

Industry Guidelines on the Safe Handling of Enzymes in the Textile Industry Supply Chain

Part I: Textile Chemical Formulating Industry





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List of Abbreviations

ACGIH:	American Conference of Governmental Industrial Hygienists
ADR:	European Agreement concerning the International Carriage of Dangerous Goods by Road (<u>A</u> ccord Européen Relatif au Transport International des Marchandises <u>D</u> angereuses par <u>R</u> oute)
aep:	active enzyme protein
AISE:	International Association for Soaps, Detergents and Maintenance Products (<u>A</u> ssociation <u>I</u> nternationale de l'industrie du <u>S</u> avon, des Détergents et des Produits d' <u>E</u> ntretien)
AMFEP:	Association of Manufacturers and Formulators of Enzyme Products
APF:	Assigned Protection Factor
CAD:	Chemical Agent Directive
CLP:	Classification, Labelling and Packaging (Regulation)
CSR:	Chemical Safety Report
DMEL:	Derived Minimal Effect Level
ECHA:	European Chemicals Agency
ELISA:	Enzyme-linked immunosorbent assay
ERC:	Enzyme REACH Consortium
ES:	Exposure Scenario(s)
eSDS:	extended SDS
EU:	European Union
FEV1:	Forced Expiratory Volume in one second
FVC:	Forced Vital Capacity
GES:	Generic Exposure Scenarios
GHS:	Globally Harmonised System
HEPA:	High Efficiency Particulate Air Filters
HRA:	Health Risk Assessment
HSE:	Health and Safety Executive
IBC:	Intermediate Bulk Containers
IUBMB:	International Union of Biochemistry and Molecular Biology (Enzyme Nomenclature Committee)
LEV:	Local Exhaust Ventilation

MAK:	German Occupational Exposure Limit (<u>M</u> aximale <u>A</u> rbeitsplatz <u>K</u> onzentration)
MS:	Member States
NIOSH:	The National Institute for Occupational Safety and Health
OC:	Operational Condition
OEL:	Occupational Exposure Limits
PEFR:	Peak Expiratory Flow Rate
PPE:	Personal Protective Equipment
RAST:	Radioallergosorbent Test
REACH:	Registration, Evaluation, Authorisation and Restriction of Chemicals (Regulation)
RMM:	Risk Management Measure
RPE:	Respiratory Protective Equipment
SDS:	Safety Data Sheet
SDIA:	Soap and Detergent Industry Association (UK)
SOP:	Standard Operating Procedure
STEL:	Short Term Exposure Limit
TCF:	Textile Chemical Formulator
TEGEWA:	Association of Manufacturers of Process and Performance Chemicals
TLV:	Threshold Limit Value
TWA:	Time-Weighted Average
ULPA:	Ultra-low Particulate Air Filters

Foreword

For decades, enzymes have been widely used in the textile industry supply chain due to their unique properties that facilitate the production of high-quality textile products and, at the same time, significantly improve the ecological footprint of the produced products.

Enzymes are proteins and, like other proteins, may act as respiratory sensitisers if individuals are repeatedly exposed to airborne dust or aerosols that contains them. Such sensitisation may ultimately lead to respiratory allergy, but it is important to note that not all individuals who become sensitised to enzymes develop allergy symptoms.

The risk of becoming sensitised at the workplace can, however, be effectively minimized by implementing risk management measures that aim to prevent the generation of airborne dust or aerosol. Risk management measures such as comprehensive process controls, smart product formulations, and functional handling instructions have all been shown to effectively protect the health of workers.

The Association of Manufacturers & Formulators of Enzyme Products (AMFEP), and the Association of Manufacturers of Process and Performance Chemicals (TEGEWA) have jointly developed this guidance document for the safe handling of enzymes in the textile chemical formulating industry; thereby providing the insight and tools to help safeguard the health of the workers in this industry. It should be emphasized that this guidance document covers the occupational conditions of the workers, end users are not in scope of this document.

This guidance document describes:

- Health hazards associated with enzymes
- Current regulatory framework concerning the use of enzymes in the textile chemical formulating industry
- Management procedures required to ensure adequate controls and staff training
- Process and equipment design to minimize and maintain low exposure levels, including recommended work practices
- Air monitoring procedures to assess enzyme exposure levels
- Recommendations on health surveillance

Note: The various chapters have different target groups, hence, it is not necessary to read through all the chapters to find the content relevant to a specific area of interest. If relevant there will be references made from one chapter to another.

The reader should keep in mind that this guidance document solely focuses on how to reduce airborne exposure to enzymes and, thus, how to avoid respiratory sensitisation at the workplace. However, workers may be exposed to other hazards at the workplace, too. To protect the health and safety of workers, a thorough health risk assessment (HRA) is generally necessary for each workplace that addresses all hazards present at this workplace. Such an HRA may also need to include other hazards associated with (some) enzymes that are not addressed in detail in this guidance document, such as skin irritation.

This guidance document reflects the state of technology and scientific understanding of controlling exposure to enzymes at the time of writing (2021). Therefore, the approaches described will be subject to changes as technical advances and scientific understanding improves.

Furthermore, only the control of enzyme exposure within the European textile chemical formulating industry has been addressed here. Although the general principles and recommendations are widely applicable, some of the guidance given may not be applicable to production sites in other parts of the world. Production plants outside of Europe must check if some elements in this guidance document are missing and/or in line with local regulation before implementing the guidance given.

Similar guidance documents on the safe handling of enzyme products are also available for the textile finishing and garment finishing industry¹, the detergent industry², the baking industry³ and the pulp and paper industry⁴.

¹ AMFEP & EURATEX (2022) Industry Guidelines on the Safe Handling of Enzymes in the Textile Industry Supply Chain - Part II: Textile Finishing & Garment Finishing Industry

<https://amfep.org/publications/amfepeuratex-industry-guidelines-part-ii-textile-finishing-garment-finishing-industry/>

² AISE: Safe Handling of Enzymes (Guideline, training materials, webinars):

<https://www.aise.eu/our-activities/standards-and-industry-guidelines/safe-handling-of-enzymes>

³ AMFEP & FEDIMA (2018): Industry Guidelines On the Safe Handling of Enzymes in the Bakery Supply Chain:

https://amfep.org/library/files/Industry_Guidelines_on_the_Safe_Handling_of_Enzymes_in_the_Bakery_Supply_Chain_-_MARCH_2018.pdf

⁴ AMFEP & CEPI (2019) Industry Guidelines on the Safe Handling of Enzymes in Pulp & Paper Manufacturing:

<https://amfep.org/publications/amfep-cepi-industry-guidelines-on-the-safe-handling-of-enzymes-in-pulp-paper-manufacturing/>

1. Introduction

The use of enzymes in the textile value chain (Figure 1) is gaining global recognition because of their eco-friendly characteristics. The enzyme technology is attractive because enzymes are highly specific and efficient, and work under mild conditions. Furthermore, the use of enzymes results in reduced process times, energy and water savings and improved product quality.

Generally, enzymes do not possess any health-related adverse effects except for the fact that they can induce respiratory allergy. Therefore, a two-part guidance document series was developed on safe handling of enzymes in the textile value chain, i.e. how to avoid the formation of airborne dust and aerosols, which if inhaled in sufficiently high amounts can lead to respiratory allergy. This issue of the guidance document series focuses on the textile chemical formulating industry (TCF) (Figure 1).

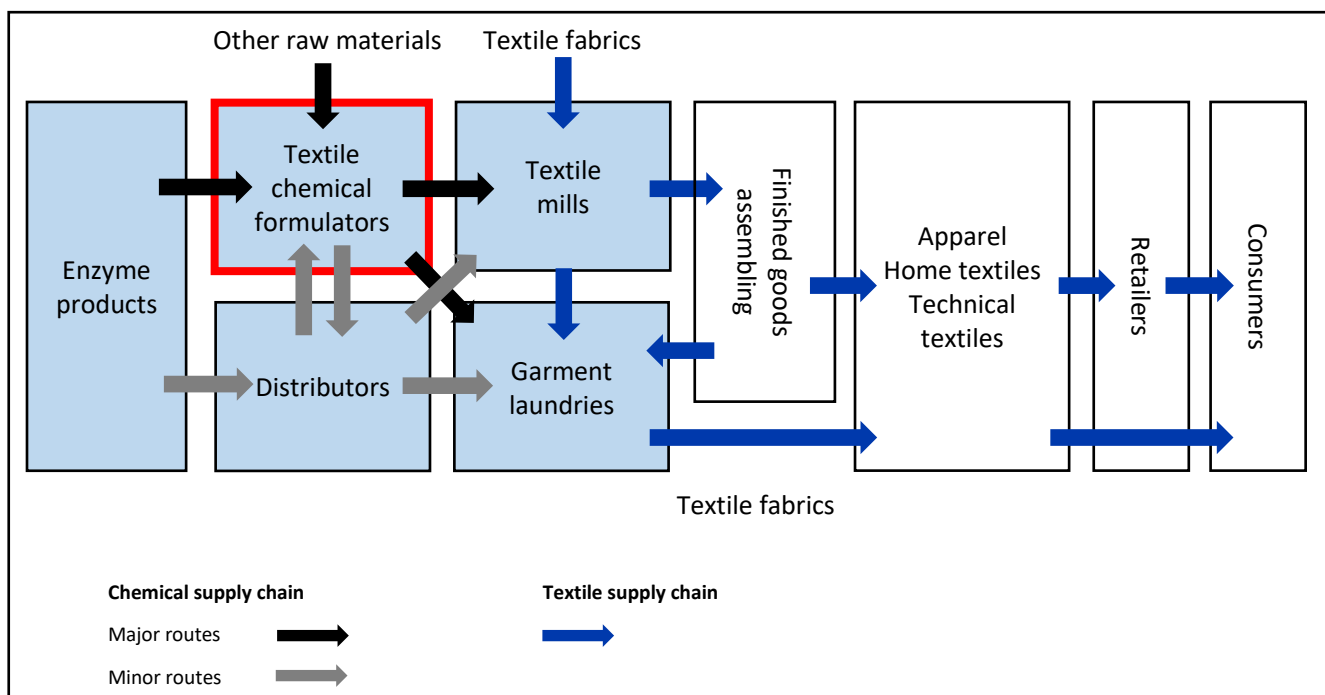


Figure 1: General enzyme value chain in the textile market. The framed red box marks the sector addressed in this guidance. Boxes coloured in blue represent sectors where enzymes are physically present.

In general, liquid enzyme products or encapsulated low dust granulated enzyme products⁵ are used in this industry, products which are received, delivered within and into sealed systems. The use of open circuits or the use of solid enzyme products which are not encapsulated are not

⁵ Exposure is controlled by encapsulation of active enzyme into granules. Granules used in technical application shall fulfil certain quality specifications so that during typically tasks, such as transfers, the encapsulation layer does not damage.

considered best practice and are thus not covered in this guidance document. Solid enzyme products which are not encapsulated, e.g. powdered enzyme products will even in low quantities generate high levels of dust, and during handling of such powdered products it will be extremely difficult to keep compliance to the occupational exposure limits (OELs) or the derived minimal effect level (DMEL).

The consequences of uncontrolled exposure to enzyme airborne dust or aerosols are well known, and the section below introduces enzymes and their benefits in the textile industry supply chain as well as the potential hazards associated with the handling of enzyme products. However, it is important to emphasize that when handled according to instructions and in well controlled industrial settings enzyme products can be used safely.

Enzymes are used in the textile industry due to their valuable and very specific properties; but what are they?

Enzymes form a special class of proteins being composed of the amino acid building blocks that are found in all types of proteins. Proteins are naturally produced by all living cells, and all living organisms – whether human, animal, plant or microorganisms – need enzymes to conduct virtually all the physiological processes which are essential for growth and life.

Enzymes act as catalysts: substances which, in very small amounts, are able to significantly speed up the rate of specific chemical reactions by significantly reducing the activation energy of the reaction; for example, the building up or breaking down of organic matter such as carbohydrates, fats and other proteins. Enzymes are highly specialized in their functionality; with each enzyme acting only on a restricted number of substances, and only catalysing one specific reaction. For example, the starch degrading enzymes (amylases), present in human saliva break down starch into smaller molecules; which can then be degraded and absorbed when entering the gastrointestinal tract.

This specificity of enzymes makes them very useful in catalysing desired reactions in industrial processes. Consequently, enzymes are extensively used in several industries including in technical (e.g. detergent, starch, textile, pulp & paper and fuel alcohol), food (e.g. dairy, baking, brewing, wine and juice) and in animal feed arenas. Commercial enzyme preparations are produced by the carefully controlled fermentation of pure cultures of selected strains of non-pathogenic bacteria, yeasts or fungi.

Enzymes are grouped into several classes according to their activity: some of the most important classes to the textile supply chain and their contribution to manufacturing and finished product quality are mentioned in Table 1.

Table 1: Examples of Enzyme classes and corresponding functionalities in the textile industry supply chain.

Application	Process	Enzyme Benefit	Enzyme classes
Pectin and protein removal (bio-scouring)	Textile pre-treatment / washing units	Saving energy, chemical use (e.g. caustic soda (NaOH) in cotton processes or chlorine in wool processes) water and time; less wastewater; gentle treatment of the woven fabrics and knit goods.	Pectinases & Lipases in some cases (vegetable fibres) Proteases (wool, silk) Xylanase (linen, jute, hemp)
Degradation of excess hydrogen peroxide	Textile pre-treatment and dyeing	Avoidance of hazardous chemicals like sulfur based reducing agents, saving of 1 or 2 wash cycles, saving of energy, water and time, reducing wastewater or loading.	Catalases
Starch removal	De-sizing	Avoidance of hazardous chemicals; gentle treatment of the woven fabrics.	Amylases
Carboxy methyl cellulose (CMC) size removal	De-sizing	Avoidance of hazardous chemicals like acids or persulfates; gentle treatment of the woven fabrics.	Amylases Cellulases
Denim finishing	Garment finishing	Increasing reliability of the process, improving product quality, reducing the handling of stones and sludge generation, decreasing machine wear, sandblasting.	Cellulases
Bleaching of indigo dyed garment articles	Garment finishing	Avoidance of hazardous chemicals like various chlorinated compounds, gentle treatment of the woven fabrics, less polluting garment wash.	Laccases
Pilling reduction, surface cleaning and antifelting finishing	Textile & garment finishing	Avoidance of hazardous chemicals; additional quality treatment and softer handle effect.	Cellulases; Proteases
Post-textile treatment process: Decolorization of textile effluents and textile bleaching	Wastewater treatment plants	Avoidance of hazardous chemicals.	Laccases

For all enzyme classes the same principles apply regarding the safe handling of enzyme-containing materials used in the textile chemical formulating industry.

Hazards associated with enzymes

Industrial enzymes have a low toxicity to humans; i.e. enzymes present no concern for endpoints like acute toxicity, genotoxicity, sub-acute and repeated dose toxicity, reproductive toxicity and carcinogenicity (1)(2)(3). However, like many other proteins, enzymes may act as allergens via inhalation. A two-step process must take place for the development of an inhalation allergy: initial sensitisation followed by elicitation (3).

Sensitisation: When allergens are inhaled in the form of dust or aerosols, they may give rise to the formation of antibodies that are specific only to them. At this stage, the sensitised individuals do not suffer from any allergic symptoms.

Elicitation: Sensitised individuals may then develop an allergy, if they are repeatedly exposed to sufficiently high airborne concentrations of the allergen concerned (4). At this stage, the individual will develop the symptoms typical for respiratory allergy such as hay fever. Some individuals may develop asthma upon continued exposure. When this condition is due to exposure in the working environment, it is called occupational allergy.

The respiratory symptoms from allergen exposure may include itching of the nose and eyes, nasal and sinus congestion and sneezing. Coughing, hoarseness, tightness of the chest and shortness of breath are all indicators of asthma. These symptoms may occur during or after working hours and they disappear within hours or a few days after the exposure has ceased. Allergy symptoms may be similar to those of the common cold, and if such symptoms occur frequently at the workplace and only rarely at weekends or during holidays, they may be the result of occupational enzyme exposure.

Allergy by inhalation caused by enzymes is similar to the respiratory allergies that are caused by well-known allergens like grass-pollen, house dust mites or cat dander; and the symptoms are similar. Some individuals are more prone to sensitisation than others are. Atopic individuals, i.e. persons already allergic to one or more of the common allergens, may develop an enzyme allergy more easily than others may. Not all atopic individuals will become allergic to enzymes and non-atopic individuals may develop an enzyme allergy if exposed to sufficiently high airborne concentrations on a regular basis.

Smokers have a markedly increased risk of becoming sensitised and developing allergy symptoms (5). There is no scientific evidence that enzymes are associated with allergy caused by skin contact or ingestion (6)(7).

In general, controlling enzyme exposure in the textile chemical formulating industry will reduce the likelihood of work-related respiratory symptoms. Enzyme handling activities that may generate airborne dust or aerosols should be prevented to minimize the risk of exposures. This subject will be addressed in the following chapters of this document.

Experience from over 50 years of handling enzyme products in the enzymes manufacturing industry as well as in the detergent industry has proven that enzymes can be safely used in the workplace (8)(9). This valuable experience and knowledge are now being applied to the textile chemical formulating industry to make it an even safer place in which to work.

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2. Regulatory requirements for Enzymes used by the Textile Chemical Formulating industry in the EU

Ensuring workers' safety is a regulatory obligation for both enzyme suppliers and enzyme users in the textile chemical formulating industry (TCFs). Safety information on the use of enzymes must be communicated by the enzyme suppliers and the appropriate risk management measures (RMMs) and operational conditions (OCs) must be implemented by the TCFs.

Exposure limits

Due to the risk of respiratory allergy, exposure to airborne enzyme dust or aerosols needs to be in control in the working environment. Two types of exposure limits are applied for enzymes used by TCFs:

- Occupational exposure limits (OEL)

An occupational exposure limit of 60 ng/m³ has been established for those enzyme products which belong to the protease class of Subtilisin. This OEL has been adopted as a regulatory exposure limit in many countries.

For details, please see **Appendix 2**, D of this Chapter.

- Derived Minimal Effect Level (DMEL)

For all enzyme products a DMEL of 60 ng/m³ is now being used within EU in REACH registration dossiers. This means that airborne exposure to all enzyme products should be kept below this limit in occupational settings of TCFs.

For details, please see **Appendix 1**, A and C of this Chapter.

Safety communication from enzyme suppliers to the Textile Chemical Formulating industry (TCFs)

- Safety Data Sheet (SDS) and Exposure Scenarios (ES)

Enzyme suppliers must communicate safe use information via the SDS under REACH. All applicable exposure limits should be stated in the SDS (OELs and DMELs). Most enzymes used by the TCFs are to date registered under REACH. Thus, for substances that are marketed above 10 tons per year in the EU, the producer must make an extended SDS (eSDS) with ESs available.

ESs provide essential information on RMMs and OCs required to control enzyme exposure to humans and releases to the environment. ES information can be appended, integrated or attached on the SDS (check for an indication in the SDS Section 1.2, 8, 11 & 12 or for any attachments after Section 16).

For details, please see **Appendix 1**, A of this Chapter.

- Labels

Enzymes may possess respiratory sensitisation potential regardless of the type of catalytic activity. Therefore, it is recommended classifying all enzymes as Respiratory Sensitiser Category 1 (H334): *May cause allergy or asthma symptoms or breathing difficulties if inhaled* in accordance with the CLP Regulation. Enzyme containing mixtures must bear labels with hazard classification so that workers are aware of the warnings. If an enzyme protein is above a certain level ($\geq 0,1\%$), a label should clearly indicate that the mixture contains enzymes as respiratory sensitiser(s). Additional pictogram and hazard/ precautionary statement is needed at higher concentration ($\geq 1\%$).

For details, please see **Appendix 1, B** of this Chapter.

Implementation of safety measures by the Textile Chemical Formulating industry (TCFs)

- Basic requirements for employers

TCFs have the obligation to implement RMMs and OCs aiming to protect the health of the workers. They must collect information, not only from SDS or labels discussed in the above section, but also from other resources, such as from this guidance document, and ensure that RMMs and OCs are in place that ensure the safe use of enzymes. This requirement is set under the Council Directive 98/24/EC⁶, commonly known as the Chemical Agent Directive (CAD).

For more details, please see **Appendix 1, C** of this Chapter.

- Exposure Scenarios (ES)

Once an ES in the eSDS is supplied to the TCFs, they have 12 months to implement necessary measures per downstream users' obligation under REACH. If it is not possible to do so, they have several options for compliance, such as carrying out a downstream user assessment. However, it is recommended as a first step to contact the enzyme supplier to discuss possible solutions. The enzyme manufactures have a long history of working together with their customers to ensure the safe use of their products along the complete supply chain and welcome any initiative that improves the safety of workers handling enzyme products.

The following appendices provide detailed information on the topics addressed earlier in this Chapter.

⁶ Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC).

Appendix 1: Main regulatory requirements in the EU

A EU REACH

Obligations of Registrants under REACH

Enzyme substances included in products destined for technical applications such as detergents, textile processing, biofuels, pulp & paper processing etc., need to be registered under the EU REACH Regulation⁷ before they can be manufactured and/or imported into the EU in a volume above 1 ton per year. It lies with the manufacturers/importers to register the substance under REACH and provide evidence that the substance can be used safely in all registered uses and along the complete supply chain. The European Chemicals Agency (ECHA) is the implementing authority on an EU level and supervises the registration process.

Activities regarding REACH implementation for enzymes are discussed and facilitated within the Enzymes REACH Consortium (ERC) created by AMFEP. Since the third and final registration deadline of May 2018, most enzymes have been registered following the guidance documents developed by the ERC.⁸

If an enzyme is in the scope of REACH registration and has been registered in tonnages >10 tons per year, then its registration dossier includes a Chemical Safety Assessment (CSA). The CSA consists of:

- Generic Exposure Scenarios (GES)
- Exposure estimation for the different routes of exposure under the conditions of use described in the GESs
- Risk characterisation; comparison of exposure levels to no or minimum effect levels

GESs have been developed based on the knowledge available to the enzyme manufacturers about the different market sectors in which their products are used. Each GES defines the RMMs and OCs required to control enzyme exposure to humans and releases to the environment for one market sector. As the available computational tools for occupational exposure are not functional for respiratory sensitisers with very low limit values, measurements of airborne enzyme (active enzyme protein) at the respective workplaces are required for the exposure assessment.

In the case of enzymes, a DMEL of 60 ng/m³ for occupational exposure has been proposed and is now being used in EU REACH dossiers for all enzymes. This DMEL has been established following a thorough retrospective review of occupational experience, correlating validated employee medical surveillance data against exposure records generated over an extended

⁷ Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC

⁸ Enzymes REACH Consortium, <http://www.enzymes-reach.org/content/welcome-enzymes-reach-consortium>

period (1).

Obligations of Downstream Users under REACH⁹

The main obligation of downstream users under REACH is to comply with the information provided in the eSDS of the enzyme manufacturers. This includes information provided in the main body of the SDS, and OCs and RMMs defined in the ES, which are typically listed in the SDS Annex. ES may be missing if 1) the single substance or all substances in a mixture are produced/imported below 10 tons per year or 2) the formulator of a mixture decided to consolidate the safe use information of the different ingredients in the main body of the safety data sheet. If an end-user does receive a consolidated SDS for mixtures, it is legally possible to request the specific ES of each ingredient from the formulator.

It shall be noted that the main body of the SDS is considered a guidance document. Downstream users of enzymes, such as the textile chemical formulating industry, are, however, legally required to comply with the OCs and RMMs listed in the respective ES. The OCs and RMMs have been defined by the enzyme manufacturer in their ES to ensure safe use of enzymes (i.e. to keep exposure below the DMEL of 60 ng/m³). If downstream users cannot comply or are unsure if they can comply with the OCs and RMMs laid out in the eSDS, then they are required to reach out to the enzyme manufacturers and jointly work on assessing the workplace in question and – if necessary – refine the respective ES. The enzyme manufacturers have a long history of working together with their customers to ensure the safe use of their products along the complete supply chain and welcome any initiative that improves the safety of workers handling enzyme products.

Alternatively, downstream users can also carry out a “downstream user chemical safety assessment” and notify ECHA about this assessment.

Downstream users may be audited by National Inspectorates that have been identified by the national Member States (MS)¹⁰. These authorities have the authority to check if users of enzyme containing products comply with their obligations under REACH.

It is important to note that downstream users are not directly required to assess compliance with the DMEL under REACH. They are solely required to comply with the OCs and RMMs that have been defined in the eSDS and to support manufacturers to define functional exposure scenarios that allow the safe use of the enzyme products. Legally binding exposure limits are solely national OELs, which are discussed further down below.

⁹ European Chemicals Agency (ECHA), “Downstream users”, <https://echa.europa.eu/regulations/reach/downstream-users>

¹⁰ European Chemicals Agency (ECHA), “National Inspectorates”, <https://echa.europa.eu/regulations/enforcement/national-inspectorates>

B CLP classification of enzymes and enzyme mixtures

The EU Regulation for “Classification, Labelling and Packaging” (commonly known as CLP Regulation)¹¹ adopts the United Nations’ Globally Harmonised System on the classification and labelling of chemicals (GHS) across all European Union countries. The regulation requires companies to appropriately classify, label and package their substances and mixtures before placing them on the market. Since 1 June 2015, it is the only legislation in force in the EU for classification and labelling of substances and mixtures.

Enzymes may possess respiratory sensitisation potential regardless of the type of catalytic activity. Therefore, it is recommended classifying all enzymes as Respiratory Sensitiser Category 1 (H334) in accordance with the CLP Regulation, unless there is scientific evidence from e.g. immunochemical/immunological testing that they do not induce a specific response. CLP Annex VI currently includes harmonised classifications for 17 enzymes.

All these 17 enzymes are classified and labelled as Respiratory Sensitiser Category 1 (H334): *May cause allergy or asthma symptoms or breathing difficulties if inhaled*. In addition to the Respiratory Sensitiser Category 1 classification, proteases in Annex VI have additional harmonised classifications, namely STOT Single Exposure Category 3 (H335), Skin Irritation Category 2 (H315) and Eye Irritation Category 2 (H319) (except subtilisin, which is classified as Eye Damaging Category 1 (H318)). The REACH registration dossier for subtilisin includes additional self-classification as Acute Toxicity Category 4 (H302), Aquatic Acute 1 (H400) and Aquatic Chronic 2 (H411). These additional classifications are due to the proteolytic activity of proteases.

A mixture containing several enzymes must be classified as a respiratory sensitiser when at least one ingredient has been classified as such and is present at or above the appropriate generic concentration limits, unless enough data on the mixture itself indicating otherwise is available and bridging is not possible. Substances that are classified as sensitisers may elicit a response, when present in a mixture in quantities below the generic concentrations or specific concentration limits for classification and must thus be indicated on the label at the lower concentrations established in Table 3.4.6 of Annex I to CLP.

Thus, for an enzyme (solid or liquid) that is a Respiratory Sensitiser Category 1 in a mixture, the general threshold concentration is 1% for the classification of the mixture (Table 3.4.5 of Annex I to CLP), and 0.1% for the inclusion on the label of the supplementary statement EUH208 — ‘*Contains (name of sensitising substance). May produce an allergic reaction*’ (Table 3.4.6 of Annex I to CLP). The threshold is considered based on active enzyme protein.¹²

¹¹ Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353, 31.12.2008, p. 1).

¹² European Chemicals Agency (ECHA), Hazard classification of industrial enzymes, June 2016 <https://amfep.org/library/files/hazard-classification-of-industrial-enzymes.pdf>

C Worker's safety and obligations along the supply chain

The Chemical Agents Directive (CAD)¹³ lays out provisions aimed at the protection of workers whose work brings them into contact with hazardous chemical agents. Under CAD, a substance is regarded as hazardous if it meets the criteria for classification as hazardous within any physical and/or health hazard classes laid down in CLP Regulation. Since most enzymes are classified as Respiratory Sensitiser Category 1, they are in the scope of CAD. There are no specific provisions for enzymes as a generic class of substances in CAD therefore enzymes are subject to the general provisions of this directive.

Where hazardous chemical agents are present in the workplace, employers must determine whether any risks to safety and health arise from their presence. The employer must be in possession of an assessment of the risk and this risk assessment must be kept up-to-date. The employer must take the necessary preventive measures to eliminate or reduce to a minimum the risks identified in the risk assessment following a hierarchy of prevention measures (described in Article 6 of CAD). Where this is not possible, the following shall be considered in order of priority:

- I. design of appropriate work processes and engineering controls and use of adequate equipment and materials;
- II. application of collective protection measures at the source of the risk, such as adequate ventilation and appropriate organizational measures;
- III. where exposure cannot be prevented by other means, application of individual protection measures including personal protective equipment.

Directives are not implemented directly into national Member States (MS) legislation but set minimum standards which MS are required to reflect in corresponding national provisions. On this basis, employers operating within the EU that are fully complying with national workplace legislation should be managing the risks from enzyme and enzymes containing products according to these principles.

In addition, REACH Regulation¹⁴ requires demonstration of adequate control of risks for identified uses and exposure scenarios should be communicated to ensure implementation of risk managements throughout the supply chain. Enzyme manufacturers have developed GESs, containing information on the safe handling of enzyme products, which are communicated downstream via the eSDS. When downstream users receive an eSDS they must check that the GESs annexed to them cover their own use of the substance and their conditions of use or take alternative actions.

¹³ Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC)

¹⁴ Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC

D Occupational Exposure Limits

Several exposure limit values for enzymes have been derived by various groups and institutions. To understand their area of application, it is necessary to briefly explain two basic principles around exposure limit values:

First, the legal obligation: Generally, two types of exposure limit values exist. On the one hand, governmental (e.g. NIOSH, ECHA) and non-governmental (e.g. ACGIH) institutes and groups may derive exposure limit values for chemicals that aim to protect workers, but which are not legally binding and predominantly act as guidance for risk assessors¹⁵. On the other hand, regulatory agencies (e.g. MAK Commission, HSE) may set exposure limit values that are legally binding and must not be exceeded. This type of exposure limit values is typically referred to as OELs, although no proper definition does exist. The European Standard EN689:2018 may be used as a basis to determine compliance with OELs.

Second, the exposure duration: Limit values are typically defined for an exposure duration of 15-minutes (often referred to as short-term exposure limit (STEL)) and/or 8-hour, but occasionally also other durations are used as benchmark (e.g. for enzymes sometimes 60-minute limit values exist). This means that the time-weighted average (TWA) exposure over the defined period may not exceed the limit value. Additionally, for some few chemicals, including enzymes, a so-called ceiling limit value has been determined by some countries. Such ceiling limit values are set where it is necessary to avoid transient excursions above the identified limit. If a ceiling limit value has been defined, then the exposure duration is irrelevant, and the exposure may not exceed the ceiling limit value at any time.

Currently, OELs have been derived for the protease subtilisin and for fungal alpha-amylase (only in the Netherlands). In the early 1970's the American Conference of Governmental Industrial Hygienists (ACGIH) established a ceiling threshold limit value (TLV) of 60 ng/m³ for the protease subtilisin. The ACGIH recommended limit has been adopted into national workplace legislation in several countries, in many cases as a ceiling limit (see **Appendix 2**). Some countries have also derived full shift exposure and/or short-term exposure limits, which are partly lower than 60 ng/m³.

Although limits for other enzymes have not been established in national or EU-wide workplace legislation, the 60 ng/m³ level is used by companies manufacturing enzymes and formulating enzyme-containing products as a benchmark applicable to all enzymes for their health risk assessments and to identify tasks where workers may need to wear respiratory protective equipment (RPE) to supplement the engineering controls that are in place.

¹⁵ It shall be noted that several countries frequently use the recommended ACGIH values as basis to set their legally binding national OELs, such as Spain and Belgium. Additionally, the OELs recommended by ECHA (previously SCOEL) have often been included in the Annex of the Chemical Agents Directive or Carcinogens at Work Directive.

Appendix 2: Examples of Subtilisin (Protease) regulatory exposure limits.¹⁶

Country	8-hr TWA limit (ng/m ³)	Short-term limit (ng/m ³)	Ceiling limit value (ng/m ³)
Australia			60
Belgium	60		
Canada (Alberta, British Columbia, Manitoba, Ontario, Quebec)			60
China	15	30	
Colombia			60
Croatia	40		
Denmark	60		60
Finland	15		60
Iceland		60	
Indonesia			60
Ireland	60	60	
Israel			60
Italy			60
Malaysia			60
Mexico			60
New Zealand			60
Nicaragua			60
Norway			60
Peru			60
Portugal			60
Singapore		60	
South Africa			60
Spain		60	
Sweden	1 glycine unit/m ³		3 glycine unit/m ³
Switzerland		60	
USA-OSHA		60	
U.S. States (California, Tennessee)		60	
Uruguay			60
United Kingdom	40		
Venezuela	60		

¹⁶ Information obtained from the GESTIS International Limits Values database (accessed on 11 December 2020) <https://limitvalue.ifa.dguv.de/> . Some of the limits may be sector specific.

Appendix 3: Definitions and explanations

aep (active enzyme protein): enzyme protein which has a catalytic activity.

Annex VI of the CLP Regulation¹⁷: A list of substances with mandatory classifications – all other end points than those listed in the Annex are liable to self-classification.

Classification: The process of evaluating available test or other data on a substance or mixture to determine if the substance or mixture meets any of the criteria for assigning a class (type) and category (severity) of hazard to the substance or mixture. Description of relevant classifications:

Applicable to all enzyme classes:

- Resp. Sens. Cat 1: Respiratory sensitiser in category 1. CLP also includes additionally the possibility to subcategorise into 1A and 1B, however this is not possible for enzymes.

Applicable only to proteases due to their proteolytic activity:

- Acute Tox. Cat 4: Acute toxicity in category 4 (harmful). For Subtilisin the route of exposure is oral intake. The oral toxicity data behind subtilisin (1800 mg/kg) is used for classification of mixtures.
- Skin Irrit Cat 2: Skin irritation in category 2 (moderate skin irritation)
- Eye Dam. Cat 1: Eye damage in category 1 (severe and irreversible eye damage, Subtilisin only)
- Eye irrit Cat 2: Eye irritation in category 2 (serious, but reversible eye irritation)
- STOT SE 3: Specific target organ toxicity – single exposure in category 3. For proteases the relevant effect in this category is respiratory irritation.
- Aquatic Acute 1: Acute toxicity towards aquatic organisms in category 1 (short term environmental hazard). For classification of mixture it is also important to know that the “M-factor” is 1.
- Aquatic Chronic 2: Chronic toxicity towards aquatic organisms in category 2 (long term environmental hazard).

Enzyme: Enzyme concentrate as defined as “substance” by REACH including constituents from manufacturing processes but excluding solvent e.g. water. In this guidance, “enzyme” refers to this definition. enzyme mixture: A formulated product with an enzyme and other formulation ingredients.

Index No.: Number assigned to substances in CLP Regulation Annex VI.

¹⁷ REGULATION (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006
EUR-Lex - 32008R1272 - EN - EUR-Lex (europa.eu)

Immunochemically identity: If two enzyme proteins cross-react with the same antibody, they are immunochemically identical.

IUBMB name and number: Enzyme nomenclature defined by Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB)
<http://www.chem.qmul.ac.uk/iubmb/enzyme/>

References

- 1 Basketter DA, Broekhuizen C, Fieldsend M, Kirkwood S, Mascarenhas R, Maurer K, Pedersen C, Rodriguez C, Schiff HE: Defining occupational and consumer exposure limits for enzyme protein respiratory allergens under REACH. *Toxicology* 268 (2010) 165–170.

3. Management and Training

3.1. Management

In general, employers are always responsible for health and safety in workplaces. The health and safety laws apply to all businesses and those determine the basic precautions and responsibilities that applies to everyone. A significant part of this responsibility is **risk management** beginning with **hazard identification**. Every type of hazard which may be potentially harmful to employees must be identified, and suitable controls must be in place to mitigate those risks. The responsibility for providing a safe place to work is not only limited to employees but also includes other stakeholders such as contractors, cleaners, visitors and others who may be affected by their activities.

Even though management faces most of the responsibility for safe workplace provision, the participation of others should not be ignored. Full participation of all employees is the most effective way to create a safe working environment – whether with enzymes or any other potentially hazardous substances. Employees should be consulted in any decision-making process regarding risk management practices and solutions.

Risk management measures should always be based on a **hierarchy of controls** (Figure 2). This means that the exposure should primarily be prevented by eliminating or substituting the hazard. If this is not possible then exposure should be controlled by isolating the hazard or reducing it by means of engineering controls and/or design. In addition, administrative controls may be used such as the imposition of safe working practices & procedures. The final measure for reducing the exposure is the use of appropriate personal protective equipment (PPE).

Risk management processes should include the management of chemicals in the workplace. The REACH Regulation (1907/2006) requires that adequate control of risks be demonstrated for identified uses of substances and gives a clear framework of precautions that must be in place before any kind of hazardous substances are used.

Safety management in the workplace should cover near miss and accident investigations, and reporting procedures for these events. Learning from such incidents is a key element for the development of a safer workplace for everyone and this can be achieved by reviewing every significant near miss or accident. The outcomes of investigations inform future risk assessments and corrective actions to prevent similar incidents happening again.

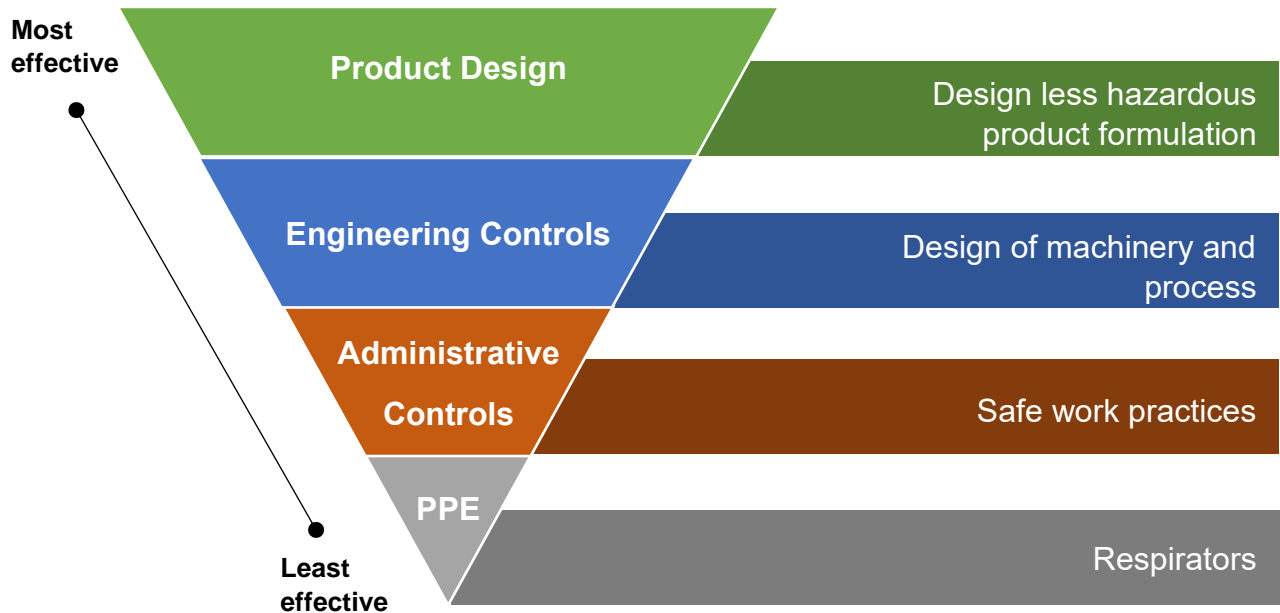


Figure 2: Controlling exposure to hazards through the hierarchy of controls (© IFF)

3.2. Continuous training

Training is a key element for raising the awareness, competence and knowledge about safety matters. All employees must have basic training in general health and safety in addition to their task specific training to gain professionalism. All workers handling chemicals and especially enzymes should also have training in the potential hazards arising from different chemicals used (such as products containing enzymes) and the appropriate precautions to take when working with these substances. Chemical safety related training should include information about the right working methods with chemicals, specific hazards and how to protect against those for example with personal protective equipment. Also, chemical product label warnings should be trained as well as potential cross reactions of chemicals present in workplace. Emergency response instructions should be trained in case of an accident. All necessary information for workplace specific chemical safety training can be found from the safety data sheet (SDS) of each product used.

Training must also be organized for others who may be exposed on site (such as maintenance personnel, external contractors), and should include background information on hazards, standard instructions and emergency instructions. Everyone attending the site for the first time should be informed and/or trained about the basics of chemical safety during their induction. Training should then be continued over time on a regular basis, and always when significant changes to processes or chemicals used are made.

From the health perspective it is important to inform everyone who might be exposed about hazards, such as respiratory sensitisers. For example, standard operational procedures (SOPs)

should be communicated to all staff so that they understand how, as well as why, they should avoid any unnecessary exposure. Even small things such as the correct way to handle empty chemical containers can make a big difference. Other important training subjects include possible symptoms of respiratory allergy, correct handling of spillages and cleaning situations as well as emergency situation procedures.

After basic training has been covered, more task specific training should be given. This should also cover the usage and maintenance of personal protective equipment (PPE): for example, how to dress, undress, cleaning and contain PPE's properly; and the key elements of how to maintain PPE's; including cleaning and checking their condition for wear and tear. Following the basic training for PPE it is essential for everyone to have the opportunity to test the effectiveness and the actual level of protection that the equipment gives. This can be done by fit testing of respiratory protective equipment and practice in a controlled environment.

The company's training program should be reviewed regularly and always when significant changes are made to its processes. Risk assessments should also provide new material for training when something new is observed or something has changed in the process. Investigations of accidents and near miss situations should contribute to the content of training to ensure that lessons are learned.

The company's safety committee is a useful group to coordinate the results of both risk assessments and near miss reports to ensure that they are taken into account in the planning of the training program.

Documenting the delivery of all training is as important as the monitoring of its comprehension. Verifying the effectiveness of every step of risk management controls is always important, but it is vital for discerning the best ways to develop them further. For example, it is good practice to collect feedback about the content of training immediately after the event in addition to collecting it at a later date, once the new knowledge has been in use.

Documentation should be extended to SOPs, which are clear and easy to be understood. SOPs are meant to describe the right way of working in each task to ensure safety and effectiveness. The risk assessments in workplace should also develop these SOPs to cover the risks present. As systems and methods of working continually evolve, it is vital that SOPs are periodically reviewed to ensure that they are still relevant and fit for purpose. It is also important to ensure and monitor that workforce continually adhere to those.

AMFEP and TEGEWA strongly encourage every vocational **school and university** providing training in textile industry practices to include training about chemical safety including enzyme related hazards in the curriculum. Knowledge about the hazards present in the industry and the control measures used to manage risks should be introduced as early as possible for every person starting in the textile industry.

In Table 2, the key learning objectives of an enzyme safety training programme are briefly summarised.

Table 2: Summary of “Enzyme Safety Training” Programme Elements

	Learning Objective	Knowledge Gained
Chapter 1	Understand the health effects of enzymes and how they are classified	<ul style="list-style-type: none"> ✓ Enzymes are classified as respiratory sensitisers ✓ Enzymes can elicit an immune response in susceptible individuals that can cause respiratory allergy and may result in occupational asthma from repeat exposures over time
Chapter 2	Understand the regulatory requirements for the safe handling of enzymes	<ul style="list-style-type: none"> ✓ The safe use information for enzymes must be communicated in the SDS, either via ES or in the main body of the SDS. ✓ A local health risk assessment must be carried out for each hazardous chemical and the conclusions must be made available to every employee, e.g. via SOPs. ✓ Employees shall support such health risk assessments and report unsafe situations
Chapter 3	Understand the management responsibility and the importance of continuous training	<ul style="list-style-type: none"> ✓ Employers are responsible for health and safety in workplaces ✓ Participation of all employees is the most effective way of creating a safe working environment ✓ Regular and targeted training is a key element for raising the awareness, competence and knowledge about safety matters
Chapter 4	Understand the hierarchy of controls for risk management strategies to minimize enzyme exposures	<ul style="list-style-type: none"> ✓ The hierarchy of controls from most effective to least effective are: product design, engineering and process design, administrative controls and finally PPE.
	Learn about the various product forms of enzymes and their risk profiles	<ul style="list-style-type: none"> ✓ The enzyme product forms from highest enzyme to lowest enzyme exposure potential are powders, liquids and low dust granulated enzyme products. ✓ The risk profile is based on the product form most likely to become aerosolized and leading to the highest enzyme exposure potential
	Identify the specific types of engineering controls that are used to minimize enzyme exposures	<ul style="list-style-type: none"> ✓ The engineering controls from most effective to least effective are e.g.: containment, ventilation enclosures, and local exhaust ventilation.
	Understand the administrative controls that are used to work safely with enzymes	<ul style="list-style-type: none"> ✓ Administrative controls include: work practice controls, training and awareness, housekeeping, and regular maintenance
Chapter 5	Identify the types of PPE to consider for appropriate selection	<ul style="list-style-type: none"> ✓ PPE selection is based on work activities and exposure potential. Respirators with a P3 air filter shall be used to prevent inhalation of enzyme aerosols. Protective clothing shall also be considered based on the work performed.
	Understand the purpose of enzyme monitoring	<ul style="list-style-type: none"> ✓ Quantify airborne enzyme exposures against established limits during worker operations ✓ Understand areas of high exposure potential and consequently to reduce the risk of sensitisation that can lead to adverse health effects. ✓ Verify that control measures are adequately protecting against exposures
	To understand the purpose and main objectives of a medical surveillance program , including the importance of early reporting and intervention	<ul style="list-style-type: none"> ✓ To Identify as early as possible, any adverse health effects which may be caused by the exposure to enzymes and provide more specific guidance on safe enzyme work practices and controls based on the results of the medical assessment ✓ Early reporting to the respective occupational health professional of enzyme related symptoms is important to prevent the progression of adverse health effects.

4. Control of Exposure during the Handling of Enzymes in the Textile Chemical Formulating industry (TCF's)

4.1. Introduction

The intent of this chapter is to prevent operator exposure to enzymes, via inhalation, during the manufacturing process of chemicals at TCFs. Ensuring workers' safety is a **regulatory obligation** for both enzyme suppliers and enzyme users.

The Chemical Agents Directive (CAD)¹⁸ lays out provisions aimed at the protection of workers whose work brings them into contact with hazardous chemical agents. Since most enzymes are classified as Respiratory Sensitisers Category 1, they are in the scope of CAD.

Where hazardous chemical agents are present in the workplace, employers must determine whether any risks to safety and health arise from their presence. The employer must be in possession of an assessment of the risk.

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

The key strategies are:

- Selection of the safest enzyme product form (liquids or encapsulated low dust granules)
- The prevention of aerosol formation from enzyme liquids by the proper plant design to prevent or minimize the formation of aerosols when using enzymes at TCFs
- The containment at source of any liquid aerosols that may be produced during handling by using closed process equipment, or enclosed equipment maintained under negative pressure by ventilation control
- The avoidance of any routine or uncontrolled spillages of enzyme-containing material, including from waste and packaging
- The clean / hygienic design of plant and equipment

The employer must take the necessary preventive measures to eliminate or reduce to a minimum the risks identified in the risk assessment following a **hierarchy of prevention measures**.

Substitution shall by preference be undertaken, whereby the employer shall avoid the use of a hazardous chemical agent by replacing it with a chemical agent or process which is not hazardous or **less hazardous** to workers' safety and health, e.g. replacing powdered enzymes

¹⁸ Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC).

by encapsulated low dust granules. Substitution can also be the choice of the right product form. Adversely to liquid or encapsulated low dust granules, powdered enzymes have a big potential of becoming airborne, hence creating a big occupational exposure risk for workers.

Referring to the 'hierarchy of controls' pyramid as can be seen in Chapter 3 (Figure 2), for the textile supply chain, reasonable elimination is only an option regarding the selection of the enzyme product form but not for the use of enzymes themselves, as the use of enzymes has incredible benefits. Instead, product design is the appropriate measure to reduce the hazard. Engineering controls, such as containment and ventilation will isolate people from the hazard. Under administrative controls, much attention should be paid to safe work practices and therefore it is of key importance to adequately train the workforce in 'enzyme safety'.

4.2. Textile Chemical Formulators

A specific questionnaire was developed by the AMFEP/TEGEWA enzyme safety taskforce; the following information was obtained from the responses of 8 textile chemical formulating companies, all members of TEGEWA.

4.2.1. Introduction: describing the process

Liquid or encapsulated low dust granulated enzyme formulations are mixed with other chemicals and mainly sold as ready-to-use chemicals for the textile and garment finishing industries.

In most cases, the mixing can be considered as a closed process.

The main purpose for the use of these chemicals are:


- De-sizing
- Bleaching process
- Stonewashing
- Biopolishing

4.2.2. Enzymes Quality and Form / Supply units


Both liquid and encapsulated low dust granulated enzyme formulations are prepared. As mentioned earlier, when powdered products are used, it is extremely difficult to keep compliance to OELs or the DMEL value. Therefore, they shall not be used and are not further discussed below.

Liquid enzyme formulations for the textile chemical formulating industry are available in 3 main supply units.


Jerrycan or canister

Packaging size (L)	Depth (mm)	Width (mm)	Height (mm)	Container weight (kg)	Example
25 - canister	290 - 302	252 - 264	457 - 469	1.2	
Material		Dimensions (mm)			
Screw cap, type 61, heated foil seal		Outer Ø 57.5 - 60.5, Inner Ø 47.0 – 50.0, Height 21.4 – 23.4			

Drum

Packaging size (L)	Depth (mm)	Width (mm)	Height (mm)	Container weight (kg)	Example
220 - drum	Ø 578 - 584		930 - 940	8.5	
Material		Dimensions (mm)			
Drum compliant with DIN ISO 20848-2, Bung closure system compliant with DIN ISO 20848-3		BCS 70x6 plastic seal (delivered detached from drum) inner Ø 57.3, BCS 56x4 aluminium seal (sealed) inner Ø 52.9			

IBC

Packaging size (L)	Depth (mm)	Width (mm)	Height (mm)	Container weight (kg)	Example
1000 - IBC	1200	1000	1160 (incl. pallet)	55.0	
Material Filling opening: Screw cap HDPE / O-ring gasket TPE, Discharge opening: HDPE/PP/aluminium film (sealed)			Dimensions (mm) Filling opening Ø 150, Discharge opening Ø 50, Fork opening Ø 100		

Encapsulated low dust granulated enzyme formulations may be supplied in:

- Disposable big bags with a fixed /removable polythene liner
- Smaller plastic or cardboard drums or boxes.



4.2.3. Storage of Enzyme Supply units

All supply units should be stored in the warehouse on pallets for ease of handling. 32 Jerrycans or 4 drums can be put on 1 ISO pallet (dimensions: 1000 x 1200 mm). Smaller pallets exist where for example only 2 drums fit on. Plastic film is wrapped around the smaller supply units for transportation. The European law for road transport dictates it as such (ADR/Directive 2008/68/EC).

It is a good practice to put maximum 3 IBC's on top of each other, depending on the allowed bearing load of the IBS themselves and/or storage rack. Please consult your IBC supplier for further guidance.

Please see picture below:



Figure 3: Storage of Enzyme Supply units.

Mother-Daughter decanting system and containment bund:

The mother daughter is a system that guarantees the continued supply of enzymes by ensuring that the black container – see picture below – is always refilled with the products. The IBC container on top is replaced when empty.

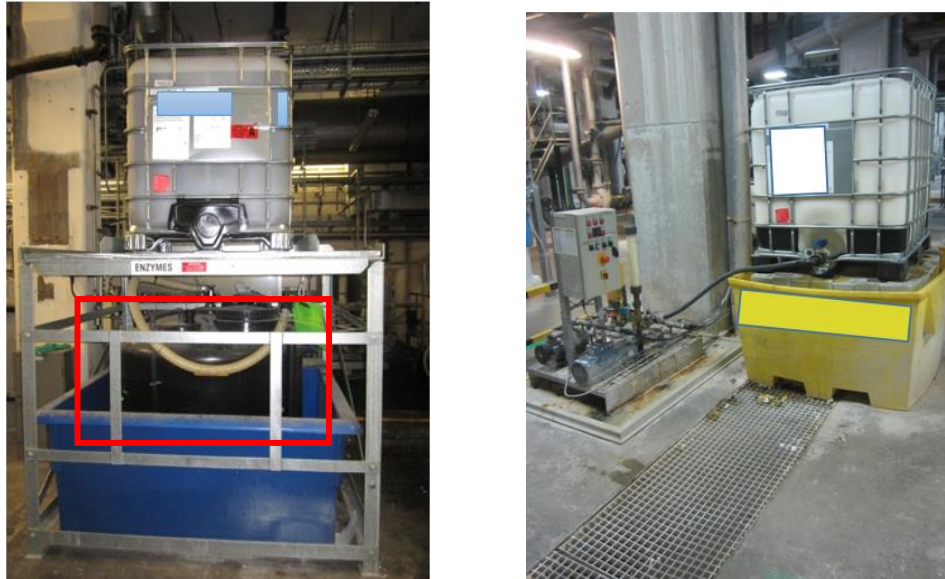


Figure 4: IBC with containment bund (black container highlighted by the red box)

4.2.4. Enzyme Exposure Scenarios for Textile Chemical Formulators

As referred to in Chapter 2, if an enzyme is in the scope of REACH registration and has been registered in tonnages > 10 tons per year, then its registration dossier should include a Chemical Safety Assessment (CSA). The CSA consists of:

- Generic Exposure Scenarios (GES).
- Exposure estimation for the different routes of exposure under the conditions of use as described in the GESs.
- Risk characterisation: comparison of exposure levels to no or minimum effect levels.

We refer to the exposure scenarios attached to the extended safety datasheets (eSDSs) that may be received from the enzyme suppliers. Depending on the process categories, e.g. open versus closed process, dedicated versus non-dedicated facilities, etc., different risk management measures (RMMs) are recommended to control workers exposure.

4.2.5. Building and Plant Design Considerations

4.2.5.1 General Principles

Buildings and plants should be designed to the extent possible to provide an environment that is easy to maintain in terms of hygiene and which minimizes the generation of aerosols by avoiding spraying, splashing, or spillage. Therefore, it is essential that clean design principles be used for buildings.

4.2.5.2 Buildings

Walls should be smooth, and sealed (e.g. painted), or clad in a smooth material that is easy to keep clean. 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 in use should be removed.

Ceilings should be smooth and give easy access for periodic cleaning.

Floors and stairs should be easy to clean.

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

Ductwork should be tubular shapes.

4.2.5.3 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.

Enzyme liquids have a significant potential for aerosol formation during handling and a risk of dust generation if spillages are left to dry out. 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 largest potential source of personal exposure to enzyme aerosols is the storage and refilling equipment for the enzyme dispersion. Interface and frequency of exposure should be eliminated or reduced as follows:

The design should prevent external spillage and spattering of fluid by:

- Limited drop heights and avoidance of splashes of liquids on surfaces (including liquid surfaces).
- Design of efficient enclosures to completely recirculate spilled liquid splashes
- Spill trays to completely collect and return the spilled material.
- Suitable sampling points
- Efficient machine setup to avoid frequent interruptions and manual intervention
- Using CIP technologies (Cleaning in Place)

In places where spills are evident or routine and have not yet been disposed of, drip pans should be provided for product removal.

The design should avoid or reduce spills, thus reducing the need for frequent cleaning of spilled material.

A. Encapsulated Low Dust Granules Handling Equipment

Conveyors/Elevators

“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 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.

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.

In case “Bucket elevators” would be used, they are subject to the same control principles as belt conveyors.

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 High-Efficiency Particulate Absorbing (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.

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.

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.

B. 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 withstand 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.

Tank Vents

We are referring also to Section 4.5. where ventilation is handled in more detail. Displaced air from enzyme storage units that is vented back into the workplace must be controlled by HEPA filtration. Please consider the fact that if the tank were stirred and/or if significant amounts of enzyme containing aerosols are formed during filling, then a HEPA filter might be blocked leading to risk of leakage e.g. at sealing points or when opening a manhole.

Air vented outside should be vented away from any intake air, and can be done without filtration, but please check your local environmental legislation when considering venting outside.

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.

4.3. Discharge of Supply Units/Waste handling

4.3.1. Discharge of Supply Units

In general, 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, in case a spillage, or release, should 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 likely that a peak exposure will occur. Personal and respiratory protection is discussed in detail in Section 4.6.

4.3.1.1. *Isolation of Discharge Process*

The best practice for discharge of supply units 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 aerosol in a direction away from the operator's breathing zone, and without allowing the aerosol to settle. Turbulent airflow should be minimized to ensure effective control and removal of airborne contamination.

An example is the use of a laminar downflow booth (see **Appendix 1**). These provide a high level of containment through 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 ≥ 1.0 m/s at all gaps or openings that lead to the outside of the room or booth (for example gaps around doors or transfer pipework), and enhanced air change rate (e.g. 5-10 air changes per hour). This will ensure that any airborne contamination is maintained within the room, or booth. This system is less efficient though than a laminar downflow booth at removal of airborne contamination or preventing 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 and the disposal of empty supply units should be handled as detailed in Section 4.3.2.

4.3.1.2. Discharge of Intermediate Bulk Containers (Rigid)

This type of rigid IBC is more commonly used for liquids. Discharge of liquids is normally done via direct connection of pipe work to the valve on the front of the IBC. We refer to Section 4.4.1 for more details about the design of the piping system and the type of valves that can be used.

Liquids IBCs may be discharged into a variety of holding tanks, 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 can 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.



Figure 5: IBC with liquid enzyme on their secondary containment; example of mother-daughter decanting system

4.3.1.3. Discharge of Drums

As with liquids IBCs, metal or plastic 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 use of pumps. The use of dip-pipes or removable “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.

4.3.1.4. Discharge of Big Bags

Filling and refilling of small silos can be done from big bags containing enzyme granulates. In this case, specialized equipment should be used, which moves material from the big bag through an almost closed system into the silos. Nevertheless, since this is not a completely closed system, dust formation can still occur. The primary mechanism for discharge of big bags is via gravity.

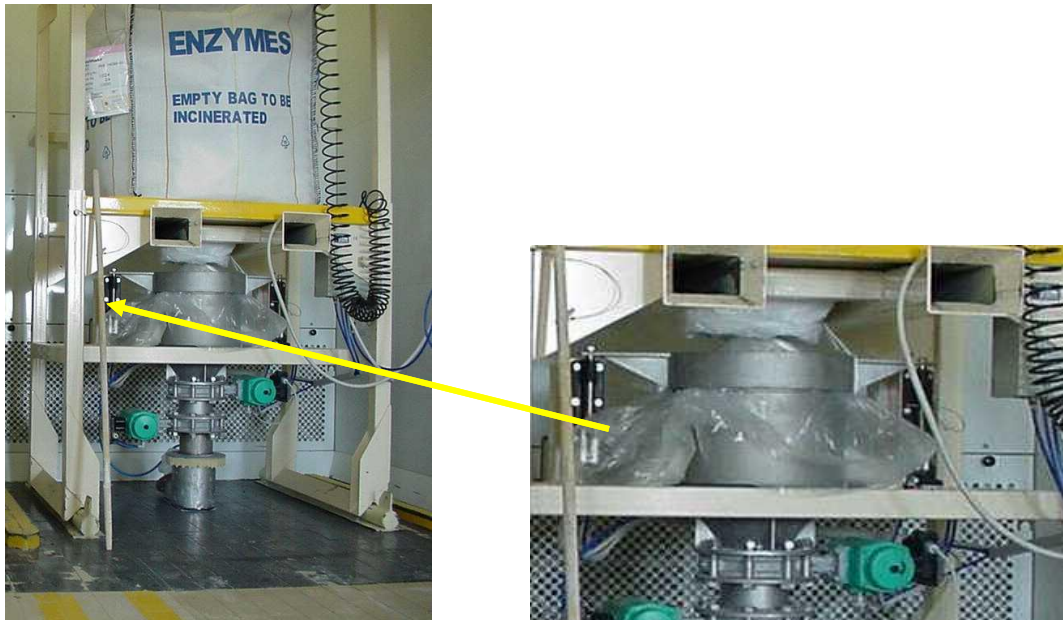


Figure 6: Inner Big-bag liner seals to discharge equipment before bag is opened.

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.

Bags should be free from any external contamination before deflation and folding.

As deflating and folding of Big-bags will create dust, 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 of the Big-bag. Vacuum for deflation may be provided by a HEPA vacuum cleaner or by connection to the local exhaust ventilation system.

Disposable Big-Bags with fixed polythene liners should be deflated and then sealed in a large polythene bag ready for disposal.

4.3.2. Disposal of Empty Supply Units

Jerrycans are normally disposed at the end-user’s site. Drums might or might not fall under the recall policy; if yes, they are taken back and rinsed.

IBC’s have a special recall policy, so-called “reverse logistics”. With every IBC delivered, documents are attached for the end-user with instructions what to do in order that a disposal company come to pick them up. Some disposal companies only reuse the metal frame and the plastic container is disposed and replaced by a new one.

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 enzyme product in order to control the exposures, especially when cleaning the IBC’s. Operators should

be trained and wear the appropriate PPE.

Please follow local regulations as they may differ from country to country.

4.4. Enzyme Transfer and Dosing

In plants, where the process layout is relatively simple, transfer of enzyme 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 pumps.

In any case, containment should be implemented to avoid the release of enzyme aerosols. Containment can be achieved by two means:

1. Complete enclosure – a physically sealed / closed system
2. Partial enclosure and ventilation control

Dosing should only be carried out using contained and controlled dosing systems.

As stated in Section 4.3.1., and as a general advice, the best practice when designing a safe discharge system for enzymes is to completely isolate the operator from the enzyme raw material, with 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.

4.4.1. Dosing of Liquid Enzymes

As a general advice, 'manual dosing' of liquid enzymes must not 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.

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, like jerrycans with venting caps and drain cocks.

Manually operated dosing should be achieved using closed transfer vessels. 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.

4.4.1.2. *Continuous Manufacturing Plant*

Although this is not current practice for TCFs, for completeness we want to describe this process. Continuous dosing plants bring together two or more metered streams of liquid and mix them together. Typically, a continuous enzyme dosing facility injects enzymes into the mixing vessel. The enzymes may be pumped directly from a supply IBC.

Liquids dosing plants are quite complex, often pressurized, and there are many points at which leaks may occur. Therefore, it is recommended that the location where enzymes are dosed in an open way be sited in a contained (authorised access) area under negative pressure to maintain an inward airflow of 1.0m/s, and with a good general ventilation (3 to 5 air exchanges per hour, as referred to in **Appendix 2** of the ECHA Practical guide 13).¹⁹

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

4.4.1.3. Batch Manufacturing Plants – Automated dosing

Liquid enzymes may be added to a batch-mixing vessel. Typically, batch-mixing vessels have a man way that can be opened either to 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 the liquid enzyme. 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 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.

The design of the piping system should be such to ensure it can be flushed while still connected, for instance by a three-way valve at the IBC to allow backflow of pipe rinse water directly to a drain near the IBC. The idea with a three-way valve is that you not just put a straight tap on your IBC, but a tap with three connections. This allows you to flush the pipe string (CIPs or just flush) without getting backflow in your IBC.

One way is product from IBC to receiving tank. The other way is pipe rinse water in. The third way is flush water out (and to sewer or collection). One must be careful if there are GMP requirements, as for example the cheaper / non-inline-fixed systems which have ball valves that cannot be cleaned on all three sides and therefore, some enzyme will remain. Note that it is important to choose the right three-way valve in terms of hygiene requirements (and therefore not the ball valve type). The valves may look differently depending on the design.

¹⁹ European Chemicals Agency (ECHA), Practical Guide 13: How downstream users can handle exposure scenarios, May 2016, https://echa.europa.eu/documents/10162/13655/du_practical_guide_13_en.pdf/2c3bc624-fb3c-4515-a581-87b79d460d38



Figure 7: Example of a hygienic three-way valve

For the dosing of liquid enzymes, underneath practices may occur:

1° Bad practice: manual dosing of liquid enzymes, with direct interface between the operator and the raw material

'Manual dosing' of liquid enzymes must not be carried out by open pouring through the manway, or over the side of any vessel. The potential for exposure to aerosol from spillage or from personal contamination is too high using a manual method. From experience it is known that this practice could result in enzyme airborne levels significantly above the DMEL of 60 ng/m³.

2° Better practice, when using manually operated dosing systems, reducing the potential of direct interface between the operator and the raw material.

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 enzymes
- Suitable transfer containers
- Local exhaust ventilation at the dispensing station
- Direct coupling of the transfer container to the process
- Positive pressure respiratory protection
- Protective overalls
- Proper handling of spillage

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.

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, as described in Section 4.3.1.3.

In general, the use of dip-pipes or removable “Drum pumps” is not recommended (see Figure 7). These are prone to cause spillage and personal contamination on removal from the drum and during storage when not in use.

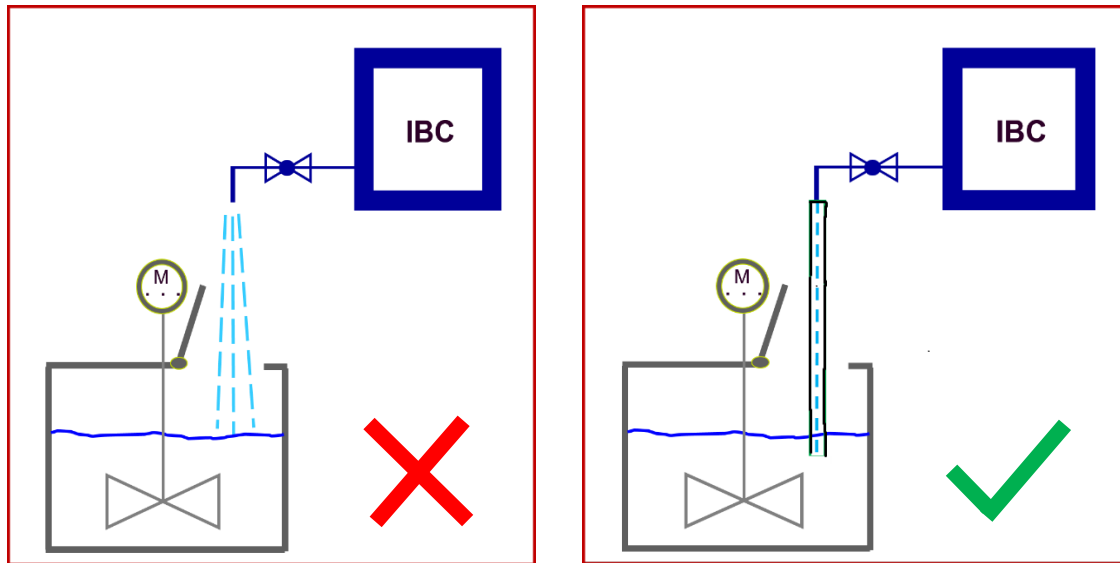


Figure 8: Advantage of using dip-pipes to reduce aerosol formation when dosing liquid enzyme

However, when necessary, the situation as described in the picture above, could be made much safer if the outlet of the IBC was provided with a flexible tubing, ending up under the surface level of the liquid (submerged loading), in this way preventing splashing of the enzyme liquid. In this situation, enzyme air monitoring has shown results that were below the DMEL of 60 ng/m³. Care should be taken to avoid exposure when removing and storing the flexible tubing from the drum.

3° Best practice: automated dosing in Batch or Continuous Manufacturing plants

Liquid enzymes may be added to a batch-mixing vessel.

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 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 may be used as a secondary protection on the air exhaust. An example of liquid enzyme transfer pumps is shown in the figure below.



Figure 9: Example of Enzyme Transfer Pump Sets (source: AISE Guidelines for the Safe Handling of Enzymes in the Detergent Manufacturing).

4.4.2. Weighing, dosing and blending of Encapsulated Low Dust Granulated Enzymes

4.4.2.1. Weighing

In large blending operations, ingredients are weighed automatically from silos and closed dosing systems before being added to the blender. However, in smaller blending and mixing operations, which is the case in most TCF facilities, this is usually not possible so that manual weighing is necessary.

Due to the nature of encapsulated low dust granulated enzyme formulations, the transfer of enzyme-containing products from a bag or box to a weighing bowl via a hand-scoop can generate significant levels of dust. This work should be done in a weighing cell (picture below) where air is constantly being removed by local exhaust ventilation. This can either be a 'down flow' booth, or a 'back flow' booth (see Figure 9). However, even when using flow booths, it is highly recommended that the operators use respiratory protection equipment RPE to minimise dust inhalation and to comply with the use instructions given by the supplier of the flow booth.

We want to emphasize that powdered enzyme products shall not be used!



Figure 10: Work practices in a back flow booth

4.4.2.2. Dosing

Encapsulated low dust granulated enzyme are sucked in by vacuum and dosed under local exhaust ventilation (LEV), preventing direct interface between the operator and the material. Where there is lack of LEV, operators should wear the appropriate RPE.

4.4.2.3. Blending

Industrial blenders exist in a wide variety of forms (ribbon, conical, rotating, horizontal, etc.) and sizes (1000 – 5.000 litre). A few different types are shown below.



Figure 11: Examples of blending equipment

Most blending operations are closed systems, although this is highly dependent on scale. In a closed system there will be no dust problems during the actual blending step, but they can occur during the filling and emptying of the blenders.

Filling a blender can also be done using closed systems, but this is purely dependent on the size of the blender. A blender which is smaller than 500 kg in size will generally be filled using bags and boxes which are emptied manually:



Figure 12: Examples of dumping stations. Powdered enzymes might be an issue in the right picture, especially if proteases are handled (uncovered arms)

This is the process step where dust formation is virtually unavoidable. In spite of clearly described working procedures, there will always be some dust formation during this operation and therefore it is strongly recommended that operators use respiratory protection equipment (RPE) and/or have strong local exhaust ventilation above and around the entrance of the blender. The blending operation itself occurs mostly in a closed system.

4.5. Ventilation efficiency and recommendations

DISCLAIMER: Ventilation requirements may vary from country to country; companies need to check the legal requirements, which are applicable in their region.

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.

4.5.1. 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 H14 (EN 1822²⁰).

The International Standard EN 1822²¹ has revised filter classifications; the recommended finishing filter class for enzymes is now H14, formerly known as class EU13 and you may still see this on some older stock or products.

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 filters operating life. This is typical of the filtration necessary for a laminar downflow booth, which re-circulates air to the working environment (see **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 Type	Classification	Efficiency
Pre-Filter	G4	95% @ 10 µm
Fine Dust Filter	F8	90 – 95% @ 5 µm
HEPA Filter	H14	99.995 – 99.9995% @ 0.3 µm

4.5.2. 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 H14 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 for sensitising substances such as 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. Taking regular readings from such gauges can be part of the plant monitoring systems.

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.

²⁰ EN 1822-1:2019 – High Efficiency Air filters (EPA, HEPA and ULPA) – Part 1: Classification, performance testing, marking

²¹ EN 1822-1:2019 – High Efficiency Air filters (EPA, HEPA and ULPA) – Part 1: Classification, performance testing, marking

4.6. 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 potential source of peak enzyme exposures, which need to be managed by a combination of equipment and proper procedure.

Cleaning up spilled enzyme granulates 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. We refer to **Appendix 2** for the maintenance and testing of equipment utilizing HEPA filters.

Liquid enzyme spillages may be washed to a drain by a soft/low pressure water hose. Spill pans may be drained down to an internal sump, from where it can be pumped directly into a product reclaim system.

Brushes, brooms, compressed air, and high-pressure water **should never** be used for cleaning spillages, as these can 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.

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 Section 4.6).

Vacuum cleaners are the preferred tool for cleaning of spillages, plant and equipment. Portable or central vacuum cleaning systems can be used. There are advantages and disadvantages to both systems;

The table in **Appendix 3** describes the options for vacuum cleaning equipment.

4.6.1. Cleaning of Spare Parts

In general, 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. 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 Section 4.3.1.1) in that it should be under negative pressure with respect to the remainder of the plant.

PPE in accordance with your plant matrix should be worn when inside the room to protect against product splashing back from the wash down. 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 Section 4.7).

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.

4.7. Personal Protective Equipment (PPE)

4.7.1. Use of Respiratory Protective Equipment (RPE)

In **standard** operational conditions, 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
- 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.

During **trouble-shooting**, 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
- Gross failure of containment or control
- Maintenance or repair of contaminated plant and equipment
- Decontamination of plant and equipment

4.7.2. Standards of Respiratory Protection

All employees required to use respiratory protective equipment must be adequately trained in its selection, use and maintenance. In some countries, it is regulated that the site doctor shall assess them as medically fit to wear and use 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 respirator selected must have an assigned protection factor (APF) adequate for the particular workplace exposure.

Divide the air contaminant concentration by the occupational exposure limit (OEL or DMEL) to obtain a hazard ratio. Then select a respirator with an APF greater than or equal to that hazard ratio. It is recommended to comply with the relevant EN standards for RPE (see e.g. EN 529:2005²² for APF of different respirator types and according to different countries).

It is highly recommended to conduct a fit testing prior to the use.

The following are examples of the type of RPE available that is often used at TCF facilities, to cover a range of contingencies.



Figure 13: Disposable respirators (FFP3) (courtesy: IFF)



Figure 14: Half-face reusable respirator (courtesy: IFF)



Figure 15: Powered Air Purifying Respirator (PAPR), (courtesy: IFF)

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 primary protection during **trouble-shooting** conditions, a higher grade of RPE will be required. The minimum standard in this instance should be P3 for airborne enzyme dust only and P3SL is effective for both dust (S) and aerosol (L).

When talking about higher grade of RPE you need to see it as a system. TM1, TM2, TM3 are the grades for masks (PAPR with tight fitting mask following: EN 12942)²³. And TH1, TH2, TH3

²² EN 529-2005 – Respiratory protective devices - Recommendations for selection, use, care and maintenance - Guidance document

²³ EN 12942:1998+A2:2008 - Respiratory protective devices. Power assisted filtering devices incorporating full face masks, half masks or quarter masks. Requirements, testing, marking

are the terms for hoods/helmets (PAPR with hood or helmet following: EN 12941)²⁴.

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. We refer to the EN 529-2005²⁵ standard for further guidance.

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 shall be used, such as a PAPR. RPE should be compatible with any other protective equipment provided, such as safety glasses, safety goggles, hearing protection, etc.

4.7.3. Other Personal Protective Equipment (PPE)

In general, skin and eye contact with enzymes, or enzyme products should be avoided through the use of suitable PPE. Proteases may irritate skin, please follow product safety data sheets.

4.7.3.1. ***Protective Clothing***

Under **standard** operational 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, gloves should be impermeable.

Safety shoes, whilst not related to enzyme safety, should also be used by all persons on site as is appropriate; rubber boots (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, such as a major spillage, 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. In addition, 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.

²⁴ EN 12941 - Respiratory protective devices - Powered filtering devices incorporating a helmet or a hood - Requirements, testing, marking

²⁵ EN 529-2005 – Respiratory protective devices - Recommendations for selection, use, care and maintenance - Guidance document

4.7.3.2. Personal Decontamination

Ideally, the plant layout 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.

Following decontamination clean work clothing should be available for use.

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 the dust or aerosol that enters the operator's breathing zone is minimised, 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 minimized by extending the side panels beyond the safe working limit of the unit. This limit is clearly marked on the inside of the walls.

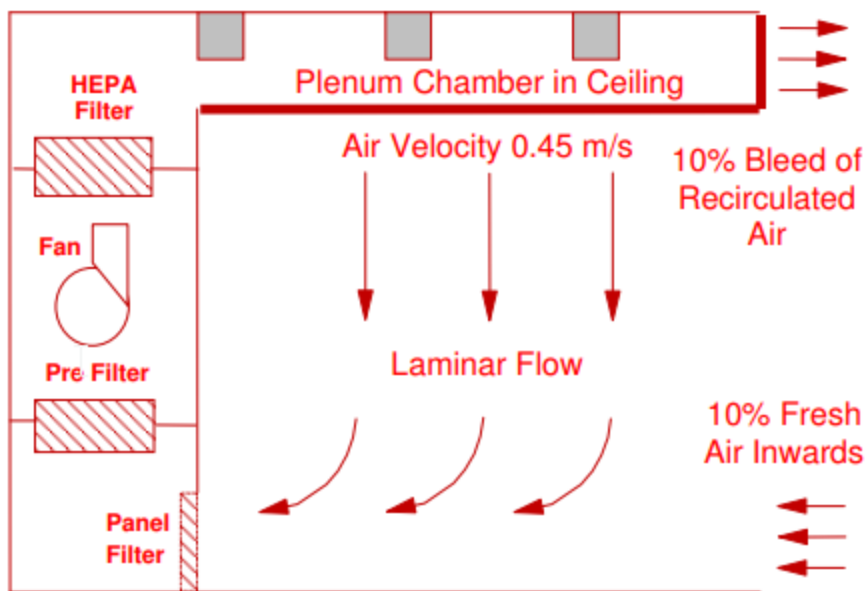


Figure 16: The Laminar Downflow Booth

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

Stage One: Panel Filter Class G 4 (replace approx. every 8 weeks)

Stage Two: Pre-filter Class F 8 (replace approx. 1 per year)

Stage Three: HEPA Filter Class H 14 (replace approx. every 3 years)

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

Appendix 2: Maintenance and testing of equipment utilizing HEPA filters

Any equipment used for transferring, or cleaning up, of enzymatic materials should be fitted with a HEPA filter on the final discharge which is rated as filter class H14 (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 Diethyl-hexyl sebacate (DEHS) 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 European Standards EN 1822-1:2019²⁶ and EN ISO 29463-2:2018²⁷. Additional test criteria for HEPA filters are covered in EN ISO 29463-3:2018 to EN ISO 29463-4:2018 and EN ISO 29463-5:2018²⁸.

Equipment containing a HEPA filter should be placed 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 should be tested in situ.

²⁶ EN 1822-1:2019 – High Efficiency Air filters (EPA, HEPA and ULPA) – Part 1: Classification, performance testing, marking

²⁷ EN ISO 29463-2:2018 – High Efficiency Air Filters (EPA, HEPA and ULPA) – Part 2: Aerosol production measuring equipment, particle counting statistics

²⁸ EN ISO 29463-3:2018 – High Efficiency Air Filter (EPA, HEPA and ULPA) – Part 3: Testing flat sheet filter media
EN ISO 29463-4:2018 – High Efficiency Air Filters (EPA, HEPA and ULPA) – Part 4: Determining leakage of filter element (scan method)

EN ISO 29463-5:2018 – High Efficiency Particulate Air Filters (EPA, HEPA and ULPA) – Part 5: Determining the efficiency of filter element

Appendix 3: Options for vacuum cleaning equipment

Description	Advantages	Disadvantages
Central Vacuum Cleaning (CVC) systems		
<ul style="list-style-type: none"> • Multiple simultaneous users possible • 7.5 meter 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 exhausters and filter / receiver to collect waste and fill dust controlled container • Dry clean-up only 	<ul style="list-style-type: none"> • 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 clean-up 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 	<ul style="list-style-type: none"> • 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 plugging • 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)		
<ul style="list-style-type: none"> • One user per PVC • May increase capacity by use of a 200 L metal interceptor drum (on wheels) with attached hose & tools • Exhaust blower with HEPA rated filter to the room • Versions available that are suitable for Liquids handling 	<ul style="list-style-type: none"> • Simple to operate • Low capital investment per unit • Malfunction affects only 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 	<ul style="list-style-type: none"> • Multiple units required to cover entire process area • Although manoeuvrable, ergonomically heavy unit (hose, tank, exhauster) to transport to clean-up 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 • In case of breach of HEPA filter, contamination will be released to the room near the operator

Mini CVCs (combination of PVC and CVC concepts)

<ul style="list-style-type: none"> • 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 clean-up only 	<ul style="list-style-type: none"> • Low ergonomic effort with minimum equipment (hose/tool) transport to clean-up 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 	<ul style="list-style-type: none"> • 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
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5. Occupational exposure assessment

5.1. Air monitoring

For this section, we refer to the exposure scenario's, the Operational conditions (OCs) and Risk management measures (RMMs) as highlighted in the REACH dossiers.

All risk characterization ratios (RCRs) should be less than one, and based on measured data from the manufacturing site. The manufacturing site should maintain a robust occupational health and industrial hygiene program, which includes periodic sampling for airborne enzymes. Additional risk management measures are implemented when estimated exposure above the derived minimal effect level (DMEL) is identified. Additional respiratory protection is required if new monitoring data reveals elevated enzyme concentrations and the problem cannot be traced to a process upset or equipment malfunction (e.g., a leaking gasket). In these cases, the level of respiratory protection that is assigned is sufficient to reduce inhalation exposures below the DMEL such that the risk characterization ratio remains below one.

In addition, the health risk assessment (HRA) for every workplace where enzymes are handled, which must be carried out under Chemical Agents Directive (CAD), should incorporate occupational exposure measurements. Due to the extremely low exposure limit values that have been derived for enzymes (see Chapter 2, **Appendix 2**), other exposure estimation approaches, such as computational models or read-across, are largely not applicable to enzymes. Various sampling protocols, which will be discussed further, provide advice on how to develop an air monitoring strategy for chemical agents.

The objectives behind monitoring of airborne dust and enzyme dust/aerosol are clear:

- It enables the quantification of employee exposures
- It enables the overall evaluation of the effectiveness of control measures.
- The results can be used to identify where control measures are found to be insufficient so that respiratory protective equipment should be worn.
- The results may also be used to identify where working practices may need to be reviewed in order to reduce exposure; i.e. less prone to create airborne exposure.

Monitoring should be prioritized based on the risk of exposure to workers. The basis for the sampling strategy in workplace air is the EN689:2018 standard. To begin with there should be a qualitative assessment of the risks as this will define the ultimate air monitoring strategy for the site. The strategy may also depend on the outcome of medical surveillance: for example, if immunological testing reveals that there is an increasing trend in the incidence of sensitisation. Moreover, the strategy will also depend on the outcomes of performance assessments of the equipment, work practices and behaviours of the workforce.

Routine air sampling is a quantitative tool to measure levels of background exposure to enzymes and dust; whereas peak sampling is used to measure high risk exposures; e.g., due to equipment defects and/or unsafe behaviour, such as using pressurized air to clean equipment or work clothes. Air monitoring includes area and personal sampling and can be undertaken with either

high or low volume samplers depending on the analytical restrictions of the type of monitoring to be undertaken.

Both **high** (up to 600 l/min) and **low flow** (2-30 l/min) **samplers** can be used.

Your enzyme supplier can be contacted for advice on measuring inhalable enzyme dust or aerosol.

Different sampling approaches may be used; although it may be necessary to follow local authority regulations or the guidance of EN standards (EN 689:2018²⁹ and EN 482:2015³⁰, Council Directive 98/24/EC (07/04/1998); ECHA Guidance, Part R.14: "Occupational Exposure Assessment").

EN482 and EN689 are the basic standards for workplace exposure measurements and all measurements carried out to compare with limit values should be done within the workers breathing zone.

Very important is the **calibration** of the sampling equipment; a typical set-up is shown in the picture below.

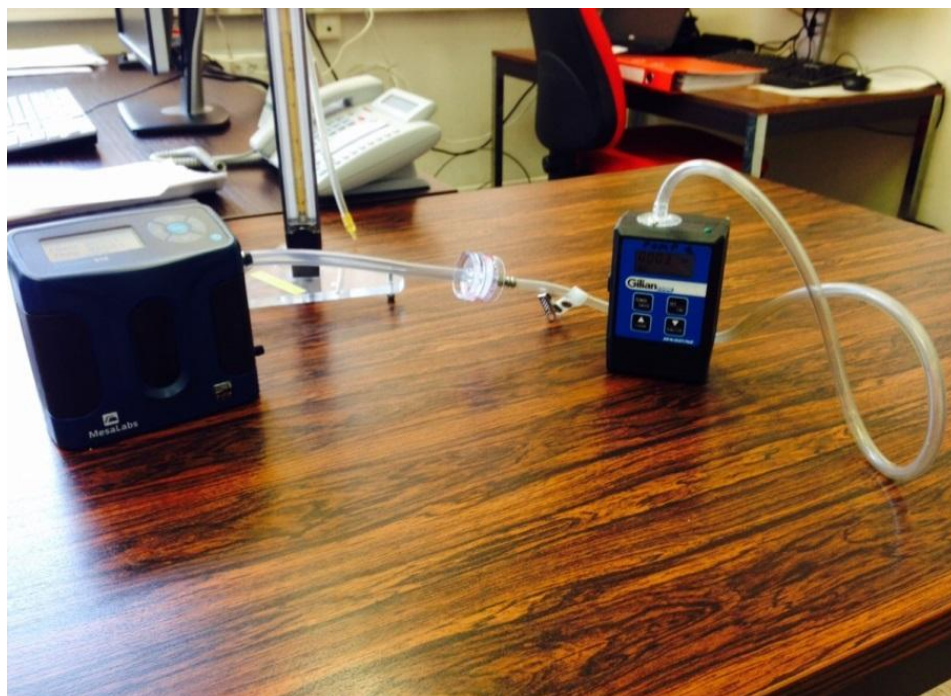


Figure 17: Calibration set-up for air sampling equipment. (Courtesy: IFF)

²⁹ EN 689:2018 - Workplace exposure - Measurement of exposure by inhalation to chemical agents - Strategy for testing compliance with occupational exposure limit values.

³⁰ EN 482:2015 - Workplace exposure - General requirements for the performance of procedures for the measurement of chemical agents.

Areas with the highest potential for exposure should be chosen as area sampling locations.

Appropriate monitoring locations can be selected in each facility by an appropriately qualified team, including industrial hygiene and manufacturing personnel.

As a general guideline, air monitoring should be conducted during the tasks most commonly associated with aerosol generation, including:

- Transfer of enzyme containing substance/mixture into containers
- Transfer of enzyme containing substance/mixture from/to containers at non-dedicated facilities (direct interface between operator and raw material)
- Sampling and quality control
- Weighing
- Mixing
- Handling of empty enzyme supply containers/bags
- Cleaning of plant and machinery
- Technical maintenance
- Any other activities of concern that are indicated by historical results of medical surveillance or air monitoring

As referred to in the introduction, monitoring should be conducted to measure employee's exposure to potential airborne enzymes during the manufacturing processes, **including material transfer**.

If there is a national limit value for workers exposure, data interpretation should be done according to EN689.

Data interpretation is perhaps the most difficult part of the whole exposure assessment and depends on the eventual use of the data, e.g.:

- Is this data going to be used to verify the effectiveness of engineering controls and the potential capital investment for the improvement of engineering controls?
- Is this data going to be used to assess the necessary respiratory protective equipment requirements?

Remedial steps should be taken immediately to resolve any exposure conditions leading to an air sampling result above the limit value (OEL and/or DMEL). When re-sampling confirms the high level, then the use of RPE or stopping production should be considered until appropriate controls can be implemented. The follow-up procedure is defined in EN689.

If the exposure in an area is above the DMEL, employees should be informed immediately and wear RPE until the measurements return to the acceptable limits.

One aspect of the exposure monitoring is the sampling, but the **analytical part** is equally important. There are two common methods, of which the **activity-based assay** is still the most practical one. The other method is an immunoassay, like **Elisa**. Please contact your enzyme

supplier for further guidance on the analytical methods.

Air sampling results, together with the outcomes of the medical surveillance programme, provide valuable information regarding the effectiveness of control measures. However, it is necessary to take into account the limitations of any exposure monitoring program, e.g.:

- No 'real-time' monitoring equipment available currently. This is only available for particles.
- Monitoring results that are less than the DMEL do not guarantee zero incidences of sensitisation.

The nature of the sampling regime means that results are always viewed in hindsight so that it might be difficult to trace back to what went wrong at the time of the sampling. Observations according EN689 should give information during sampling.

In cases where there may be a lack of available qualified internal resources, a certified consultant (industrial hygienist) should be contracted to conduct the air monitoring; and a certified laboratory employed to carry out the air monitoring analysis.

For the components of an air monitoring program, please consult the AISE "Guidelines for the safe handling of enzymes in detergent manufacturing".³¹

5.2. Health surveillance

This chapter is intended to guide occupational health professionals in implementing the current best practice for the health surveillance of workers at risk of exposure to **enzymes**. The protocols recommended in this document may be refined by occupational health specialists based on historical results obtained from their specific area of the textile chemical formulating industry (TCFs).

The content of this chapter is based on the "Current Best Practice for the Health Surveillance of Enzyme Workers in the Soap and Detergent Industry", issued in March 2001 by the Medical Sub-Committee of the UK Soap and Detergent Industry Association (SDIA). It also includes, with the exception of some modifications, recommendations given in that publication.

It should be emphasized that enzymes generally have a low order of toxicity. There are only two relevant toxicological end points:

- **Respiratory allergy**, which is an intrinsic hazard for all enzymes, and
- **Skin irritation**, which is an intrinsic property of enzymes belonging to the class of proteases and only relevant for this class of enzymes

Different enzyme classes are used in the Textile Industry (See Introduction, table 1).

As described previously in this guideline, enzymes are proteins and, like other proteins, may act as respiratory sensitisers if individuals are repeatedly exposed to airborne aerosols that contains them. Such sensitisation may ultimately lead to respiratory allergy, but it is important to note that

³¹ AISE (2018), Guidelines for the safe handling of enzymes in detergent manufacturing, https://www.aise.eu/documents/document/20180405111438-aise-enzymes_safe_handling-v2-2-march_2018.pdf

not all individuals who become sensitised to enzymes develop symptoms. Therefore, the aim of health surveillance will be to identify those workers who become sensitised and to prevent that such sensitised workers develop allergy symptoms.

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

Health surveillance is recommended for employees that are exposed to enzymes in the textile chemical formulating industry. In some countries, employers may be obliged to provide occupational health service if there is a known risk of identifiable disease.

The objectives of health surveillance related to enzyme exposure include:

- Protecting the health of individual employees by the earliest possible detection of any adverse effect which may be attributed to enzyme exposure.
- Assisting in the evaluation of measures taken to control enzyme exposure.
- Collecting and maintaining objective data to detect and evaluate hazards to health.
- Giving guidance on how to continue working in an environment where enzyme exposure cannot be avoided, based on the outcome of medical assessments.

Respiratory allergy, which is also called Type 1 allergy, is the only sort of allergy caused by enzyme exposure. Enzymes do not cause allergy via skin contact and, to date, enzymes have not been associated with food allergy.

It is essential to understand that developing a respiratory allergy is a **two-stage process** (5).

The induction (sensitisation) stage: It begins with the individual being exposed to airborne allergens in the form of dust or wet aerosols. If this exposure is sufficiently high, and lasts for a sufficiently long period of time, the individual may become sensitised.

The elicitation stage: A sensitised person does not show any allergy symptoms, but the immune system has been activated and specific IgE antibodies have been generated. The presence of specific IgE antibodies can be detected by a skin test or a RAST analysis of the blood. If a sensitised person is repeatedly exposed at sufficiently high level and for sufficiently long periods of time, allergy symptoms may develop, and the person is now allergic.

The difference between being sensitised and being allergic is determined by the appearance of allergic symptoms. A sensitised person has no symptoms and sensitisation by itself is not a disease, whereas an allergic person will always present allergic symptoms when exposed to the allergen in question. Sensitisation is the early warning that an allergy may develop. However, prompt and correct intervention may prevent the development of a fully blown allergy.

In the case of enzyme allergy, recent literature suggests that the exposure level required for **elicitation** of an allergy is higher than the exposure level required for **inducing** sensitisation. Therefore, it is of key importance to prevent peak exposures (6).

If a person develops an enzyme allergy, it will be a workplace related allergy, and symptoms may develop during or after working hours. In most cases the symptoms will disappear when the

exposure ceases, for example at weekends or during vacations. Symptoms are identical to those presented by allergies towards common allergens. In order of appearance and increasing severity these are:

- itching and redness of the mucous membranes
- watery eyes/nose
- sneezing
- hay fever
- hoarseness or shortness of breath
- coughing
- tightness of the chest
- asthma

The first symptoms to appear will usually be less severe, such as watery eyes or sneezing. If the individual is continually exposed to the allergen for a long period of time, more and more severe symptoms may appear, and in some cases, these may become chronic.

It is, therefore, vital that swift and appropriate intervention should take place as soon as possible; preferably before any further symptoms appear.

Some people are defined as being “**atopic**”, which means that they are allergic to one or more of the common allergens like pollen and house dust mites. It has been long discussed whether atopic individuals are at a higher risk of developing allergy, but there is no clarity on this point. Smoking has been identified as a factor which can increase the risk of becoming sensitised and of developing symptoms.

Some enzymes may cause **skin irritation**. These enzymes all belong to the class of proteases, which degrade protein. No other class of enzymes possesses this characteristic. The irritation will appear as redness of the skin, and only after intensive contact. The irritation will be localised and disappears after the skin contact with the protease enzyme has ceased. Skin irritation should not be mistaken for a skin allergy, as enzymes do not cause skin allergies (7,8).

An enzyme allergy is exclusively an occupational health hazard for people working in the enzyme manufacturing industry; or for downstream users such as workers handling enzymes as raw materials in the textile chemical formulating industry. Several studies have shown that consumers of products that contain enzymes in today’s market are not at risk. Therefore, an enzyme allergy is the result of an occupational exposure and its cause will always be found in the working environment.

5.2.1. Guidance for a Health Surveillance programme

Elements of this programme could be:

- A pre-employment testing
- **Medical history** could be assessed with particular reference to, for example, asthma, allergic rhinitis, eczema, urticaria, allergies, chronic lung disease and any medication.
- **A respiratory questionnaire** could be completed including details of smoking habits.

Examples of such pre-employment and periodical questionnaires are given in the AISE “Guidelines for the Safe Handling of Enzymes in Detergent Manufacturing” (see chapter 5A).

- **Assessment of lung function** could be made using a suitable spirometer and following an accepted standardized procedure and protocol in order to minimise measurement errors. The parameters that could be measured are FEV1, FVC, PEF, R.
- **Immunological Tests**, e.g. **skin prick** or **serological tests** could be performed. The purpose of immunological monitoring is to monitor the appearance of sensitisation among the workforce, revealed by the development of specific IgE antibodies. It is important to remember that sensitisation is not a disease: it is an indication that a person has been exposed, and may be on their way to developing an allergy.



Figure 18: Skin prick testing

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 an increased frequency of medical surveillance of such workers may be appropriate.

In this case, we also suggest a workplace (root cause) investigation should be conducted to ensure that exposures are in control. If possible, it is important to understand if a positive immunological test is related to a specific incident (higher exposure than normal work) or if it cannot be ruled out that normal work operations might result in sensitisations. In that case risk management measures must be improved to prevent reoccurrences.

Those with **abnormal findings** to the respiratory questionnaire which (in the opinion of an occupational health professional) could be due to enzymes; and those with impaired lung function according to spirometry readings; should have immediate further assessment.

Those who show a **continuing downward trend in lung function** should be carefully assessed regarding the need to remove them from further work with enzymes.

References

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6. Concluding Remarks & Acknowledgements

In this document, the authors have demonstrated the importance of controlling dust and aerosol exposure throughout the supply chain of the textile chemical formulating industry. This control is achieved based on a holistic approach: from a technical perspective in the form of equipment and processes, and through operator behaviours and effective management. The advice and best practices provided in this document should be read in conjunction with local guidelines and current regulations where applicable.

Should you require further guidance on enzyme safety, you are recommended to contact your enzyme supplier.

This document will be updated as new and significant insights become available.

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