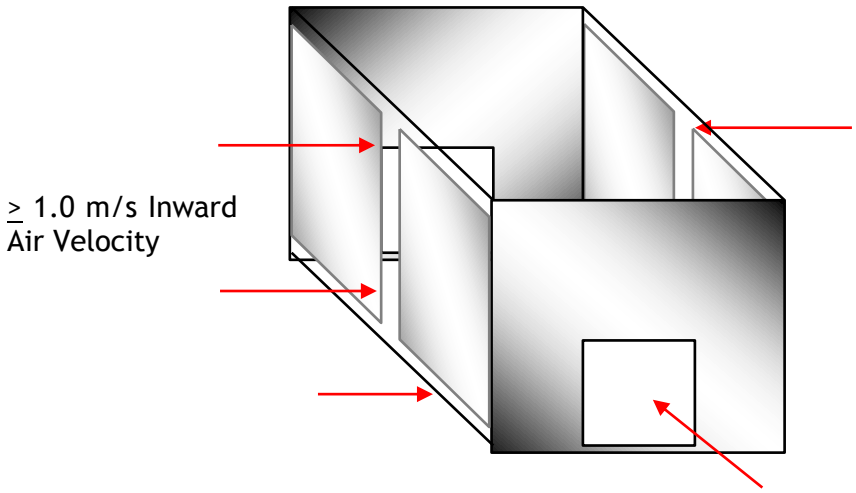


Figure 7 – Schematic Diagram of a Packing Machine Enclosure (Roof removed for clarity) illustrating the Minimum Inward Airflow Through All Openings

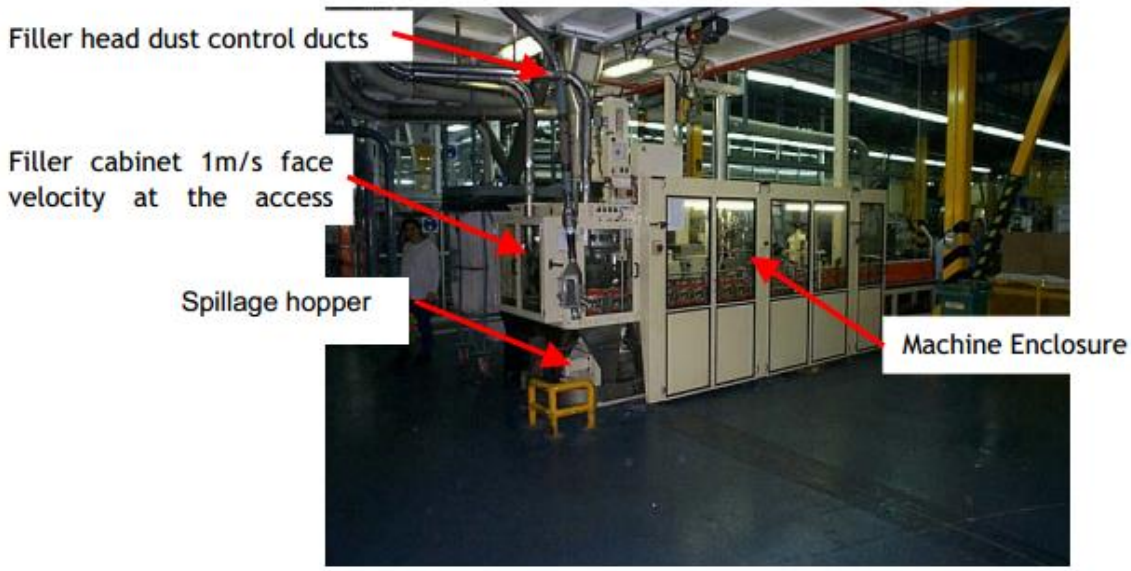


Figure 8: Carton Filling Machine

A common design fault is to attempt to collect spillage from the filling heads by using the existing ventilation control system without undertaking suitable modifications to separate out powder for rework or to ensure there is sufficient carrying capacity of the available airstream. In this instance the normal practice is to provide ventilation control to the packing enclosure via the collection hoppers that are positioned beneath the filling heads. Once the hoppers, or the ductwork below them, become blocked then ventilation control of the enclosure is reduced, or even lost completely.

There are two approaches that can be adopted:

- Design the ventilation control system with sufficient airflow to ventilate the filler cabinet and the spillage hoppers. The powder carrying capacity of the available air stream should be sufficient to prevent powder fallout from the airstream and blockages occurring in the hoppers and ductwork.
- Incorporate a powder separation facility to remove excess powder from the ventilation system prior to the filtration unit, or provide separate ventilation control and spillage recovery systems to the packing machine enclosure

Spillage recovery is discussed further in 5.10.5.

In any event the ventilation control should always be interlocked with the operation of the packing machine to ensure that the machine cannot be operated if the ventilation is not operating, or the efficiency has dropped to a level at which control has been lost. This can be achieved via the use of static pressure gauges located at strategic points within the ventilation system, or ductwork, of each packing machine.

Views of a carton filling machine and a bottle filling machine, illustrating some of the principles discussed above, are shown in Figures 8 and 9.

Figure 9: Bottle Filler Machine

5.10.4. Local Exhaust Ventilation

When filling packs with powder, direct control of the dusty air displaced from the carton or bag by local exhaust ventilation is the best practice to contain a major source of dust. Local exhaust ventilation is normally in addition to the ventilation provided to the enclosure, but may supplement it in providing additional extract air to achieve the required face velocities at openings, carton exits, etc.

The points controlled for each type of filling machine include:

- Carousel type carton filling machines - ring extraction above the cartons for the entire time the carton is filling plus about 60 degrees of travel beyond to catch the lingering dust in the carton headspace.
- Vertical form fill and seal machines - extraction of dust directly from the bag forming tube
- "In-line" filling machines (bags / cartons) – local extraction at the top of the bag or carton

5.10.5. Spillage Recovery in Packing Machines

5.10.5.1. Powders

Spillages can frequently occur beneath the filling head(s). In a high-speed machine this can result in a significant build-up of powder that can interfere with the machine performance as well as contaminate the exterior of cartons causing both safety and quality issues. Spillage can be minimized by good machine design (e.g. no carton–no fill), effective maintenance, and accurate set-up.

Spillages that do occur may be removed safely by constructing spillage trays, or hoppers, beneath the filling heads that can be designed to be emptied without the need for an operator to open the machine enclosure, by using either a portable vacuum cleaner or a ventilation control system, or a separate vacuum transfer system. The latter two options can be used to recycle powder directly to the process.

The spill trays should be designed with steep sloping sides, to direct powder towards a collection point from where it can be removed. Depending upon the properties of the powder, this may require the additional use of vibrators to prevent the powder from sticking to the sides of the spillage hoppers, and to assist powder flow.

Spillage recovery using the ventilation control system requires very careful design to ensure that the system does not become blocked and lead to a loss of containment / ventilation control.

5.10.5.2. Liquids

Spillages of liquid products may be collected in spill pans and drained down to an internal sump within the packing machine. From here it can be pumped directly into a product reclaim system, or into another container awaiting rework or disposal.

Collection containers should be designed to prevent the generation and release of enzyme aerosols.

5.10.6. Access into Packing Machine Enclosures

From time to time it will be necessary for an operator to open a packing machine enclosure to carry out a task such as clearing jammed cartons or bottles, cleaning spillage, cleaning sensors, adjusting filling heads, or re-filling scoop magazines or in-pack offers, etc.

As far as is practicable, the packing machine and its controls should be designed to minimize the need for frequent access into the enclosure. It should be possible to make all minor adjustments from outside.

Access into packing machine enclosures carries a risk of exposure to product dust and/or aerosol containing enzymes. When this is necessary, the only practical control to prevent exposure is the proper use of respiratory protective equipment, which must be fitted before the access doors to the machine, is opened. This is discussed in detail in 5.15.

5.11. Tabletting

Tabletting should be considered as a process, rather than a packing operation. The process involves compressing detergent powder into a formed, tablet-like, shape. It involves the application of force to the detergent powder, and as a result the encapsulated enzyme may be damaged. This can, by design, be minimized. Because of the higher risk of damage, a higher degree of control may be needed for the tabletting process than for powdered products.

The spillage, dust and debris which builds up within the tabletting machine during the tabletting process may contain a higher proportion of damaged encapsulate than would be encountered in a normal packing machine. For this reason the tabletting machine should be considered as an item of process equipment, and not a packing machine. The same constraints should apply for access into, cleaning, and maintenance of this equipment, as would apply to other enzyme process plant. This will rely heavily on the use of respiratory protective equipment, which will be discussed in detail in 5.15.

5.11.1. Tablet Machine Enclosure

The design of the enclosure should follow the basic principles for packing machines discussed in 5.10.

5.11.2. Tablet Reject and Tablet Conveying

The speed of the tabletting process, and thus the numbers of tablets conveyed, means that there may also be a risk of exposure to dust and enzymes from

- Dust or debris adhering to the exterior surfaces of the tablets
- Tablets that have not been formed correctly
- Damaged tablets
- Abrasion of tablets during conveying
- Rejected tablets / reject collection

Whilst on a per-tablet basis, exposure as a result of the associated dust and debris is probably insignificant [if the process is designed correctly], it may be significant when considering the large numbers of tablets conveyed, and the potential for a build-up of dust and debris in the conveying system. Therefore tablet-conveying systems should be fully enclosed and ventilated.

Tablets which are rejected because they are damaged, not correctly formed, or underweight should be rejected and collected under controlled conditions, similar to those discussed in 5.11.2

Tablets should only be handled using fully enclosed and controlled systems until packed into closed / sealed retail packs.

5.12. Product Reclaim, Rework and Trade Returns

Reclaim and rework of a product occurs when it does not meet a quality specification or has been incorrectly packed [over or under weight]. It also occurs when the product is packaged in a faulty container, or is returned from the trade as surplus material.

Reclaim of a packed product is often a manual operation, unit by unit. This means that there is a close interface between the operator, the product, and the packaging. It is essential that exposure to dust and aerosol is properly controlled during this type of operation. Because of the likelihood of handling leaking containers, operators in this area need to wear RPE for complete protection. With high potential for exposure when handling leaking product containers, central rework or scrapping stations should be isolated from other operations.

Granulating product that is reclaimed for blending back into the manufacturing process has a higher risk of containing damaged enzyme encapsulates. Reduction of enzyme exposures comes from minimizing enzyme encapsulate break-up in the reclaim processes, controlling the addition rate of reblend product to levels proven to keep operating area dust levels within limits, and providing enclosed and ventilated process and packing equipment.

Dry reclaim of granulate product is preferred to avoid the additional expense of remanufacturing the product via a wet route. Typically, most of the packed product is returned to the process from package scrapping operations or from exhaust ventilation filter fines, with control of the dosing rate to meet product quality targets. Most of this section describes the steps to be taken in packing reclaim operations.

Wet granulated product recycle is necessary when the ingredients are good but remanufacturing of the product is required to meet quality targets. This recycle step avoids the need for waste disposal to the environment. To prevent enzyme exposures in that part of the process from the drying tower to finished product mixing (see 5.7), belt conveyors and other equipment that transport the base granule, which could contain enzymes from recycled powder, need to be enclosed and ventilated as described in 5.5.

Liquid product reclaim also needs to be enclosed either via a dedicated pump and piping system or via containers that are filled and emptied with attention to avoiding vented enzyme aerosols and avoiding spills.

5.12.1. Manual Reclaim of Powders

The whole reclaim process should be carried out within the containment of a booth controlled by effective ventilation. This includes operations to open packs or cartons, to tip out product, to collect reclaimed product, and to dispose of contaminated packaging.

Disposal of packaging is often neglected and in many instances empty packs, contaminated with powder and/or dust, are removed from the booth prior to compaction and collation. This results in exposure of the operator to airborne dust, personal contamination [clothing, shoes, etc.] and powder spillage.

The booth design should facilitate the safe collation and disposal of packaging. Nothing should be drawn back through the controlled working opening [Figure 10].

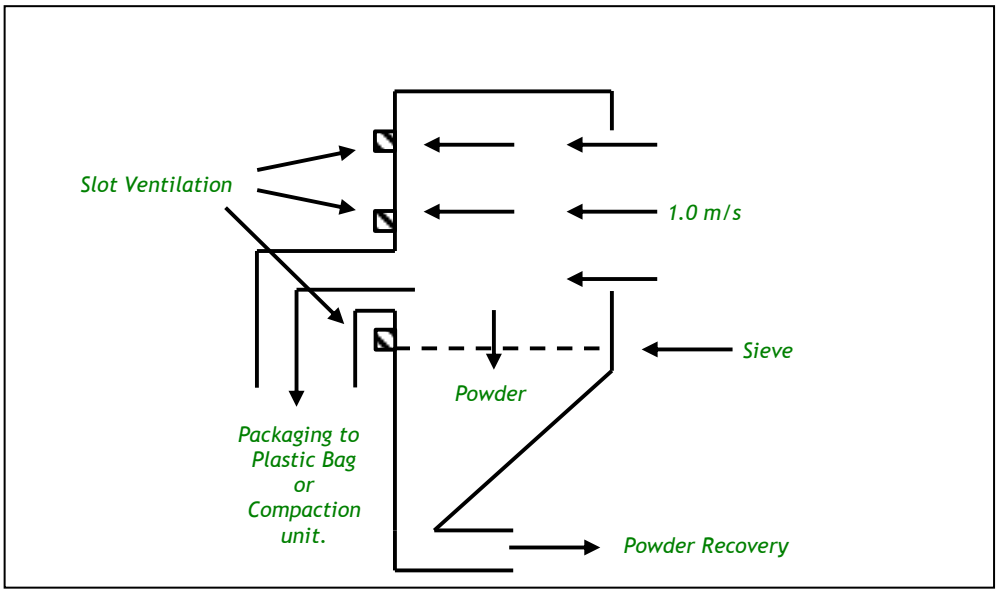


Figure 10. Schematic design of a reclaim booth.

Powder from this booth may be collected in a fixed hopper from which it is directly reintroduced into the process, or it may be conveyed to a hopper or directly back to the process by an enclosed conveyor or dense phase vacuum transfer [see 5.7.2].

Big-bags are often used for the accumulation of reclaimed powder, and its eventual re-introduction into the process. The re-use of Big-bags in this way has to be carefully managed as the process can lead to significant exposure if the bags become externally contaminated, worn and/or damaged, or they are deflated and folded in an uncontrolled manner.

A better option is to convey reclaimed powder directly to storage, and / or into the process, without any additional handling such as may be required when using tote bins or big bags.

Operators undertaking manual reclaim of powders should always use suitable respiratory protection as secondary protection. Whilst full control of the actual reclaim process is possible, there is always a risk of exposure from handling packs outside of the reclaim booth that may be faulty, damaged, partially open, or externally contaminated. The use of respiratory protection is thus essential for this type of task and is discussed in detail in 5.15.

5.12.2 Rework of Tablets

To rework rejected tablets back into the product it is necessary to break the structure of the tablet down to an extent where the resulting powder is a suitable consistency to be returned into the manufacturing process for re-tabletting. We have already discussed in some detail the importance of maintaining the integrity of the encapsulated enzymes during handling of enzymes and the manufacture of the product, and this type of process is no different. It is essential that the equipment used to break down reject tablets minimizes the amount of encapsulate damage and enzyme release.

Important factors to consider for a tablet rework system are:

- The application of sufficient force to just break down the tablet with minimal damage to the encapsulates
- All moving equipment clearances in the product stream should be greater than the diameter of the enzyme granulate to minimize shear damage
- Having a fully enclosed and ventilated design
- Controlling the addition rate of reworked product so that slightly higher enzyme dustiness does not cause dust problems in the tablet press and tablet handling system

The analytical methods described in Chapter 10 can be used to assess the extent of encapsulate damage due to the process and guide process improvements to minimize release of enzyme dust.

As there is the potential for the powder to contain some damaged encapsulate, or at least more damage than in normal finished powder, the handling, transfer and dosing of the reclaimed powder should be carried out by fully contained processes, and preferably automated to remove any manual interface.

5.12.3 Manual Reclaim of Liquids

Essentially the same basic exposure control requirements as used for powders are necessary for the manual tipping and reclaim of enzyme liquids. However, the risk from handling full bottles, cartons and empty liquids packaging is somewhat lower than for powders, although dried out residues from spillages or overfilled containers may present a risk from dust inhalation.

Bottles or cartons should only be opened and poured out within an enclosed and ventilated reclaim booth. For heavy-duty liquids that are slow to pour, the packs may be mounted upside-down in a frame, or on spikes, and left to drain fully. Liquids are best drained into a hopper, and then pumped directly back into the process or into a storage vessel (see 5.7.1) taking care that any microbiological (spoilage) risks are addressed.

5.12.4 Automated Reclaim Systems

There are a variety of automated systems for product reclaim, but these are not very common. The basic action destroys the packaging and separates it from the powder, or the liquid. The motion is normally quite violent, thus high specification containment and ventilation control is required. Inward air velocity at any minor gaps or at any openings in the enclosure [i.e. inlet, outlets, etc.] should meet the recommendation already discussed for plant and equipment ($\geq$ 1.0 m/s).

For powders and tablets, the machinery should not damage the enzyme encapsulates present in the powder. This can usually be ensured by minimizing any potential for crushing of encapsulates between surfaces, or shearing between moving parts.

Collection and conveying of the reclaimed product and packaging should be under contained and controlled conditions to prevent the release of dust and or aerosol. The re-use of Big-bags to store reclaimed powder is not recommended.

5.12.5. Disposal of Waste Packaging from Reclaim Operations

Waste packaging will contain some traces of enzyme powders, or enzyme liquids. Therefore packaging should be handled carefully to avoid exposure to dust or aerosol. The best practice option is to collect together packaging for disposal as soon as the carton, or bottle, is emptied as part of the reclaim operation, thus avoiding any secondary handling of packaging.

For powders, empty cartons should be placed into a large polythene sack that can be tied up when full. Alternatively they can be placed into a ventilated compaction unit which then "extrudes" the compacted packs into a closed polythene liner. Containment and control of automated compaction units should follow the same basic principles as the process plant.

For liquids, "empty" bottles pose little exposure risk unless they contain sufficient traces of the product to generate spillage, or they are compacted or shredded in which case the forces involved are normally sufficient to generate aerosols. Any such the facility should be contained and controlled as is the process for plant and equipment. Care should be taken to avoid the spillage of liquid from "empty" bottles by ensuring that they are suitably drained.

Third-party waste recycling companies should be informed of the hazards and risks associated with the handling and processing of packaging that is potentially contaminated with an enzyme product.

5.13. Filtration of Extract Air From Ventilation Control Systems

The treatment of extraction air contaminated with enzyme dust and/or aerosol will depend upon the type of plant and/or equipment that is under control, the degree of contamination, and the location into which the extract air is discharged. Most countries already have legislation concerning the concentration of particulates that can be discharged to the external atmosphere. Legislative requirements regarding venting of exhaust air should always be adhered to first, followed by the guidance in this document.

5.13.1. Enzyme Handling Plant and Equipment

Most local exhaust ventilation systems are directly exhausted outside in accordance with local environment emission regulations and in a location which prevents intake back into the building. However, if the local exhaust ventilation discharge is purposely recirculated back into the workplace, then extra filtration is needed to prevent the discharge of enzyme dust and/or aerosol back into the working environment. In this case the minimum standard of filtration is considered to be HEPA filtration, to at least EU13.

HEPA filters are normally preceded by one or two pre filters to remove the bigger particle sizes, preventing the HEPA filter from blocking up, and thus prolonging the HEPA filter's operating life. This is typical of the filtration necessary for a laminar downflow booth which re-circulates air to the working environment (Appendix 1).

Depending on the expected dust loading, the equipment suppliers can recommend suitable pre-filters, but a typical three-stage system would be comprised of the elements in the following table:

Filter	Eurovent Specification	Typical Efficiency
Pre Filter	EU4	90%
Fine Dust	EU8	90%
HEPA	EU13	99.995%

5.13.2. Finished Powder Handling - Plant and Equipment

The minimum standard of filtration required is to EU8 (see above) and after filtration extract air should be discharged externally to the building. This standard of filtration is typically provided by bag, sock, or cartridge type filtration systems. Finished powder handling normally generates a significant dust load for the associated filtration systems, therefore some form of automated filter cleaning systems are required. Reverse jet cleaning is the most efficient self-cleaning system and is recommended. Mechanical cleaning systems that shake the internal filters are generally far less efficient.

5.13.3. Re-Circulated Air Systems

It is not recommended that air from enzyme controlled systems is re-circulated to the working environment.
Air that is to be returned to the working environment for example from a down flow booth must be filtered to HEPA standard, to at least EU13 and must be appropriately validated. In North America, there is a specific consensus standard called ANSI/AIHA Z9,.7-2007 (Recirculation of Air from Industrial Process Exhaust Systems). This consensus standard provides design and operational requirements for the recirculation of exhausted air from systems which require special precautions like enzymes.

Filtration systems used for this purpose should be monitored for performance via the use of static pressure gauges, which will alarm in the event of a filter failure. Best practice is to link this alarm into the plant control systems to activate an automated shutdown procedure. Taking regular readings from such gauges can be part of the plant monitoring systems, and can prevent automated shut-downs by use of timely maintenance procedures.

Relatively inexpensive dust penetration detection instruments are also available to quantify the amount of dust that passes a filter. However these are not appropriate for liquid aerosols.

5.14. Dealing With Spillages, and Cleaning of Plant and Equipment

The use of improper or improvised clean-up methods can result in generation of airborne enzymes. This can result in the exposure of operators in the immediate area of any cleaning operation and in adjacent areas via general ventilation. Clean-up operations are a significant source of peak enzyme exposures, which need to be managed by a combination of equipment and proper procedure.

Cleaning up spilled enzyme encapsulates, liquids, and enzyme products should be done with the use of a vacuum cleaning system fitted with HEPA filtration. The air inflow at the vacuum tool provides some containment of dusts or aerosols at the pickup point. Normal industrial vacuum cleaning systems without HEPA filtration should not be used, as the filtration systems will not adequately remove enzyme dust and/or aerosol before it is returned to the working environment.

Brushes, brooms, compressed air, and high pressure water **should never** be used for cleaning spillages, as these will either generate significant airborne dust and / or aerosol, or leave behind a wet residue, which can dry out to form a fine dust. Vacuuming followed by wet mopping is preferred. Smaller spillages may be washed to drain by a soft / low pressure water hose.

Depending on the size of a liquid spillage the use of a sorbent material can be considered. The contaminated sorbent must be shovelled up and placed into a sealed plastic bag / plastic container and disposed of by incineration, or through the wastewater treatment plant [however this will require additional handling controls and disposal of the contaminated packaging]

Respiratory protection should be used for all cleaning / spillage operations because the risk of exposure is always high (see 5.15).

Vaccum cleaners are the preferred tool for cleaning of spillages, plant and equipment. Portable or central vaccum cleaning systems can be used. There are advantages and disadvantages to both systems, as follows:

The table that follows describes the options for vacuum cleaning equipment.

Description	Advantages	Disadvantages
Central Vacuum Cleaning (CVC) systems • Multiple simultaneous users possible • 7.5 metre hoses + tools • Metal tubing network with multiple branches, each with multiple hose connections, to serve defined use zones over a large process area • High vacuum exhauster and filter / receiver to collect waste and fill dust controlled container • Dry cleanup only	• Convenient plug in valves around area at known spill locations • High reliability, with system maintenance, to encourage operators to clean up spills promptly • Minimum equipment (hose/tool) to transport to cleanup site • Emptying waste container can be centrally controlled • Lowest frequency and magnitude of exposures from emptying collected waste at a central, off-line location • Single system to manage versus multiple units	• CVC malfunction affects entire system • Highest initial capital investment • Operators must be trained to purge pipework for long enough to get the waste all the way to the filter/receiver to minimize tubing pluggage • Ownership by department or group, not by an individual user • High energy consumption since it runs continuously when process is running • Low efficiency with high / excessive number of users • Long hoses difficult to handle, easy to damage
Portable Vacuum Cleaner (PVC) • One user per PVC	• Simple to operate • Low capital investment per unit • Malfunction affects only	• Multiple units required to cover entire process area • Although manoeuvrable, ergonomically heavy unit

• May increase capacity by use of a 200 L metal interceptor drum [on wheels] with attached hose & tools • Exhaust blower with HEPA rated filter • Versions available that are suitable for Liquids handling	one unit • Mobile, can relocate to other process areas • Can assign clear ownership to an individual / location • Energy efficient – on only when needed • Shorter hoses are lightweight • Shorter hoses are less likely to be damaged	(hose, tank, exhauster) to transport to cleanup site if required to be lifted) • Emptying 200 L drum risks major dust exposure and ergonomic effort to operator • Location for emptying must be managed or risk major dust exposures to adjacent people – takes time to roll PVC to off-line area which inhibits timely emptying for next user • Significant maintenance effort is required for PVCs; not designed for continuous service like CVC
Mini CVCs (combination of PVC and CVC concepts) • 2 to 4 simultaneous users per system • Limited tubing network with hose inlets for small area within larger process area • Medium vacuum exhauster and filter / receiver to collect waste and fill removable container • Dry cleanup only	• Low ergonomic effort with minimum equipment (hose/tool) transport to cleanup site • Emptying waste container can be in off-line area • Medium frequency and magnitude of exposures from emptying collected waste at an off-line location • Malfunction only affects part of operating area • Clear ownership can be assigned	• Medium capital investment - several units can serve process/packing areas • Maintenance effort for multiple equipment systems required • Manual emptying of dust from unit has higher risk of dust exposure and ergonomic effort than CVC but less than PVC • Medium energy consumption with lower vacuum requirement than CVC – runs when process area is running

Cleaning of Size Change Parts

It is recommended that there is an isolated and ventilated area specifically for the purpose of cleaning size change parts (i.e. machine parts removed for product changeover). Change parts should be transported to the cleaning bay/area in a rigid solid sided container to minimize spills. The area should fulfil requirements similar to an isolated discharge area (see 5.6.1) in that it should be under negative pressure with respect to the remainder of the plant. An example where containment is by the use of an isolated room is shown in Appendix 2.

For cleaning parts vacuuming followed by low pressure warm water is the recommended method. Vacuum cleaners must meet the specifications detailed above. Wash water should drain into a closed system, and be dealt with along with the other factory effluent in the treatment plant.

As this is an operation with a high potential for exposure to dust and / or aerosol therefore respiratory protection must be worn as a safeguard (see 5.15).

5.15. Respiratory Protective Equipment (RPE)

5.15.1. Use of Respiratory Protective Equipment (RPE)

In **normal** situations, the use of RPE should always be considered as **secondary** protection where a risk assessment has shown that there is a potential for exposure despite the presence of engineering controls, e.g.

- "On-line" maintenance
- Access into filling machine enclosures
- Product reclaim
- Dealing with small spillages
- Cleaning
- Quality Sampling

RPE should also be used where, due to a failure of a critical engineering control, there is a very significant risk of a peak exposure, e.g. during discharge of enzymes.

In **abnormal** situations RPE may be required as **primary** protection. In this instance the standard of RPE should be identified by a risk assessment for the task, including the likely level of exposure. Abnormal situations include:

- Major spillage of enzyme raw material
- Dealing with, and repair of, damaged enzyme supply units
- Major spillage of enzyme product
- Gross failure of containment or control
- Maintenance or repair of contaminated plant and equipment
- Decontamination of plant and equipment

5.15.2. Standards Of Respiratory Protection

The selection of suitable RPE will depend upon the task, the potential level of exposure, and whether the RPE is required for primary or secondary protection. The time for which RPE needs to be worn should also be taken into consideration as should comfort, fit, and compatibility with other PPE, to ensure that there are no issues that could result in incorrect use, or misuse.

The following are examples of the type of RPE available that is often used [or available] in detergent manufacturing plants, to cover a range of contingencies.

- Disposable orinasal masks (which must be well-fitted)
- Re-usable orinasal masks and cartridge filters
- Full face masks and cartridge filters
- Full face positive pressure masks
- Positive pressure blouses / hoods

The efficiency that is required to provide the necessary protection should be determined by undertaking a risk assessment for the particular task. The recommended minimum standard of respiratory protection is provided below.

For any task where RPE is used as protection against enzymes, or enzyme products under **normal** operating conditions, the minimum standard that should be used is P2 for airborne dust only, and P2SL for airborne aerosol, but this should be confirmed via risk assessment.

This standard is also sufficient for most tasks carried out where a low-level but infrequent exposure may occur, or where the RPE is required only as secondary protection.

For primary protection under **abnormal** conditions a higher grade of RPE will be required. The minimum standard in this instance should be P3 for airborne dust only, and P3SL for airborne aerosol. Again this should be confirmed by risk assessment. If it is identified that greater protection is required, or because of the duration of the task comfort may be an issue, then positive pressure respiratory protection should be used. In the event that personal decontamination is necessary, respiratory protection may need to be waterproof to enable the operator to shower whilst still wearing it.

All employees required to use respiratory protective equipment must be adequately trained in its selection, use and maintenance. The site doctor should assess them as medically fit to wear and use respiratory protection.

In the event that normal orinasal face masks cannot be used because the employee has significant facial hair, e.g. a beard, large moustache, etc, and a good face seal cannot be achieved against the skin, then positive pressure respiratory protection should be used. RPE should be compatible with any other protective equipment provided, such as safety glasses, safety goggles, hearing protection, etc.

5.16. Personal Protective Equipment (PPE)

Enzymes are not skin sensitisers, but some are skin irritants. Detergent products are usually high pH and are also irritants, or may also contain other irritant materials. Therefore skin and eye contact with enzymes, or enzyme products, should be avoided with the use of suitable personal protective equipment.

5.16.1. Protective Clothing

Under **normal** operating conditions all employees, contractors and visitors should use the relevant personal protective equipment and work clothing appropriate for the areas they visit or for the tasks they undertake. Often this will be mandated by site policy.

For handling liquid products the contact surfaces of gloves should be impermeable, but for powders cotton gloves should suffice.

Safety shoes, whilst not related to enzyme safety, should also be used by all persons on site as is appropriate; wellingtons [with safety caps] may be required for major wet cleaning operations.

Decontamination facilities [showers] and a change of protective clothing / work clothing should be available for employees in the event that personal contamination occurs.

Under **emergency** conditions the personal protective equipment should be identified from a risk assessment for each task.

Normal work clothing should be changed / laundered as per site policy, and contaminated work clothing should be changed as soon as is possible depending upon the degree of contamination, and in accordance with the following guidance for personal decontamination. Also contaminated work clothing must not be worn in areas such as in offices, meeting rooms, control rooms, canteen, etc as this presents a risk of exposure

outside of the manufacturing / process area. For maintenance or high risk tasks, where personal contamination is likely, a disposable work wear is an option.

5.16.2. Personal Decontamination

Ideally, the plant lay-out should allow the most convenient and shortest distance from potential exposure areas to personal decontamination facilities. Showers should be available for personal decontamination at the end of shift, after undertaking abnormal tasks, or in the event of an emergency.

Documented procedures should be available for undertaking personal decontamination after undertaking abnormal tasks where the potential for personal contamination is high.

Following high risk tasks, contaminated clothing should be removed whilst still wearing respiratory protection. Clothing should be placed into a plastic bag for disposal or laundering. Special water soluble bags for contaminated clothes are available. It may also be necessary for an operator to shower whilst initially wearing respiratory protection to avoid exposure to airborne enzyme dust and/or aerosol. Therefore the respiratory protection may need to be splash proof / waterproof.

Following decontamination clean work clothing should be available for use.

Chapter 5 - Appendix 1: The Downflow Booth

The downflow booth is designed to provide the best practicable operating environment for handling hazardous materials, affording maximum protection to operators. The booths can be designed in a variety of sizes and shapes depending on the nature of the operation.

Low turbulence (laminar) displacement air is supplied vertically from the ceiling plenum. This sweeps down over the operational area ensuring maximum dilution and removal of airborne dust and/or aerosol. To ensure operator safety an average vertical air velocity of 0.45m/s is required. It also ensures that no dust or aerosol can enter the operator's breathing zone, as long as the operators' head is above the source of contamination.

The booth is maintained under slightly negative pressure to the surrounding area ensuring full containment of materials. The negative pressure creates a 10% influx of air into the booth at floor level to "sweep" air contaminated with dust and/or aerosol into the filtration system. Turbulence from draughts across the open face of the booth is minimised by extending the side panels beyond the safe working limit of the unit. This limit is clearly marked on the inside of the walls.

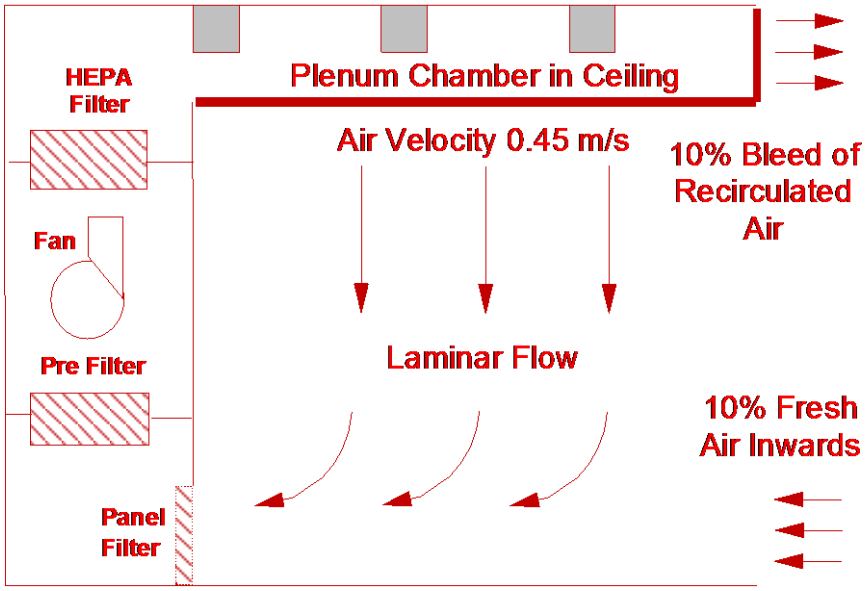


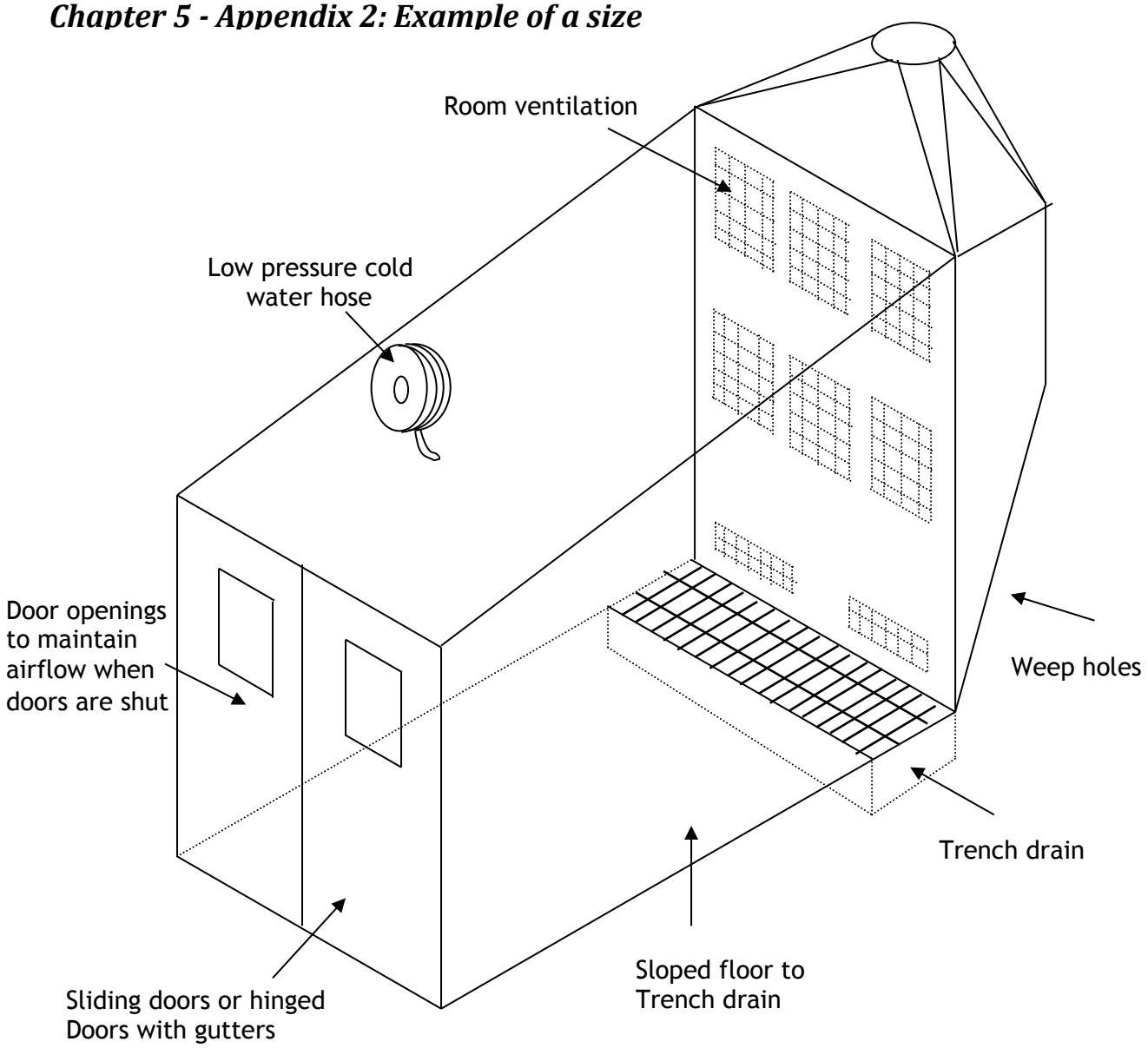
Figure 11. The Laminar Downflow Booth

Extracted air is treated via a three-stage filtration system before being recycled to the working environment:

Stage One	: Panel Filter Class EU 4	(replace approx. every 8 weeks)
Stage Two	: Pre-filter Class EU 8	(replace approx. 1 per year)
Stage Three	: HEPA Filter Class EU 13	(replace approx. every 3 years)

Each filtration system is monitored via a static pressure gauge, e.g. a Magnahelic or Photohelic gauge.

Chapter 5 - Appendix 2: Example of a size



Parts Cleaning

The parts cleaning station is an enclosed area where change parts and other equipment are cleaned.
It is an isolated room with sufficient exhaust ventilation to maintain a recommended 1m/s face velocity across the door as shown. PPE in accordance with your plant matrix should be worn when inside the room to protect against product splashing back from the wash down.

Cool low pressure water is used for cleaning whenever possible. The use of hot or high pressure water should be minimized because they produce high levels of aerosol. Water from parts cleaning runs down the sloped floor of the room and drains to the plant effluent system.

Chapter 5 – Appendix 3: Maintenance and testing of equipment utilising HEPA filters

Any equipment used for transferring, or cleaning up, of enzymatic powder should be fitted with a HEPA filter on the final discharge which is rated as filter class H13 [(1)]. It is essential that such equipment functions according to the required specification. HEPA filters can be purchased "off-shelf" from a number of suppliers with a challenge test certificate indicating compliance to a specific filter class. However, damage may occur during storage or transit so they should be inspected before being fitted by the machine supplier or trained company personnel. If there are doubts over the integrity of the filter it can be challenged in situ by use of a liquid particle test aerosol such as Dispersed Oil Particulate (DOP) paraffin oil or DEHS (Diethyl-hexyl sebacate) or equivalent aerosol [(2)] prior to being used in the workplace.

Criteria for suitable aerosol substances and the equipment and methodology for challenge testing of HEPA filters is set out in the British and European Standards BS EN 1822-1:1998 [(1)]) and BS EN 1822-2:1998 [(2)].

Additional test criteria for HEPA filters are covered in BS EN 1822-3:1998 to 1822-4:2000 and 1822-5:2000 [(3-5)].

Equipment containing a HEPA filter should be place on a scheduled maintenance program. The interval for maintenance should be determined by robustness of equipment, usage of equipment etc. Equipment should be checked for physical damage (e.g. seals intact, no cracks in internal housing, no loose screws etc) and, if deemed necessary, the filter performance tested in situ.

References

[(1)]BS EN 1822-1:1998 – High Efficiency Air filters (HEPA and ULPA) – Part 1: Classification, performance testing, marking

[(2)]BS EN 1822-2:1998 –High Efficiency Air Filters (HEPA and ULPA) – Part 2: Aerosol production measuring equipment, particle counting statistics

[(3)]BS EN 1822-3:1998 – High Efficiency Air Filter (HEPA and ULPA) – Part 3: Testing flat sheet filter media

[(4)]BS EN 1822-4:2000 – High Efficiency Air Filters (HEPA and ULPA) – Part 4: Determining leakage of filter element (scan method)

[(5)]BS EN 1822-5:2000 – High Efficiency Particulate Air Filters (HEPA and ULPA) – Part 5: Determining the efficiency of filter element

Chapter 6 - Performance assessment of equipment and behaviour

Operator exposure to total dust and enzyme dust and aerosols in both granule and liquid operations can be correlated with poor plant performance, poor plant hygiene and lack of adherence to operating procedures. A monitoring programme is needed to check that control systems are effective for current formulations, or to assess whether control systems need to be improved ahead of formulation upgrades.

Sensitisation is believed to be primarily due to short duration peak exposures as well as on-going lower/background exposures. Up until now the Industry has relied heavily on air sampling to detect exposure sources. Additional semi-quantitative tools have been developed to supplement air sampling for the detection and ranking of sources of exposure due to dust release and/or product spillage arising from equipment defects and/or unsafe behaviour (1).

The following tools are described in this chapter:

6.1 Semi quantitative assessment of containment
6.2 Assessment of equipment performance and maintenance
6.3 Detecting and ranking peak exposure sources
6.4 Behaviour Observation System

A successful program requires properly trained individuals for conducting the assessments and doing the appropriate follow-up.

6.1. Semi quantitative assessment of containment

Visual assessment is an effective and simple tool to help detergent manufacturing sites identify areas where containment has been lost and there is a need to take immediate corrective action.

This assessment focuses on the first two of the four Hygiene Operational Guidelines:

1. Containment at source of any dust or liquid aerosol formation
2. Avoidance of recurring routine or uncontrolled spillages
3. Avoidance of personal contamination
4. Handling of empty containers with appropriate controls

Guidelines 3 and 4 will not be covered in this section, as they will be effectively managed through safe practices, personal protective equipment and the Behaviour Observation System.

6.1.1. Approach

Look for locations where enzyme dust or spillage is visible or where regular skin contact occurs. This provides real-time feedback for taking immediate corrective action to clean up the spill and to establish long-term fixes of defective equipment in order to prevent spill recurrence.

6.1.2. Survey process/frequency

Each operating department with enzyme containing material should have a survey process to gather and document performance data. ***Appendix 1*** provides a flowchart as an example on how to gather performance data although the detail will be site specific.

All employees should participate in completing surveys and reporting results, and scoring should be consistent across the site. Initially, surveys should be completed in each operating department according to an agreed schedule and should be completed randomly through the shift versus always at the same time. Surveys should also be completed following maintenance activities but **prior** to start-up to ensure that no enzyme spillages have occurred during or remain after the maintenance procedure.

In general, frequency should be set based on compliance. Sites and departments with strong continued performance (based on compliance level) with less than 1.0% of employees being sensitised in the last 12 months can reduce survey frequency (e.g. daily or weekly). Frequency should increase if compliance deteriorates.

Appendix 2 Gives an example of a ranking system for an assessment of containment to be used during the semi quantitative assessment tours.

6.1.3. Compliance target setting and reporting

A compliance target can be set for the assessment of containment (e.g. 90% of the assessed locations show no visible dust/liquid or recurring spillages outside the containment areas). The trend in compliance percentage can be used to indicate if there are recurring issues with equipment defects and/or behaviours. All results, including trend analysis, should be reported periodically and shared with all employees at safety meetings.

6.1.4. Corrective actions and follow-up

Remedial steps should be taken immediately to clean visible dust/liquid outside the containment areas and fix equipment defects. The recurring spillages should be eliminated with a clear action plan.

6.2. Assessment of equipment performance and maintenance

Without routine maintenance, the performance of equipment such as local exhaust ventilation systems may degrade over time. Spills of enzyme containing products may occur due to equipment leakage, operating procedure or process malfunction. The causes of recurring spillage need to be identified and corrected to minimize enzyme exposures.

6.2.1. System monitoring and maintenance

An effective system Monitoring and Maintenance program ensures that the appropriate plans are developed and implemented to keep Local Exhaust Ventilation systems operating within ±

10% airflow and ± 20% static pressure of baseline design conditions. This will reduce the amount of time spent cleaning the build-up that occurs in the ductwork, thus reducing exposure time.

Topics that should be included in a system Monitoring and Maintenance plan include:

- Daily visual checks of the system
- Scheduled airflow and static pressure measurements to ensure operation within baseline conditions, which are documented at system start-up
- Scheduled duct and equipment inspections and cleaning
- Scheduled mechanical lubrication and maintenance for the fan, filter, and airlocks
- Record keeping requirements

Employees required carrying out system monitoring and maintenance must be trained and competent.

6.2.2. Organizational and procedural principles

Key organizational and procedural principles include:

- Clear accountability in the plant organization for the maintenance and performance of engineering controls
- Clear site change management procedures to ensure that systems are tested at start up after changes to prove that the control specifications have been met and documented and that there is proof of performance of changes

For further details on the organizational and procedural principles, refer to Chapter 4, Management and Supervision.

6.3. Detecting and ranking peak exposure sources

This section describes a system, and the equipment necessary, to identify sources of peak exposure and recommends a tool for prioritising those sources for elimination. Peak exposures may occur from a specific task (e.g. cleaning a spill, clearing of jams) or due to intermittent or continuous emissions from the plant or process. Both tasks and equipment sources should be considered.

6.3.1. Approach

The three primary factors to consider in the decision to conduct the survey are:

- Changes in process, equipment and/or formulation
- Deterioration of compliance with Hygiene Operational Guidelines
- Increasing levels seen in the routine air sampling results

The following are criteria to help to pick priority areas and work tasks accordingly:

1. Risk assessment
2. Semi-quantitative assessment of containment
3. Air Sampling Data
4. Incident investigation reports (***Chapter* 9** provides an example on how to conduct and report an incident investigation)
5. Health surveillance data
6. Employee feedback

6.3.2. Guide for peak exposure location and sampling

It is not necessary to take air samples for every source. If there is visible dust or liquid aerosol, either visible to the naked eye or via backlighting, one can assume that there is an exposure above the OEG and take immediate corrective action.

The potential sources for peak exposure to dust can be located based on:

- **What is visible to the naked eye**
- **Backlighting by a high intensity light source**. For this, the key specifications to have are power of 250W and beam diameter less than 100mm (i.e. Torch / flash light, key specification is a light with a xenon bulb with polished reflector)
- **Direct reading monitors using an area** (Sam 2500) **or a portable sampler** (Malvern Portable Airborne Particle Counter Model HHC 3012, 5012 or equivalent). Although both samplers only measure total dust, it is generally recognized that an out of OEG limit for total dust will also potentially present an out of OEG limit for enzyme dust. The Sam 2500 has visual warning lights to warn of an out of limit and the results can be downloaded onto a graph to give the time, and size of the peak

Direct reading light scattering instruments will give an indication of liquid aerosol but are not sufficiently accurate to provide precise exposure measurements.
As control improves, or even before, it is recommended to supplement these techniques with focused air sampling (see section 7.2.2) to ensure that corrective actions have been effective.

Ideally, the sampler should be placed within 1 metre from the potential peak exposure source and at a height level within the breathing zone. The sampling duration should be at least 15 minutes or for the duration of the potential peak exposure task. For this, the analytical method may need to be adjusted to higher sensitivity, as the amount of enzymes collected on the filter may be significantly lower (see chapter 10, Analytical Procedures).

Each source should be measured at least 6 times to determine an average value and range of exposure.

6.3.3. Ranking peak exposure sources

It is often useful to rank peak exposure sources in terms of risk. The ranking should take account of exposure level, frequency of exposure, number of people exposed, the ability to anticipate the exposure and PPE practices. ***Appendix 3*** gives an example on how to rank peak exposure sources using a criticality index.

Unless there is good reason to do otherwise, arbitrarily decide to tackle the highest ranking items. An example of a good reason to do otherwise would be if a lower item had a known and significant history of causing sensitisation.

6.3.4. Corrective actions and follow-up

The high-risk sources should be eliminated with a clear action plan. In the meantime, remedial steps should be taken immediately to reduce peak exposure. Operators should be informed immediately and the appropriate actions should be taken (e.g. assess the need for PPE, conduct an investigation, etc.). The effectiveness of the peak exposure reduction/elimination plan needs to be verified by using the same techniques outlined

above in section 6.3.2. The peak exposure survey can be updated periodically as needed, following the approach outlined in 6.3.1.

6.3.5. Feedback to employees

All employees should be informed of the high risk and priority sources of exposures targeted for elimination. They should also be informed of the progress as part of regular safety meetings.

6.4. Behaviour observation system (BOS)

The intent of observing behaviours is to ensure that unsafe behaviour leading to exposure in the workplace is confronted and corrected and the safe behaviour is reinforced. This provides a simple and yet a powerful tool to eliminate unsafe behaviour "before the fact". Many exposures related incidents are the result of unsafe behaviour. Below is an example of one approach used on how to set-up, carryout and follow-up a successful Behavioural Observation System. ***Appendix 4*** provides an example for the Overall Behaviour Observation cycle.

6.4.1. Elements of a behavioural observation system (bos)

- Selection of critical behaviours
- Organizational involvement
- Trained observers
- Data evaluation and feedback
- Program goal and change procedure
- Guidelines for observations and confrontations

6.4.2. Selection of critical behaviours

Identify those behaviours that have a high potential for exposure to enzymes. Useful sources of information are:-

1. Safe working practices
2. Talk with personnel about hazardous jobs or tasks
3. Air sampling data
4. Semi-quantitative assessment of containment data
5. Health surveillance data

6.4.3. Survey scheduling and organization involvement

Surveys should be completed in each operating department according to an agreed schedule and should be completed randomly across all shifts.
All levels of the organization should participate in BOS.

Below is an example of frequencies used.

- Plant manager — Once per month
- Operations manager — Once per week
- Shift Manager, Operators — As often as necessary for 1 BOS per shift

6.4.4. Observer's task

All observers must be trained and competent to undertake behavioural observation. The observer should:

- Plan the tour
- Stop for 10-30 seconds at each location
- Observe and confront
- Correct non-compliant behaviour
- Follow up on items noted that are not related to behaviours (e.g. eye wash fountain malfunction)

Guidelines for persons carrying out observations and confrontations are:

- Address the unsafe behaviour and not the person. Be fair and consistent!
- Determine why the error was made; there may be a valid reason. Listen!
- Never confront in front of others
- Never accuse the person of making the mistake on purpose
- Talk as grown-ups
- Never refer to previous mistakes
- Show how to do the job safely
- Show you care about the person's health and safety and the advantage to the Business
- Do not accuse the person. Describe and do not evaluate the unsafe behaviour

6.4.5. Data evaluation and feedback

- Results are analysed for each behaviour in the following way:

  Number of safe observations
  ---------- X 100 = % Safe
  Total number of observations

- Results are analysed for the whole survey in the following way:

  Total number of all compliant observations
  ---------- X 100 = % Safe
  Total number of all observations

- Line charts are used to track more effectively the evolution of each behaviour as well as overall performance of BOS

- Teams get feedback on the results at least once every month

- Behaviours should be analysed by department, work area or shift to address problem areas

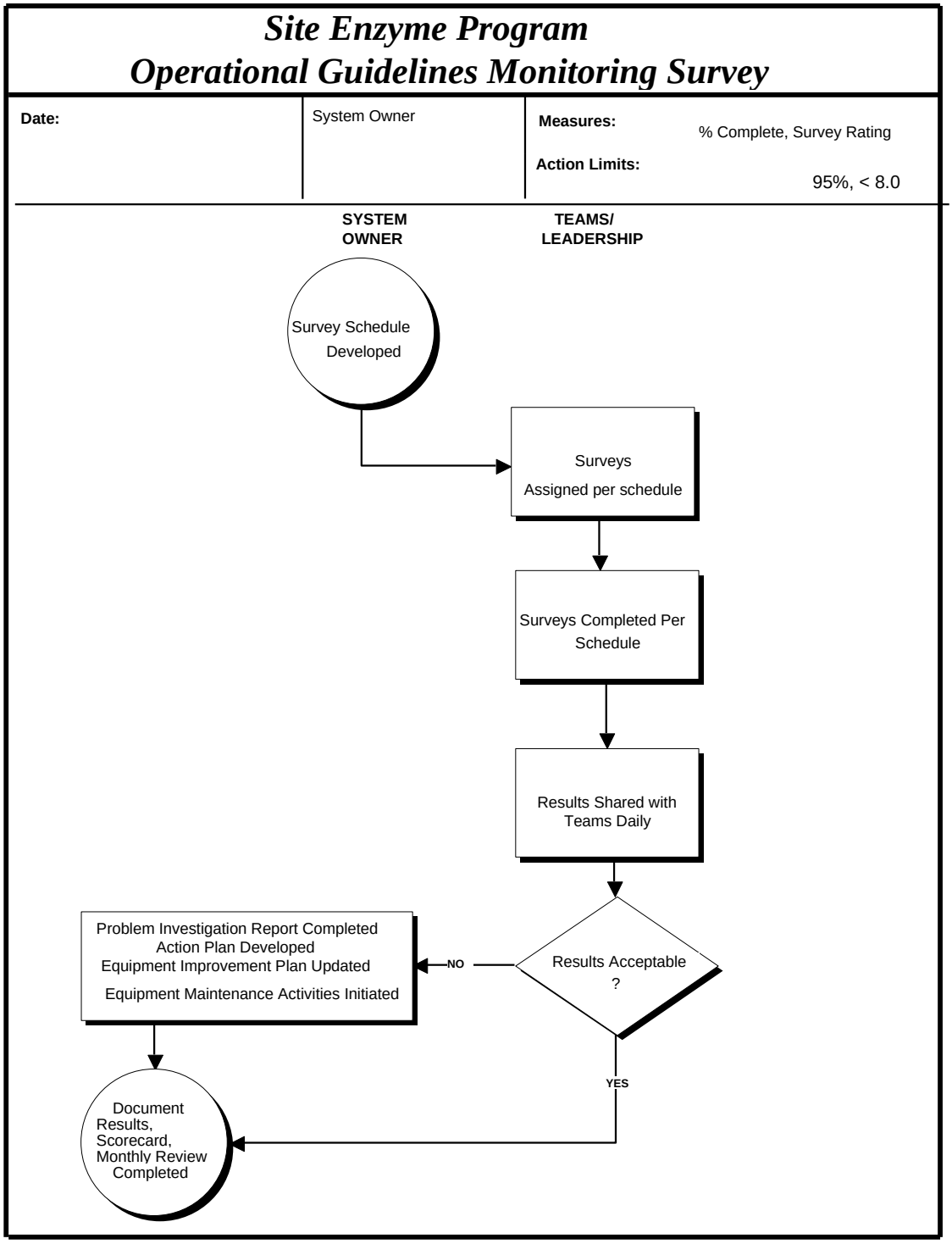
6.4.6. Goal-setting

Goals are stated for each individual behaviour in the checklist such as:

- 100 observations with safe behaviours above 95%
- Three consecutive months with safe behaviour above 95%
- When safe behaviour goals are achieved the checklist is changed and other critical behaviours are included. A short checklist (e.g. 4-10 behaviours) makes the system easier to administer and sustainable as the observations last only 15-20 min
- Listed behaviours must be clear and specific so that everybody observing the same situation would come to the same conclusion
- Outcomes can be included if they are the immediate results of unsafe behaviours. The disadvantage is that only group feedback is possible
- BOS should be open to address unsafe behaviours not included in the checklist

An example of a BOS survey sheet is provided in **A*ppendix 5***.

Chapter 6 - Appendix 1: Site Enzyme Program Operational Guidelines Monitoring Survey



Chapter 6 - Appendix 2: Example of a ranking system for a semi-quantitative assessment of containment

CATEGORY	DEPARTMENT	RATING LEVEL DESCRIPTIONS					
		9-10	8	7	6	5	0-4
Containment at source of any dust or liquid aerosol formation **&** Avoidance of recurring routine or uncontrolled spillages	Packing Lines	**No visible dust** present outside of dust control containment or enclosed spillage contain- ment.	2-3 teaspoons per packing line area of total spillage out- side catch trays or on exposed conveyor/equip- ment surfaces. Unenclosed catch trays/line contain <1 cup total spillage.	>2-3 teaspoons per packing line area of total spillage outside catch trays or on exposed conveyor/equip- ment surfaces. Unenclosed catch trays/line area contain about 1 cup total spillage.	>2-3 teaspoons per packing line area of total spillage out- side catch trays or on exposed conveyor/equipment surfaces. Unenclosed catch trays/line area contain >1 cup of spillage.	>1 cup per packing line area of spillage outside catch trays or on exposed conveyor /equipment surfaces. Unenclosed catch trays/line area contain >1 cup of spillage and are close to overflowing.	>1 cup per packing line area of spillage outside catch trays or on exposed conveyor /equipment surfaces, and unenclosed catch trays are overflowing onto floors or other moving equipment.
	Making/ Packing/ Product Feed/ Scrapping	No visible dust/powder present outside of dust control containment or enclosed spillage contain- ment.	<1 cup of total spillage/dust per floor area, not in main traffic aisle. <1 cup spillage in catch trays/floor. No visible raw enzymes or raw enzyme dust in any raw enzyme area.	1-2 cups of total spillage per floor area, not in main traffic aisle. N visible raw enzymes or raw enzyme dust in any raw enzyme area. Minimal amount on beams equip- ment.	>2 cups total spillage per floor area. A few raw enzyme prills/granules visible in raw enzyme area. Some accumu- lation of dust powder on o/h beams/equipment.	>2 cups total spillage per floor area. 1-2 teaspoons of raw enzymes visible in raw enzyme area. Some accumu- lation of loose dust/powder on o/h beams.	>10 cups spillage per floor area including raw enzymes. Excessive accumulations of dust/powder on o/h beams and equipment and catch trays overflowing onto floors.
	Distribution	No visible dust/powder present outside of dust control containment or enclosed spillage contain- ment.	<1 cup total spillage per floor area of visible dust/powder on floors, equipment or on overhead beams/equipment. Case conveyor/ULF trays per area have <1 cup spillage in total. No spillage in main traffic aisles.	1-2 cups total spillage out- side catch trays or on floors/ equipment per floor area. No spillage in main traffic aisles.	>2 cups total spillage outside catch trays or on floors/ equipment per floor area. 1-2 spills (several teaspoons) in main traffic aisles.	Conveyor/ULF catch trays have >10 cups of dust/ powder overall but are not overflowing. >2 cups total spillage on floors, several spills in traffic aisles.	>10 cups of total spillage on floors with spillage in walk-ways and driving aisles.

NOTES:

1. The rating level is equivalent to the compliance level percentage (e.g. a 90% compliance level would have an equivalent rating of 9).
2. For any packing line or any floor area with spillage of any amount from above knee level to overhead, the maximum rating achievable is 7.0.
3. The extent of packing line areas or floor areas is defined on a case by case basis.
4. This matrix was written for monitoring visual dust/powder in Dry Granules Operations. The same applies for aerosols/liquids in Liquids Operations. It is just a matter of change in terminology.
5. Survey frequencies

Compliance Level	Survey frequency
<80%	Shiftly
80% - 90%	Daily
>90%	Weekly

Chapter 6 - Appendix 3: Criticality index rating guidelines

The approach is to:

1. Assign a rating of 1-4 to factors R1 to R4 described below

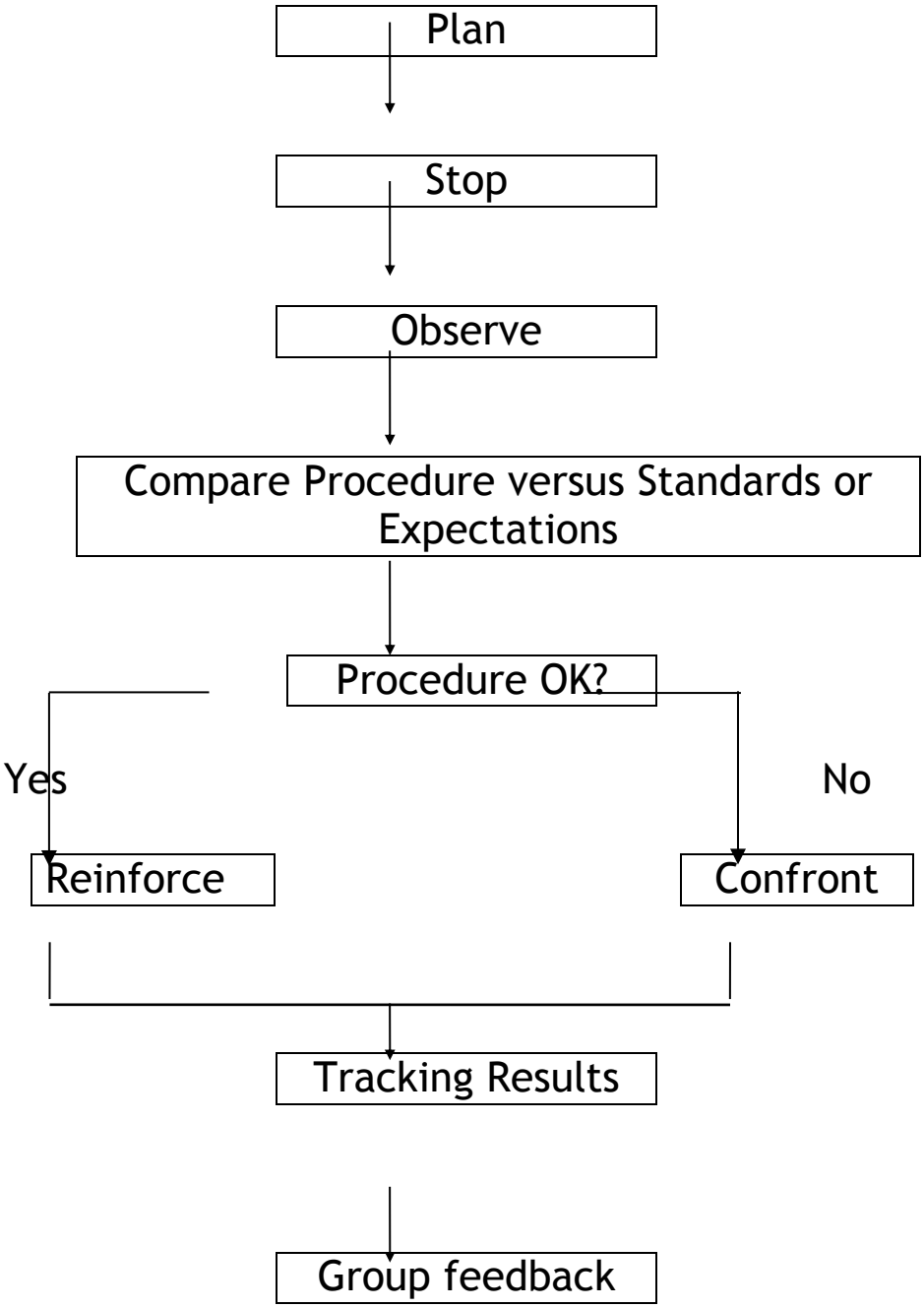
2. Calculate "Criticality Index" (CI = R1 X R2 X R3 X R4)

	Rating			
Critical factor	**1**	**2**	**3**	**4**
Exposure Level (R1)	No airborne dust/liquid either visibly or via backlighting.	• Intermittent leak or spill outside breathing zone may be observed visibly or via backlighting.	• Intermittent spillage overhead or in breathing zone.	• Continuous leak/spill **or** • Visible dust in air or on surface **or** • Dust/liquid observed continuously in air via backlighting.
No. of Events (R2)	< 1 per shift	1-4 per shift	5-8 per shift	≥ 9 per shift
Average No. of People Exposed Per Event (people within 3m or 10 ft.) (R3)	1	2	3	>3
Ability To Anticipate And Get Mask On In Time (R4)	Scheduled maintenance. (e.g., entering filter)	Could expose adjacent workers. (e.g., changeover)	Repetitive task with exposure potential. (e.g., repetitive clean up)	Production pressures for immediate response. (e.g., jam)

Important Note

Criticality index is an empirical scale. Absolute numbers don't mean anything in them. It is relative ranking that is important.

Observation Cycle



Chapter 6- Appendix 5: Bos Survey

AN EXAMPLE OF A BOS SURVEY

Date	Observer

Correct PPE in use	Criteria for observation	Pass	Fail	Positive Feedback given	Corrective Feedback given
3M half mask carried on person	Making Department				
Dust mask worn	PPE area, bag tipping				
Safety glasses carried on person					
Safety glasses worn	Walking through eye protection zone				
Safety glasses worn	When driving fork lift truck				
Goggles worn	Working in Pumping area / Perfume area				
Rubber Gloves	Handling chemicals/equipment				
Disposable overalls worn	Involved in clean out working in enzyme area				
Goggles worn	Drivers when unloading road or rail tankers				

Spill elimination/clean up

Indicate below any spills noted on your survey route and action taken to clean up and prevent any further spills.

Spill Observed At	Action taken	Fixed.	Not Fixed	Logged in Zone Book	Spill Cleaned up

EWF/SS Check list

Location	Pass	Fail	Location	Pass	Fail
Eye wash 1			Eye wash 5		
Eye wash 2			Eye wash 6		
Eye wash 3			Eye wash 7		
Eye wash 4			Eye wash 8		

Chapter 6, References

1. Peters, G., Johnson, G.Q. and Golembiewski, A. (2001) Safe use of detergent enzymes in the workplace. Applied Occupational and Environmental Hygiene (accepted for publication).

Chapter 7- Routine air monitoring programme

The intent is to monitor the airborne dust and enzyme levels in the workplace. The routine air sampling is a quantitative tool to measure the level of background exposure, whereas the peak sampling could be used to measure peak exposure, for example due to equipment defects and/or unsafe behaviour. Air monitoring includes area and personal sampling and can be undertaken with either high or low volume samplers depending on the analytical restrictions.

Area sampling is used to evaluate the effectiveness of control measures and trends in performance; it can also provide an indication of employee exposure and is typically done at a fixed location. Personal sampling involves a low volume device, which is worn by the operator and can be used to evaluate individual employee exposure by job description or as total cumulative exposure where job rotation applies.
However the use of personal sampling is limited by the lowest limit of detection of the methodology (sampling and analyses combined).
Normally, both total and enzyme airborne dusts are measured in powder detergent manufacturing operations. Only enzyme aerosol is measured in liquid operations.
Evaporation of liquid precludes gravimetric measurement of total liquid detergent aerosol.

7.1. Approach

The air monitoring program is not a substitute for operating to high standards of hygiene and housekeeping but is valuable for checking the working environment for dust and enzyme aerosols. It can be used in conjunction with the semi-quantitative tools described in Chapter 6 for Performance Assessment of Equipment and Behaviour.

7.2. Components of an air monitoring programme

The following six components collectively represent the routine air monitoring program:

- Training
- Air sampling equipment
- Air sampling strategy
- Data analysis and interpretation
- Follow-up with employees
- Corrective actions and validation

7.2.1. Training

A trained and competent person should oversee the air monitoring program. This individual is responsible for establishing the sampling plan (e.g. sampling frequency, location and sampling time), selection of air monitoring equipment, data evaluation, assessment of the adequacy of control measures and training of individuals collecting the samples. The individuals performing these tasks should be adequately trained in the operation of sampling equipment.

The collection of reliable and accurate air sampling data requires training on the following:

- Operation and maintenance of the sampling equipment
- Calibration of sampling equipment
- Data collection (e.g. sample time, flow rate, location, operations, employee work practices)
- Sampling plan
- Understanding of the basic analytical requirements, including handling, storage and transport of filters
- Maintenance of sampling equipment

Training should involve a practical demonstration of sampling and equipment calibration. The practical demonstration of skill should be repeated at least every 12 months.

7.2.2. Air sampling equipment

High volume samplers are commonly used for enzyme air sampling. Samplers typically operate at 300-600 litres/minute and sampling times of up to 4hrs may be necessary to demonstrate compliance with internal occupational exposure limits. The higher volume samplers (600l/min) may be used for solid particles and the lower volume samplers (300l/min) for liquid aerosols. This can normally be done by the same HV sampler, but after flow rate adjustment. Some of the new high volume samplers have flow rate controllers, with which the flow rate can be adjusted to the target flow.
Experience has shown that liquid aerosols will pass through the filter material if the sampler volume is too high. Whatman GF/C glass fibre filter pads are generally used for these samplers. High volume sampler manufacturers include Bendix Sensidyne Incorporated, GMW Graseby (Anderson), Newton Instruments (Galley), Tisch. See section 10.4.1. for the filter type to be used.

Alternatively low volume samplers can be used for personal sampling or area sampling.
These have a flow rate of 2-3 litres /minute for personal sampling, or 20-30 litres/min for area or targeted sampling. They can use a glass fibre, PVC or Teflon filter. Low volume pumps are made by a variety of vendors such as Gillian Instrument Corporation, SKC Incorporated and Casella instruments.

There are advantages and disadvantages for both types of samplers. High volume samplers normally need to be calibrated by the supplier and calibration routinely checked by the user. They collect large volumes in a short period of time, which allows for a greater detection limit. Low volume samplers are easier to calibrate and the pumps used for personal sampling do not require external electrical source for operation. More sensitive analytical methods may be needed. In areas with flammable solvents explosive proof samplers are available.
The low volume samplers with a flow rate of 20-30 litres/min provide the option of area or targeted sampling; i.e. if the exposure at a certain operation or equipment should be measured, these samplers will allow such assessment. This is particularly important when mapping and identification of potential exposure sources are made.
It is important to keep air samplers very clean to avoid sample contamination. The filter holder should be protected from contamination when not in use and cleaned before each sampling campaign. Cleaning with a substance that denatures protein contamination and dries quickly (e.g. ethanol) is advised. The equipment should be allowed to dry completely before sampling because moisture can weaken the filter and increase the risk of tearing the filter pad during handling.

7.2.3. Air sampling strategy

Each site should have a system to ensure that the air sampling program is representative of the overall operation. Each enzyme used within the site should be monitored as the use of a single enzyme as an indicator of airborne levels of other enzymes in use is not reliable. The following factors should be in place to ensure the program delivers accurate data representative of the operation.

7.2.3.1. Sampling Schedule

The system for data tracking should verify that samples are taken at random times on all shifts (day and night). There is an exception called targeted sampling, which is discussed later. It is recommended that samples be also taken when there is no operation. This will establish the background level in the workplace and serves as the baseline for the air sampling results obtained during production.

7.2.3.2. Sampling Frequency

For each unit operation, representative area samples should be taken on a regular basis. It is recommended that samples are taken at least daily, rotated around the shift pattern.
In packing halls, sampling frequency should reflect the complexity of the operation.

7.2.3.3. Sampling Duration

Sample duration may vary depending on the objective (up to 4 hrs for high volume sampling and 8 hrs for personal monitoring), and the variability within the process. See section 6.3.2 for peak air sampling.
Sampling duration should also reflect the sensitivity of the analytical method (LOD or the limit of detection of the enzyme in question), enzyme levels in the facility and the air sampling rate of the equipment (type of sampler).

7.2.3.4. Sampling Locations

Areas with the highest potential for exposure should be chosen as area sampling locations. Sampling frequency should depend on results of previous measurements. Appropriate monitoring locations can be selected in each facility by a team including industrial hygiene and manufacturing personnel. As a general guideline, some companies have found monitoring at the following locations important:

- Where the enzyme supply container is discharged
- Enzyme dosing area at dosing units
- Mixing or blending of finished product
- In the powder / liquid storage area
- Finished product storage / transfer areas
- At the head of each packing machine
- At the packing reject station
- In the area set aside for recovery of powder
- Handling of empty enzyme supply containers
- And, wherever medical surveillance results indicate some areas/activities of concern Section 6.3 on "Detecting And Ranking Peak Exposure Sources" can be used to help identify additional locations.

7.2.3.5. Sampler Positioning

Air samplers are designed so that dust samples are collected in the same way that an operator would inhale dust.
The sampler head of the high volume sampler should be placed in a position equivalent to the operator's breathing zone (typically 1.5 meters above the floor). The filter head is precisely manufactured so that the speed of air flowing into the filter is similar to the speed of air breathed in (1.25 m/sec). In terms of distance from the source, exact sampler locations should be decided on a case-by-case basis following the outcome of the risk assessment and the location of any potential peak exposure sources. To ensure the reproducible location of the samplers, the position can be clearly marked on the floor.

7.2.3.6. Targeted Sampling

Some operations have a relatively high potential for generating dust or aerosol, like cleaning, maintenance, rework, troubleshooting…. Where such operations are part of the routine air monitoring program, samples should be taken during a period of activity.

7.2.3.7. Sampling Procedure

Filters can be weighed before and after taking the air sample to determine total airborne dust before conducting the analyses for enzymes. Care should be taken not to damage or contaminate your filter before or during analyzes.
Filters should be removed from the sampling device as soon as possible after the sampling process is completed. Further details on filter handling are outlined in Chapter 10, Analytical Procedures.

7.2.3.8. Sampler Calibration and Maintenance

Sampling pumps should be calibrated according to the manufacturers' instructions and recommended frequency.
Low volume personal samplers should be calibrated before each use and the primary calibration device sent away for certification once a year. Calibration of the high volume samplers should be checked at regular intervals. It is advisable to have the flow meter and orifice plates calibrated against an international standard at least once every twelve months.
Modern high volume samplers often have calibration facilities built into their electronics.

7.2.3.9. Observations

Operators should record any non-routine conditions and behaviours happening in the area during sampling that may affect the results, such as spills, maintenance, and intervention without PPE etc. Observations should be logged along with the results.

7.2.4. Data analysis and interpretation

There are many methods for analyzing results. One example uses a statistical concept called Capability Ratio (Cpk). A further useful performance indicator is the Upper Control Limit (UCL), which is illustrated in ***Figure 1***.

7.2.4.1. Definition and Use of Cpk

$$Cpk = \frac{\text{OEG Value - Average Value}}{3 \times \text{Standard Deviation}}$$

Where:

- Cpk = Capability Ratio
- OEG Value = Value of Occupational Exposure Guidelines (see chapter 3)
- Average Value (AVG) = Arithmetic mean for data from sampler location
- Standard Deviation = the standard deviation calculated assuming normal distribution of data

CpK is a measure of how capable a system is of delivering results below the OEG: the greater the CpK, the higher the capability. Given that the OEG is a fixed value, a lower average value and a lower standard deviation make a system more capable
A target can be set for Cpk. For example, a Cpk of 1.0 means 99.7% of all results are below the OEG value. The trend in Cpk values calculated for a sampling location can be used to indicate if an area is considered to be in control (i.e. Cpk > 1) or out of control (i.e. Cpk <l).

The value of the CpK in relation to the monitoring data is shown below:

Capability Ratio	**Air Monitoring Data**
CpK > 1	AVG + 3SD < OEG
CpK = 1	AVG + 3SD = OEG
CpK < 1	AVG + 3SD > OEG

Sampling frequency at each location can be based on Cpk with the help of a competent person. For area sampling, a minimum of 30 data points should be used to calculate the Cpk. Cpk should be updated at least quarterly; the oldest results used should have been attained no more than 16 weeks previously.

7.2.4.2. Definition and Use of UCL

UCL is a fixed level based on performance of several locations. Typically it is 50% of the OEG. Results at each location should be recorded on a control chart. Sampling results should be plotted as a function of time ***(Figure 12)***.

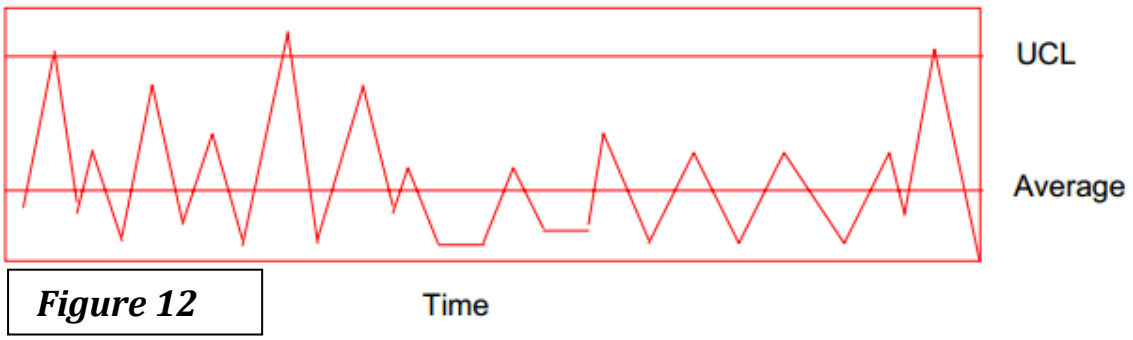


Figure 12

It may also be valuable to compare similar locations across sites for new equipment/process commissioning.

7.2.5. Corrective actions and follow-up

Remedial steps should be taken immediately to resolve any exposure conditions leading to an air sampling result out of the OEG limit. When re-sampling confirms the high level, then stopping production should be considered.
Actions that may be taken when individual results are above the OEG value or above the UCL as well as the % of routine sampling locations with Cpk<1 are discussed in Chapter 6.
A follow up check is needed to ensure that corrective action is effective and exposures have been eliminated.
Historical data for total dust, enzyme dust and enzyme aerosols should be kept for at least 10 years. Personal sampling data is kept as part of the personal file and needs to be maintained for at least 40 years or according to legislative requirements.

7.2.6. Feedback to employees

If an area is above the OEG limit, employees should be informed immediately and wear RPE until results are within limits. When the Cpk results are within limits but the air sampling data is above the UCL, it should be decided on a case-by-case basis if PPE should be mandatory.
The individual results above the OEG limit or above the UCL, as well as the % of routine sampling locations with Cpk<1, should be reported periodically to all employees and shared during the safety meetings. The report should include a summary of the basic causes found during the investigation and corrective actions that were recommended and the status of implementation.

Chapter 8 - Health surveillance

This chapter is intended as guidance to assist occupational health professionals in implementing the current best practice for the health surveillance of enzyme workers in the European detergent industry. The protocols recommended in this document may be refined by occupational health specialists based on history of results from their specific industry.

The Medical Sub-Committee of the UK Soap and Detergent Industry Association (SDIA) published the revision of its recommendations for the health surveillance of employees engaged in the manufacture of enzymatic washing products in March 2001: Current Best Practice for the Health Surveillance of Enzyme Workers in the Soap and Detergent Industry (1). This chapter is based, with the exception of some modifications, on the recommendations given in that publication.[4]

The Soap and Detergent Association of the U.S. (now called ACI) also published in 1995 the Work Practices for Handling Enzymes in the Detergent Industry which described current medical monitoring practices of enzyme workers (2).

8.1. Definition

Health surveillance is the periodic medical examination of workers potentially exposed to enzymes.

8.2. Objectives

The objectives of health surveillance include:

- Protecting the health of individual employees by detecting, at as early a stage as possible, adverse changes which may be attributed to exposure to hazardous substances
- Assisting in the evaluation of measures taken to control exposure
- Collecting and maintaining objective data to detect and evaluate hazards to health

Health surveillance is indicated for employees who are, or are liable to be, exposed to a substance hazardous to health when:

- The exposure of the employee to that substance is such that an identifiable disease or biological effect may be related to the exposure and
- There is a reasonable likelihood that the disease or effect may occur under the particular conditions of his work and
- There are valid techniques for detecting signs of the disease or the effect
- Surveillance is likely to further the protection of the employees' health

[4] Acknowledgement: We would like to express thanks to the SDIA (now called the UK CPI) for sharing a summary of good practices in using enzymes for all-European use. Members of the SDIA Working Group included P. Nicholson, M. Cathcart, J. Lewis, Professor Sir A. Newman Taylor and P. Oliver.

8.3. Pre-placement testing

1. A history should be taken with particular reference, for example, to asthma, allergic rhinitis, eczema, urticaria, allergies, chronic lung disease and any medication.

2. A respiratory questionnaire should be completed (Appendix 1), (,3,4,5,6,) including details of smoking habits. Appendix 1 is based on the International Union Against Tuberculosis and Lung Disease (1984) IUATLD questionnaire.

3. Assessment of lung function should be made using a suitable spirometer to estimate forced expiratory volume in 1 second (FEV 1), forced vital capacity (FVC), FEV1/FVC ratio and peak expiratory flow rate (PEFR) (Appendix 2), (7,8,9,10,11,12,13,14,15,16,17,18,19,20).

4. Immunological Tests e.g. skin prick or serological tests should be performed (Appendix 3).

5. A physical examination may be carried out at the discretion of the occupational health professional who should have received approved training in occupational medicine.

   Subjects with significant findings such as a history of asthma, allergic rhinitis or other respiratory disease or poor lung function should be assessed carefully. On the basis of history and examination findings, the Occupational health professional will make suitable recommendations in accordance with local legislation regarding the employee fitness to work with enzyme products and of any adjustments or special requirements. Such recommendations shall be based on formal risk assessment and sound clinical judgment.

8.4. Temporary Workers

In the case of occasional or temporary workers, the medical selection and surveillance procedures will depend on the duration and degree of exposure. Where there is significant exposure for one month or more, the protocol for "new employees" should be applied.

8.5. Employees working with enzymes

During the first 24 months of employment, individuals should have six-monthly health surveillance and thereafter a minimum of every 12 months.

The review should include:

- Periodic Respiratory Questionnaire
- Spirometry
- Immunological Test

Those with normal findings may continue to work until the next examination.

Those who have developed a positive immunological test result to enzyme and have no other adverse findings may continue to work with enzymes, although increased frequency of surveillance of such workers may be appropriate initially.

Those with abnormal findings to the respiratory questionnaire, which estimated by an occupational health professional, could be due to enzymes, and those with impaired lung function on spirometry require immediate further assessment and should be re-tested within one month or at the discretion of occupational health professionals. Those who show a continuing downward trend in lung function should be assessed as to the need for removal from further work with enzymes.

Employees with clinical symptoms of enzyme induced respiratory disease should have their fitness to work assessed by the occupational health professional.

Enzyme workers should be trained to recognize symptoms and encouraged to report to the occupational health centre any symptoms which could be related to enzyme exposure. There should be careful monitoring of the respiratory sickness absence of enzyme workers with appropriate follow up action by the Occupational health professional.

8.6. Record Keeping

To comply with legal requirements, all relevant records must be kept for a minimum of 30 years or more according to national legislation after employment has terminated. Clinical information obtained from health surveillance should be maintained in confidential personal medical records.

8.7. Data interpretation and follow-up

The results of an individual's immunological tests should be given to each employee. They are of practical relevance for individual employees, since they may permit the identification and correction of individual contributory or causative factors such as failure to follow job safe practices. Therefore a new sensitisation may warrant further investigation as described in chapter 9. Nevertheless positive immunological responses are not an accurate predictor of the likelihood that a person will develop respiratory symptoms such as those of asthma or hay-fever.

Group results of immunological test results also assist in the evaluation of workplace control measures. Group data should be used to monitor the effectiveness of hygiene and engineering programmes at factories and within individual departments. Such data will help prioritise areas for improvement. However the validity of the use of health surveillance data to monitor compliance is affected by group size.

Chapter 8 - Appendix 1: The respiratory questionnaire

It is anticipated that applicants will complete a general health questionnaire at pre-placement and that this questionnaire will include questions relating to previous employment and any exposures to chemicals, fumes or dust. Thus the intent of the respiratory questionnaire is solely to detect existing respiratory symptoms.

In the health surveillance of those working with respiratory sensitisers, sensitivity is more important than specificity. If the surveillance procedure generates false positive results, these may be eliminated easily by further clinical assessment. However, unidentified false negative results will place some employees at risk of ill health by continuing to expose them to the same environment and chemical hazard.

To aim for maximum sensitivity, the use of a questionnaire based on that published by the International Union Against Tuberculosis and Lung Disease (IUATLD) in 2001 and which has been validated extensively is recommended (see Appendix 1: annex 1 and 2) with the following modifications:

- Minor rewording to produce separate pre-placement and periodic questionnaires and to allow use at intervals other than annually
- The removal of questions to elicit symptoms of chronic bronchitis
- The addition of questions to elicit symptoms of rhinitis and conjunctivitis
- Rewording to amalgamate very similar questions into one question
- The addition of an enquiry about smoking habits

The occupational health specialists should assess the significance of any reported symptoms and should identify any smokers. Smoking cessation advice is particularly important for those working with respiratory sensitisers, since smoking promotes IgE production and damages the respiratory mucosa and mucociliary clearance mechanisms.

Annex 1 – Pre-placement respiratory questionnaire

MEDICAL IN CONFIDENCE **(PLEASE PRINT)**

Last Name:		First Names:
Birth Date: Day Month Year	Department:	Proposed Work/Job Title:

*Your health history is most important in evaluating your health. Please complete this **CONFIDENTIAL** questionnaire as accurately as possible and return it directly to **Occupational Health**. Answer all questions by placing a tick in a YES or NO box and by printing the word(s) or number(s) answer as required.*

	Yes	No	For medical use only
1. Does your chest ever feel tight or your breathing become difficult?			
2. Have you ever had an attack of wheezing or whistling in your chest?			
3. Have you ever had an attack of shortness of breath that came on during the day when you were not doing anything strenuous?			
4. Have you ever had an attack of shortness of breath that came on with exercise?			
5. Have you ever been woken at night by an attack of shortness of breath or coughing?			
6. Have you ever woken up with a feeling of tightness in your chest first thing in the morning?			
7. Which of the following statements best describes your breathing? a. I never or only rarely get trouble with my breathing. b. I get regular trouble with my breathing, but it always gets completely better. c. My breathing is never quite right.			
8. Has a doctor ever told you that you have asthma?			
9. Have you ever had an attack of asthma?			
10. Have you had an attack of asthma any time in the last 12 months?			
11. Are you currently taking any medicines, tablets or inhalers for asthma?			
12. Other than when you have a cold, have you ever had: a. Sneezing, running or blockage of the nose? b. Itching or watering of the eyes? c. Are you currently taking any medicines or tablets for these symptoms?			
13. Have any of the problems described in question 12 occurred at any time in the last 12 months?			
a. Have you ever smoked cigarettes? If yes, how many did you smoke a day?…….…….. For how many years?……..…….. b. Do you currently smoke cigarettes? If yes, how many cigarettes do you smoke a day?……			

Please sign this questionnaire
I declare to the best of my knowledge that the answers to the questions above are complete and accurate.

Signature..... ……
Date.....
..... **.....** **.....**
Signature of Occupational Health Nurse **Print name of Occupational Health Nurse** **Date**

Annex 2 – Periodic Respiratory questionnaire

MEDICAL IN CONFIDENCE **(PLEASE PRINT)**

Last Name:	**First Names:**	**Employee number:**
Department:	**Job Title:**	**Date of Birth:**

*Your health history is most important in evaluating your health. Please complete this **CONFIDENTIAL** questionnaire as accurately as possible and return it directly to **Occupational Health**. Answer all questions by placing a tick in a YES or NO box and by printing the word(s) or number(s) answer as required.*

	Yes	**No**	**For medical use only**
1. Since your last examination has your chest ever felt tight or your breathing become difficult?			
2. Since your last examination have you had wheezing or whistling in your chest?			
3. Since your last examination, have you had an attack of shortness of breath that came on during the day when you were not doing anything strenuous?			
4. Since your last examination, have you had an attack of shortness of breath that came on with exercise?			
5. Since your last examination, have you been woken at night by an attack of shortness of breath or coughing?			
6. Since your last examination, have you woken up with a feeling of tightness in your chest first thing in the morning?			
7. Which of the following statements best describes your breathing? a. I never or only rarely get trouble with my breathing. b. I get regular trouble with my breathing, but it always gets completely better. c. My breathing is never quite right.			
8. Since your last examination, has a doctor told you that you have asthma?			
9. Since your last examination, have you had an attack of asthma?			
10. Are you currently taking any medicines, tablets or inhalers for asthma?			
11. Since your last examination, other than when you have a cold, have you had: a. Sneezing, running or blockage of the nose? b. Any itching or watering of the eyes? c. Are you currently taking any medicines or tablets for these symptoms?			
12. Have any of the problems described in question 11 occurred at any time in the last 12 months?			
13. Since your last examination: a. Have you ever smoked cigarettes? If yes, how many did you smoke a day? b. Do you currently smoke cigarettes? If yes, how many cigarettes do you smoke a day?			

Please sign this questionnaire

Signature.....
Date.....

....
.....

Signature of Occupational Health Nurse **Print name of Occupational Health Nurse** **Date**

Chapter 8 - Appendix 2: Lung function testing using a spirometer

Accepted standardised procedures and protocol should be followed to reduce measurement errors (e.g. Miller et al, 2005, (12, 13) - Cotes et al, 1997, (9)).

The following standardised approach to spirometry is recommended:

- A volumetric spirometer is preferred, to allow direct observation of the graph during the performance of the forced expiratory manoeuvre
- The spirometer should conform to the performance criteria of the American Thoracic Society
- Spirometry should be administered by trained and competent staff, since testing and interpretation require both skill and training
- A routine maintenance and calibration programme must be in place
- Guidelines should be followed with respect to calibration procedures, leak checks and BTPS correction factors to minimize measurement errors
- The nurse should enquire about current illness and/or medication that may affect test results or dictate the postponement of the procedure
- Feedback to nurses about performance in obtaining satisfactory spirometry results forms an integral part of the quality control of the surveillance programme
- Hygiene measures should be in place to prevent the transmission of pathogens
- Spirometry should be performed in the standing position
- The nurse should observe for any signs of dizziness or syncope
- The number of test indices should be limited i.e. to FVC, FEV1, FEV1/FVC ratio, PEFR, to reduce the false positive rate

For a forced expiratory manoeuvre to be acceptable there must not be:

- Unsatisfactory start to expiration (i.e. excessive hesitation, false start or an excessive extrapolated volume greater than 5% of FVC or 0.15 litres, whichever is the greater)
- Coughing during the first second of expiration
- Early termination of expiration - the plateau on the volume time curve should last at least 1 second and expiration length should be at least 6 seconds and optimally 10 seconds
- Valsalva manoeuvre
- Leak
- Obstructed mouthpiece e.g. due to the tongue or dentures

For the test indices to be considered reproducible:

- The first and second largest measurements of FVC must not vary by more than 150mls
- The first and second largest FEV1 must not vary by more than 150mls
- The greatest single values for FEV1 and FVC must not come from the last test performed. (FEV1 and FVC may be derived from separate expiratory manoeuvres)
- A minimum of three trials should be completed

Once acceptable and reproducible spirometry results have been obtained, the results should be interpreted by the trained and competent person, who should bear in mind the limitations of "% normal values".

The practice of classifying values of FEV1 and FVC of less than 80% of normal has no biological basis, although some studies show that for adults of average age and height, 80% of predicted FEV1 and FVC is close to the fifth percentile, i.e. boundary of normal. Using a fixed value of 80% results in shorter, older adults being more readily classified as

abnormal and taller, younger adults being classified erroneously as normal. Similarly, defining a fixed lower limit of normal for FEV1/FVC ratio is not recommended in adults, since FEV1/FVC is related inversely to age and height. Ideally, normal ranges should be based on calculated fifth percentiles.

During periodic health surveillance a 15% fall in FEV1 or FVC over one year is regarded to be clinically significant. Assuming measurement error has been excluded, such reductions in lung volume merit further investigation.

"Abnormal" or borderline spirometry test results should be referred to the occupational health professional for interpretation and follow up.

Performance of Forced Expiratory Manoeuvres

Check spirometer calibration
Explain test
Prepare subject
    ask about smoking, recent illness, medication, etc.
Instruct and demonstrate test to subject
    correct posture with head elevated
    inhale completely
    position mouthpiece (open circuit)
    exhale with maximal force
Perform manoeuvres
    have subject assume correct posture
    have subject take the deepest possible inspiration inhale completely; and without hesitation
    place mouthpiece in mouth and close lips around mouthpiece
    exhale maximally as soon as lips are sealed around mouthpiece
    repeat instructions as necessary, coaching vigorously
    repeat for a minimum of 3 manoeuvres: no more than 8 are usually required
Check test reproducibility and perform more manoeuvres as necessary

Chapter 8 - Appendix 3: Immunological tests

Sensitisation to allergen is defined as the development of specific IgE. The demonstration of an immunological response to allergen does not establish the presence of disease, but indicates sufficient exposure to allergen to stimulate a detectable immunological response. Two types of immunological methods are available for determining sensitisation, the skin prick test and serological tests such as the radioallergosorbent test (RAST), UniCAP system and the enzyme-linked immuno-sorbent assay (ELISA). The choice of methodology within each company will take account of many factors, including those set out in Table 1.

Serological tests are useful:

- As a quantitative measure of specific IgE antibody when monitoring of an individual is required
- When individuals have been taking antihistamines which suppress skin prick test reactions
- In individuals with skin disease which is so extensive that skin tests are difficult to perform or where there is dermatographism
- In groups of employees in countries where skin prick tests may not be practicable or acceptable
- In a situation where reanalysis or supplementary analysis (e.g. towards other enzymes or enzyme components) could be useful

However, serological testing requires an invasive procedure (blood sampling via venepuncture), is relatively costly and the results are not available immediately. The skin prick test is less invasive, provides immediate results and is generally less expensive. Local regulatory and legal aspects relating to each type of immunological test must be verified for compliance (an occupational health physician should make recommendations to management about legal aspects of testing).

Skin Prick Test Procedure

Several disposable devices (e.g. hypodermic needles and lancets) are available for skin prick tests. Expert medical advice and training are needed to ensure that the test is performed competently, effectively and in a consistent manner.

An appropriate technique is as follows:

Reasons for the procedure should be explained to the employee. Instructions should be given to report any delayed skin reaction coming on some hours after the prick test and arrangements should be in place to confirm any such reaction.

Testing may be performed by a suitably trained and competent nurse. Training in the procedure should ensure standards consistent with those at a specialist led allergy clinic.

The volar surface of the forearm is used. Employees should be tested with:

- Negative control – suitable diluent (e.g. physiological saline or 50% glycerol/50% physiological saline)
- Positive control – (histamine e.g. 1:1,000 histamine phosphate or 10mg/ml histamine dihydrochloride)
- Enzyme reagents (i.e. for the enzymes to which the individual has been exposed)

Skin prick test reagents should be prepared using samples provided by the relevant enzyme suppliers specifically for that particular purpose. These samples are normally prepared from enzymes preparations free from contaminants and are well characterised.
Skin prick test reagents must be prepared in facilities that comply with the principles and guidelines of good manufacturing practice (as described in Commission Directive 2003/94/EC dated 8 October 2003).

Raw enzyme material should never be used for SPT because of possible impurities, such as minor amounts of secondary enzymes, which can lead to confusion in interpreting results. The enzyme supplier can provide advice on the concentration of the skin prick test reagent to be used in practice. A concentration of 50 µg enzyme protein per milliliter of reconstituted material has been shown to deliver valid results. The reagent must be sterile.

A NEGATIVE control is used to identify false positive responses through non-specific reactions to the needle or dermatographism. A POSITIVE control is used to confirm whether the skin prick test is valid i.e. to identify false negative responses to allergen extracts as may occur with the use of certain medications, in particular antihistamines.

Skin test reagents should be properly stored according to the instructions of the supplier. Expiry dates should be checked on a regular basis.

One drop of the skin test solution is placed near a marked (felt tip pen) area of the arm. The tip of a 26G hypodermic needle is passed through the drop and inserted into the skin at an angle so that the skin may be lifted on the bevel or the tip of a lancet is pressed into the skin at an angle through the drop. The needle/lancet is withdrawn and the excess solution is wiped off immediately with a paper tissue (taking care not to transfer any solution to the adjacent sites). Each solution is pricked into the skin once only. A fresh needle/lancet must be used for each prick test.

The skin prick test sites should be inspected at 15 minutes. The test is considered valid if a wheal of at least 3mm diameter is obtained with the positive control (in the presence of a flare). A reaction is considered to be positive if:

- The enzyme reagent produces a wheal of at least 3mm diameter with flare (where there was no reaction to negative control), or
- A wheal of at least 3mm greater than any wheal reaction to the negative control with flare

It is recommended that each wheal is measured (and the presence/absence of a flare recorded) and the size in millimetres entered in the employee's medical records.

Skin prick tests should not be performed at skin sites with active dermatitis.

Although skin prick testing is considered to be a safe procedure, adverse events, such as large local reactions may occur in some individuals. Systemic symptoms are less likely with prick tests for inhalable allergens than either skin prick tests for food allergens or with intra-cutaneous tests. However, it is recommended that full emergency equipment and drugs should be on hand for treatment of potential anaphylaxis.

Serological Test Procedure

Venepuncture for serological tests should be performed by a trained and competent nurse in the occupational health unit or in a clean, quiet and well-illuminated room. The procedure should be explained to the employee. The employee should be asked whether they have ever fainted during venepuncture. If they have, venepuncture should be undertaken with the employee lying down.

Once collected, the blood should be centrifuged to separate off the serum. The serum sample should be stored refrigerated (for short-term storage) or frozen (for longer-term storage) in a dedicated medical refrigerator/freezer until samples are transported to the testing laboratory with appropriate documentation. Only accredited/certified (GLP) laboratories should be used for serological tests. A record log should also be maintained to record the details of samples sent. Once received, the results of serological tests should be entered in the employees' medical record and the employee should be informed of the result.

Serological test principles

There are several in vitro test methods for the determination of circulating allergen specific IgE antibodies in human serum, e.g. RAST, UniCAP System, and ELISA. All these methods are based on the same principle; the formation of a solid phase/allergen/human IgE/anti-human IgE/indicator complex. The allergen of interest (e.g. enzyme) is covalently bound to a solid phase (paper disc, cellulose immunoCAP, plastic microtitre well). If there are any allergen specific IgE antibodies in the serum of the examined person, they react with the solid phase bound allergen. Any non-specific/unbound IgE is washed away and enzyme or radioactive labelled antibodies against human IgE are added to form a complex. Again, after incubation, unbound enzyme/radioactive labelled anti-human IgE is washed away. In the case of methods using enzyme labelled anti-human IgE a suitable substrate or development agent is added to the complex. The endpoint is the measurement of the radioactivity, fluorescence or colour reaction (depending on the method used). To evaluate the test results, the response in the patient's serum sample is compared directly against calibrators or normal control sera. The solid phase preparation is a critical step in all methods and should be optimised. The enzyme samples used in the preparation of the solid phase are representative concentrate batches as supplied by the manufacturer. The advantage of commercial methods such as the UniCAP System is that the solid phase reagents (i.e. immunoCAPs) are standardised and quality controlled.

The RAST method was the original method developed for serological analysis but methods have been evolving and one of the new methods is the UniCAP System. This is more sensitive and faster than the RAST method, with a lower background and broader detection range. The specific IgE antibody data generated by the UniCAP System is based on WHO-IgE standards. The results are expressed as both kilo units of allergen specific IgE antibody per litre (kU_A/l) and as a Class or ranking which relates to the amount of specific IgE antibody (e.g. undetectable, low, moderate, high etc.) present in the serum sample.

Table 1: Factors influencing choice of immunological test

Scientific aspects		
	Skin Prick Test	Serology
Advantages	□ **Immediate results** □ **May be more sensitive for some allergens**	□ **Quantitative** □ **No risk of adverse reactions** □ **Serial sampling possible to monitor changes in response** □ **Serum can be stored and used for subsequent baseline investigations**
Neutral	ϒ **Robustness**	
Disadvantages	□ **High level of skill/training required for standardisation and reproducibility** □ **Possibility of adverse reaction (local irritation)** □ **Not quantitative** □ **Affected by some medications and skin condition**	□ **Requires special preparation of reagents** □ **Reliant on specificity of reagents** □ **Results not immediate** □ **Invasive blood sampling required** □ **Risks associated with handling and transportation of biohazardous material**
Logistics		
	Skin Prick Testing	Serology
Advantages	□ **Relatively inexpensive**	□ **Less training of Occupational Health staff required**
Disadvantages	□ **Requires initial training of occupational health staff** □ **Possible medico-legal restrictions in some countries**	□ **Very expensive**
Industrial relations		
	Skin Prick Testing	Serology
Advantages	□ **Familiarity**	□ **Blood sampling may already be carried out as part of health surveillance**
Disadvantages	□ **Perception of positive response as an adverse effect** □ **Discomfort**	□ **Fear of needles**

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Chapter 9 – Monitoring and performance assessment follow-up

There are many contributing factors that can give rise to exposure to enzymes. The intent of this chapter is to provide an integrated approach to interpret and follow-up on the different data generated in operation. Chapters 6, 7 and 8 outlined the data interpretation and follow-up for the specific performance assessment tools, air monitoring and health surveillance. Below is an example of one approach used on how to effectively analyse, interpret and follow-up on the different data generated in operation in an integrated way. The methodology has proved to be effective in improving enzyme safety (1).

9.1. Approach

Look beyond the immediate cause to identify basic causes as to why operation management systems did not prevent a situation. This allows people to look beyond the immediate situation and find ways to improve system capability.

9.2. Process

Conduct a cause and effect analysis to investigate an incident when the basic/root cause(s) are unclear. Once the potential basic/root cause(s) have been identified a report needs to be issued summarising the plan for immediate corrective actions and basic/root cause elimination.

This process is used to identify system-based reasons (basic causes) why some locations are high risk or why a location is out of control. This can be applied to process monitoring as well as health surveillance.

9.2.1. Multi-Cause Analysis (MCA) (see *Appendix 1*)

As an example, an out of OEG limit air sampling result could occur because a fume hood face velocity was less than the design specified value. That is an immediate cause and should be fixed as soon as possible. However, the basic cause may be that the monitoring and maintenance program did not detect deterioration in the fume hood performance. Fixing the basic cause should ensure all equipment is adequately maintained and monitored in the future and not just the fume hood. ***Appendix 2*** provides examples of how this can be applied to air monitoring.

9.2.2. Problem Investigation Report (PIR) (see *Appendix 3*)

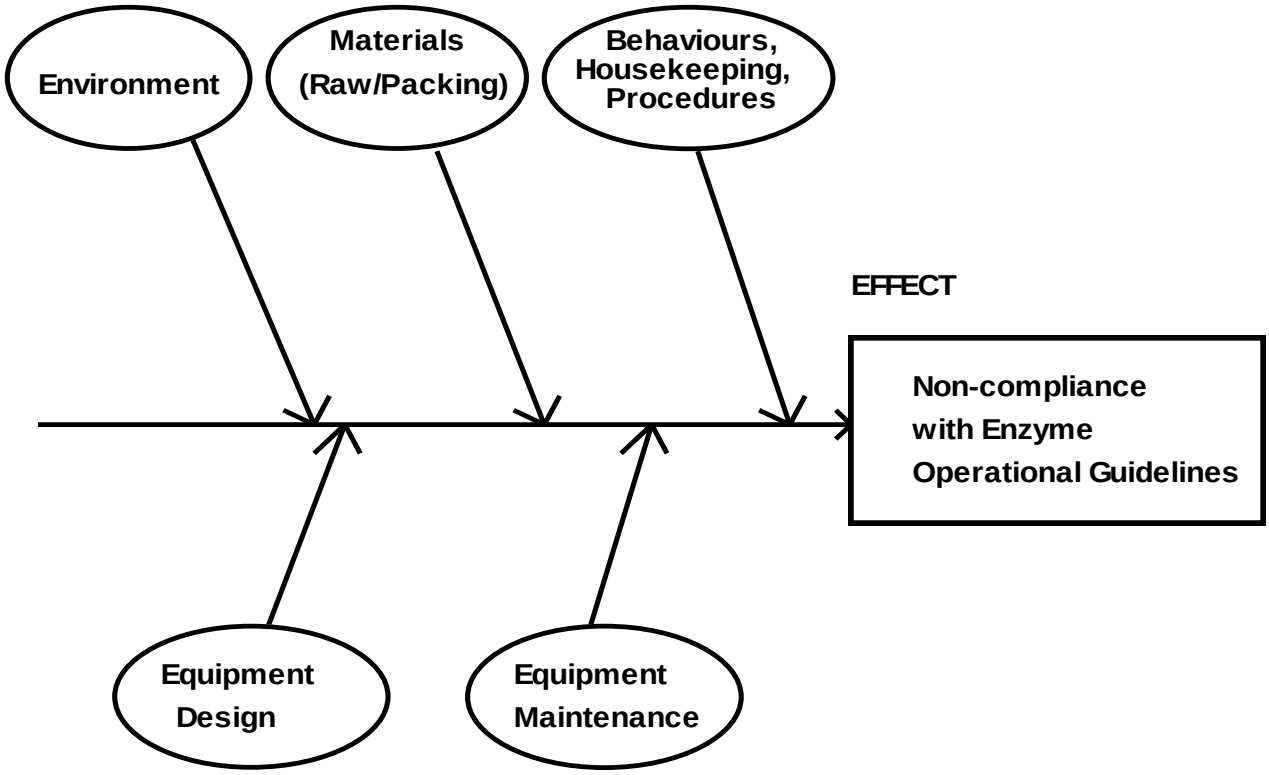
PIR includes the outcome of investigation as well as corrective actions and feedback. For example:

- To correct and monitor bad operating practices that could cause unnecessary exposure add these behaviours to the Behaviour Observation System (BOS) observation list (Chapter 6, Appendix 5).

- Equipment maintenance and design defects should be discussed in the team meetings and added to the maintenance programme with timed action steps. The Criticality Index Rating Guidelines (Chapter 6, Appendix 3) can be used to prioritise activities.

Chapter 9 - Appendix 1 : Multi-cause Analysis

MULTI-CAUSE ANALYSIS



Action Steps	Owner	Comp. Date	% Comp.
1.			
2.			
3.			
4.			
5.			

Chapter 9 - Appendix 2: Multiple cause-analysis applied to air sampling

Basic Cause	Example	Action
1. Knowledge	Employees don't know how to take air samples, calibrate pump, or use/maintain controls	Train and qualify
2. Not enforcing Safe Practices	Employees know how but do not follow department Safe Practices	Line management reinforces Safe Practice compliance
3. Engineering	Employees use controls/follow Safe Practice but aerosol is still released from equipment	Identify if emission is due to inadequate design of equipment or monitoring and maintenance. Address as appropriate
4. Feedback Systems	Employees are focused on production volume or quality and are too busy to follow Safe Practices or carry out monitoring and maintenance	Management to increase weighing for IHandS on overall performance appraisal and reinforce Safe Practices
5. Methods/Procedures	A particular way of doing a job was not recognized, as a potential source of aerosol or Safe Practice was inadequate. Consequently controls/Safe Practices were not devised or implemented or were inadequate	Review the procedure for conducting Hazard Analysis or Job Safety Analyzes upgrade as necessary
6. Inadequate inspection and maintenance	The face velocity at the hood was only 80% of the specified value	Reinforce inspection and maintenance of all equipment
7. Employee placement	Employee unable to perform task due to physical limitation	Unlikely to be a factor in air sampling

Chapter 9 - Appendix 3: Problem investigation report

PROBLEM INVESTIGATION REPORT

DEPARTMENT: _____ **DATE:** _____
INVESTIGATIVE TEAM: _____
DATE OF INCIDENT: _____ **@ TIME:** _____

1. **Item**

2. **Circumstances Under Which Problem Occurred**
(Describe the circumstances under which the deviation occurred).

3. **Immediate Corrective Action and Expected Results**
(Describe the short-term fix(s) taken to alleviate the immediate problem).

4. **Analysis of Causes**
[Complete Cause and Effect Analysis and follow process flow on backside of this page before identifying root cause (s)].

GENERAL ROOT CAUSES
SAFETY/ENZYME BASIC CAUSES

1. Skills development is required to perform the job effectively.
2. Current best practice/method was not followed.
3. Raw or Packing materials have influenced current operating specifications.
4. Inspections/Maintenance Programs do not meet current needs.
5. Equipment does not meet current Plant requirements.
6. A supporting system does not meet customer needs (Support provided by internal or external
7. suppliers).
Learned through experience current method,
8. system, approach or work process doesn't exist or does not meet current plant needs.
Business needs and plan are no longer aligned.
9. (i.e.: cost impact may influence the outcome/change).
10 Training is required to perform the job safely.
11. Task and employee are not aligned.
12.. Safe Practices are not followed.
13. There is a problem with the design.
14. P.P.E. does not meet current demands.
15. Inspections/Maintenance Programs do not meet current needs.
16. Equipment does not meet current plant standards.
17. Employee worked unsafe.
18. Learned current method is unsafe.

5. **Do you believe the action plan will eliminate the root cause:** (i.e.: incident will no longer impact the result).

6. **Will this report be shared across the Site/Network**?
(Is there an opportunity to Search and Reapply?). YES / NO

Chapter 9, References

1. Peters, G., Johnson, G.Q. and Golembiewski, A. (2001) Safe use of detergent enzymes in the workplace. Applied Occupational and Environmental Hygiene, Vol. 16: 389-396.

Chapter 10: Analytical procedures

The analysis of the concentration of enzymes in air is necessary to confirm that exposure to enzymes is adequately controlled. Detergent manufacturers usually develop their own methods or obtain them from the enzyme supplier. Essential for the methods used for analysing enzymes in air is that they should have a very low detection limit. The concentration of enzymes in e.g. production samples may also be relevant to analyse, and in this situation it is important that the methods should have the capacity to measure enzymes in the presence of detergent. Enzyme analyses are time-consuming with manual procedures that have demanding personnel requirements. For this reason some companies use automated methods. Aside from economics and ease of use, either method (i.e. manual or automated), is suitable as long as the required sensitivity and reliability are ensured and the method has been validated.
In this chapter we will address the principles of enzyme analyses and explain how to analyse filters from air sampling. In addition a section will discuss the analysis of enzymes in product samples and in enzyme raw materials. Another section will also describe the principles of protein determination in enzyme raw materials.

10.1. Principles of Enzyme Analysis

10.1.1. Sample preparation

The actual enzyme analysis is usually preceded by a sample preparation step where the enzyme is brought into aqueous solution. Representative sampling, complete dissolution and preservation of enzyme stability are essential to ensure correct analysis.

10.1.2. Methods to Assess Enzymes in Sample Solutions

Two broad categories of analytical methods are available for enzyme analysis: activity-based assays and immunoassays, such as ELISA (**E**nzyme **L**inked **I**mmuno **S**orbent **A**ssay).

Each technique will be discussed briefly, without going into specific methodology or technical details. More detailed/specific information on the analytical methods can be supplied by the enzyme manufacturers.

10.1.2.1. Enzyme activity-based assays

Field of application

(Active) enzymes in dissolved sample preparations derived from finished products, enzyme raw materials, enzyme raw material dustiness tests, and factory air monitor filters

Principle

The activity-based method measures catalytic active enzymes in a solution. The principle is based on the enzyme catalysed conversion of an appropriate substrate into a product under well-defined conditions. Catalytic activity is followed photometrically by

monitoring the change in substrate or product concentration at the appropriate wavelength. Some assays use special additives which form coloured complexes with substrate or reaction products to facilitate easy detection.

Enzyme levels are measured relative to standard solutions prepared from an analytical standard of known activity.

The activity method is simple, specific and rapid. Simple basic equipment (manual methods) and advanced auto analysers are available commercially from laboratory equipment suppliers.

Analytical Limits

The analytical limits may vary from assay to assay. Example: the detection limit for Savinase (a typical detergent protease) is of the order of 1.5 ng enzyme protein/ml. The quantification limit is approximately 2.5 ng/ml. In contrast, enzymes belonging to the class of cellulases will often have higher analytical limits.

One should be aware that if the sample contains more than one enzyme reacting with the substrate used in the activity analysis, then it will not be possible to distinguish whether the analytical response is due to one or the other enzymes. Such situations will occur for air monitor filters if more than one enzyme product belonging to the same class are used in the production line e.g. more than one protease product.

10.1.2.2. Immuno assays (ELISA)

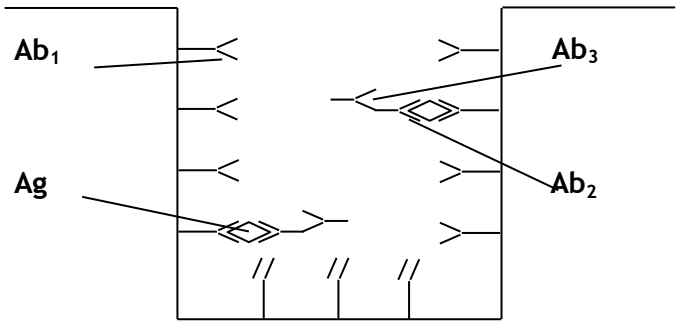
Field of application

Enzyme (protein) in dissolved sample preparations derived from enzyme raw material dustiness tests and factory air monitor filters.

Principle

The ELISA method (**E**nzyme **L**inked **I**mmuno **S**orbent **A**ssay) measures immunochemically active enzyme, i.e. enzymes being recognized by specific antibodies. Generally, the most common ELISA system used is a sandwich ELISA.

The principle is illustrated in the figure below:



The antigen (**Ag**), e.g. enzyme A is bound onto a microplate, which has been coated with a primary antibody ($\mathbf{Ab_1}$) to the antigen in question.

A secondary antibody ($\mathbf{Ab_2}$) to the antigen is bound to Ag, followed by an enzyme-conjugated antibody ($\mathbf{Ab_3}$). The enzyme catalyses a colour reaction which is proportional to the quantity of antigen. The signal is detected photometrically using a microplate reader.

A standard is applied on each microplate and the concentration of the antigen under investigation is calculated relative to the readings from the analytical standard of known concentration.

The time for analysis is approximately 5 hours.

Equipment necessary for performing the test can be more or less automated, depending on needs. It is therefore not feasible to give specific recommendations on this.

Reagents/substrates needed are:

- Antibodies from two different species to the antigen in question, e.g. polyclonal monospecific rabbit anti-enzyme A and polyclonal goat anti-enzyme A
- Enzyme-conjugated antibody, e.g. rabbit anti-goat immunoglobulin/ peroxidase

Limit of quantification

The limit of quantification may vary from assay to assay. Example: The limit of quantification for Savinase is of the order of 0.1ng enzyme protein/ml.

10.1.3. Pros and Cons for Enzymatic Activity Methods vs ELISA for dust analysis

The pros and cons for enzymatic activity methods vs ELISA re filter dust analysis are summarised in the below table:

	Pros	Cons
ELISA	□ Low limit of determination □ High specificity □ The same principle and instrumentation is used for all methods □ Measures immunochemical response □ May be able to separate between (not closely related) enzymes of similar classes	□ Demands very clean room and equipment □ Demands trained staff working with high accuracy □ Demands specific antibodies □ Time consuming assay procedure □ Costly
Activity methods	□ Based on commercially available substrates □ Relatively easy to set up and run	□ Assay principle and instrumentation should be considered for every new enzyme □ Limit of determination sometimes borderline □ May not be able to separate enzymes of similar classes □ Environmental enzymes (e.g. amylases) may produce high, variable background interference)

10.2. Enzyme activity units

Currently, there is no agreed common international method for each enzyme activity type. Individual enzyme suppliers have their own favoured methods of analysis and usually their own definition of the unit. This restricts any attempt to compare enzymes with apparently similar activity characteristics by simple inspection of the vendors' enzyme data sheet and specifications.

In addition many detergent manufacturers have their own internal methods, tuned to their own needs and enabling them to compare enzymes from different vendors. Enzyme activity is often expressed in arbitrary units, e.g. changes in absorbance, increase in reducing groups, amount of converted substrate expressed in milligrams or micromoles per unit of time.

Enzyme activity is measured relative to standard solutions prepared from an analytical standard of known activity. Conversion of activity into protein level is simple for mono-component enzyme product once the enzyme-protein content of the analytical standard - as well as activity - are known. For multi-component enzyme products the relationship between activity and enzyme protein content of a sample is not always easily established. Standard enzyme preparations for analytical purposes are available from enzyme vendors.

With regards to analysis of air monitor filters, it is essential to remember, that in order to document compliance to the DMEL, TLV or OEG, the activity units measured on the filters must be converted into enzyme protein content.

10.3. Filter Analysing from Air Sampling

10.3.1. General Aspects and Requirements

Airborne enzyme is normally collected on glass fibre filters (Whatman GF/C or Gelman) in high-volume samplers that samples 300-600 l/min (Newton Galley or equivalent). *It should be noted that glass fibre filters may not be appropriate for all enzyme types. Information on appropriate filters can be obtained via the enzyme supplier.*

Typically, sampling is carried out in pre-defined sampling locations over periods of 15 minutes to 4 hours on a shift to shift or a day to day basis, at random times. Shorter sampling periods are used when short duration 'peak exposures' are suspected, while longer periods are used to monitor average airborne concentrations. Sampling positions should be appropriate in a factory to monitor the highest exposure potential within a location.

The filters are sensitive to humidity and they must be handled with extreme care to prevent contamination. When not in use keep the filters in separate clean containers. To measure total inhalable dust, filters can be weighed before and after use. This enables the total dust levels to be assessed gravimetrically, while the enzyme dust collected can be analysed using activity or ELISA methods. Care must be taken not to contaminate the filters, written procedures on how to handle the filters should be in place. Analysis of the filters should be carried out as soon as practicable after sampling.
If not analysed immediately, the filter should be stored frozen until analysis. If the filter is to be send for analysis at another location, the filter should be transported frozen i.e. on dry ice.

The airborne enzyme concentration is calculated from enzyme on filter (ng protein or enzyme units)/ sampling rate (m^3/min.) x sampling time (min).

Method sensitivity should be sufficient to detect at least 10% of the OEG for each enzyme type. It should also be noted that reduced sampling periods require high sensitivity methods, as the amount of enzyme collected on the filter is significantly lower. Typically, ELISA methods have higher sensitivity, and are less susceptible to interferences, but require a higher level of expertise to perform and require specialised equipment.

Low volume samplers, 25 l/min, can be used instead of high volume samplers. Low volume samplers are especially well suited for monitoring of exposure at a specific process step or equipment. If using a sufficiently sensitive analytical method, the low volume sampler may also be used for short term (20 min) peak exposure measurements at a specific process step or equipment. The low volume sampler can be equipped with Teflon filters which give the enzyme higher stability when sampling in humid conditions.

Personal samplers are used to monitor an individual's average exposure. The duration of the personal sampling must be sufficient to cope with the limit of quantification of the applied analytical method, approx. 4-8 hours.

10.3.2. Validation of Monitoring Filter Pad Analysis

To properly assess the levels of airborne enzyme collected, experiments should be performed to validate the recovery efficiency of enzyme aerosols and dust from filter collection media in different sample matrices. This can be accomplished by performing a series of enzyme spiking experiments which investigate the following areas:

- Enzyme recovery efficiency with background matrix present
- Confirmation of background matrix response to a given assay substrate
- Stability of enzyme in background matrices

Note - Determining the overall effect that different background matrices have on enzyme levels from actual air collection pads is difficult to assess because the amounts and ratio of enzyme to background matrix collected is unknown. For further details and ideas on how to investigate these effects, it is recommended that you contact the supplier directly.

10.3.3. Enzyme Recovery Efficiency with Background Matrix Present

Aerosol (Liquid) Sample Preparations

It is recommended that all spike solutions be made in H_2O using a known concentration of background matrix and enzyme to most closely represent enzyme aerosols in a plant situation. All spike solutions should be spiked evenly to the selected filter media, as well as the respective elution buffer without filter media.

(NOTE - Background matrix concentrations should be representative of levels which are collected onto actual filter pads in a real plant situation).

Dust Spike Sample Preparations

It is recommended that a known amount of background matrix and ground enzyme be spiked (weighed) directly onto the selected filter media and the respective elution buffer without filter media.

(NOTE - when grinding enzyme granules be sure to follow safe handling procedures as recommended by the supplier).

Assaying Spike Preparations

Both aerosol (liquid) and dust spike preparations should be eluted in assay buffer and run according to the recommended procedure as outlined by the supplier.

Calculating Enzyme Recovery Efficiency

Compared to the nominal levels, the accuracy of spike solutions can be very low (<50%). Therefore, it is recommended that the level of enzymes used in determining enzyme recovery efficiency should be based on direct assay of the spikes in their associated matrix.

To determine enzyme recovery efficiency, the results of the samples prepared without filter pads should be used as the benchmark for expected activity at each concentration level. These results should be compared to the results of the samples prepared with filter pads to calculate a recovery percentage. Based on typical assay and sample preparation error, a recovery rate of 50% is usually acceptable but typically higher results are strived for.

Factors which typically influence recovery efficiency are:

- Enzyme stickiness to preparation materials and filter media
- Enzyme is inactivated by formulation matrix
- Enzyme is inactivated in a dilution of the formulation matrix
- The formulation interferes with the assay reaction
- A combination of the above factors

Problems with enzyme stickiness can be reduced or investigated by looking at other filter media alternatives or by pre-coating filter pads with various surfactants before use. Further experiments can also be performed to determine if the enzyme is being inactivated by formulation matrix or if the formulation matrix is interfering with the assay reaction (see below).

Once a recovery factor is obtained it should be incorporated into the calculation steps of the respective method followed for determination of airborne enzyme from air collection filters. *(NOTE - Typical enzyme recovery of dust samples is essentially 100% and therefore no recovery factor needs to be incorporated into the calculation step; however, enzyme recovery of aerosol samples can be quite low and the proper recovery factor obtained through performing the necessary spiking experiments should be incorporated into the calculation steps).* The enzyme supplier should be able to assist with recommended baseline recovery factors for a given enzyme and filter media. However, whenever there is any deviation from the recommended filter media or any change in the enzyme formulation/matrix, a revalidation of recovery efficiency should be performed.

10.3.4. Confirmation of Background Matrices Response to a Given Assay Substrate

Matrix blanks should be checked at known concentrations to determine a baseline response to a given substrate. Further, known enzyme spikes should be added to matrix blanks to check for interferences. Typical inactivation or interfering factors include: pH

change in dilution/assay buffer upon addition of the formulation sample, chemical inactivation of the enzyme in the formulation or a dilution of it, and chemical interference of the assay reaction.

Stability of Enzyme Background Matrices

The stability of the preparations made in a given formulation matrix should be assessed by reassaying at various time intervals to ensure no inactivation or interference problems.

10.4. Product and Enzyme Raw Material Analysis

10.4.1. Active Enzyme in Product and Enzyme Raw Materials

Sampling

Samples should be representative for the bulk material in order to obtain meaningful results.

Bulk materials which are not completely homogeneous, such as detergent powders, require a special method of sampling. A sample splitter which does not crush or grind particles should be used. The method starts from packed (e.g. 5 kg) samples which require further size reduction using a rotary sample splitter prior to the final sampling using an appropriate sample divider for production of the "analytical" sample. Smaller packs can be sampled by direct use of an appropriate sample divider.

Great care should be exercised to avoid inhalation of dust produced during sampling of enzyme-containing products. The sample divider should be placed in a fume cupboard or a suitable mask should be worn.

Analysis

Activity-based analysis is the preferred technique for the determination of the level of active enzymes in a product and enzyme raw materials. A high degree of method sensitivity is not essential as samples of this type usually contain a significant amount of enzymes. Methods should be robust and insensitive to interference by detergent ingredients. Enzyme levels are measured relative to standard solutions prepared from an analytical standard of known activity.

10.4.2. Methods to Assess Dustiness of Enzyme Raw Materials

The first step in a series of primary control measures towards the prevention of operator and consumer exposure to enzyme dust is the product design. Granular products are designed to encapsulate the enzyme protein under a protective coating to greatly reduce the formation of airborne enzyme dust. The technology of encapsulation has greatly improved over the years, resulting in encapsulates that are stronger, more resistant to abrasion, and which thus remain largely intact throughout the supply chain as long as the processing equipment does not significantly damage the raw material. Where poor quality material is used the equipment shear forces may result in unacceptably high dust levels.

There are currently two main methods used in the detergent industry to ensure that encapsulates meet a certain quality and thus comply with the requirements for the first step in primary control.

These are:

- **Vertical Elutriation Test**
- **Heubach Attrition Test**

Both tests are useful as tools to monitor production quality, or as material acceptance checks at receiving sites, though neither test is entirely predictive of raw material dustiness in actual use. The Elutriation test can be used to:

- Assure the quality of encapsulate received into our plants re 'free' enzymatic dust
- Assure likewise the quality of the finished product

The Heubach test can be used to:

- Assess the batch variation in strength or durability of encapsulates, and
- Predict how encapsulates may be affected by a given process

Enzyme suppliers should use an appropriate method to ensure that the encapsulates they supply are sufficiently robust to withstand the detergent manufacturing process. The dust specification will be dependent on the enzyme type and the test (either Heubach or Elutriation) used in product quality control. It is important to consult the enzyme supplier for the dust specification.

Each test will now be described briefly, without going into specific methodology or technical details.

10.4.2.1. Vertical Elutriation Test

Test Objective

To quantify the amount of free enzyme dust associated with supplies of enzyme encapsulates, or enzymatic powders.

Free enzyme dust presents a potential occupational exposure hazard when handling or discharging encapsulates, and when handling or packing the finished product.

Test Principle

A set quantity of encapsulate (60g) is placed in a flow of air under standard conditions for a period of 40 minutes, at an air velocity of 0.8m/s. The air flow through the bed of encapsulate is designed to move the granules around gently to remove dust, but not to cause severe abrasion by violent fluidisation. The equipment is designed such that the separation of particles classed as inhalable (<100um[5]) is achieved over this period.

Particles that are separated from the bulk sample are collected by filtration of the air stream. The filter can then be analysed gravimetrically for dust, and chemically for enzyme (by either activity or ELISA methods).

[5] American Conference of Governmental Industrial Hygienists (ACGIH) 1993. Threshold limit values for chemical substances and physical agents. ACGIH, Cincinnati, Ohio.
European Committee for Standardisation (CEN) 1993. Workplace atmospheres – Size fraction definitions for measurement of airborne particles. CEN Standard EN 481, Brussels.
Nieboer, E., Thomassen, Y., Chashchin, V., Odland, J.O. 2005. Occupational exposure assessment of metals. JEM 7: 411-415.

Repeatability

Typically, the cv of the Elutriation method is in the range of 20 – 30%. This may be a function of the relatively large sample size (60g) and the design of the elutriation chamber, which provides a steady laminar flow to effect a consistent separation of particle sizes.

10.4.2.2. Heubach Test

Test Objective

To ascertain the strength/durability of the enzyme encapsulates by subjecting them to a physical force and measuring the amount of dust generated as a result of this attrition.

The encapsulation of enzymes has already been described as the primary control measure. This test is used to quantify the resistance of the encapsulates to attrition/abrasion.

Test Principle

A sample of encapsulate (typically 20g) is placed in the Heubach equipment on top of a fine mesh platform. The sample chamber contains a series of four steel balls, which are rotated by means of a motor driven impeller. The steel balls subject encapsulates to physical force, whilst air is pumped through the mesh platform to fluidise away any dust that is created as a result of the abrasion process. In common with the elutriation test, the dust is filtered out of this air-stream for gravimetric and chemical analyses. The equipment can also be operated in Elutriation-only mode, where the steel balls are removed prior to addition of sample.

Repeatability

Typically, the cv for the Heubach test lies in the range of 30-50%, somewhat higher than the elutriation test.

10.5. Protein determination

There are many analytical techniques for establishing the amount of protein in a sample. Unfortunately, results will vary dependent on the method used. For reasons of harmonisation it is recommended to use the nitrogen content as a basis to calculate protein concentrations in enzyme reference materials for dust analysis or samples for setting enzyme dust limits. Nitrogen content can be measured either by Kjeldahl analysis or by Elemental analysis. Both methods have proven to be in mutual good agreement. Protein content is calculated by multiplying the nitrogen value with a factor 6.25. This factor is an accepted average when the exact protein mass to nitrogen ratio is not exactly known. Nitrogen response from non-protein components, like amino acids and ammonium salts, should be subtracted out, if these compounds and quantities can be verified.

Total nitrogen by Kjeldahl*:*

The sample is digested in sulphuric acid at elevated temperature with copper (II) sulphate acting as catalyst to produce ammonium sulphate. The ammonia is liberated by steam distillation under alkaline conditions and is collected in boric acid. Nitrogen content is then determined by titration with hydrochloric acid.

Total nitrogen by Elemental Analysis by Micro-Dumas Combustion:

The sample, enclosed in an ultra-pure tin combustion capsule is dropped into the top of a combustion tube which is held at 1200 degrees C and contains granulated chromium III oxide combustion catalyst. A pulse of pure oxygen is admitted to generate a flash combustion at 1700 degrees C. The resulting gas-phase combustion products are transported by helium carrier gas into a reduction column with fine copper at 600 degrees C to reduce all nitrogen oxides to nitrogen gas. Water vapour from the sample is removed by a gas trap. Nitrogen content is then determined by gas chromatography.

Samples for setting enzyme dust limits (standard batch samples) should be representative for the enzyme preparation as used in the enzyme raw material. Different ways are used by enzyme and detergent manufacturers to express protein content. This may be enzyme protein or total protein (including non-enzyme protein and lower molecular weight peptides). The latter expression is the more conservative one and takes into account that not all of the antigenic components may be known.

10.6. Reporting and Record-Keeping and Auditing

Any records pertaining to results from air monitoring for levels of enzymes should provide sufficient information to determine:-

- Calibration of equipment
- Raw and finished data
- Reports – (written and/or graphical)
- Staff training records

Records may be kept in any format but in all cases the information should be readily retrievable and in an easily understood form. It should be kept in such a way that the results can be compared with health records if required.

Records of monitoring should be available to employees and/or their representatives (dependant on country this may be a legal or voluntary requirement), and to inspectors appointed by a relevant enforcing authority or an employment medical advisor.

Depending on legislative requirements, or a company's own in-house practice, records should be archived in a manner that is readily retrievable. The retention period of records will normally be in strict conformance with legislative requirements (e.g. to match that of health surveillance records of employees).

Chapter 11 - Auditing Enzyme Operations

To ensure the effectiveness of the control measures taken to limit occupational exposure to enzymes, regular audits of the operation systems and equipment are necessary. Audits should cover engineering design and construction, operational systems and maintenance, health surveillance and analytical and management systems. This chapter describes an audit system based on system compliance. This should be supplemented with performance auditing which checks compliance by assessment of the results of the control measures (termed monitoring in this document). This includes the analysis of air monitoring data, behavioural observations, plant tours and interviews. These aspects of performance auditing are covered in detail in chapters 6 and 7.

Personnel trained and proven to be competent in both enzyme auditing techniques and operational systems should lead the audits. An effective audit programme should assess the systems periodically, typically at least every 12 months using internal or external resources. Competent plant personnel carry out internal audits, and competent personnel from outside the plant (though not necessary from another company) carry out external audits. A scoring system may be used to evaluate compliance (see Appendix 1 for an example) and there should be a follow-up procedure for action on the audit results. An example of an Auditing Process is provided in Appendix 2 of this chapter.

11.1. Engineering Design and Construction

This part of the audit should show that appropriate measures for engineering and equipment design are incorporated in the construction of enzyme facilities and operating systems to protect employees. The recommended standards for engineering design, ventilation, cleaning systems etc were described in detail in chapter 5. The purpose of the audit is to assess the plant against these standards.

Factors which need to be considered in designing an audit programme for design and construction are listed below.

- Managing Change
- Dust and Aerosol Control
- Technical Documentation
- Cleaning systems
- Base Powder Handling and Dosing Systems
- Enzyme Storage and Dosing
- Finished Product and Mixing
- Rework /Recycle (Making)
- Packing Equipment
- Online Rejects / Scrapping (Finished Product)
- Laboratory
- Finished Product Warehouse

11. 2. Operating Systems and Maintenance

The audit should also ensure that safe operating and equipment maintenance procedures are used for all enzyme systems, and that trained and competent personnel design, construct, operate and maintain the enzyme systems.

Listed below are factors which need to be considered in designing an audit programme for operating systems and maintenance.

- Monitoring and Maintenance
- Detecting and Ranking Peak Exposure Sources
- PPE/RPE
- Training
- Safe Systems of Work
- Health Surveillance
- Air monitoring programme

Chapter 11, Appendix 1: Audit Checklist

Engineering Design and Construct

Managing Change	**Score**
A system is in place and is documented to show that risks, design best practice for changes to equipment, raw materials and new installations have all been considered	
Dust and Aerosol Control	
There are dust control systems in place to an appropriate design that provide control and containment of sources of dust or aerosol. Fines recovery from these systems are fully enclosed to prevent exposure	
Technical Documentation	
There are flow diagrams showing orifice plates, baseline data, balance calculations, fan curve. Filter and exhaust system design calculations. Drawings of filter and fan with equipment specification. CVC system flow diagram, design calculations filter and exhauster sizing, equipment specification. There is an effective system in place to ensure that changes to the baseline are monitored and recorded	
Cleaning Systems	
Central vacuum cleaning (CVC) systems or portable vacuum cleaners (PVCs) are available for clean-up of spills and cover most areas routinely needing cleaning For Liquids: Clean-up methodologies include wet mopping, low pressure and temperature water wash down. All PVCs are fitted with HEPA filters	
Base Powder Handling Equipment	
Powder handling equipment is enclosed enough to prevent gross spillage. Conveyor openings and enclosures have containment velocity of 0.5m/s to 1m/s to prevent exposure to dust outside equipment	
Enzyme Storage and Addition	
There is a designated area for storage and addition systems. Addition rooms are ventilated and under negative pressure. Enzyme bag addition systems and bins are under negative pressure with containment velocity at the bag opening Surge bins are fully enclosed and vented, dusty air disposed to DC. Enzyme addition conveyors and weighing equipment are fully enclosed and leak free For Liquids: Isolated unloading/addition room under negative pressure as powders area is bunded all pumps and transfer lines are leak free design	
Finished Product and Mixing	
Conveyors are leak free and have 1m/s containment velocity at openings. Mix drum is fully tight and has 1m/s containment at openings .Powder transporters are leak free and loaded under dust control hood For Liquids batch tanks/day tanks are vented outside above the breathing zone. Transfer pumps have leak free mechanical seals with isolation valves and lines are leak free with welded joints preferred to flanges	

Rework and Recycle (Making)	Score
Systems for rework, recycle, and re-blend filter fines and process waste are enclosed enough to prevent gross spillage. Minimum operator intervention for transferring wet or dry scrap For liquids: the method for handling scrap product produces no spills or aerosol generation. Scrap containers are clearly marked and spill free	
Packing Equipment	
Packing equipment is fully enclosed to prevent spillage. Conveyors and hoods have negative pressure to achieve dust containment at openings. Belt and roller conveyors for cartons, cases and bottles have spill trays to contain spills. Dosing and filling equipment is under negative pressure for containment at openings For Liquids: Filler head is under negative pressure spills are contained within filler. Spill trays/pans contain minor spills on conveyors and belts. All filler header tanks are ventilated to the outside above the breathing zone	
Rejects and Scrap	
Packing scrap, rejects, quality check and powder recovery systems are enclosed to prevent gross spillage and are under negative pressure.1m/s containment at openings For Liquids: Recovery is done under negative pressure conditions in dedicated area or room	
Laboratory	
There is a dedicated enzyme analytical work area. Operations with raw enzyme or enzyme containing finish products are done in a fume cupboard or ventilated enclosure with 1m/s containment velocity. CVC, PVCs are available for spills	
Warehouse Equipment	
Conveyors do not damage the product and have spill trays. There is spill control equipment available i.e. vacuum cleaners and absorbent mats. Overhead conveyors have spill trays to prevent spills below	

Operational Systems and Maintenance

Compliance	**Score**
There is an effective system to identify sources of dust and spills and data for > 12 months show that effective action has been taken to eliminate basic cause if exposure prompt action is taken to improve equipment and control when necessary There are >12 months data from monitoring systems to show compliance with the OEGs housekeeping standards, spill elimination programme and behavioural observation system (BOS)	
Monitoring and Maintenance	
There is an effective system for maintaining and monitoring dust control systems, >12 months data shows that systems are in control. A maintenance program exists and repairs are carried out promptly Condition of clean up equipment is monitored and maintained (CVS and PVC) Are housekeeping practices (use of containment and clean up equipment acceptable?	

PPE	
Personal Protective Equipment (PPE) is available and maintained Areas to use PPE are displayed in the plant	
Training	
There are qualified hygiene engineering resources in place. There are qualified enzyme program leaders in place. Employees and contractors are knowledgeable about potential health effects, control measures and responsibilities. Training and re-qualification take place on 12 monthly basis at a minimum for employees and contractors	
Safe System of Work	
There are written operating procedures in place for enzyme materials and product maintenance and cleaning	
Air Sampling	
There is an air-sampling programme and samples are collected according to requirements. All areas are within control limits There is an effective system to track, communicate and follow up on air sampling results	
Plant Tours	
There is documentation to show that actions are taken when exposures occur Did the plant tour verify there were no raw enzyme materials or finish product spills from handling equipment? Are all the air sampling locations within the control limits?	
Medical	
There is a health monitoring programme for all employees exposed to enzyme operations Health checks are carried out at least every 12 months	

Chapter 11, Appendix 2: Guidelines for Audit Rating

0	Nothing has been done
2	Some attempt has been made but no effective implementation Shows some effort/focus in the past but activity is not evident at present Major system deficiencies which need to be addressed
4	Unreliable and unsatisfactory systems, much room for improvement A system exists and results tracked but it is not widely understood or communicated No system owner exists
6	Systems are partially implemented System owner identified Systems being able to deliver results but not sustained over previous 6 months
8	Implemented and effective Systems delivering solid results and have been sustained over the past 6 months There are no major outages
10	Sustained long term results with full system and results documentation Unlikely to be any system improvements identified Model system is approaching excellence

Glossary

Glossary	
Amylase	Enzyme which acts on starch
Antibodies	Molecules which mediate an immune response following induction by an antigen
Atopics	People who show symptoms in response to a variety of common antigens
Brush conveyor	
Cam-lock	Quick operating hose or piping connectors with a shaped nozzle on one side that fits into a matching cap on the other. Levers on the sides of the cap operate mechanical cams to lock the nozzle into the sealing surface inside the cap
Capability ratio	A measure of the deviation of an airborne enzyme level from the OEG, which takes account of the variability in sequential measurements (see 7.2.4)
Cellulase	Enzyme which acts on cellulose
Central vacuum cleaning system	High vacuum cleaning system with central filter and multiple tubing branches serving use zones with many hose connections throughout the process area (see section 5.14 for details)
Dense phase vacuum transfer/pneumatic conveying	Conveying design which uses a high ratio of solids to conveying air and low air velocity in the pipe to transport granulated materials in a way that minimizes particle break up. Conveying can be done over short distances under vacuum or over longer distances with positive pressure
Detergent matrix effects	The greater antigenic potential of enzymes when administered in the presence of detergent formulation
Disc conveyors	Pipe shaped conveyor which moves solids through the pipe by the action of a series of discs connected by a cable. The movement of the discs by the cable sweeps a discrete amount of powder through the pipe.
Dilute phase pneumatic conveying	See lean phase pneumatic conveying
Drag conveyor	A series of metal or plastic sweeps, connected on both ends to chains driven from the head of the conveyor housing. The sweeps are dragged along the bottom of the housing which moves powder to the drop point at the end of the housing.
Drum pumps	A pipe shaped pump, driven by air, that can be inserted into the bung opening on a drum to empty it
Dry-break coupling	A two part coupling which can only be disconnected when both halves are in a sealed condition
Elemental analysis	A method to determine total nitrogen using a combustion technique (section 10.6)
Elutriation test	A test based on determination of the initial dustiness of the raw material
Epitopes	Part of a protein molecule which is responsible for an antigenic response
Kjeldahl analysis	A method to analyse total protein by determining the nitrogen content (section 10.6)

Lean-phase pneumatic conveying	Conveying design which uses a low ratio of solids to air to move granulated materials through a pipeline. Because of the higher air velocities, these are not used to transport fragile materials. Materials can be moved short distances under vacuum and long distances under positive pressure.
Lipase	Enzyme which acts on lipids
Manway	Opening in a tank or pressure vessel large enough to allow a person to enter the equipment. Also known as access ways.
Orinasal masks	Masks covering nose and mouth
Potentiation	An increased immunological response to an enzyme as a result of the simultaneous exposure to another enzyme
Protease	Enzyme which acts on protein
Proteolytic	Able to break down proteins
Rhinitis	Hay-fever (runny nose and itchy eyes)
Screw conveyors	Shaft wrapped with a helical shape of metal (or flights) that rotates in a rounded housing. The close clearance of the rotating flights with the housing wall results in a linear motion which pushes granulated materials the length of the housing
Sensitivity	Frequency with which a test is able to predict positive responses out of all true positive responses
Sensitisation	The induction of antigen specific IgE antibodies
Single diaphragm pumps	A rubber or other flexible membrane is pushed by air pressure into a curved housing to displace liquid from the housing into the connected piping system. Check valves are needed at the entry and exit of the pump housing to prevent backflow.
Specificity	Frequency with which a test is able to predict negative responses out of all true negative responses
Spirometry	Measurement of lung function
Subtilisin	A protease derived from Bacillus subtilis or closely related species
Vibratory feeds	A horizontal pan with an induced external vibration that moves granulated materials horizontally in a gentle motion to avoid granulate break up