Socio-economic analysis (SEA) on possible phase out of respiratory sensitisers in consumer and professional products: the case of enzymes

Final Report

Association of Manufacturers and Formulators of Enzyme Products (AMFEP)

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Executive summary

Introduced in 2020 as part of the wider European Green Deal strategy, the Chemicals Strategy for Sustainability (CSS) identified the generic risk approach (GRA) as an efficient regulatory tool and proposed that it gradually becomes the default option for the most harmful chemicals. In its current form, the GRA applies to substances with carcinogenic, mutagenic and/or reprotoxic properties (CMRs) found in consumer uses. The European Commission (EC) is currently reviewing a potential extension of the GRA under the REACH Regulation (European Parliament and European Council, 2006) which would involve expanding its existing scope to additionally cover the full list of the CSS' "most harmful chemicals" on top of CMRs, including endocrine disruptors, persistent, mobile and toxic chemicals and chemicals falling under further hazard classes such as specific target organ toxicity and respiratory sensitisation. Furthermore, the range of uses considered would be expanded to include professional uses.

This socio-economic analysis (SEA) report was commissioned by the Association of Manufacturers and Formulators of Enzyme Products (AMFEP) to provide evidence on the potential impacts a possible extension of the GRA may have on manufacturers, formulators and downstream users of food, feed, and technical enzymes in Europe. These GRA scope revisions, if implemented, will likely have a significant impact on the European enzyme industry because of the following features of the enzyme products within the new GRA scope:

- **Product characteristics:** all enzymes are classified as respiratory sensitisers.
- **User characteristics:** there are consumer and professional uses of enzymes. Around 34% of all enzymes used (volumed basis) in the EU would fall within the scope of the GRA.

This SEA assesses the impacts of a hypothetical ban of all enzymes applications within the scope of the GRA. The likelihood of the ban or justification of proposed changes to the GRA scope were not considered.

Many industries will become less sustainable if enzymes are banned

It is estimated that a potential ban could have an extensive impact on many consumer and professional uses, ranging from reducing end-product quality and performance, to removing it from the market in the absence of suitable alternatives. In most of the cases, the sustainability benefits when using enzymes would be lost, thereby undermining the objectives of the CSS. Some examples of specific impacts include:

- **Food enzymes:** cheese production would not be possible without enzymes which are critical for cheese making process (they are responsible for milk clotting) - The EU cheese market is estimated to be worth €30billion/year (AMFEP, 2022a);
- **Feed enzymes:** the lack of enzymes would reduce feed digestibility and availability of nutrients - and an increased excess nutrient flow in animal manure (e.g. phosphorus) could have negative impacts on the environment. The higher quality feed ingredients required would increase prices, resource consumption, and may lead to shortages in available feedstock;
- **Technical enzymes:** efficiency and sustainability of detergent formulations would be reduced (e.g. enzymes are responsible for high washing-performance even at low temperatures), and some medical diagnostic tests (e.g. diabetes and COVID tests) could not be manufactured without enzymes.

Impact on EU enzyme industry

The EU manufactures and/or imports around 3,500 different final formulated enzyme products totalling around 230,000 tonnes/year. The estimated total value of European enzyme production in 2022 was approximately €2.1 billion, and the industry employs around 7,900 people. The EU-27's enzyme market is highly innovative, and it is estimated that R&D spending between 2013-2022 totalled approximately €2.7 billion, which helps maintain the EU's global leadership in enzyme technology. If the EU does not maintain this leadership, another regional power (e.g. China or US) will likely take over the global leadership, leaving the EU with a competitive disadvantage (economically, politically and on innovation).

Around 34% of the European total of manufactured and imported final formulated enzyme products (78 thousand tonnes per year) fall within the revised scope of the GRA. This corresponds to a market value at risk of €624 million million/year. Professional uses would be primarily affected by a ban of food and feed enzymes, whilst banning the use of enzymes in detergents would mostly impact consumer uses.

In addition to the EU consumers being deprived of hundreds of products which are produced more sustainably because of the use of enzymes in their production (see below), An extension of the GRA and the potential ban of enzyme products would likely trigger the following responses from enzyme manufacturers:

- **Most likely short-term response:** continue producing in the EU-27 for uses outside the GRA scope and exports outside the EU-27.
- **Likely long-term response(s):** some companies may need to cease production at EU-27 sites due to insufficient demand to maintain all current enzyme producers.

Formulators and downstream users of enzyme products for professional and consumer uses would need to reformulate (e.g. use of enzymes in feed and detergent applications) and / or cease sales of their products containing enzymes (e.g. craft cheese and diabetes tests) when they are critical in their production processes which cannot be replaced.

This SEA monetised some of the economic impacts of these likely responses to a potential ban of enzyme products. Assuming that the ban would take effect in 2025, it was estimated that enzyme product manufacturers would lose profits of around €1.6 billion in present value (PV) over the period 2026-2029 (€411 million per year PV). This economic cost would be further amplified by a wide range of additional costs for downstream users (e.g. reformulation costs, loss of revenue or higher energy costs), none of which were quantified in this study due to time limitations. For example, the EU cheese market alone is estimated to be worth €30billion/year. **Around 1,444 employees, including those working directly in the enzyme manufacturing industry and those employed across the supply chain are estimated to be made redundant.** The cost of this unemployment was estimated at €315 million.

An EU enzyme ban will deprive the EU from meeting other sustainability and health objectives

In total, the costs to the enzyme manufacturers alone of a potential ban were estimated in the short term (e.g. over a 4-year period) to be at least €2 billion. This estimate excludes several other costs which go beyond economic impacts, such as costs to the environment, human health, and end-users. Some examples of these

additional, yet equally important impacts which could not be monetised are:

- **Environmental impacts:** greater food wastage due to reduced product shelf life (e.g. in bread production), increase in energy consumption and greenhouse gases pollution due to reduced efficiency using unsuitable alternatives (e.g. less efficient food/feed processing alternatives, or use of less efficient alternative substances in detergent products);
- **Human health impacts:** risks from less effective cleaning and inability to properly monitor glucose levels for diabetes. Around 32.3 million adults were diagnosed with diabetes in the EU in 2019 (OECD, 2019). The cost of managing diabetes in Europe totalled €149 billion in 2019, representing roughly 9% of EU member states' healthcare budgets (European Parliament, 2019).;
- **End-user impacts:** reduced choice for consumers who increasingly demand more sustainable products, lower quality of products (incl. lost functionality, reduced durability, and performance) and higher costs associated with increased prices triggered by lower supply and / or more expensive inferior alternatives to enzymes increasing the cost of production.

Following the results from this SEA, **AMFEP recommends that enzyme product manufacturers (and formulators) are provided with an exemption from a potential ban of enzyme products resulting from the revision of the GRA scope.** The lack of suitable alternatives to enzymes, combined with significant economic and social costs, as well as adverse impacts to human health and the environment justify a regulatory exemption from a ban on enzyme containing products. The potential extension of the GRA to respiratory sensitizers needs to be carefully evaluated against the significant sustainability benefits which enzymes provide on other policies which the EU wishes to address (e.g. EU Green Deal, Bioeconomy Strategy, Industrial Strategy, Farm-to-Fork, Circular Economy Action Plan, CSS, and Zero Pollution Action Plan, etc). By only looking at the intrinsic hazard of enzymes being respiratory sensitizers, without considering documented safe use and the significant market disruptions a ban would entail, the Commission would be ignoring all the sustainability drivers for their use.

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List of abbreviations

AB Enzymes	Associated British Foods Enzymes
A.I.S.E.	International Association of Soaps, Detergents and Maintenance Products
AMFEP	Association of Manufacturers and Formulators of Enzyme Products
AoA	Assessment of alternatives
CLH	Harmonised classification and labelling
CLP	Classification, Labelling and Packaging of chemicals
CMR	Carcinogenic, mutagenic or reprotoxic
CSS	Chemicals Strategy for Sustainability
DU	Downstream User
EC	European Commission
ECHA	European Chemicals Agency
EDs	Endocrine disruptors
EGD	European Green Deal
EFSA	The European Food Safety Authority
EU	European Union
FTE	Full-time equivalent
GHS	United Nations' Globally Harmonised System
GRA	Generic approach to risk management
MAF	Mixtures Assessment Factor(s)
PBT	Persistent, bio-accumulative and toxic chemicals
PV	Present Value
REACH	Regulation (EU) No. 1907/2006 on the Registration, Authorisation and Restriction of Chemicals
R&D	Research and Development
RMMs	Risk management measures
RMOs	Risk Management Options
SAGA	Suitable alternatives are generally available
SEA	Socio-economic analysis
SRA	Specific risk assessment
SVHC	Substances of very high concern
vPvBs	Persistent and very bio-accumulative

1 Introduction

1.1 Purpose of this study

The purpose of this socio-economic analysis (SEA) is to assess potential impacts of a possible extension of the generic approach to risk management (GRA) under the REACH Regulation ((EC) No 1907/2006)[1] to enzymes.

The study is commissioned by the Association of Manufacturers and Formulators of Enzyme Products (AMFEP) who represents the enzyme industry in Europe. Following discussions with the European Commission's (EC) contractor, AMFEP wants to use the evidence produced in the SEA to inform the EC about the potential consequences of a theoretical phase-out of food, feed and technical enzymes used in some categories of consumer and professional products.

1.2 What are enzymes?

Enzymes are proteins that act as catalysts i.e. they speed up processes in every living organism and accelerate chemical reactions. Without enzymes, those chemical reactions would either not occur or would run too slowly. They are effective in very small amounts, biodegradable, water soluble and generally non-toxic[2]. They help provide environment-friendly products to consumers by using less energy, water and raw materials and generating less waste.

According to AMFEP, enzyme products are used to make and improve everyday consumer and commercial products (AMFEP, 2022b). They are used in the manufacturing of foods and beverages, in animal nutrition, textiles, household cleaning, and in biofuels for cars and energy generation. More specifically:

- **Food** – Enzyme products are widely used by the food industry for processing raw materials and producing a large number/variety of food products, such as starch, dairy, bakery, meat and fruit products, as well as fruit juices, beer and wine. The European Food Safety Authority (EFSA) has developed a short video that presents enzymes and their use in the food chain (EFSA, n.d.).
- **Feed** – Enzyme products are widely used as feed additive by the animal feed industry to enhance the digestibility of feeding stuff (e.g., grain or grass), increase nutritional value and can contribute to reduce waste.
- **Technical** – Enzyme products are used in numerous technical applications, such as in detergents (laundry and dishwashing detergents), pulp and paper manufacturing (e.g. to remove ink in paper recycling), textile processing and fabric finishing, leather production, and ethanol production.

1.3 Policy context

1.3.1 Current chemicals regulatory framework

With chemicals being part of our everyday lives, they require close monitoring to protect human health and the

[1] For further details see: https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12959-Chemicals-legislation-revision-of-REACH-Regulation-to-help-achieve-a-toxic-free-environment_en

[2] For further details see: https://amfep.org/about-enzymes/safety/consumers-safety/

environment whilst maintaining their sustainable use. The existing EU legal framework for chemicals which comprises around 40 pieces of legislation aims to ensure that the required level of protection and safety is provided by each member state (European Commission, n.d.).

The two key legislations for the assessment and management of chemicals in the EU are the REACH Regulation (EU) No. 1907/2006 on the Registration, Authorisation and Restriction of Chemicals (European Parliament and European Council, 2006) and the CLP Regulation (EC) No. 1272/2008 on Classification, Labelling and Packaging of chemicals (European Parliament and European Council, 2008).

"*REACH aims to improve the protection of human health and the environment through the better and earlier identification of the intrinsic properties of chemical substances*" (European Commission, n.d.). The 'Registration of Substances' (TITLE II) of the REACH regulation imposes a general obligation for manufacturers and importers of chemicals to collect and register data about their substances, mixtures and their uses in the central database of the European Chemicals Agency (ECHA) (European Commission, n.d.). Hence, it puts the burden of proof on the industry responsible for identifying and managing risks from chemicals which they place on the market (ECHA, n.d.). If the risks are not adequately controlled, relevant authorities incl. the Commission or individual Member States can restrict their use, for example through authorisation requirements (ANNEX XIV) or EU-wide restrictions (ANNEX XVII).

Ultimately, companies should substitute the substances with the highest risk profile, referred to as "substances of very high concern" (SVHC), with suitable alternatives (European Commission, n.d.). Currently, certain substances classified as carcinogenic, mutagenic or reprotoxic (CMRs), persistent, bio-accumulative and toxic chemicals (PBTs) or very persistent and very bio-accumulative (vPvBs) may be identified as SVHCs under REACH (ECHA, n.d.). Other types of substances, including endocrine disruptors (EDs) or respiratory sensitisers, may be classified on a case-by case basis as SVHCs if they are found to be of 'Chemicals of equivalent concern' to CMRs, PBTs or vPvBs.

REACH Article 68(2) authorises the Commission to restrict a substance if it fulfils the criteria of being a CMR and if it could be used by consumers (on its own, in mixtures or articles). This is referred to as the generic approach to risk management or the 'Generic Risk Assessment' approach (GRA) (see more **Box 1.1)**. This procedure allows the European Commission to implement a restriction solely based on a substance's intrinsic hazard properties, i.e. there is no requirement to show that there is an unacceptable risk.

REACH is complemented by the CLP which obliges manufacturers, importers and downstream users of substances or mixtures to provide a classification, label and packaging for their unwanted substances before placing them on the market (ECHA, n.d.). The classification criteria in the CLP help identify substances' hazard classes such as physical, health or environmental hazards. Once the hazard class is identified, it needs to be communicated to the user. This is achieved through appropriate labelling.

Both the classification and labelling of some hazardous substances are harmonised across the EU to manage any potential risks in a systematic way. These harmonised risks assessments primarily concern the SVHC (ECHA, n.d.). Some other substances might be required to use the harmonised classification on a case-by-case basis. The harmonised classifications are listed in Annex VI to the CLP Regulation. A substance must be self-classified when it has no harmonised classification in Annex VI (to the CLP), but it does have hazardous properties (ECHA, n.d.). Mixtures are not subject to harmonised classification and labelling (CLH) hence they must always be self-classified before being placed on the market.

The existing regulation under REACH and CLP also applies to enzyme product producers. Currently, most of them are listed in Annex VI to the CLP, i.e. they have a harmonised classification (AMFEP, 2008), whilst the remaining enzyme products are self-classified. Proteases have additional classification due to their catalytic activities (Amfep, 2008). Regardless of the classification method, all enzymes and enzyme mixtures are classified as respiratory sensitiser 1.

1.3.2 Revision of REACH

REACH requires a review every 5 years to monitor progress in the achievement of its objectives (European Commission, 2018a). The most recent REACH review finalised in 2018 established that REACH is effective, efficient, coherent, relevant and generates EU added value (European Commission, 2018b). In addition, it identified opportunities for improvement such as further simplification and burden reduction (VVA, 2022). In the subsequent year, the Commission presented the European Green Deal (EGD) (European Commission, 2019) to provide the basis for its policy objectives to integrate sustainability considerations across different policy areas. In an attempt to address the recommendations for improvement from the second revision of REACH, the EGD announced the subsequent adoption of a Chemicals Strategy for Sustainability (CSS) (European Commission, 2020) targeting risks posed by harmful substances. The key action arising from the CSS is the ongoing revision of REACH, conditional on the results of an impact assessment. The revision is led jointly by The Commission's Directorate Generals for Internal Market, Industry, Entrepreneurship and SMEs (DG GROW) and DG Environment (DG ENV) (European Commission, 2022).

The ongoing revision is considering a number of potential reforms to the REACH. Each of them is being evaluated in targeted technical studies. The list of proposed revisions includes the following (CMS Law-Now, 2022; European Commission and DG GROW, 2021):

- Extension of the GRA to additional hazard classes and to professional uses;
- Reforms of the authorisation and restriction process of REACH, including the concept of essential use in authorisations and restrictions;
- Revision of the registration requirements, including increased information requirements to enable identification of all carcinogenic substances and substances with critical hazard properties (including effects on the nervous and the immune systems), registration of certain polymers of concern, and information on the overall environmental footprint of chemicals including GHG emissions;
- Introduction of Mixtures Assessment Factor(s) (MAF);
- Simplifying communication in supply chains;
- Revision of the provisions for dossier and substance evaluation;
- Revision of provisions for control and enforcement including stronger border controls and the creation of a European Audit Capacity for REACH, and;
- Provision of sufficient and appropriate standard information requirements on the intrinsic properties of a substance to identify endocrine disruptors.

The revision follows the EC's Better Regulation provisions (European Commission, n.d.) and will assess the impact of any changes to REACH for four main categories of impacts:

- Protection of human health and the environment;

- Use of animal testing;
- Functioning of the internal market, and;
- Competitiveness and innovation of European industry and businesses.

1.3.3 Extension of GRA

The CSS identifies the GRA as one of the most efficient measures which can achieve its goals of better human health and the environment protection against harmful chemicals by taking preventive action. The application of the GRA across legislation generally bans the most hazardous substances from most consumer uses. The CSS concludes that such preventive approach is simpler, faster, provides clear signals to all parties from industry and downstream users to enforcement authorities, and incentivises substitution and innovation (European Commission, 2020). Nevertheless, the majority of EU chemicals are currently assessed on a case-by-case basis, following the 'specific approach to risk management' (SRA) (see **Box 1.1**).

Box 1.1: CSS approaches to risk management

The CCS introduces two possible approaches to the risk management for unwanted substances: specific risk assessment (SRA) and generic risk assessment (GRA) (Ricardo, 2021). They are defined as follows:

GRA: *A 'generic approach to risk management' in an automatic trigger of pre-determined risk management measures (e.g. packaging requirements, restrictions, bans, etc.) based on the hazardous properties of the chemical and generic considerations of their exposure (e.g. widespread uses, uses in products destined to children, difficult to control exposure). It is applied in a number of pieces of legislation on the basis of specific considerations (e.g. characteristics of the hazard, vulnerability of certain population, groups, non-controllable or widespread exposure* (European commission, 2020).

SRA: *Specific risk assessments consider the hazard, the use of the substances and related specific exposure scenarios for humans and the environment, and risk management measures are triggered based on their outcomes* (European Commission, 2020).

The CSS aims for the GRA to gradually become the default option for what the CSS identifies as the "most harmful chemicals"[3]by extending the scope of Art. 68 (2) of REACH (AMFEP, n.d.; European Commission, 2020). At first, the Commission wants to extend the GRA to ensure that consumer products do not contain chemicals that are carcinogenic, mutagenic, reprotoxic, persistent, bioaccumulative and toxic, and/or endocrine disrupting . Secondly, the Commission plans to examine an extension of the GRA to cover further existing or yet to be established hazard classes, including hazard classes on chemicals affecting the immune, neurological or respiratory systems and chemicals toxic to a specific organ (European Commission, 2020). The extension of the GRA will allow the limited use of these most harmful chemicals where they are proven essential for society. The CSS announced that the essentiality criteria are yet to be defined as part of process separate from the REACH revision. The form to be taken by the criteria remains to be defined.

In addition to the extension of the GRA to other hazard classes, the CSS also seeks to establish the same level of protection as applied to consumers to professional users, i.e., to workers outside industrial settings and those

[3] Chemicals meeting the classification criteria for Category 1 in any of the following existing or yet to be established hazard classes: carcinogenicity, germ cell mutagenicity, reproductive toxicity, respiratory sensitisation, endocrine disruption, persistent, bioaccumulative and toxic substances,, immunotoxicity, neurotoxicity.

self-employed workers such as farmers or construction workers (VVA, 2022). This is because these types of users are expected to be prone to high exposure or emissions from the unwanted substances.

Table 1.1 summarises the scope of the current and revised GRA outlined in the CSS.

Table 1.1: Current and revised GRA scope in CSS

	Current GRA scope	Revised GRA scope
Uses covered	• Consumer uses	• Consumer uses • Professional uses
Hazard classes covered	• CMR cat. 1A and 1B	• CMR categories 1A and 1B • ED (HH and Env) • PBT/vPvB • STOT (SE and RE) • Respiratory sensitisers • Substances affecting the immune or neurological systems

Source: (VVA, 2022) and (European Commission, 2020).

The two proposed changes to the GRA scope that will have the largest impact on the EU enzyme industry is inclusion of chemicals classified as respiratory sensitisers. This is because all enzymes are classified as respiratory sensitisers (AMFEP, 2012). Furthermore, enzyme products are used in all types of uses, including consumers and professionals (as defined in REACH), both of which may potentially be banned by means of the GRA extension. If respiratory sensitisers are banned as a result of the expanded scope of the GRA, the enzyme industry would effectively be only permitted to sell their products to industrial users and/or export their products outside the EU.

1.4 Project scope and objectives

This study assesses socio-economic impacts of a possible extension of the GRA under the REACH Regulation for the EU manufacturers, formulators, and downstream users of enzymes. For the purpose of this assessment, the potential GRA extension is assumed to be equivalent to a ban of all substances with respiratory sensitiser properties that are intended for consumer and professional uses. Hence, despite all enzymes having properties of respiratory sensitisers (AMFEP, 2012), the scope of the analysis is limited to the list of enzyme uses and hazard classes considered in the revised GRA scope (see **Table 1.1**).

Despite food and feed enzymes being regulated by separate legislative frameworks and being subject to pre-market approval from the European Food Safety Authority (EFSA), it is assumed that they would be banned like other technical applications of enzymes (already in the scope of registration under REACH) due to consumer uses and professional uses.

Table 1.2 provides an overview of the consumer and professional enzyme uses which fall under a potential ban resulting from the revised GRA. The products are grouped into five product categories: food, feed, technical: detergents, technical: industrial application and technical: other uses. The list of uses is non-exhaustive and is

aimed at illustrating the scale of GRA impact on the enzyme industry.

Table 1.2: Example enzyme uses in SEA scope

Product category	Products for consumer uses	Products for professional uses
Food	• Use of flour containing enzymes by consumers to bake bread • Other do-it-yourself food applications containing enzymes	• Use of flour containing enzymes by craft bakers • Use of (an) enzyme product(s) as food processing aid(s) by craft/artisan cheese makers • Use of (an) enzyme product(s) in starch factories where workers fall under the definition of professional users (i.e., craft starch factories) • Use of (an) enzyme product(s) as food processing aid(s) by craft wineries/breweries • Use of (an) enzyme product(s) as food processing aid(s) by craft fruit juice producers • Use of (an) enzyme product(s) by craft oil producers • Other uses of enzyme products by craftsmen using enzyme products as processing aids • Use of enzymes by cooks in restaurants to treat meat
Feed	N/A	• Use of animal feed with enzymes by farmers • Use of enzymes approved as feed additives according to Commission Regulation 1831/2003 by feed millers for the production of animal feeds
Technical: detergents	• Use of detergents containing (an) enzyme(s) by consumers to wash clothes or dishes	• Employees at hospital wash medical device with Use of enzyme-containing detergents by employees at hospitals for cleaning medical devices. • Use of cleaning agents containing enzymes by employees of cleaning services for the cleaning of hard surface facilities/sites (e.g., hospitals, corporate facilities, public buildings) • Professional laundry and dish washing
Technical: industrial application	N/A	• Treatment of water/sewage with enzyme products by employees at sewage/waste treatment centers

Product category	Products for consumer uses	Products for professional uses
Technical: other	• Cosmetics containing enzymes • Medical diagnostic kits for diabetics (blood glucose testing)	• Employees at hospital/clinic/COVID center Use of diagnostic kits containing enzyme(s) by employees at hospital/clinic/COVID center.

Source: AMFEP

1.5 Structure of this report

The remainder of this report is structured as follows:

- **Section 2** outlines the socio-economic analysis method used to assess the possible impact of a ban on respiratory sensitisers on the enzyme market.
- **Section 3** sets out the baseline scenario, i.e. the situation in which no additional regulatory action is taken, by providing information on the variety of enzyme products produced and the size and composition of the enzymes market, including enzymes classified as respiratory sensitisers.
- **Section 4** assesses whether any alternatives exist based on information provided by AMFEP members through targeted questionnaires and interviews, as well as information identified in consulted literature.
- **Section 5** examines the 'ban' scenario by assessing the possible responses to a ban on the use of respiratory sensitisers and the consequential supply chain responses.
- **Section 6** provides information on the impacts, i.e. the costs and benefits, of the proposed ban. These costs and benefits include the economic impacts, environmental and health impacts, social impacts and impacts on EU end-users of banned enzyme products.
- **Section 7** summarises the key findings of the study and makes recommendations for the proposed revision of the GRA scope.

2 SEA method

2.1 Introduction

The socio-economic analysis (SEA) has been carried out in accordance with ECHA's SEA Guidance (ECHA, 2008). It seeks to assess the impacts, i.e. costs and benefits, of the potential ban based on the definition used by ECHA in the Annex XV dossier by estimating the 'net' impacts relative to the baseline scenario, which is the current situation in the absence of a restriction. As per ECHA's Guidance, the analysis has been carried out from society's perspective rather than the perspective of the enzymes sector.

The work was carried out between June and August 2022 in order to deliver results before the end of August 2022, following AMFEP's discussions with the Commission's contractor.

An inception meeting was held online on 21st June 2022, which was attended by representatives of the AMFEP Secretariat and several AMFEP members i.e. private companies manufacturing enzymes. The meeting provided an opportunity to better understand how the enzyme sector may be affected by the proposed REACH revision, in particular the potential GRA extension.

It was also an opportunity for companies to comment on a draft questionnaire in order to ensure that all questions were relevant to the sector and would be well understood by relevant stakeholders and that no essential questions were missing.

The inception meeting was followed by the stakeholder consultation process, which forms the basis of the analysis carried out in this SEA report and began on 1st July 2022. The consultation process consisted of the distribution of an Excel-based questionnaire to five AMFEP members and follow-up telephone interviews in the last week of July.

The purpose of these interviews was to enable a more in-depth exchange of information on specific topics, including market size, value chain and functions of enzymes in products within the scope of the GRA extension. Research and development activities undertaken to reduce or eliminate exposure to respiratory sensitisers and possible alternatives to final (formulated) enzyme products were other topics covered during the interviews, alongside the likely response of companies to an implementation of a potential ban of respiratory sensitisers for consumer and professional uses.

2.2 Policy scenarios assessed

This SEA seeks to assess the impacts, i.e., costs and benefits, of a potential GRA extension. If a substance falls under GRA, there are multiple risk management options that can be triggered (see Section 1.3), but it is not possible to predict the exact measures that would be implemented and when. Instead, this SEA assesses the impacts of a potential ban of enzyme products due to their respiratory sensitiser properties, as per advice from the Commission's contractors. The impacts are derived relative to the baseline scenario, which is the current situation in the absence of a ban.

The assessment is focussed on affected AMFEP members enzyme products, but where possible the data has been extrapolated to the entire EU market. Further details on the approach are also provided in the relevant sections where the results are presented.

2.3 Method used

To derive indicative EU estimates for enzyme product use volumes, the indicative market share of AMFEP members' participating in the study (see more details in Section 2.4) was used to extrapolate survey data to the EU. The exact EU market share of AMFEP respondents is not known, but the following information was used to derive a reasonable approximation:

- The global market share of AMFEP survey respondents' is 85% (Guerrand, 2017);
- The EU market share of all (including non-respondents) AMFEP members is 90% (AMFEP, 2022a)
- AMFEP comprises 28 full members.

Given that the five AMFEP members providing data in the survey have a significant total global market share (85%), the remaining 23 AMFEP members and any remaining enzyme product manufacturers not affiliated with AMFEP are likely smaller companies with lower market shares. In the absence of further information it is assumed that the five survey respondents have a similar market share in the EU and globally (i.e., 85%).

The total EU market volumes were derived from the respondents' data by uplifting it by the missing 15% of the EU market.

2.4 Data collection sources

The Excel questionnaire focused on gathering data on the number and volume of final (formulated) enzyme products manufactured, imported and sold as well as the number of final (formulated) enzyme products functional within mixtures and articles. Corresponding information on sectors and users (i.e. industrial, professional and consumers) was also gathered, to allow for a breakdown of the data based on whether it would be in the scope of a potential revision of the GRA.

Information on employment and the supply chain of enzyme product manufacturers was also collected. Furthermore, the questionnaire was used to gather data on costs of R&D carried out to reduce the risks arising from enzyme respiratory exposure, and information on existing downstream user alternatives to enzyme products. The questionnaire also sought to understand the companies' possible responses to a ban of respiratory sensitisers resulting from the GRA extension revised under REACH.

As illustrated in **Figure 2.1**, five companies provided data through the Excel questionnaire and through interviews. These are all major enzyme products manufacturers and formulators (i.e. none of the companies are SMEs). The companies also responded to follow-up questions, which improved the overall accuracy of the data. The information was then aggregated to preserve the confidentiality of individual responses. The stakeholder data was complemented with information found in literature suggested by the AMFEP Secretariat and AMFEP members as well as additional sources identified through desk-based research.

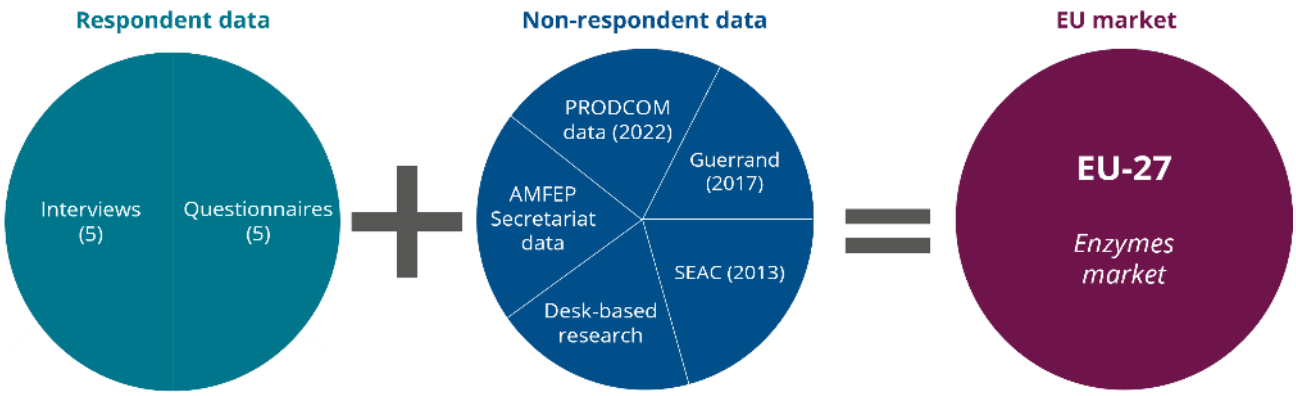


Figure 2.1: Method and data used to derive total impacts at EU-27 level

According to the data collected, the questionnaire respondents account for around 85% of the global enzymes market. The data collected is therefore considered to be sufficiently representative for extrapolating data to the entire EU market in a meaningful way.

The price year used in the analysis is 2022 and a discount factor of 4% has been used to calculate present values of impacts.

3 Baseline scenario

3.1 Introduction

As set out in ECHA's official guidance document on the preparation of a socio-economic analysis, a baseline scenario describes the "*situation in the absence of the proposed restriction (or any further Risk Management Options (RMOs))*" (ECHA, 2008, p.50.). The baseline scenario does not necessarily reflect the current situation as the expected implementation of new legislation of relevance, other than the restriction, or the modification of existing legislation over the timescale of the SEA should be considered according to ECHA (2008). Any other relevant expected developments such as a voluntary action should also be taken in account in the baseline scenario.

Sections 3.2 and 3 provide information on the uses of enzymes within the EU and uses of enzymes within the scope of the GRA, respectively. Sections 3.4 and 3.5 detail the volume of enzymes manufactured/imported within the EU-27 and the EU enzymes market, while Section 3.4 describes the existing EU regulations that are relevant.

3.2 Uses of enzymes within the EU

Enzymes are protein-based catalysts which are produced by fermentation (AMFEP and A.I.S.E., 2022). They are required by all living organisms, including humans, to conduct the physiological processes essential for growth and life. They act as catalysts that speed up the rate of specific chemical reactions and are used make and improve everyday consumer and commercial products, in industries from food and beverage, animal nutrition and textiles through to household cleaning, biofuels and energy generation (AMFEP, 2022c).

Enzymes are readily biodegradable, they generally exhibit no specific environmental toxicity and are hence not classified for the environment. In particular, industrial enzymes have an excellent safety profile, with little ability to cause adverse responses in humans (AMFEP, 2022c).

Enzyme products are available in liquid and solid formulations. Liquid formulations are a solution of the enzyme protein in water with several additives including stabilisers and salts, whilst solid enzyme products can be enzyme granulates (i.e., enzymes which are granulated with salts) or enzyme powder or immobilised enzymes (i.e., enzymes adsorbed onto a solid support) (Novozymes, 2022a).

Products containing final (formulated) enzyme products have a number of benefits, primary of which is the reduced environmental impact of manufacturing and consumer use of enzyme containing products. **Box 3.1** below highlights the benefits of using enzyme products in terms of climate change mitigation.

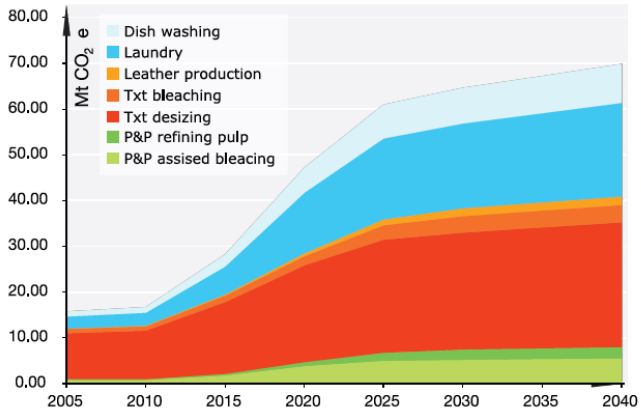
Box 3.1: Enzyme products contribution to the mitigation of climate change

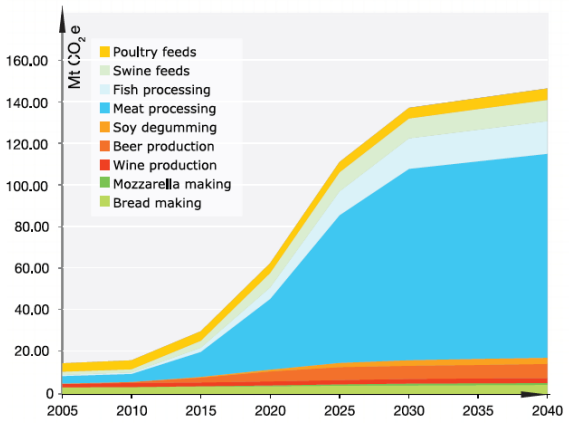
The World Wildlife Fund (2009) has estimated the global efficiency improvements that enzyme products could enable in the food sector and traditional industries. By 2030, enzyme products could indicatively save (compared to the baseline):

- up to 139 million metric tons of carbon dioxide equivalent ($MtCO_2e$) in the food industry; and
- up to 65 $MtCO_2e$ in traditional industries (detergents, textiles, pulp and paper).

This is equivalent to the CO_2 emissions released by consuming 430 million barrels of oil or taking nearly 40 million cars off the road (AMFEP, 2022d).

The following figures present emission reductions achieved by industrial biotechnology in the food and traditional industries, assuming industrial biotechnologies reach a market penetration of 100% by 2030.





Source: Bang et al. (2009)

In addition to having a positive impact on the environment, enzymes have a number of key societal benefits. **Table 3.1** below summarises the key societal benefits of enzyme products per sector (note: it is not an exhaustive list).

Table 3.1: Societal benefits from the use of enzyme products

Enzyme market category	Societal benefits of enzyme products
Food	• Improves the quality of food (for instance by standardising the results of a baking process, so that goods look similar and are reliably produced) and improves the safety of food • Increases the digestibility of food and reduces allergenicity (for instance it reduces the allergenicity of milk and helps milk become more acceptable to the infant) • Reduces the use of other raw materials and reduces energy consumption • Helps respond to special dietary needs, for example enzyme products facilitate the production of low-salt processed meats, and enable millions of people with lactose and gluten intolerances to digest dairy and bakery (e.g., bread) products
Feed	• Reduces the amount of inorganic phosphates farmers need to add, which in turn reduces the amount of phosphorus in animals' waste that ends up in the environment • Reduces the amount of certain chemicals released to the environment (e.g. reduced nitrogen excretions) by improving the availability of chemical uptake (Pan et al., 2017). • Enzymes enable producers to optimise animal production in a sustainable way e.g. more meat per animal or same amount of meat cheaper. • Enzymes enable feed efficiency improvements with cost savings
Technical - Detergents	• Enables low temperature washes, and as a result reduces energy consumption, CO_2 emissions and costs for consumers • Breaks down soils and stains and thus achieves improved washing performance • Contributes to making detergents more environmentally friendly, by reducing the chemical load to the environment and reducing the amount of raw materials used in detergent manufacturing (e.g. by improving compaction)

Enzyme market category	Societal benefits of enzyme products

Technical – all other applications	• Textiles
	  ○ Reduces and removes the chemical load to the environment
	  ○ Enables mild processes at neutral pH and low temperatures, avoiding the use of treatment (e.g. reducing the amount of acids and bases used in the processing of textiles) and reducing water consumption
	  ○ Increases the lifetime of textiles
	• Leather
	  ○ Less chemicals, surfactants and solvent used
	  ○ Shorter processing times
	• Bioenergy
	  ○ Bioethanol supply to the society
	• Pulp and paper
	  ○ Reduces the chemical load and energy consumption
	  ○ Ensures better paper quality
	• Wastewater treatment
	  ○ Increases the efficacy of Chemical Oxygen Demand (COD) removal, thereby further improving the quality of the effluent
	• Medical diagnostics
	  ○ Rapid and inexpensive medical tests including glucose monitoring for diabetics

Sources: AMFEP (2022b); Novozymes (2013); and Interviews (2022) with enzyme products manufacturers and formulators (n=5)

In addition to the environmental benefits described above, enzymes are used in both Food and Feed products to remove hazardous substances. Both zearalenone and fumonisin B1 – B3 have hazard profiles relating to human health and consequently are included in the EU Commission Regulation No 1881/2006 which sets maximum levels for certain contaminants in foodstuffs. Moreover, European Commission Recommendation 2006/576/EC, which limits Fumonisin (B1 & B2) and zearalenone in Feed and Food materials (e.g., maize), respectively. The enzyme Fumonisin esterase is able to detoxify fumonisin (B1 - B3) by cleavage of the toxins' diester bonds and removal of the tricarballylic acid (TCA) side chains. This is effective showing a reduction of up to 87% of fumonisins in corn dry milling (which is a standard process for the production of corn flour). Also, the enzyme has been tested in the production for corn gluten and maize flour porridge with up to 100% fumonisin reduction (AMFEP, 2022e). Zearalenone hydrolase is able to significantly reduce zearalanone content in a number of different food processes. For example, corn oil is susceptible to zearalanone contamination, but by treating corn germs before oil production zearalanone content can be reduced by up to 51% (AMFEP, 2022f). Zearalenone detoxification with a zearalanone hydrolase of more than 90% has also been reported in Chang et al. (2020). Reducing these hazardous microtoxins/contaminants are critical for food safety, thus the use of enzymes in Food and Feed products are essential to human society.

Furthermore, enzyme products enable various industries to guarantee high quality and stability of products. For example, cotton treated with enzyme products does not generate pilling (fluff) - it looks better and lasts longer. In the fruit juice industry, enzyme products make the fruits easier to press and the juice clearer, resulting in higher fruit yields. Moreover, enzyme products also improve the efficiency of industrial processes:

- Enzyme reactions are often carried out under mild conditions enabling the use of simple and widely available equipment;

- Enzyme reactions are highly specific with high reaction rates;
- Enzymes increase the yields and minimise unwanted by-products; and
- Small amounts of enzymes are needed in order to carry out chemical reactions even on an industrial scale. The use of enzyme products thereby leads to lower storage space requirements compared to alternative processing aids.
- Enzymes reduce the environmental impact of manufacturing by reducing the use of raw materials (including chemicals, water, and energy) and the amount of waste generated.

Table 3.2 below, summarises key enzyme product uses by the four main enzyme market categories ('Food', 'Feed', 'Technical – detergents' and 'Technical – all other applications').

Table 3.2: Enzyme products use per sector

Enzyme market category	Downstream user	Function of enzymes
Food	Industrial users and professional users (bakers)	Enzyme products are used as processing aids in many different applications, including fresh-keeping of bread and other baking applications, brewing, grain milling and food processing. Numerous products are produced with the help of enzyme products, such as: • bakery products (e.g. bread and cookies); *see **Box 3.2** for more information* • dairy products (cheese, lactose-free milk, infant milk formulas, yoghurt etc.); • meat products; • fruit products, beer and wine; • sweeteners (starch modification/hydrolysis); and • many others (e.g. salad dressings, mayonnaise and baby food). The use of enzyme products is significant for some food products and processes, for instance clotting milk for the production of cheese and quark and the saccharification of starch into sugar.
Feed	Industrial users (formulators) and professional users (farmers)	Enzyme products are used as ingredients in animal feed to improve the quality of the product and enhance its digestibility by livestock. As such, enzyme products improve the nutrient availability of the product to the animal and enable the use of lower quality feed. Thus, the use of enzyme products is significant. For example, the enzyme phytase breaks down phytate, which together with phytic acid accounts for around 50–80 % of the total phosphorus present in pig and poultry diets, to release the bound phosphorus but also other essential nutrients to give the feed a higher nutritional value.
Technical - Detergents	Industrial users (formulators), professional users and consumers	Enzyme products are used as ingredients in various household care products, such as laundry and dishwashing detergents, as well as products used in industrial and institutional cleaning and industrial laundry. Enzyme products make detergents more efficient in removing grease, soil, starch and protein stains during a washing cycle. They are also considered essential for improving the performance of low temperature washes and the compaction of detergents. As a result, fewer chemicals are used in this application. EU Ecolabel[4] restricts the use of sensitisers, therefore detergents containing enzymes (as respiratory sensitisers) would be excluded – however, enzymes have been derogated due to

[4] "Ecolabelling" is a voluntary method of environmental performance certification and labelling. An ecolabel identifies products or services proven environmentally preferable overall, within a specific product or service category.

Enzyme market category	Downstream user	Function of enzymes
		acknowledgement that they have a good safety profile and are essential in order to achieve the overall goals of the European Green Deal.
Technical – all other applications	Industrial users	Enzyme products are used as processing aids in textile processing and fabric finishing. Enzyme products are needed for some textiles (e.g. denim), whilst for others they enhance the sustainability of the product (resulting in long-lasting textiles). For instance, enzyme products are important for: • Cold bleaching of denim, replacing the chemical bleaching process; • Denim abrasion, replacing stone wash; and • Biopolishing, removing protruding fibres from cotton for long lasting clothes. Most cotton derived textiles are processed with enzyme products. Enzyme products are also used as processing aids in leather production, for instance for: • Improving the quality of soaking, liming (to remove hair), and bating (to remove residues of non-collagen protein and other material); • Degreasing, i.e. improve fat dispersion and the production of waterproof and low-fogging leathers. The use of enzyme products is needed for the leather industry, especially since the use of various chemicals has been replaced by enzyme products, which has made the process more sustainable. In addition, enzyme products are used as processing aids for ethanol production, to break down the starch and cellulose into fermentable sugars. Enzyme products are also used for biopolymer production (where they catalyse polymerization). Enzyme products are used in the biofuel industry as processing aid for manufacturing of bioethanol and biodiesel for non-fossil based energy sources for transport. Enzyme products are needed for ensuring the efficient use of raw materials, accelerating the fermentation process, reducing the treatment time, controlling viscosity, and improving yields. Enzyme products are used as processing aids in pulp and paper manufacturing to remove ink and control pitch, treat starches for paper applications, enhance bleaching, improve the softness of tissues and improve filtration and dewatering. Enzyme products are needed for reducing the use of chemicals and energy, and for ensuring a better quality of paper. Enzyme products are used as processing aids in wastewater treatment to give a good boosting effect and clarify wastewater by degrading organic matters. Enzymes are essential for many medical diagnostic kits. Most notable is blood glucose measurements for diabetics.

Sources: AMFEP (2022b); (Novozymes, 2013); and Interviews (2022) with enzyme products manufacturers and formulators (n=5)

Box 3.2 describes two examples of the use of enzymes in the food industry. Firstly, the use of maltogenic amylase in white bread and secondly, asparaginase breaking down acrylamide in starch-based foods.

Box 3.2: Detailed example of enzymes in the food industry

The enzymes such as maltogenic amylase are used in white bread to reduce staling[5] and asparaginase are used to reduce the formation of acrylamide in starch-based foods. See the following bullet points for more

[5] Staling is a highly complex phenomenon with 'firming' being the most well-known and important symptom.

information:

- Amylases (e.g., maltogenic amylase) can be added to the dough to degrade damaged starch, which is fermented by the yeast before the bread making stage. This process reduces staling. Doubling the volume of this one specific enzyme keeps white bread fresh for 3 more days and thereby lowering the disposal rate of old bread from 24% to 19%. This results in a reduction of 20kg of CO_2e from the end-of-life phase of the bread (AMFEP, 2022b).
- Acrylamide is an unwanted (hazardous – carcinogen) substance that can be formed in multiple starch-based foods when heated, due to the natural presence of certain sugars and amino acids. Enzymes (e.g., asparaginase) enable reduced acrylamide formation in affected baked goods and other foods by up to 95% without compromising on taste, texture, flavour or smell. The enzymes offer a solution to healthier baking and also an answer to acrylamide challenges in specific baked goods.

Source: AMFEP (2022b)

3.3 Uses of enzymes within the scope of the GRA

Under the existing REACH regulation, there are no hazard properties of enzymes that are likely to trigger a potential REACH restriction or authorisation requirement. However as explained in Section 1.3, the potential extension of the GRA, could mean that enzymes used for **professional and consumer uses** are within the scope of a future REACH restriction, as enzymes are classified as respiratory sensitisers. This is an intrinsic hazard property of all enzymes, which means that all enzymes are classified as respiratory sensitisers.

Uses of enzymes and their relevance for GRA is detailed below, based on the EC contractors survey (DG GROW, 2022). **Table 3.3** sets out the hazard classes covered under the proposed expansion of the GRA scope and their relevance to final (formulated) enzyme products. It shows that the only hazard classification relevant to enzymes is 'respiratory sensitisers'.

Table 3.3: Hazard classes covered under the GRA and their relevance to final (formulated) enzyme products

Hazard classes	Hazard classes covered under the proposed GRA scope and their relevance to final (formulated) enzyme products			
	Manufacturing substances with these hazard classes	Using in mixtures	Using in articles	I do not know if substances display these properties
Endocrine disruptors (ED) with effects for human health	No	No	No	N/A
Endocrine disruptors (ED) with effects on the environment	No	No	No	N/A
Persistent, bioaccumulative and toxic substances (PBT)	No	No	No	N/A
Very persistent and very bioaccumulative substances (vPvB)	No	No	No	N/A
Substances with specific target organ toxicity, single exposure (STOT SE)	No	No	No	N/A
Substances with specific target organ toxicity, repeated exposure (STOT RE)	No	No	No	N/A

Immunotoxic substances	No	No	No	N/A
Neurotoxic substances	No	No	No	N/A
Respiratory sensitisers	Yes	Yes	Yes*	N/A

Table notes:

- This table answers specifically Q18 of the EC contractors survey: "Q18. Are you manufacturing, using in mixtures or using in articles, substances in the following hazard classes?"
- Result based on survey responses (n=5). There is consistency between respondents. The only variation (noted by a *) related to use of enzymes in articles where some respondents noted that it only applies if the enzyme is 'functional' in the article.

In the EC contractors survey, they ask questions (e.g. Question 20) related to the number of substances used (e.g. as a raw material input to make a product) for each relevant hazard classification. In relation to enzyme production, all enzymes manufactured will be classified as respiratory sensitisers regardless of the raw materials used. Therefore, 100% of enzymes manufactured will be respiratory sensitisers.

Table 3.4 sets out who uses the final (formulated) enzyme products broken down by use types. It shows that enzymes have industrial uses, professional uses, and consumer uses. The only exception is animal feed products which are only available to industrial and professional users (e.g. farmers) and are not available to the general public. Furthermore, the GRA only applies to professional and consumer uses – industrial use is included partly for completeness but also because if downstream customers (e.g. professionals and consumers) cannot buy their products due to a ban, they would be 'indirectly' affected by the GRA.

Table 3.4: Who uses the manufactured final (formulated) enzyme products

Enzyme market category	Industrial use	Professional use	Consumer use
Food	Yes	Yes	Yes
Feed	Yes	Yes	No
Technical - detergents	Yes	Yes	Yes
Technical - all other applications	Yes	Yes	Yes

Table notes:

- Result based on survey responses (n=5) where the most frequent response is presented. Not all companies produce enzyme products for each market category and therefore these markets were not relevant/appliable (n/a) for some companies. N/A responses were therefore excluded even if it was the most frequent response.

When sold as a final (formulated) enzyme product for downstream use, the enzyme is functional and viewed as a respiratory sensitiser. However, some enzymes are non-functional but may remain in the product. This is common in food products since enzymes are mostly used as processing aids (Commission Regulation (EC) No 1332/2008), and as such they fulfil their technological function during food production and will not have a technological function in the final food product. This is commonly achieved through heat or pH treatments, or substrate depletion. Therefore, only consumer and professional uses of functional enzymes are in the scope of this SEA.

Table 3.5 shows that for each enzyme market category some products exist whereby the enzyme is still 'functional' within a mixture (as defined under REACH), and therefore the respiratory sensitisation hazard is still present. However, there are risk management measures (RMMs) in place that limit exposure risk to ensure their

safe use (see Section 4.2).

Table 3.5: Are any of the final (formulated) enzyme products within a mixture?

Enzyme market category	Are any of the final (formulated) enzyme products within a mixture?		
	Industrial use	Professional use	Consumer use
Food	Yes	Yes	Yes*
Feed	Yes	Yes	N/A
Technical - detergents	Yes	Yes	Yes
Technical - all other applications	Yes	Yes	Yes

Table notes:

- Result based on survey responses (n=5) where the most frequent response is presented. Not all companies produce enzyme products for each market category and therefore these markets were not relevant/appliable (n/a) for some companies. N/A responses were therefore excluded even if it was the most frequent response except in the case of feed for consumer use as this is not relevant as it is not available to consumers.
- * - indicates that some companies indicated a different response as it is depends on the specific consumer product(s). However, "Yes" is noted in such instances as it relates to the presence "any" final product within each market category that contains a functional enzyme.
- Note that the GRA only applies to professional and consumer uses – Industrial use is included partly for completeness but also because if downstream customers (e.g. professionals and consumers) cannot buy their products due to a ban, they would be 'indirectly' affected by the GRA.
- ECHA (2022a) defines a mixture as *"a mix or solution of two or more substances"*. Under the EU chemicals legislation, mixtures are not considered substances. Examples of mixtures are paints, shampoos, and detergents.

Table 3.6 shows that when it comes to articles (as defined under REACH) enzymes may no longer be 'functional' in the final product, and the presence of any hazard depends on the application. In general, final (formulated) enzyme products are mostly mixtures, with a few exceptions where the product is viewed as an article under REACH – specifically medical diagnostic tests.

Table 3.6: Are any of the final (formulated) enzyme products within an article?

Enzyme market category	Are any of the final (formulated) enzyme products within an article?		
	Industrial use	Professional use	Consumer use
Food	No	No	No
Feed	No	No	N/A
Technical - detergents	No	No	No
Technical - all other applications	No	Yes	Yes

Table notes:

- Result based on survey responses (n=5) where the most frequent response is presented. Not all companies produce enzyme products for each market category and therefore these markets were not relevant/appliable (N/A) for some companies. N/A responses were therefore excluded even if it was the most frequent response except in the case of feed for consumer use as this is not relevant as it is not available to consumers.
- Yes - shows that one or more companies indicated "Yes" – when asked if there was the presence of "any" final product within each market category that contains a functional enzyme. This was found to only occur in Technical – all other applications as a result of medical diagnostics tests.
- Note that the GRA only applies to professional and consumer uses – Industrial use is included partly for completeness but also because if downstream customers (e.g. professionals and consumers) cannot buy their products due to a ban, they would be 'indirectly' affected by the GRA.
- ECHA (2022a) defines an article as *"substances used to produce things that have a special shape, surface or design."* When the special shape, surface or design determines the function to a greater degree than the chemical composition, these are called articles under the legislation. Examples of articles are bicycles, batteries, and CDs.

As noted in Sections 1.3.3 and 1.4, the extension of the GRA means that respiratory sensitisers will be within the revised scope when used in products for professionals and consumers[6], resulting in a possible ban on enzymes in such products. Appropriate RMMs are already implemented to reduce the level of exposure to respiratory sensitisers for workers during manufacturing (AMFEP, 2022h). For consumers and professionals using products containing enzymes safety is ensured via improved product forms (e.g. encapsulated products) and/or appropriate instructions of use. However, these measures seem not be considered under the revised GRA. This will lead to impacts on professional and consumer uses, as well as indirect impacts for uses not in the scope (i.e., industrial uses) as the demand for their products will be affected.

3.4 Volumes of enzymes made/imported within the EU-27

3.4.1 Volumes of enzymes made within the EU-27

Europe is the leading producer of enzyme products, accounting for around 80% of the global enzymes market in 2019 (AMFEP, 2022a). According to PRODCOM (2022), Europe's total sales of produced enzyme products amounted to 260,259 tonnes in 2020. The manufacture of enzyme products in Europe is concentrated in five countries as shown in **Figure 3.1**. In 2020, Denmark, Finland, Belgium, France and Germany accounted for 250,374 tonnes, or 96%, of the total volume of enzyme products sold by European manufacturers (PRODCOM, 2022). Denmark (53%) and Finland (24%), alone, produced 77% of the total volume of enzyme products sold in the EU that year, while Belgium (8%), France (7%) and Germany (4%) accounted for a further 19% (PRODCOM, 2022). A detailed breakdown of the quantity of enzyme products sold by European countries can be found in Appendix 1 under **Appendix Table 1**.

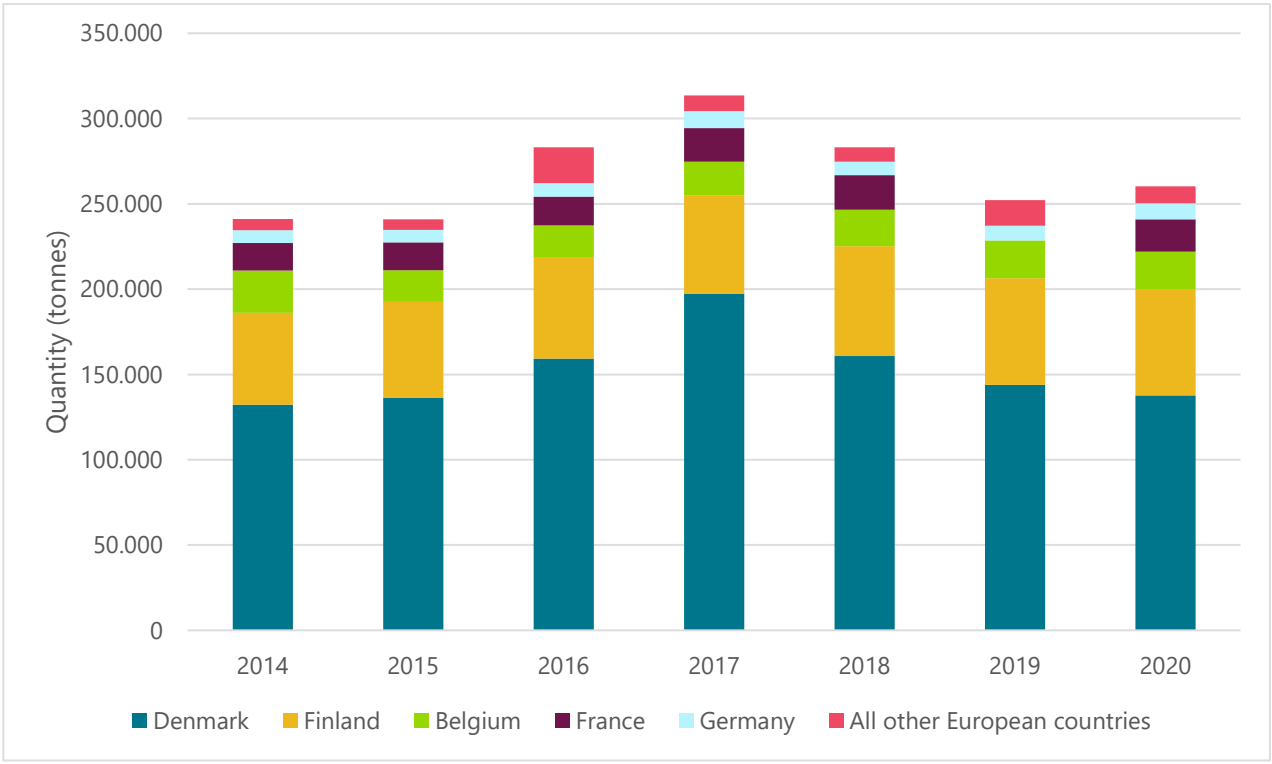


Figure 3.1: Sold production volume of enzyme products in the EU (by country), 2014 – 2020

[6] It should be noted that enzymes used in industrial processes are still outside of the extended GRA's scope.

Source: Derived from PRODCOM (2020)

Note: "all other European countries" refers to all other countries that were listed in the PRODCOM database shown in **Appendix Table 1**.

3.4.2 Volumes of enzymes used within the scope of the GRA

Table 3.7 sets out details on the total number of final (formulated) enzyme products made and/or imported in the EU-27 and those that would fall within the scope of the proposed revision to the GRA based on data gathered for this project from the 5 leading EU manufacturers of enzymes. The table shows that there are around 3,500 formulations which are either made or imported into the EU-27, of which all (100%) would have a respiratory sensitisation hazard classification. It is estimated that 40% of formulations (n=1,410) would be within the proposed scope of the GRA (as set out in **Table 1.2**).

Table 3.7: Total number of final formulated enzyme products within the scope of the GRA

Enzyme market category	Number of final (formulated) enzyme products made in or imported into the EU-27			Share (%) of total number of final (formulated) enzyme products that would be in the scope of a revised GRA
	Total	… that are respiratory sensitisers	… that would be in the scope of a revised GRA	
Food	2,400	2,400	550	23%
Feed	200	200	200	100%
Technical - detergents	650	650	650	100%
Technical - all other applications	300	300	10	3%
TOTAL	**3,550**	**3,550**	**1,410**	**40%**

Table notes:

- The total number of final (formulated) enzyme products is the sum of formulations made by each company and extrapolated to account for those EU companies that were not surveyed
- Result based on survey responses (n=5), but not all companies produce enzyme products for each market category. Data from these 5 companies are representative for the entire EU-27 market (i.e., they account for the majority of the EU-27 market). The results have been extrapolated to account for those EU companies that were not surveyed.
- The number of formulations reported are rounded to the nearest 50 (or nearest ten if less than 50)

Whilst the total number of final formulated enzyme products within the scope of the proposed changes to the GRA is a useful indicator for certain types of impacts, it is also important to know the corresponding volumes.

As detailed in Chapter 4, enzymes are very effective which means that only a small amount is required to delivery its intended functions. Enzyme products are available in liquid and solid formulations, and the volumes reported in **Table 3.8** include the liquid content (e.g. water), as this was the sales tonnage data that was readily available to collect in a short period of time. Volumes reported in this SEA will therefore not match the REACH registration

data which relates to the the enzyme concentrate dry matter for technical enzyme applications only.[7] Furthermore, the totals presented are based on survey data which has been extrapolated to provide a best estimate for the EU-27 market. The volume of final (formulated) enzyme products reported here (~230,000/year) are close to those reported in **Figure 3.1** (~250,000 tonnes/year using PRODCOM data) but will not match since they are derived from two completely different datasets and methods.

Table 3.8: Volume of final formulated enzyme products within the scope of the GRA

Enzyme market category	Total annual volume (tonnes) of final (formulated) enzyme products			Percentage (%) of total volume of final (formulated) enzyme products that are made in the EU-27 and/or imported that are within the scope of the GRA?	Total annual volume (tonnes) of final (formulated) enzyme products that are made in the EU-27 and/or imported that are within the scope of the GRA
Enzyme market category	**Manufactured (M)**	**Imported (I)**	**Manufactured and imported (M+I)**		
Food	35,150	3,700	38,850	4%	1,700
Feed	40,900	3,150	44,050	67%	29,600
Technical – detergents	83,850	8,800	92,650	51%	47,150
Technical – all other applications	47,850	6,650	54,500	0.2%	100
TOTAL	**207,750**	**22,300**	**230,050**	**34%**	**78,550**

Table notes:

- The total volume of final formulated) enzyme products is the sum of volumes made/imported by each company and extrapolated to account for those EU companies that were not surveyed
- Result based on survey responses (n=5) but not all companies produce enzyme products for each market category. Data from these 5 companies are representative for the entire EU-27 market (i.e., they account for the majority of the EU-27 market). The results have been extrapolated to account for those EU companies that were not surveyed.
- The volume of final formulated) enzyme reported are rounded to the nearest 50 tonnes / year. The tonnage data reflects what is termed a 'representative annual average' rather referring to a specific year. This was done to mitigate risks of using specific years of historical data which may have been skewed due to the impacts of COVID-19.
- The totals presented are based on survey data which has been extrapolated to provides a best estimate for the EU-27 market. The volume final (formulated) enzyme products reported here (~225,000/year) are close to those reported in **Figure 3.1** (~250,000 tonnes/year using PRODCOM data) but will not match since they are derived from 2 completely different datasets and methods.

Table 3.8 shows that nearly 230,000 tonnes of final formulated enzyme products are either manufactured or imported into the EU-27 per year, whereby imports only account for ~10% of the total volume that is manufactured in and imported into the EU-27. It also shows that around 34% of the total volume of final formulated enzyme products (~79,000 tonnes per year) manufactured in and imported into the EU-27 is within the scope of the GRA. The remaining total annual tonnage (~66%) is deemed to not be directly within the scope of the GRA. This volume may, however, be indirectly impacted as downstream products manufactured using industrial enzymes may be impacted by a revised GRA. The enzyme market categories most impacted by a

[7] Whilst some respondents provided dry matter volumes, all respondents provided volume data for final formulated enzyme volumes, so this is reported in this SEA. It is also relevant to note that "*industrial enzymes are used in a variety of applications, some of which require their registration under the so-called REACH Regulation*" (ERC, n.d.) For food and feed enzymes no registration is required by any EU Regulation. Therefore, using just REACH tonnage data would under-report volume data.

revision of the GRA would be 'feed' and 'technical – detergents' applications. Only a small proportion (volume basis = 4%) of 'food' applications is directly within the scope of the GRA and most technical applications that are not detergent-related applications are outside of the scope of the GRA.

Around 92% of what is either made or imported into the EU is sold to customers within the EU-27 (See **Table 3.9**). What is exported (8%) is relativity small in comparison but aligns with what is imported (~10%). This shows that enzymes made in the EU-27 are typically sold within the EU-27 with imports and exports somewhat cancelling each other out and may relate to specialist food products.

Table 3.9: Proportion of EU sales within and outside the EU-27

Enzyme market category	Total volume (tonnes) of final (formulated) enzyme products manufactured and/or imported into the EU-27 that would be within the scope of the GRA	
	Sold within the EU	Sold outside the EU
Food	77%	23%
Feed	99%	1%
Technical - detergents	87%	13%
Technical - all other applications	97%	3%
TOTAL	**92%**	**8%**

Table notes:

- Result based on survey responses (n=5) but not all companies produce enzyme products for each market category. Data from these 5 companies are representative for the entire EU-27 market (i.e. they account for the majority of the EU-27 market).

Finally, companies were asked to estimate how the market over the next five years will change per year for products that are within the scope of the GRA. As set out in Table 3.10 the overall market is expected on average to increase by 5.1% per year, with growth expected in each market category. This growth rate is aligned with historical growth rate for the sector whereby between 1996 and 2010, the market value of the enzyme sector more than doubled based on an average annual growth rate of 4.9% (eftec, 2019).

Table 3.10: Expected EU-27 market trends over the next 5 years

Enzyme market category	How you do expect the EU-27 market for final (formulated) enzyme products that are within the scope of the GRA to change per year (+/-) over the next 5 years
Food	5.4%
Feed	3.5%
Technical - detergents	6.3%
Technical - all other applications	4.0%
AVERAGE	5.1%

Table notes:

- Result based on survey responses (n=5) but not all companies produce enzyme products for each market category. Data from these 5 companies are representative for the entire EU-27 market (i.e., they account for the majority of the EU-27 market).

3.5 EU enzymes market

This section provides context to the scale of impacts caused by a possible ban and highlights the importance of the enzyme sector to the EU in terms of employment and market value. It also looks at the enzyme market globally. It highlights different aspects of the market, such geographical clusters and key downstream user industries.

3.5.1 Key global market actors

Europe is the largest enzyme producing region in the world (AMFEP, 2022a). According to Sarrouh et al. (2012) the United States and Japan have also been major producers of enzyme products. Denmark is the largest producing country with companies such as Novozymes and Danisco - a company acquired by DuPont's Nutrition & Biosciences Business in 2011 and transferred to IFF under a merger agreement in 2021 (IFF, 2022) – located there. Germany and the Netherlands have also been important European producers due to the presence of companies like BASF and DSM. Companies from India and China were expected to become relevant players in the concentrated enzyme market in the future (Sarrouh et al., 2012). Domestic production of enzyme preparations in China has increased by an average CAGR of 9.03% between 2008 and 2017 (Daxue Consulting, 2020).

The Association of Manufacturers and Formulators of Enzyme Products (AMFEP) represents the enzyme industry in Europe. AMFEP represents 28 full member organisations and a further two associated member organisations (AMFEP, 2022i). In total, AMFEPs members represent 90% of the European enzymes market (AMFEP, 2022a).

The enzymes market was dominated by six companies in 2012, with Novozymes, DuPont's Nutrition & Biosciences Business (now under IFF), DSM, BASF, Associated British Foods (AB Enzymes), and Captive Production, accounting for more than 90% of the global enzyme market (De Guzman, 2013). In 2015, Novozymes, DuPont and DSM were still among the leading global producers of enzyme product accounting for more than 75% of the global market, with AB Enzymes (8%), BASF (3%), Christian Hansen (2%), Kerry and Soufflet Biotechnologies being other important European manufacturers of enzyme products (Guerrand, 2017). **Figure 3.2** provides the global market share of the key producers of enzyme products as of 2015.

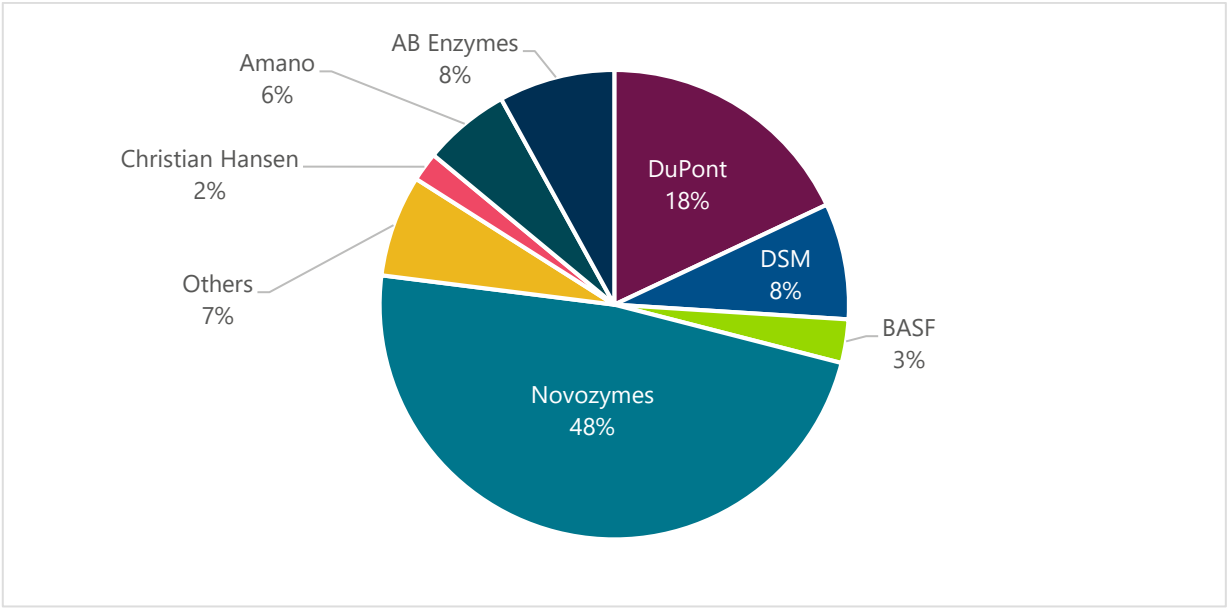


Figure 3.2: Global market share of enzyme products by company, 2015
Source: Guerrand (2017).

3.5.2 Global market

In 2010, the global enzymes market reached an estimated value of nearly €2.5 billion, where both technical enzyme products and enzyme products used for food and beverages accounted for around 30% each (eftec, 2019). Between 1996 and 2010, the market value of the enzyme sector more than doubled based on an average annual growth rate of 4.9% (eftec, 2019).[8] In 2010, the leather and bioethanol segments had the highest value within the technical enzyme market , whilst the milk and dairy market was the leading market segment with respect to enzyme products for the food and beverages sector (Sarrouh et al., 2012).

The value of the global enzymes market in 2012 was close to the 2010 market value, between €2.33 and €2.72 billion (De Guzman, 2013; eftec, 2019). Whilst having accounted for approximately 48% in 1996, enzyme products used in detergents only comprised 23% of the global enzyme market value in 2012, as illustrated in **Figure 3.3**. Enzyme products for other technical applications, e.g., textile and personal care applications and leather as well as pulp/paper processing, together accounted for 22% of the global market value in 2012.

[8] See OECD (1998) for 1996 figures on global enzymes market.

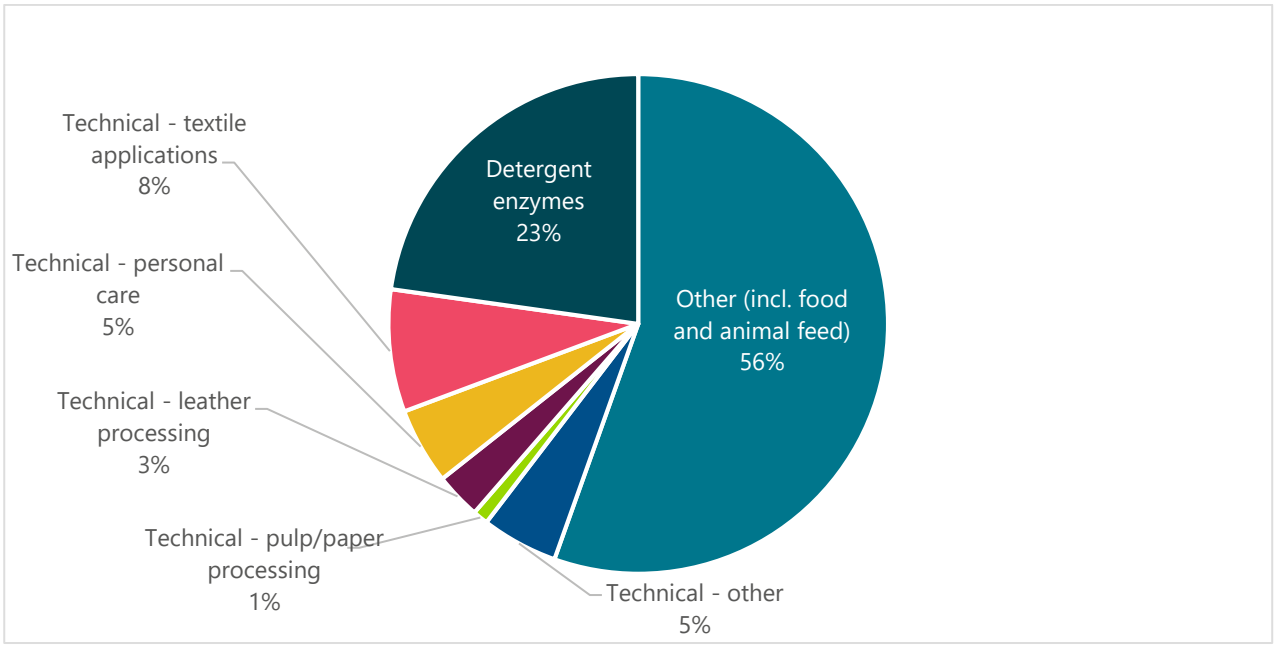


Figure 3.3: Global enzymes market share by application in 2012
Source: De Guzman (2013)

As shown in **Figure 3.3**, enzyme products for the food & beverage sector accounted for the biggest share (35%) of the total market value followed by enzyme products for cleaning agents and the animal feed sector accounting for 25% and 20%, respectively. The market shares of each sector have, however, not changed significantly between 2012 and 2015, as can be seen in **Figure 3.3** and **Figure 3.4**. The increase of per capita income in emerging economies leading to increased demand for processed food and beverages is one reason behind the significant growth of the food and feed sector (Guerrand, 2017).

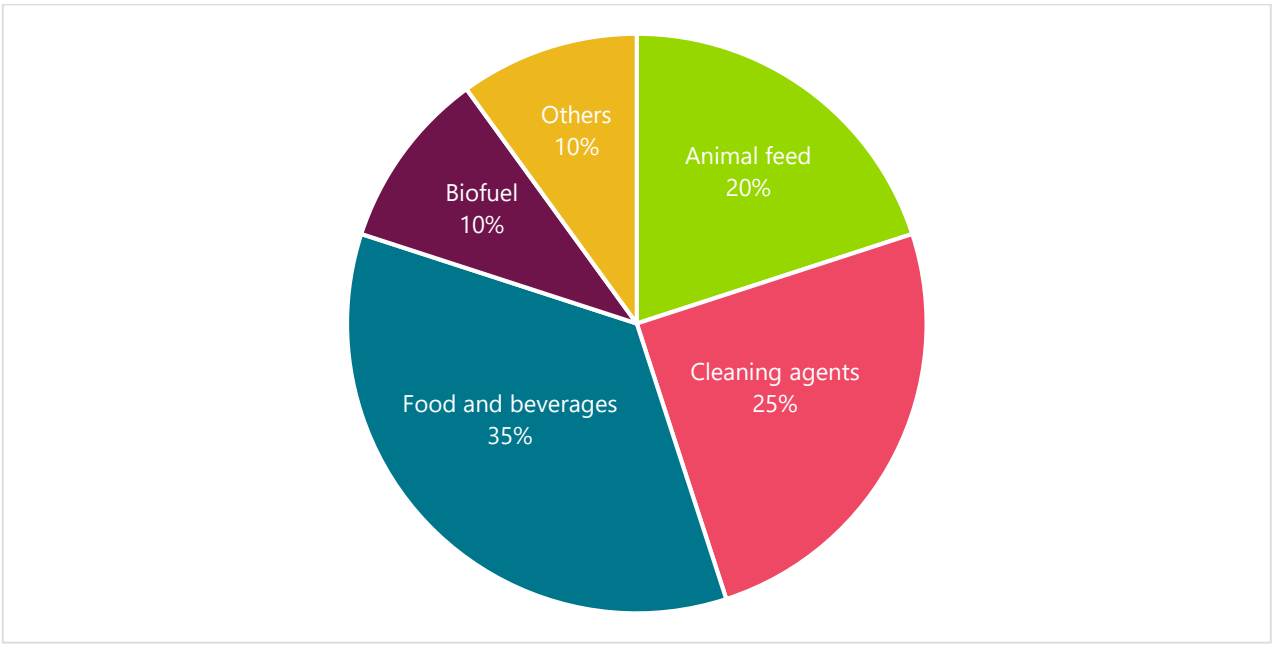


Figure 3.4: Global enzyme products market share by application (based on value), 2015

Source: Guerrand (2017)

In 2016, the global enzymes market was estimated between €4.5 billion and €5 billion[9] (Guerrand, 2017). By 2018, the global market value was estimated to be €6.02 billion (Bano et al., 2017). The growth of the global enzymes market from 1996 to 2018 is represented in **Table 3.11**.

Table 3.11: Change in global enzymes market value (1996-2018)

Market value (estimated)	Year	Source
€0.49 billion - €1.25 billion	1996	(OECD, 1998)
€2.5 billion	2010	(Sarrouh et al., 2012)
€2.33 billion - €2.72 billion	2012	(De Guzman, 2013)
€4.5 billion - €5 billion	2016	(Guerrand, 2017)
€6.02 billion	2018	(Bano et al., 2017)

Note: figures presented are undiscounted and converted from dollars to euros using average exchange rate for their respective year.

3.5.3 EU market

According to PRODCOM (2020) the total value of European enzyme production in 2020 was approximately €2.11 billion. **Table 3.12** shows that Denmark accounted for 58%, (€1,223 million) of European enzyme production and that the remaining significant producing countries – Finland, Germany, France, Lithuania, and Belgium – accounted for a further 38.5%. A detailed breakdown of the production values of all European countries from 2014 to 2020 can be found in Appendix 1 under **Appendix Table 2**.

Table 3.12: Production value of enzyme products in Europe (2020) - PRODCOM

Country	Production value (in € million) in 2020	Percentage share
Denmark	1,223	58.0%
Finland	264	12.5%
Germany	192	9.1%
France	159	7.5%
Lithuania	121	5.8%
Belgium	75	3.6%
Other	75	3.5%
Total	**2,109 (or 2.11 billion)**	**-**

Source: PRODCOM (2022)

Table 3.13 estimates the value of the final formulated enzyme products market in the EU-27 and the market value that would fall within the scope of the proposed revision to the GRA based on data gathered for this project from the five leading EU manufacturers of enzymes. The total market size estimated of €2.09 billion/year is similar to that derived from the PRODCOM data in **Table 3.12** (~€2.11 billion in 2020). This validates the survey data,

[9] Converted using average annual exchange rate for 2016: $1 = €0.904 (https://www.exchangerates.org.uk/USD-EUR-spot-exchange-rates-history-2016.html#:~:text=Currency%20Menu&text=This%20is%20the%20US%20Dollar,rate%20in%202016%3A%200.904%20EUR.)

which is the preferred dataset for this analysis since it provides a breakdown by enzyme market category and is able to distinguish the market within the scope of the GRA.

Table 3.13: EU-27 enzyme market value – derived from survey data

Enzyme market category	Annual EU-27 market value for final (formulated) enzyme products (in € million/year)	
	Total	Total within the scope of the GRA
Food	680	30
Feed	396	266
Technical - detergents	642	327
Technical - all other applications	372	1
TOTAL	**2,090 (or 2.09 billion)**	**624**

Table notes:

- Result based on survey responses (n=5) but not all companies produce enzyme products for each market category. Data from these 5 companies are representative for the entire EU-27 market (i.e. they account for the majority of the EU-27 market).
- The total value of final formulated enzyme products is the sum of sales revenue generated within the EU-27 by each company and extrapolated to account for those EU companies that were not surveyed
- Companies were asked to provide the low and high sales prices by enzyme market category. There was large variability across the companies that provided data due to niche/specialist products having a high price. Therefore, unit prices used are based on the average of reported sale prices. A conservative approach was used taking the average of the low prices received combined with lowest of the high price received (and thereby seeking to exclude prices of niche products).

Figure 3.5 provides a further breakdown of the total enzyme market within the scope of the GRA (€624 million/year) by end-user categories. This provides insight into who may be affected by a potential ban on the use of enzymes within the scope of the GRA. For the food category, professional users are directly affected, whilst there may be indirect impacts on industrial users if demand falls from professional and consumer applications. In the feed industry, the main actors affected are professional users, whilst banning the use of enzymes in detergents will mostly impact consumers.

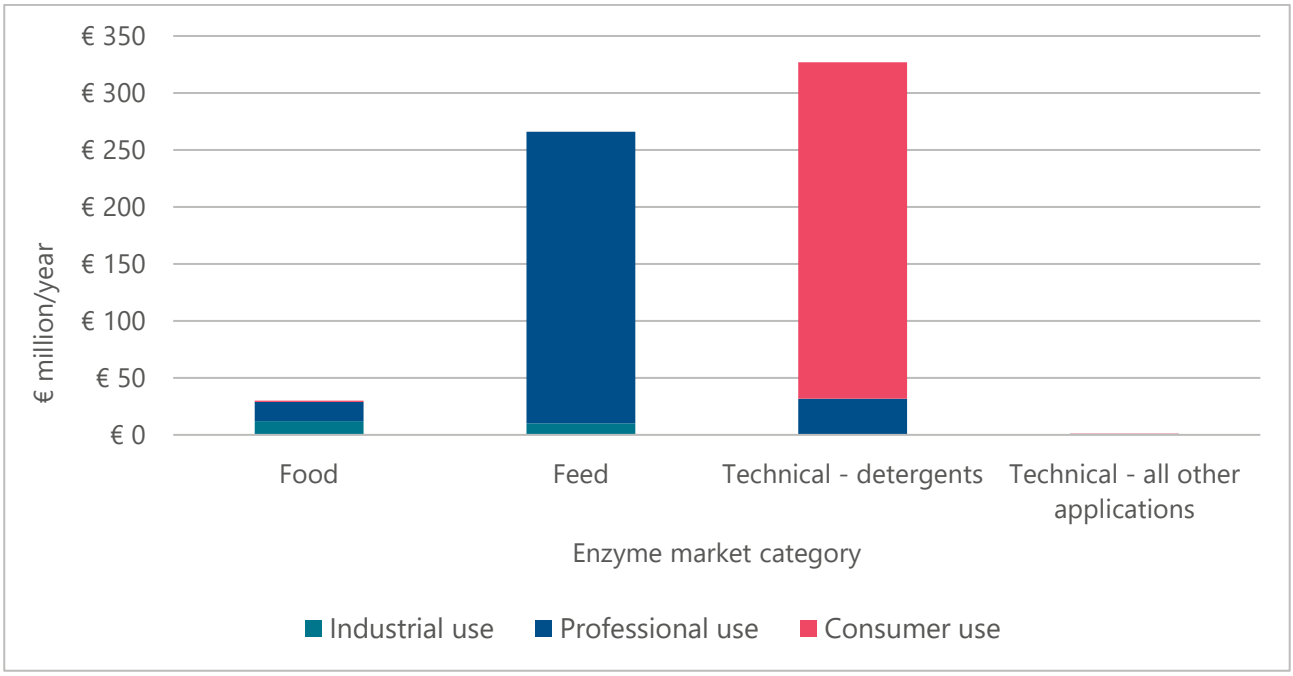


Figure 3.5: Breakdown of EU enzymes market value, within scope of GRA, by end-user category

Source: Interviews (2022) with enzyme products manufacturers and formulators (n=5)

Finally, **Figure 3.6** illustrates how the total enzyme market within the scope of the GRA (€624 million/year – assumed relevant for the year 2022) is expected to grow over time based on an annual 5.1% growth rate as set out in **Table 3.10**.

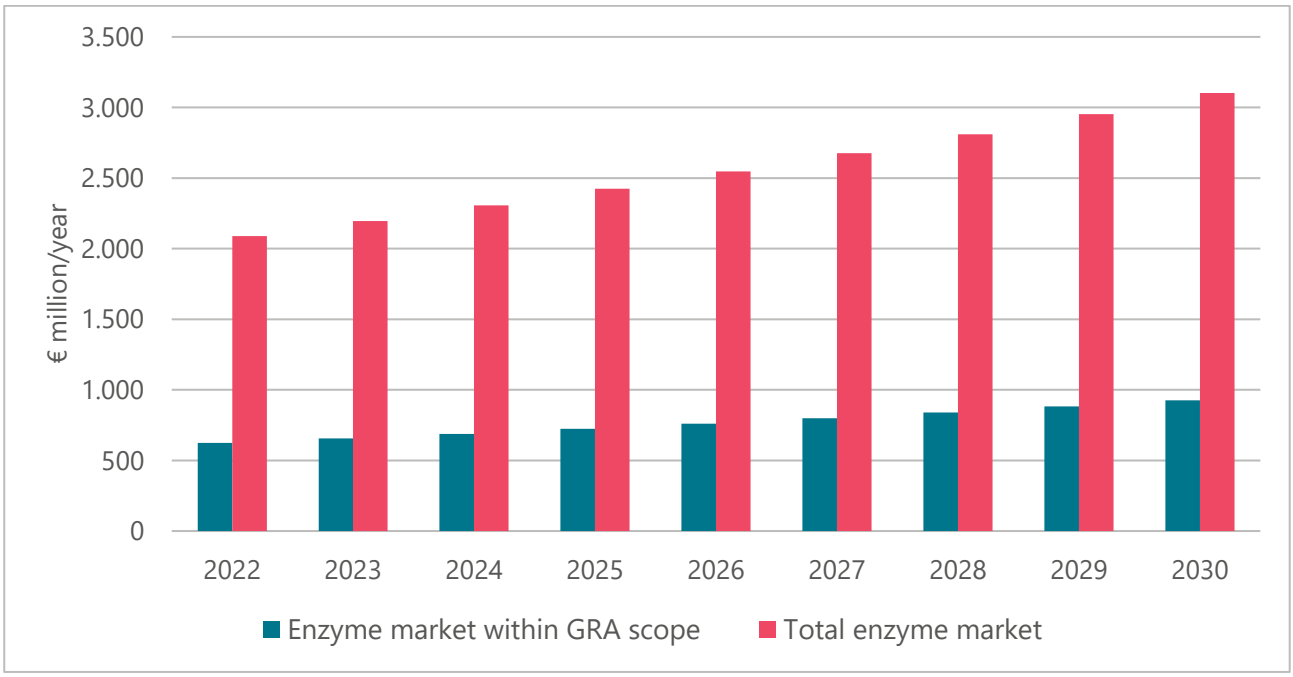


Figure 3.6: Projected EU-27 market value of enzymes over time (2022-2030)

Source: Interviews (2022) with enzyme products manufacturers and formulators (n=5)

3.5.4 Employment

It is estimated that around 6,700 people are directly employed in the EU's enzyme's market (manufacturing, import/export and distribution) and that it supports a further 1,200 indirect jobs (contractors/external service providers). **Table 3.14** shows figures for estimated total employment and annual expenditure on salaries for the European enzymes market by extrapolating employment data from the survey responses of the five surveyed AMFEP member firms.

Table 3.14: Employment in European enzymes market

	Total number of jobs	Total annual expenditure on salaries (in € million)
Direct employment	6,700	648
Indirect employment (i.e., contractors or external service providers)	1,200	100
Total	**7,900**	**748**

Table notes:

- Result based on survey responses (n=5). Data from these 5 companies are representative for the entire EU-27 market (i.e., they account for the majority of the EU-27 market). The results have been extrapolated to account for those EU companies that were not surveyed.
- Total number of jobs is rounded to the nearest 100.
- Total expenditure is rounded to the nearest € million.

There is limited information available on employment in the wider enzyme industry value chain, but information on the wider biotechnology sector, which the enzyme industry is a part of, was found. According to a study published by the European Association for Bioindustries, the industrial biotechnology sector as a whole supported around 94,000 direct full-time equivalent (FTE) jobs in Europe in 2013, (Debergh et al., 2016).

Of the 94,000 direct jobs attributed to the industrial biotechnology sector, of which the enzyme industry accounted for 4%, or 3,760 FTE jobs (Debergh et al., 2016). The report also shows that the total value chain supports a significantly higher number of jobs, over five times the number of direct jobs (486,000 FTE jobs). **Figure 3.7** shows the breakdown of the FTE jobs for each part of the industrial biotechnology value chain in 2013.

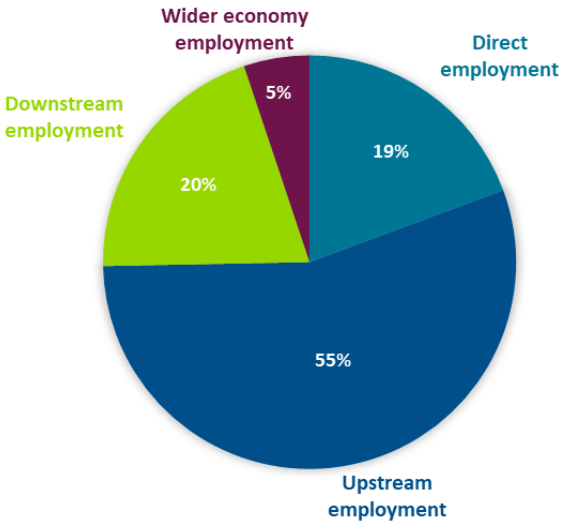


Figure 3.7: Shares of total employment in the European industrial biotechnology sector per value chain segment
Source: Adapted from estimates presented in Debergh et al. (2016)
Note: Wider economy refers to employment induced by spending of employees in the biotechnology industry.

As shown in **Figure 3.7**, the majority (55%) of the employment in the industrial biotechnology sector is found amongst upstream suppliers, whilst direct employment and downstream user employment are similar at around 20% each. If the enzyme industry value chain is comparable to the wider biotechnology sector, it is therefore expected that the total employment in the value chain is considerably higher than what is presented in **Table 3.14**. Using the relationship between direct employment and total employment in the value chain (total value chain in ~5 times the direct employment) found for the industrial biotechnology sector, the total employment related to the enzyme industry value chain would be some 33,000 employees.

3.5.4.1 End-use sector employment

Information on employment for the European enzyme market's end-use sectors was limited. However, a report on behalf of the International Association of Soaps, Detergents and Maintenance Products (A.I.S.E.) analysing the impacts of the Chemicals Strategy for Sustainability does provide some information on employment for this end-use sector. Ricardo (2022) explain that the 4,500 businesses within the EU-27's Soaps, Detergents and Maintenance Products sector employ more than 100,000 people. Roughly 80 large businesses are responsible for over 50% of this employment (Ricardo, 2022). Considering that the detergents sector accounted for 23% of global demand for enzymes in 2012, as shown in **Figure 3.3**, this provides a general idea of the potential scale of employment across the European enzyme market's end-use sectors.

3.5.5 Research & Development (R&D)

According to AMFEP (2022f), the EU leads the global market for enzyme technology. As shown in Section 3.5.1, this is largely driven by the fact that the industry's leading companies are also based in Europe.

Table 3.15 shows the estimated expenditure on R&D for the European enzymes market from 2013 to 2022, which totalled approximately €2.7 billion. The table shows that the majority of R&D spending went towards improving the cost efficiency of enzyme products. A significant amount was also spent on developing new markets/applications for enzyme products. Finally, the reduction/elimination of exposure to respiratory sensitisation during manufacture and use of enzymes made up relatively small shares in total R&D expenditure over the ten-year period.

Table 3.15: Expenditure on R&D across European enzymes market (2013-2022)

R&D category	Expenditure (in € million) on R&D (2013-2022)
Reduce/eliminate exposure to respiratory sensitisers during manufacture of enzymes	100
Reduce/eliminate exposure to respiratory sensitisers during use of enzymes	50
Cost efficiency (to make final (formulated) enzyme products cheaper or more efficient)	1,450
New markets/applications of final (formulated) enzyme products	1,090
Total for all R&D categories	**2,690 (or 2.7 billion)**

Table notes:

- Result based on survey responses (n=5). Data from these 5 companies are representative for the entire EU-27 market (i.e., they account for the majority of the EU-27 market). The results have been extrapolated to account for those EU companies that were not surveyed.
- Expenditure figures are presented in 2022 values.
- Expenditure figures are rounded to nearest €10 million.

In contrast to **Table 3.15**, **Table 3.16** shows the estimated expenditure on future R&D of enzyme products across the European enzyme market from 2023-2033, which increases by 27% in total. This data was estimated for each of the five survey respondent firms, who make up the majority of the market, and was extrapolated to account for the EU market as a whole. **Table 3.16** shows increases in expenditure for each of the R&D categories, with improving cost efficiency and the development of new markets/applications making up the overwhelming majority of R&D expenditure.

Table 3.16: Future expenditure on R&D across European enzymes market (2023-2033)

R&D category	Future expenditure (in € million) on R&D (2023-2033)	Percentage increase from 2013-2022 period
Reduce/eliminate exposure to respiratory sensitisers during manufacture of enzymes	140	38%
Reduce/eliminate exposure to respiratory sensitisers during use of enzymes	70	37%
Cost efficiency (to make final (formulated) enzyme products cheaper or more efficient)	1,750	21%
New markets/applications of final (formulated) enzyme products	1,450	33%
Total for all R&D categories	**3,410 (or 3.4 billion)**	**27%**

Table notes:

- Result based on survey responses (n=5). Data from these 5 companies are representative for the entire EU-27 market (i.e., they account for the majority of the EU-27 market). The results have been extrapolated to account for those EU companies that were not surveyed.
- Expenditure figures are presented in undiscounted (2022) values.
- Expenditure figures are rounded to nearest €10 million.

3.6 Existing EU regulations

Understanding the applications of enzyme products in different downstream sectors (described in Section 3.4) is crucial for determining which other regulations are relevant to the enzymes sector and whether these regulations already adequately manage the health risk arising from the use of enzyme products classified as respiratory sensitisers.

Enzyme products within the scope of the revised GRA are used as processing aids in food products, quality and digestibility enhancers in feed, sustainability enhancers in textiles as well as for the purpose of improving the performance of detergents. In some cases, enzyme products are essential substances in the production processes (e.g. denim production).

Enzymes are already regulated at various levels, i.e. production, workplace and product level. At the workplace level, manufacturers and downstream users are responsible for complying with workplace safety requirements set by various competent authorities. At the product level, meanwhile, enzyme products are regulated differently depending on the use, whereby their use in the food and animal feed sector is usually regulated by food additive regulations, while industrial uses of enzyme products are usually regulated by chemical regulations. The regulations, other than REACH, applying to the enzyme sector either directly or indirectly via their downstream uses are summarised in **Table 3.17**.

Table 3.17: Legislation (other than REACH) applying to the enzyme market and relevant downstream sectors

Enzyme market sector	Regulation number & name	Summary
All	Regulation (EC) No 1272/2008 Regulation on the classification, labelling and packaging of substances and mixtures (CLP)	Sets uniform requirements for the classification, labelling and packaging (CLP) of chemical substances and mixtures in accordance with the United Nations' Globally Harmonised System (GHS) Responsibility for the identification of hazards and classification mainly lies with manufacturers, importers and downstream users of those substances or mixtures.
	Regulation (EC) No 2017/542 Amending Regulation (EC) No 1272/2008 by adding an Annex on harmonised information relating to emergency health response	An amendment to the above regulation, serving as a comprehensive guide on the implementation of Article 45 and Annex VIII Relates to emergency health responses
	Directive 98/24/EC 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work	laying down minimum requirements for the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents that are present at the workplace or as a result of any work activity involving chemical agents.
Food	Regulation (EC) No 1332/2008 Regulation on food enzymes	Harmonises rules on food enzymes such as conditions for use in food and labelling requirements
	Regulation (EC) No 1331/2008 Regulation on establishing a common authorisation procedure for food additives, food enzymes and food flavourings	Establishes a common procedure for authorising food enzymes, additives and flavourings
	Regulation (EC) No 1130/2011 Amending Annex III to Regulation (EC) No 1333/2008	Establishes a list of approved food additives for food additives, enzymes, flavourings and nutrients and the conditions for their use

Enzyme market sector	Regulation number & name	Summary
	Regulation (EC) No 1169/2011 Regulation on the provision of food information to consumers	Describe labelling requirements for food enzymes
Feed	Regulation (EC) No 1831/2003 Regulation on additives for use in animal nutrition	Standardises feed additives authorisation procedure Lays down rules for the labelling and supervision of these substances
	Regulation (EC) No 429/2008 Regulation on detailed rules for the implementation of Regulation (EC) No 1831/2003	Provides the framework for implementation of Regulation (EC) No 1831/2003 (above) Additives for aquatic animals are included under this regulation
	Regulation (EC) No 885/2009 Amending Regulation (EC) No 378/2005 as regards reference samples, fees and the laboratories listed in Annex II	Amends Regulation (EC) No 378/2005 which lays down detailed rules for the implementation of Regulation (EC) No 1831/2003 (above) The testing required by the Community Reference Laboratory is amended to reduce the number of evaluations performed by laboratories and reduce fees where appropriate.
Technical	Regulation (EC) No 528/2012 Regulation concerning the making available on the market and use of biocidal products	Enzymes are not biocides and hence not in scope of the BPR per se. Only preservatives (PT-6) used in enzyme products need to comply with the provisions of the BPR.
	Regulation (EC) No 648/2004 Regulation on detergents	Protection of the environment from surfactants in detergents by imposing minimum standards for primary and ultimate biodegradability Harmonisation of rules limiting content of phosphate and phosphorus compounds Enzymes must be listed on labels regardless of their concentration within the detergent
	Regulation (EC) No 66/2010 Regulation on the EU Ecolabel	Framework for awarding the EU Ecolabel The lifecycle of a product/service is assessed relative to similar ones and awarded if found to have lower environmental impact.
	Regulation (EC) No 1223/2009 Regulation on cosmetic products	Creates stringent requirements for cosmetics products, updating them to consider use of nanomaterials and simplifies procedures for companies and regulators A safety assessment and "responsible person" designated for ensuring safety compliance are required Labelling and packaging requirements are outlined
	Regulation (EC) No 1935/2004 The regulation sets out the general principles of safety and inertness for all Food Contact Materials.	The regulation sets out the general principles of safety and inertness for all Food Contact Materials. Other related regulations on specific materials may be applied depending on food contact materials.

The potential REACH revision of the GRA scope leading to a restriction on respiratory sensitisers aims to prevent the associated health consequences. The ECHA Guidance for the preparation of an Annex XV dossier for restrictions (ECHA, 2007) indicates that a restriction is not necessary/justified if "*the risk would be sufficiently reduced by compliance with already existing legal requirements and that Community wide compliance could be achieved via enforcement. [In such cases], the Authority is requested to document this conclusion in the relevant parts of the restriction format and submit the documentation to the Agency Forum and Member State C[ompetent] A[uthoritie]s*". An analysis of the extent at which other existing community-wide regulations cover the health risks posed by respiratory sensitisers (i.e. enzyme products in this study) in an adequate way in combination with worker safety requirements has therefore been conducted.

As shown in **Table 3.17**, enzyme products used by the food sector are already regulated under regulations (EC)

No 1332/2008, 1331/2008, 1130/2011 and 1169/2011. They seek to harmonise rules to facilitate trade within the EU and guarantee consumer health and rights. They do not, however, consider the health effects associated with the manufacturing of food enzymes. Regulation (EC) No 1332/2008 clearly indicates that food enzymes *"[which] pose a safety concern to the health of the consumer at the level of use proposed"* cannot be placed on the market. Furthermore, in line with Regulation (EC) No 1331/2008, any food enzyme product to be placed on the market can only be authorised conditional on the results of a risk assessment, putting a particular focus on the product's risk to human health. Regulation (EC) No 1169/2011 requires companies to appropriately label their products to inform about their health impacts. Hence, food enzyme products which are currently placed on the EU market already meet the highest standards with regards to consumer health concerns dictated by existing regulation.

Similarly, existing EU regulation on feed places emphasis on both human and animal health. Regulation (EC) No 1831/2003 states that feed additives must undergo safety assessments before authorisation whilst Regulation (EC) 429/2008 establishes requirements of physio-chemical, toxicological and eco-toxicological tests and a safety assessment to ensure this. In particular, Regulation (EC) 429/2008 refers directly to enzyme products' effect on the respiratory system and provides specific criteria to be met by products. It also requires producers to provide supporting evidence that airborne levels of dust or mist will not constitute a hazard to the health of users/workers.

Technical enzyme products are similarly regulated with a focus to facilitate EU trade. Regulations (EC) No 648/2004, 66/2010, 66/2010, 1223/2009 and 2023/2006 refer to detergents, the EU Ecolabel, cosmetics and safe packaging for food respectively. Each regulation has a strong focus on health effects of products it legislates. For example, the EU Ecolabel regulation requires products to be given the EU Ecolabel to provide evidence showing the net environmental balance between the environmental benefits (and costs) and health and safety aspects. Whereas respiratory sensitising substances are excluded from EU Ecolabel, enzymes are derogated acknowledging their essentiality to achieve the overall goals of the EGD and their history of safe use.

Overall, legislation relevant to enzymes and enzyme products focuses on facilitating trade between Member States by harmonising and simplifying rules and creating standards to ensure human health and wellbeing.

4 Information on possible alternatives

4.1 Introduction

As noted in (ECHA, 2008), an alternative is a possible replacement for a substance and it should be able to replace the function that the substance performs without increasing the overall risks to human health or the environment. In addition to 'drop-in' (i.e., like for like) alternative substances, alternatives processes are also assessed (as these would also remove the need for the potentially restricted substance to be used). There are AoA guidance documents listed on ECHA's Substitution to Safer Chemicals webpage (ECHA, 2022b), such as OECD (2021), which outline more information on how to substitute hazardous chemicals with safer alternatives. In summary, a typical AoA will identify whether an alternative substance (or process) is:

- Technically feasible (i.e., reproduce the same level of functionality)
- Economically feasible (i.e., the costs of replacement are viable)
- Available (i.e., in sufficient quantity within the region)
- Reduced risks / hazard profile (i.e., reduced risks to human health and the environment)

This section will include information on R&D undertaken to minimise exposure from respiratory sensitisers, technical requirements of enzymes (used in Food, Feed, Detergents, and other industrial applications), information on possible/known alternatives to enzymes, necessary steps and time required to transition away from their use.

4.2 R&D carried out by the enzyme industry to date to minimise exposure

All enzymes are inherently respiratory sensitisers. This notwithstanding, enzymes are not volatile, the risks associated with the use of enzymes come from exposure to aerosol and dust. These can be mitigated by reducing levels of exposure to these and in turn, reducing the likelihood of a person experiencing adverse respiratory reactions. It was noted during the interviews with AMFEP members that investment in this area (making existing products safer through reduced levels of exposure) is directed through R&D and product stewardship programs which include education/training of customers and evaluating exposure potential of products and applications.

The enzyme industry has invested in processes that reduce exposure to respiratory sensitisers both during the manufacturing of enzymes, as well as during the use of enzymes. As noted in Section 3.5.5, the EU's total R&D spend on final (formulated) enzyme products was approximately €2.6 billion (€2,630 million[10]) between 2013 and 2022. Further to this spending, it is forecast that R&D spending will increase by 27% over the next 10 years; therefore, totalling €3.3 billion (€3,340 million[10]) between 2023 and 2033. **Table 3.15** demonstrates that the previous decade of R&D has been more focussed on improving cost efficiencies and entering new markets / developing new products (that contain final (formulated) enzyme products). However, in this chapter the R&D processes concentrated around reducing/eliminating exposure to respiratory sensitisers during manufacture and use are discussed. There are a number of different processes that can achieve this reduction; for example, reduction of exposure during the manufacturing of final (formulated) enzyme products can be achieved by

[10] This was rounded to the nearest €10 million to avoid false accuracy.

introducing a closed system. Moreover, to reduce workers exposure enzymes can be delivered in forms that reduce the generation of aerosols/dust (e.g. encapsulated granules, liquids etc.). Consumer products containing enzymes are also designed to minimise exposure during use (e.g. detergent capsules, single dose tablets etc.). This reduces the levels of inhalation exposure via the generation of aerosols/dust, which is the exposure route of concern for respiratory sensitisers.

Furthermore, development of new encapsulated products reduces end-user exposure to respiratory sensitisers. When describing R&D carried out to reduce exposure to respiratory sensitisers during use, an AMFEP member added that major R&D efforts to increase enzyme catalytic activity against specific substrates had resulted in less enzyme being present in the end-product, which led to reduced exposure (to respiratory sensitisers).

In addition to the examples above, AMFEP members implement in their manufacturing facilities the necessary engineering controls to reduce manufacturing operators' exposure to respiratory sensitisers (through reduction of dust). Additional elements of an enzyme safety programme include equipment maintenance, medical surveillance, work practice controls, employee training and air sampling (within the facility) to measure the effectiveness of control measures.

R&D and product stewardship programmes have enabled companies, who manufacture enzymes and use enzyme in processes, to work safely with enzymes without adverse health effects. Consumers and professional users of enzyme containing products can safely use these products without health effects due to safe product design. Further to this, the enzyme industry is continuously looking to improve their products and reduce potential exposure to respiratory sensitisers.

4.3 Technical requirements that alternatives need to meet

For centuries, enzymes have acted as natural catalysts to help people optimise yield from their raw materials/processes. Improved process efficiency and products characteristics (e.g., reduction in process time and/or improvement to product shelf-life) from use of enzymes significantly reduce the ecological footprint of products; therefore, professional users can sell products that use less energy, water and raw materials and generate less waste (AMFEP, 2022g).

Moreover, safety of the users of products made with enzymes is of utmost importance, and enzymes have an excellent safety profile with little ability to cause adverse responses in humans – they pose no risk of acute toxicity, repeat dose toxicity, genotoxicity, carcinogenicity, or reproductive and developmental toxicity. The important exception is the intrinsic potential of enzymes, like other proteins, to act as respiratory sensitisers. Sensitisation by itself does not cause symptoms, but repeated exposure to the same enzyme can cause a sensitised person to develop allergy symptoms at a later point (AMFEP and A.I.S.E., 2022).

Enzymes provide a level of functionality that other substances cannot match; they enable producers to reduce ingredient costs by rendering ingredients such as emulsifiers and gluten redundant (AMFEP, 2022g). Furthermore, baking enzymes can considerably increase both the efficiency and sustainability of the baking production process, as the same baking result can be achieved at lower temperatures. This reduces energy consumption (and the resulting greenhouse gas emissions) and associated costs. **Table 4.1** includes a list of enzyme classes, their contribution to the baking industry and the corresponding sustainability benefits.

Table 4.1: Examples of various enzyme classes and corresponding benefits in the baking industry

Enzyme class	Contribution	Sustainability benefits
Fungal alpha-amylase	Ensures desired end-product characteristics such as volume, crust colour, and crumb structure	Higher quality final products
Lipase	Improves crumb structure and crumb colour	Higher quality final products and less waste during production
Phospholipase	Improves dough strength and stability, loaf volume and crumb softness	Higher quality final products and less waste during production
Xylanase	Improves dough stability, bread appearance and texture, superior volume of baked goods	Higher quality final products
Glucose oxidase	Improves gluten strengthening	Higher quality final products and less waste during production
Amyloglucosidase	Improves bread crust colour and bread volume	Higher quality final products and reduction in energy consumption (reduced baking times)
Maltogenic amylase	Improves moistness, softness, and texture of baked goods	Higher quality of final product, reduction of energy consumption, reduced amount of raw materials as well as reduced amount of food waste
Protease	Reduces the strength of flour protein, thereby reducing mix time and elasticity and increasing the extensibility and softness of the dough.	Reduction of energy and water consumption, as well as reduction in food waste and higher quality final products
Cellulase	Improves dough conditioning and nutritional profile in whole wheat or whole grain breads	Higher quality final products
Asparaginase	Reduced acrylamide formation	Healthier final products

Source: (AMFEP, 2022g)

4.4 Information on possible/known alternatives

As mentioned in Section 4.2, the only viable alternatives for DUs are processes or substances that do not involve enzymes. In general, enzymes were brought into industry as safe substances that – in certain circumstances – could remove unwanted chemicals (e.g., phosphates in animal feed). Furthermore, enzymes act catalytically and can repeat their job over and over, resulting in high activity levels at very low concentrations. This property makes enzymes more efficient than 'single-use' chemicals and thus reduces the volume of product required to achieve a function[11]. From an environment and health standpoint, achieving the overall goal of the European Green Deal would be considerably harder, possibly leading to a regression (with respect to the green transition), if enzymes can no longer be used.

Common for all four enzyme product categories is that using alternatives would reduce the effectiveness of the process and reducing the quality of the output. In some instances, the 'known' alternative would be the substance previously used, that has been replaced by enzymes. For example, if the enzymes used in flour (by craft bakers) were removed, then the bakers would have to revert back to using emulsifiers. As explained in Section 4.4.1 below, this would produce an inferior product. Furthermore, enzymes generate environmental benefits, primarily by reducing energy required to manufacture products (see **Table 4.1** for examples of sustainability benefits of enzymes in the baking sector). More specific examples of possible alternatives specific to each enzyme product categories are included in the subsections below.

[11] For example, comparatively smaller volumes (per wash) of washing detergents containing enzymes are required to achieve the same level of performance as washing detergents that do not contain enzymes - see Section 4.4.3 for more information.

4.4.1 Food

In addition to naturally occurring enzymes in flour, final (formulated) enzymes are added to flour that is used by craft bakers (i.e., professional users). They were first introduced to replace the use of emulsifiers (for example, monoglyserides or steryl lactalyse) and increase the output of bakers whilst also improving the quality of the product (e.g., reduced staling/extended lifespan). A return to the use of emulsifiers would result in the loss of a number of beneficial properties currently provided by enzymes. For example, enzymes help achieving right texture to bread, prevent staling and transform nutrients from flour to more digestible forms for humans. Therefore, without the addition of enzymes, flour would vary in quality between batches, the final product would be inferior and consequently, food waste would increase (which goes against the EU's green objectives) and economic pressure would increase on bread production.

For starch factories where workers can fall under the definition of professional users (i.e., craft starch factories), enzymes are used in order to ensure starch products have high purity. This industry processes starch-containing raw materials like maize, wheat, rice and potatoes into starch, proteins, and fibres. The starch can be sold as a product or further modified. By further using enzymes, starch can also be transformed into a wide range of carbohydrates (e.g. maltodextrin, glucose syrup; dextrose) and with additional process steps into polyols. The end products are used in a variety of downstream applications, particularly food but also feed and other industrial applications. Since there is no viable alternative substance or process that can replace the use of enzymes, it would not be possible to reliably produce high purity starch products (often used in intravenous feeding) if enzymes where banned.

Currently, enzymes are used in most steps of the process of producing grain and starch, leading to technical and environmental benefits as well as to a wide range of different products. Examples of applications, process steps and enzyme benefits are listed in **Table 4.2**.

Table 4.2: Examples of applications of enzymes and related benefits in grain and starch processing

Application	Process step	Enzyme benefits	Enzyme class examples
Degradation of the grain structure, breaking down the fiber network to release starch and protein fractions	Grain milling and separation	• Increased starch yield and purity / reduced cereal, water and energy input • Cleaner non-starch fractions (protein and fiber) • Reduced drying needs / reduced energy consumption • Reduced waste	Xylanase Arabinofuranosidase Cellulase
Transformation of the starch macromolecules into smaller molecules	Liquefaction	• Avoidance of harsh chemicals (acid) / no need for acid-resistant equipment / enhanced worker safety • No need for extensive pH neutralization / reduced load at the ion exchange step/reduced water use (compared to acid-based process) • High flexibility in process conditions (pH, temperature) • Very wide range of final products / stability, purity and quality of the syrups	Alpha-amylase

Application	Process step	Enzyme benefits	Enzyme class examples
Extensive conversion of the liquefied starch into sugars	Saccharification	• High yield and purity • Specific cleavage of bonds in amylose and amylopectin • Very wide range of final products	Alpha-amylase Beta-amylase Glucoamylase Pullulanase Maltogenic amylase
Removal of insoluble particles form syrups	Saccharification	• Speeding up filtration / improving yield and purity • Improve syrups' clarity	Lysophospholipase
Converting glucose into a mixture of glucose and fructose	Isomerization	• High yield and purity • Increased sweetness	Glucose isomerase

Source: (AMFEP, 2022a)

Similarly, if the enzymes used in brewing and wine making were banned, the products (which are important for both the European economy and cultural heritage) would become inferior in quality. Enzymes are widely used during different wine making steps providing a broad range of effects, such as to maximise juice yield, improve aroma compounds, flavour enhancement, colour extraction in red wines, and contribute to the removal of dissolved unwanted colloidal particles and pectin substances during wine stabilisation and filtration. Moreover, enzymes used in beer help to increase brewhouse capacity by up to 25%, reduce costs and meet sustainability and attenuation targets, without compromising on taste. Therefore, the impacts of banning enzymes from use in brewing and wine making (craft companies who are viewed as professional users) would be severe in terms of quality, waste, and emissions.

Enzymes are used extensively in the dairy industry. Every year, approximately nine million tonnes of cheese are consumed in the EU and with a value of €30 billion the cheese market is of high value to the European economy (AMFEP, 2022a). Milk clotting can take place without enzymes, using a highly energy intensive filtration process and the resulting product resembles cheese, but is of a much lower quality. The use of enzymes is an important element in reducing the carbon print of cheese production. Besides the milk clotting enzymes other enzymes used in cheese production are lipases and lysozyme - lipase is used to generate piquant taste notes in specific cheeses such as provolone. The alternative (to the use of enzymes) is to let this happen by natural fermentation. However, this involves a high risk of spoilage and, subsequently, increased food safety risk. The use of enzymes in the dairy industry results in a green and sustainable production method of essential food products that would not exist without the use of enzymes. The use of enzymes helps to reduce the dairy sector's carbon footprint and CO_2 emissions by producing dairy products efficiently with minimal energy requirements. Furthermore, and most importantly, enzymes help the dairy industry to produce nutritious, healthy, and great-tasting food products that are essential foods in the European diet.

4.4.2 Feed

Enzymes are prevalent in animal feed used by farmers; they have many benefits as they improve digestibility and lower excretion of nutrients into the environment[12]. Enzymes also promote better gut health and less incidence of gut problems what could require use of antibiotics in animals. Further to this, enzymes improve yields and decrease the volume of animal feed required to achieve the same results (i.e., less food is required per animal).

[12] The enzyme enables the Feed to have better phosphorus (phytase), energy (phytase, xylanase, glucanase, mannanase), amino acid and nitrogen (phytase, xylanase, glucanase, mannanase) digestibility and therefore reduces the amount of these environmentally harmful substances released by the animal (through excretion).

There is no like-for-like alternative to the use of enzymes in animal feed; therefore, if enzymes could not be used, the feed would contain, for example, increased amounts of phosphorus (i.e., phosphate) which ends up in the environment through excretion. Feed millers who produce animal feeds would also be affected by the lack of viable alternatives to enzymes in feed, as more raw materials/ingredients would be needed which increases the production costs.

A considerable part of the phosphorus that occurs naturally in feed ingredients of plant origin is bound in the form of phytate. Therefore, phytate bound phosphorus is not absorbed by the animal and largely excreted into manure (and thus, into the environment). Phosphorus is an important macronutrient for animal growth and has been usually added in form of inorganic phosphorus to animal feed in intensive livestock production. Phytase (6-phytase EC 3.1.3.26, 3-Phytase EC 3.1.3.8) is an enzyme that hydrolyses phytate. The enzyme is used to release existing phosphorus in animal feed for poultry, swine and aquaculture. In this way phytase does not only increase the digestibility, but also decreases the release of phytate bound phosphorus into the environment via livestock manure (AMFEP, 2022a).

4.4.3 Detergents

Enzymes have been proven to provide excellent cleaning performance for equipment used for food manufacturing, whilst using low concentrations and under mild conditions (e.g. lower temperatures) (AMFEP, 2022c), resulting in lower consumption of chemicals. Enzymes are non-corrosive and do not damage surfaces of instrument, rubber gaskets, etc., so the (surfaces of the) products being cleaned last longer (AMFEP and A.I.S.E., 2022).

In detergents enzymes are viewed as alternatives to environmentally hazardous substances (e.g., phosphate in a laundry products), with a proven superior washing performance (Wood and Ramboll, 2022). Traditionally used surfactants act by forming micelles and are 'used up' during the wash processes. Replacing parts of the conventional detergent ingredients with enzymes therefore reduce the total amount of detergent required per wash. Consequently, using enzyme-based detergent formulations leads to a significant reduction of CO_2 emissions from both the manufacturing and use of detergent ingredients (AMFEP, 2022a).

Box 4.1 outlines the comparative cleaning ability of a non-enzyme (alternative) detergent with that of an enzyme-containing detergent at both 40°C and 20°C.

Box 4.1: Case study of enzymes in detergents[13]

Figure 4.1 shows an example of improved stain removal performance at reduced temperatures with the use of enzyme-containing detergent (EU regular liquid detergent without and with 0.006% lipase protein) compared to an enzyme-free detergent at a higher temperature. Washing performance of detergents at low temperatures has been improved with increasing enzyme usage since 1985, while the average washing

[13] Converted using average annual exchange rate for 2021: $1 = €0.8458 (https://www.exchangerates.org.uk/USD-EUR-spot-exchange-rates-history-2021.html

temperature in the EU has decreased from 62°C to 41°C.

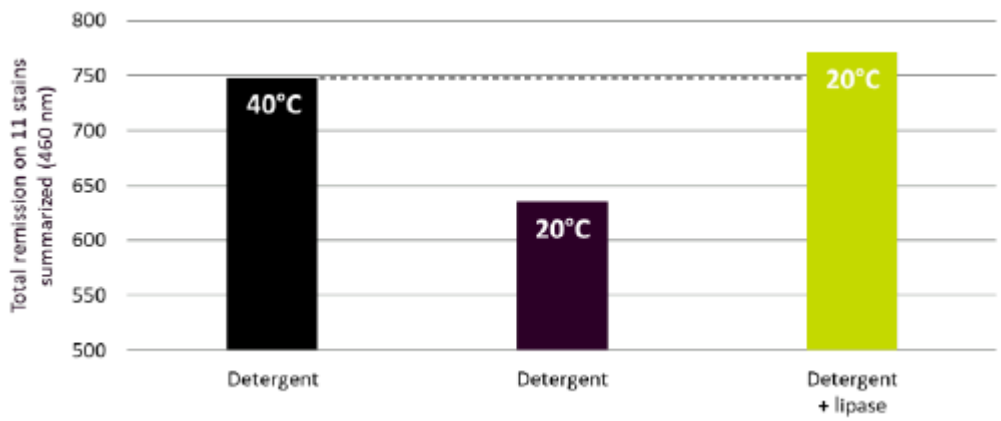


Figure 4.1: Example of stain removal at reduced temperature with use of enzymes

One of the main innovations of the industry is the compact detergents products. Compaction means that the product is, amongst others, more concentrated (i.e., less detergent is needed) and the chemical load to the environment is reduced. Water use is also reduced and there are savings in fuel as less product is transported. For example, between 1997 and 2017 the average detergent dosage was halved and the aggregated reduction in detergent volume used was estimated as 30 million tonnes over the period.

In conclusion, enzymes contribute significantly to cleaning performance and minimise the impact on the environment, since they have a high performance at low concentrations in the formula.

Source: (AMFEP and A.I.S.E., 2022)

4.4.4 Other technical uses

Other technical applications utilise enzymes – for example, the use of enzymes to break down non-food energy sources in the conversion of agricultural waste to biogas. Without the inclusion of enzymes, technical adaptions would need to be introduced (to increase agitation of tanks). This requires more energy to power the additional agitation, which increases the greenhouse gas (e.g., CO_2) emissions and reduces the final product yields.

A very important use of enzymes is in diagnostics tests. One of the most recognised diagnostic methods used by consumers is blood glucose measure for management of diabetes. The first glucose biosensor was developed in 1975 (Singh et al., 2019). Another example is that of hospital/clinic/Covid-19 centre diagnostic kits, where enzymes (especially proteases) play a key role in viral diagnostics - they aid in isolating viral genetic material by breaking down internal peptide bonds. They also limit the degradation of this material by deactivating nucleases. In diagnostics, these processes are known as lysis processes (Novozymes, 2022b). There are no alternative substances or processes that can replace the functionality that enzymes have in diagnostic tests; without enzymes, the sensitivity of diagnostic tests (including PCR analysis) will significantly decrease. The impacts of which would be severe to those who rely on blood glucose tests in order to manage their diabetes or use of a PCR test for those who require knowing whether they have caught Covid-19.

4.5 If substitution of enzymes was required, steps, time and associated costs

4.5.1 Introduction

Enzymes are unique in their ability to catalyse reactions while posing minimal risk to human health and the environment. In order to avoid regrettable substitution (replacement of a substance with an alternative that potentially increases the risks to human health and the environment), it is likely that a number of uses will not be able to revert back to 'old' previously used technologies that were replaced by enzymes. Although previously used chemicals were not always hazardous[14], enzymes have allowed for the removal of these 'unwanted' substances from products. An example of this is the use of enzymes to remove lactose from milk, so those who are lactose intolerant are able to drink (lactose-free) milk.

Regrettable substitution was mentioned as a concern by the detergents sector, who noted that the risk of regrettable substitution in 'non-essential' products had already been highlighted by Euratex[15] (Ricardo, 2022). For example, replacing a classified substance that is controlled by safe use (that the risk has already identified, and (risk reducing) measures are in place) with a substance with less (eco)toxicological data, or with a more hazardous substance that is 'outside' the scope of a potential ban, have potential implications for human health.

As previously explained, there are no alternatives available for enzyme manufacturers and formulators since the respiratory sensitiser classification is an intrinsic property of all enzymes. Any substitution efforts, as a result of a ban of respiratory sensitisers, will therefore have to occur at the DU level. AMFEP does not have information on substitution steps, time needed or associated costs that DUs would incur if they could no longer use enzymes. Furthermore, as noted in Section 5, the most likely response of professional users who use final (formulated) enzyme products is to reduce their production (to solely industrial users who are outside of the scope of the GRA) or to cease production and not relocate (outside of the EU).

However, the previous work completed by Ricardo (2022) includes information on substitution steps (and costs) if the detergents industry was no longer able to use final (formulated) enzyme products. Therefore, Section 4.5.2, details the discussions included in that report, this can be used as a reference guide for the other enzyme sectors (i.e., Food, Feed, etc.) showing that some reformulation may need to occur, and that without this, the turnover from the sector will be reduced.

4.5.2 Detergent industry

The detergents industry notes that a ban of respiratory sensitisers could cause the withdrawal of consumer products (see **Table 3.2** for examples) that contain final formulated enzyme products that are deemed not to be safe (due to their respiratory sensitisers classification) (Ricardo, 2022).

Enzymes have been safely and widely used in consumer laundry products in the EU for a number of decades. **Table 4.3** outlines the three key product categories where enzymes are used, and the market value for each of these product categories.

Table 4.3: Product categories of enzyme use and their market value

Product Category of Enzyme Use	Market Value of Product Category

[14] With the notable exception of acrylamide, which is carcinogenic and is removed from food products through the introduction of enzymes.

[15] European Apparel and Textile Confederation, representing the interests of the European textile and clothing industry at the level of the EU institutions." For more information: https://euratex.eu/about-euratex/

Consumer Laundry Care	€15.3 billion
Consumer Automatic Dishwash	€3.2 billion
Professional Laundry	€0.5 billion

Source: (AMFEP and A.I.S.E., 2022)

A.I.S.E. highlights that 95% of their product portfolio would be affected by proposed changes to CLP and GRA, and it is anticipated that 56% of these products will, as a consequence, need to be reformulated (Ricardo, 2022). Further to this, responses suggested that 6% of the portfolio affected by the expansion of the GRA could be subject to derogations (Ricardo, 2022). **Box 4.2** outlines the evidence collected related to the EU soaps, detergents and maintenance products sector's capacity to substitute and/or reformulate that has been considered in this analysis.

Box 4.2: Substitution and/or reformulation of products that may be affected by proposed changes to CLP and GRA

25 businesses were surveyed to gather evidence as to the extent to which they may implement specific actions resulting from the adoption of policy changes and their likely scale, especially including substitution and/or reformulation.

They concluded that some substitution and/or reformulation is likely, and businesses will attempt to maximise this where economically viable; however, this is only likely to mitigate around 56% of total potential market withdrawals resulting from regulatory changes and time taken to implement.

Source: (Ricardo, 2022)

Figure 4.2 demonstrates that if businesses do not substitute and/or reformulate at all, and do not obtain derogations for any substance use, the EU soaps, detergents, and maintenance products sector could lose between -12% and -15% of their turnover. The best available evidence suggests that businesses will be able to substitute and/or reformulate 18% of their product portfolios (in terms of total sector turnover). In any of these cases, turnover losses are not expected to vary significantly from the central estimate (Ricardo, 2022).

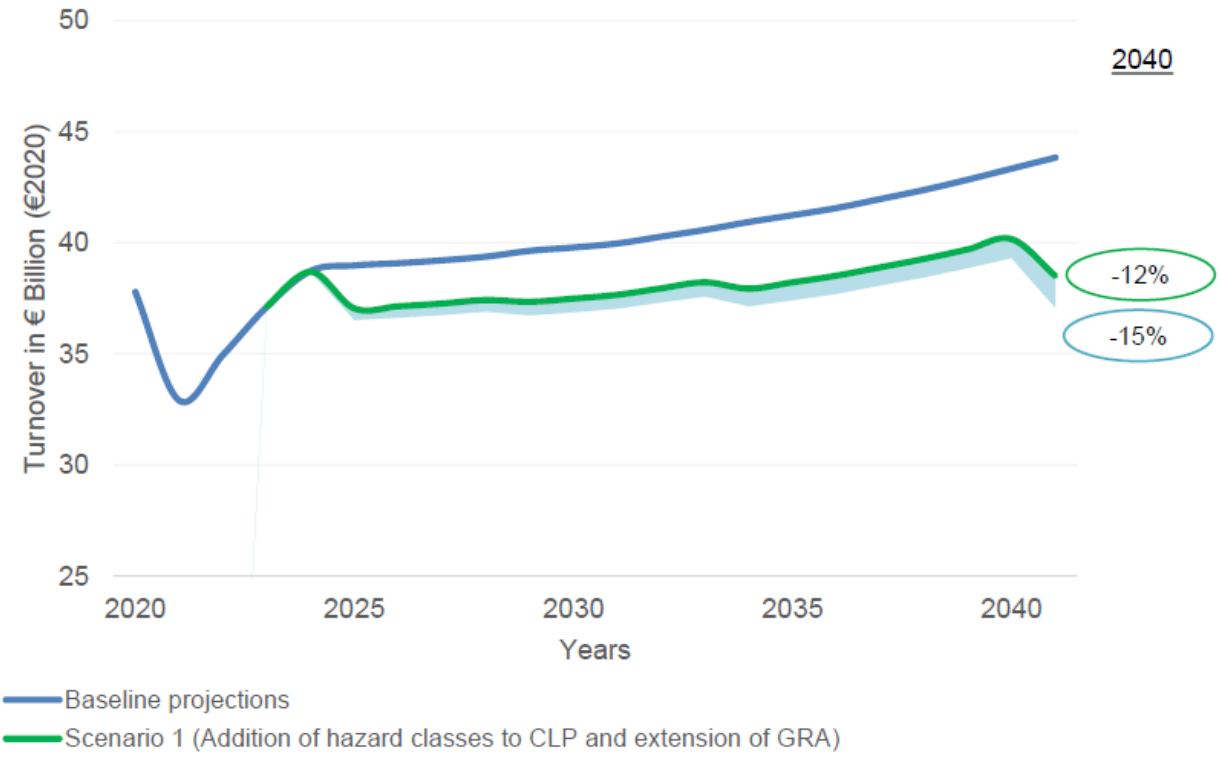


Figure 4.2: Illustration of the sensitivity of the estimated impacts on the turnover of the EU soaps, detergents and maintenance products sector against the baseline scenario (€ 2020) to expected substitution and/or reformulation
Source: (Ricardo, 2022)

Additionally, substitution and reformulation could affect the quality and attractiveness of the substances and/or products sold by the EU soaps, detergents and maintenance products sector. This could impact the EU soaps, detergents and maintenance products market, especially in the face of international competition (Ricardo, 2022).

5 Description of the 'ban' scenario

5.1 Introduction

This section assesses impacts of a potential change in the GRA scope effectively leading to a ban on use of enzyme products set out in **Table 1.2** and similar products placed on the EU market by other companies. As the exact scope of this REACH revision is unknown, this assessment assumes that all enzyme products are banned from being used due to their respiratory sensitiser property from 2026 onwards (it is unlikely that any 'ban' e.g., via a REACH restriction would enter into force earlier than 2026).

The study aims to provide evidence regarding a possible ban of enzyme products within the scope of the revised GRA and the associated impacts, however, it does not assess the likelihood of such a ban.

The subsequent subsections set out the possible and most likely responses to such a ban for enzyme manufacturers (Section 5.25.2) and downstream users of enzymes (Section 5.3). The impacts of the most likely response(s) are further assessed in Section 6.

5.2 Enzyme manufacturers

As part of the questionnaire enzyme products manufacturers (who may also be formulators) were asked to identify their most likely response to the proposed restriction from the following list of suggested responses:

- Seek to reformulate by using an alternative process to avoid the need for respiratory sensitisers substances for producing final (formulated) enzyme products
- Seek to reformulate to use alternative substances (to respiratory sensitisers substances) to continue producing final (formulated) enzyme products
- Continue producing in the EU-27 but only selling the final (formulated) enzyme products (manufactured using respiratory sensitisers substances) to industrial users within the EU-27 and companies outside of the EU-27
- Cease production of final (formulated) enzyme products in the EU-27 and relocate production site/increase capacity at existing site(s) outside of the EU-27
- Cease EU-27 production of all final (formulated) enzyme products and no relocation of production outside the EU
- No action required - We are unaffected by a possible ban on the use of respiratory sensitisers in consumer and professional uses

The respondents (n=5) overall responded in a similar manner, meaning there is more confidence in the most likely response. The results summarised in **Table 5.1** show that the respondents consider only two possible likely responses. The first and most likely response indicates that in the short-term following a ban, enzyme product manufacturers will continue producing in the EU-27 and selling the final (formulated) enzyme products to industrial users within the EU-27 and companies outside of the EU-27 only i.e. stop selling their products to consumer and professional users. However, it is not economically viable for manufacturers producing enzymes to only supply for industrial uses, particularly for manufacturers whose products are primarily sold to industrial users. The second likely response gives a long-term perspective and suggests that companies will cease EU-27

production of all final (formulated) enzyme products (without relocating their production outside the EU), due to insufficient volumes to justify maintaining production at EU sites. All other possible responses are highly unlikely with justifications included in the table.

Table 5.1: Possible responses to a ban by enzyme manufacturers

Possible responses	Overall ranking	Justification
Seek to reformulate by using an alternative process to avoid the need for respiratory sensitising substances for producing final (formulated) enzyme products	5 - Definitely would not do this	Enzymes are respiratory sensitizers Cat. 1. This is an intrinsic hazard and there are currently no means to produce enzymes without this hazardous property.
Seek to reformulate to use alternative substances (to respiratory sensitisers substances) to continue producing final (formulated) enzyme products	5 - Definitely would not do this	There is no way to make final (formulated) enzyme products without them being classified as respiratory sensitisers due to intrinsic properties of final (formulated) enzyme products
Continue producing in the EU-27 but only selling the final (formulated) enzyme products (manufactured using respiratory sensitisers substances) to industrial users within the EU-27 and companies outside of the EU-27	1 - Most likely response	This is deemed an initial most likely response by most companies. However, many note that the remaining market will not be large enough for all companies and therefore some companies are likely to cease production
Cease production of final (formulated) enzyme products in the EU-27 and relocate production site/increase capacity at existing site(s) outside of the EU-27	4 - Unlikely response	This is deemed unlikely as some companies don't have sites outside the EU27 and don't view the remaining market large enough to justify the large investment required to relocate
Cease EU-27 production of all final (formulated) enzyme products and no relocation of production outside the EU	2 - Likely response	This is deemed a possible long term most likely response by many companies. Some companies believe that the remaining market will not be large enough for all companies and therefore some companies are likely to cease production
No action required - We are unaffected by a possible ban on the use of respiratory sensitisers in consumer and professional uses	5 - Definitely would not do this	This scenario is very unlikely because most companies are solely based on enzyme products only and it is not possible to make enzymes that are not respiratory sensitizers

Table notes:

- The results are based on survey responses (n=5). Data from these 5 companies are representative for the entire EU-27 market (i.e., they account for the majority of the EU-27 market).

5.3 Downstream users of enzymes

Due to the tight timescales of the project, it was not feasible to do any meaningful consultation directly with downstream users. Instead, enzyme products manufacturers (who may also be formulators) were asked, as part of the questionnaire, to identify what they thought would be the most likely response of their customers to a potential ban. The following list of suggested responses was included in the questionnaire:

- Reformulate - seek to use an alternative substance to fulfil the function of final (formulated) enzyme products
- Reformulate - seek to use an alternative process to fulfil the function of final (formulated) enzyme products
- Reformulate product (including changes in form and functionality) and change instructions on how to use their product - (e.g., to compensate for the loss of function provided by final (formulated) enzyme products)
- Cease sales of their affected products in the EU-27 (cannot make their product without final (formulated) enzyme products) but continue to sell to customers outside the EU-27
- Cease production of their affected products in the EU-27 (cannot make their product without final (formulated) enzyme products) and relocate production outside the EU-27
- Cease production of their affected products in the EU-27 (cannot make their product without enzymes)
- Other (please specify)

Table 5.2 summarises the possible responses to a ban on enzymes by their downstream users for each product affected.

Table 5.2: Possible responses to a ban on enzymes by downstream users of enzymes

Enzyme market category	Products affected within the scope of the GRA	Most likely responses	Supporting justification for response
Feed	Use of animal feed with enzymes by feed millers and farmers.	Reformulate using alternative substances. This reformulation would likely occur upstream (i.e., customers would have to reformulate feed diets).	Animal requirement would have to be covered by the addition of other ingredients to ensure that the improvements seen with enzymes are obtained e.g., feed millers would need to use alternative solutions to add more nutrients to feed.
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft fruit juice producers.	Reformulate using an alternative process to fulfil the function provided by enzyme products / cease sales of affected products with no alternatives within the EU-27.	Downstream users would need to go back to conventional processes that do not require enzymes. Some downstream users will not have the capacity to invest in alternative processes and would have to cease production as a result.
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft wineries/breweries.	Reformulate using an alternative process to fulfil the function provided by enzyme products / cease sales of affected products with no alternatives within the EU-27.	Many wineries would not be able to change their production processes and may have to cease production/sales in the EU. Some wineries would have to return to conventional processes.
Food	Use of (an) enzyme product(s) as food processing aid(s) by	Reformulate using an alternative process to fulfil the function provided by	Downstream users would need to go back to conventional processes that do not require enzymes. Some downstream users will not have

Enzyme market category	Products affected within the scope of the GRA	Most likely responses	Supporting justification for response
	craft/artisan cheese makers.	enzyme products / cease sales of affected products with no alternatives within the EU-27.	the capacity to invest in alternative processes and would have to cease production as a result.
Food	Use of (an) enzyme product(s) by craft oil producers.	Reformulate using an alternative process to fulfil the function provided by enzyme products / cease sales of affected products with no alternatives within the EU-27.	Downstream users would need to go back to conventional processes that do not require enzymes. Some downstream users will not have the capacity to invest in alternative processes and would have to cease production as a result.
Food	Use of (an) enzyme product(s) in starch factories where workers fall under the definition of professional users (i.e., craft starch factories).	Cease sales of affected products within the EU-27 with no alternatives.	Downstream users will not have the capacity to invest in alternative processes and would have to cease production as a result.
Food	Use of enzymes by cooks in restaurants to treat meat.	Cease sales of affected products with no alternatives within the EU-27.	Downstream users will not have the capacity to invest in alternative processes. Enzyme manufacturers would also not be able to justify R&D for this downstream use segment as it only forms a small portion of business. Downstream users would have to cease production as a result.
Food	Use of flour containing enzymes by consumers to bake bread.	Reformulate using an alternative process to fulfil the function provided by enzyme products and change instructions for use of product by consumers / cease sales of affected products with no alternatives within the EU-27.	Quality of flour products is very dependent on use of enzymes. Downstream users would be able to reformulate with compromises to quality. Some smaller downstream users may not have the capacity to reformulate and would have to cease sales within the EU.
Food	Use of flour containing enzymes by craft bakers.	Reformulate using an alternative process to fulfil the function provided by enzyme products / cease sales of affected products with no alternatives within the EU-27.	Some downstream users would go back to conventional processes that would negatively affect quality. The others, such as craft bakers will not be able to replace enzymes which contribute to the quality of their products and will consequently lose business. Alternatives to enzymes are too difficult to obtain for them (e.g., developing yeast strains that already include necessary enzymes in sufficient quantities or using genetically modified wheat) due to knowledge and investment constraints.
Technical - detergents	Employees at hospital wash medical device with use of enzyme-containing detergents by employees at hospitals for cleaning medical devices.	Reformulate using alternative substance to fulfil the function of enzyme products (including changes to form and functionality) and change instructions for use of product.	Enzymes are commonly used and effective for the cleaning of medical devices and surfaces. Alternative detergents would be formulated with more surfactants, meaning a change in effectiveness and cleaning methods as a result.
Technical - detergents	Use of cleaning agents containing enzymes by employees of cleaning	Reformulate using alternative substance to fulfil the function of enzyme	Enzymes are commonly used and effective for the cleaning of medical devices and surfaces. Alternative detergents would be formulated with

Enzyme market category	Products affected within the scope of the GRA	Most likely responses	Supporting justification for response
	services for the cleaning of hard surface facilities/sites (e.g., hospitals, corporate facilities, public buildings).	products (including changes to form and functionality) and change instructions for use of product.	more surfactants, meaning a change in effectiveness and cleaning methods as a result.
Technical - detergents	Use of detergents containing (an) enzyme(s) by consumers to wash clothes or dishes.	Reformulate using alternative substance to fulfil the function of enzyme products (including changes to form and functionality) and change instructions for use of product.	Detergent manufacturers would replace enzymes with additional surfactants and other chemicals such as older product formulations that are no longer used, meaning a change in effectiveness and cleaning methods as a result.
Technical - detergents	Use of detergents containing (an) enzyme(s) by professionals to wash clothes or dishes.	Reformulate using alternative substance to fulfil the function of enzyme products (including changes to form and functionality) and change instructions for use of product.	Detergent manufacturers would replace enzymes with additional surfactants and other chemicals such as older product formulations that are no longer used, meaning a change in effectiveness and cleaning methods as a result.
Technical - all other applications	Agricultural waste material conversion to biogas.	Reformulate using alternative substance to fulfil the function of enzyme products.	Biogas sites would need to adapt the technology to stir and agitate more of the raw material to make it usable for microbes.
Technical - all other applications	Cosmetics containing enzymes (maybe).	Reformulate using an alternative process to fulfil the function provided by enzyme products / cease sales of affected products with no alternatives within the EU-27.	Cosmetic producers would replace some products however, for a number of products there are no alternatives that replace the function of enzyme products and downstream users would need to cease sales within the EU.
Technical - all other applications	Employees at hospital/clinic/COVID centre use of diagnostic kits containing enzyme(s) by employees at hospital/clinic/COVID centre.	Reformulate using an alternative process to fulfil the function provided by enzyme products / cease sales of affected products with no alternatives within the EU-27.	For certain kinds of testing, downstream users will not be able to reformulate end products (e.g., COVID/virus tests, and glucose monitoring tests for diabetics).
Technical - all other applications	Enzymes in biodegradable food packaging materials.	Cease sales of affected products within the EU-27 with no alternatives and relocate production outside the EU-27.	It is not possible to produce biodegradable plastics without enzymes.
Technical - all other applications	Treatment of water/sewage with enzyme products by employees at sewage/waste treatment centres.	Reformulate using an alternative process to fulfil the function provided by enzyme products / cease sales of affected products with no alternatives within the EU-27.	Enzymes support the breakdown of cellulose-based fibres, reducing viscosity and enabling better digestion of solid waste by microbes. Efficacy would have to be compensated with other chemicals.
Technical - all other applications	Use of diagnostic kits/test strips by consumers to (e.g., diabetes tests).	Reformulate using an alternative process to fulfil the function provided by	No known alternatives exist, as such companies would need to conduct R&D or cease production.

Enzyme market category	Products affected within the scope of the GRA	Most likely responses	Supporting justification for response
		enzyme products / cease sales of affected products with no alternatives within the EU-27.	

Many respondents noted that their downstream users would need to reformulate and or cease sales of their enzyme containing products within the EU-27. Across a range of products/end-uses (enzymes used in diagnostic kits, detergents, wastewater/sewage treatment, baking, etc.) enzymes played critical functions in creating/enabling key characteristics that would, in most cases, cannot be replicated by other substances (to the same level). While the respondents identified products where enzymes could be replaced with alternatives these were also accompanied with negative impacts such as efficiency and quality trade-offs. **Table 5.2** shows that a ban on enzymes would have far reaching impacts on several downstream user industries.

6 Impacts of a ban

6.1 Introduction

This chapter assesses impacts of a potential ban on the use of enzyme products within the scope of the GRA (See **Table 1.2**) within the EU-27 based on the most likely response(s) assessed in Section 5. The chapter covers:

- Environmental and human health impacts of a ban (Section 6.2);
- Impacts on EU end-users/consumers (Section 6.3); and
- Employment impacts (Section 6.4); and
- Economic impacts (Section 6.5).

All relevant impacts are assessed where possible at an EU-27 level (i.e., covering the whole market). Any monetary estimates that have been discounted are accompanied with the following bracket: (PV - present value). A 4% discount rate has been used, as recommended by the European Commission (EC, 2017), an analytical period up to 2029 and values are shown in 2022 prices.

6.2 Environmental and human health impacts of a ban

As noted earlier, it was not possible within the timescales available for this study, to quantify and/or monetise the environment and human health impacts of a potential ban on enzymes within the scope of the GRA. **Table 6.1** qualitatively summarises a vast range of environmental and human health impacts that have not been quantified in this report. Whilst these impacts have not been monetised, this does not mean they are insignificant. Many of these are substantial costs and should therefore be given the same weight as the quantified costs, when considering net impacts to society.

Table 6.1: Environmental and human health impacts of a ban on use of enzymes in certain downstream user products

Enzyme market category	Product affected	Description of impact	Types of environmental and/or human health impact
Food	Use of flour containing enzymes by craft bakers.	There would be a reduction in production process efficiency and product shelf life.	• Greater food wastage • Increase in energy consumption and greenhouse gasses pollution from production process
Food	Use of (an) enzyme product(s) by craft oil producers.	There would be a reduction in production process efficiency.	• Increase in energy consumption and greenhouse gasses pollution from production process
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft/artisan cheese makers	Enzymes could be replaced by highly energy intensive filtration process which would resemble cheese but with lower quality.	• Increase in energy consumption and greenhouse gasses pollution from production process

Enzyme market category	Product affected	Description of impact	Types of environmental and/or human health impact
			• People would have to consume less healthy alternatives compared to enzyme containing cheeses
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft wineries/breweries	Producers would have to use alternatives with poorer quality that would reduce production process efficiency.	• Increase in energy consumption and greenhouse gasses pollution from production process
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft fruit juice producers	Producers would have to use alternatives with poorer quality that would reduce production process efficiency.	• Increase in energy consumption and greenhouse gasses pollution from production process
Feed	Use of feed additives by feed millers for the production of animal feeds	Animal nutrition would require additional ingredients as well as an increase in volume of feed per animal.	• Increase in energy consumption and greenhouse gasses • Increase in pollutants to the environment • Higher quality feed ingredients required which increase price and may lead to shortages in available feedstock
Feed	Use of animal feed with enzymes by farmers	Animal nutrition would require additional ingredients as well as an increase in volume of feed per animal.	• Increase in energy consumption and greenhouse gasses • Increase in excess nutrient flow could have negative impacts on the environment
Technical - detergents	Use of detergents containing (an) enzyme(s) by professionals to wash clothes or dishes	Increased energy usage associated with replacement of enzymes.	• Increase in energy consumption and greenhouse gasses
Technical - detergents	Use of detergents containing (an) enzyme(s) by consumers to wash clothes or dishes	Detergent producers would have to substitute enzymes with substances that are potentially harmful and would increase the volume, time and temperature that items need to be cleaned at.	• Increase in pollutants to the environment • Increased energy consumption and greenhouse gasses
Technical - detergents	Use of cleaning agents containing enzymes by employees of cleaning services for the cleaning of hard surface facilities/sites (e.g., hospitals, corporate facilities, public buildings)	Detergent producers would have to substitute enzymes with substances that are potentially harmful and would increase the volume, time and temperature that items need to be cleaned at.	• Increase in pollutants to the environment • Increased energy consumption and greenhouse gasses • Human health implications from less effective cleaning processes

Enzyme market category	Product affected	Description of impact	Types of environmental and/or human health impact
Technical - detergents	Employees at hospital wash medical device with use of enzyme-containing detergents.	Detergent producers would have to substitute enzymes with substances that are potentially harmful and would increase the volume, time and temperature that items need to be cleaned at.	• Increase in time and costs to clean medical devices • Increase in pollutants to the environment • Increased energy consumption and greenhouse gasses • Human health implications from less effective cleaning processes
Technical - all other applications	Use of diagnostic kits/test strips by consumers to (e.g., diabetes tests)	Downstream users would need to reformulate or cease production until an alternative exists.	• Diabetics would face serious health implications as glucose monitoring is essential. For example, increase in health care costs e.g. from visits to emergency room from improper blood glucose measurement
Technical - all other applications	Treatment of water/sewage with enzyme products by employees at sewage/waste treatment centres.	Increase in time required for waste processing as well as introduction of potentially harmful alternative substances.	• Increased energy consumption and greenhouse gasses • Increase in pollutants to the environment
Technical - all other applications	Enzymes in biodegradable food packaging materials	Enzymes are essential in biodegradable plastics - downstream users of enzymes would need to cease production.	• Environmental and opportunity costs of offsetting plastics with biodegradable plastics.
Technical - all other applications	Employees at hospital/clinic/COVID centre use of diagnostic kits containing enzyme(s) by employees at hospital/clinic/COVID centre.	Cease production of Covid/virus diagnostic test kits.	• Human health costs
Technical - all other applications	Agricultural waste material conversion to biogas	Biogas sites would need to adapt technology to stir and agitate more of the waste material to promote higher microbial activity.	• Increased energy consumption and greenhouse gasses

Notes:

1. Impacts are on impacts reported in survey responses (n=5). Data from these 5 companies are representative for the entire EU-27 market (i.e. they account for the majority of the EU-27 market).

6.3 Impacts on EU end-users/consumers

As noted earlier, it was not possible within the timescales available for this study, to quantify and/or monetise all the impacts of a potential ban on enzymes within the scope of the GRA. **Table 6.2** qualitatively summarises a vast range of end-user/consumer impacts that have not been quantified in this report. Whilst these impacts have not been monetised, this does not mean they are insignificant. Many of these are substantial costs and should therefore be given the same weight as the quantified costs, when considering net impacts to society.

Table 6.2: End-user/consumer impacts of a ban on use of enzymes in certain downstream user products

Enzyme market category	Product affected	Description of impact	Types of end-user/consumer impact
Food	Use of flour containing enzymes by craft bakers.	Reformulation and cease of production of products with no alternatives.	• Reduced consumer choice • Increase in price of baked items (e.g., bread) • Lower quality products with shorter shelf life.
Food	Use of flour containing enzymes by consumers to bake bread.	Reformulation of consumer-use flour products.	• Increase in price of flour and related food items (e.g., bread) • Lower quality food items with shorter shelf life.
Food	Use of enzymes by cooks in restaurants to treat meat.	Restaurants would not be able to offer certain meat food items.	• Reduction in consumer choice
Food	Use of (an) enzyme product(s) by craft oil producers.	Producers would need to reformulate products.	• Increase in price of craft oils for consumers
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft/artisan cheese makers.	Cheese producers would need to reformulate products.	• Increase in price of cheese for consumers • Less consumer choice
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft wineries/breweries.	Craft wineries/breweries would need to reformulate and cease production of products with no alternatives.	• Increase in price for consumers • Less consumer choice • Lower quality products for consumers
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft fruit juice producers.	Juice producers would need to reformulate and cease production of products with no alternatives.	• Increase in price for consumers • Less consumer choice • Lower quality products for consumers
Feed	Use of feed additives by feed millers for the production of animal feeds.	Feed millers would need to reformulate products, introducing additional ingredients and potentially leading to increase in feed per animal.	• Increase in price of meat for consumer
Feed	Use of animal feed with enzymes by farmers.	Feed millers would need to reformulate products, introducing additional ingredients and potentially leading to increase in feed per animal.	• Increase in price of meat for consumer
Technical - detergents	Use of detergents containing (an) enzyme(s) by consumers to wash clothes or dishes.	Detergent producers would need to reformulate products with alternatives that are not as effective.	• Increase in price for consumers • Less consumer choice • Lower quality products for consumers
Technical - detergents	Use of cleaning agents containing enzymes by employees of cleaning services for the cleaning of hard surface facilities/sites (e.g.,	Detergent producers would need to reformulate products with alternatives that are not as effective.	• End-users of facilities would face potential health implications

Enzyme market category	Product affected	Description of impact	Types of end-user/consumer impact
	hospitals, corporate facilities, public buildings).		from spaces that are no longer as clean.
Technical - detergents	Employees at hospital wash medical device with use of enzyme-containing detergents.	Detergent producers would need to reformulate products with alternatives that are not as effective.	• End-users of hospital facilities would face potential health implications from spaces that are no longer as clean.
Technical - all other applications	Use of diagnostic kits/test strips by consumers to (e.g., diabetes tests).	Downstream users would need to reformulate or cease production until an alternative exists.	• End-users face health implications because of inadequate testing.
Technical - all other applications	Treatment of water/sewage with enzyme products by employees at sewage/waste treatment centres.	Increase in time and resources required for waste processing as well as introduction of potentially harmful alternative substances.	• Increase in price for waste treatment services for consumers. • Potential health and environmental implications for society as a whole.
Technical - all other applications	Enzymes in biodegradable food packaging materials.	No alternatives to enzymes in biodegradable plastics – producers would need to cease production.	• Reduced consumer choice for greener plastic alternatives.
Technical - all other applications	Employees at hospital/clinic/COVID centre use of diagnostic kits containing enzyme(s) by employees at hospital/clinic/COVID centre.	No alternatives to enzymes in diagnostic kits for COVID/viruses – producers would need to cease production.	• Negative cost and health implications for health workers and patients
Technical - all other applications	Cosmetics containing enzymes (maybe).	Cosmetic producers would need to reformulate and cease production of products with no alternatives.	• Less consumer choice • Increase in price of consumer products for consumers

Notes:

1. Impacts are on impacts reported in survey responses (n=5). Data from these 5 companies are representative for the entire EU-27 market (i.e. they account for the majority of the EU-27 market).

6.4 Employment impacts

Impacts on EU employment are directly linked to reduced production/sales of enzymes that fall with the scope of the GRA that assumed to be banned from 2026. As set out in the SEAC guidance on calculating costs associated with unemployment (SEAC, 2016), it is assumed that increases in unemployment, due to a ban on the use of specific chemicals will be temporary, as resources will be redeployed to the production of other goods and services after a certain period of time. The SEAC approach thus accounts for the distributional effects (e.g. any increase in jobs from use of inferior alternatives used by downstream users instead of enzymes).

The survey respondents imply that between 15-20% of their workforce will be made redundant if a ban of enzymes falling under the scope of the GRA is implemented. In order to be conservative, we assume the lower bound of 15% of jobs lost (direct and indirect), using the employment numbers reported earlier in **Table 3.14**. The number of jobs at risk (1,444) is expected to be much higher than the conservative estimate presented in **Table 6.3** since they only take into account jobs lost directly by the enzymes industry and their use of contractors

(indirect). However, the impacts of these job losses alone are significant with an estimated societal cost of €315 million (PV).

Table 6.3: Summary of employment impacts

Impact on employment at...	Minimum number of jobs at risk	Total value of jobs lost 2026 (PV - € million)
Enzyme manufacturers	1,225	€ 272
Use of contractors by enzyme manufacturers	219	€ 43
Downstream users (of enzyme products no longer available)	unknown	Unknown
Minimum number of jobs at risk	**1,444**	**€ 315**

Notes:

1. Jobs at risks does not include downstream users of enzymes, which means that the value to society is underestimated. Jobs at risk are estimated to be 15% of the numbers employed directly or indirectly by enzyme manufacturers
2. The approach to valuing jobs is in line with SEAC guidance (SEAC, 2016).
3. Average gross annual salary data is based on average salary using survey data (n=5). Data from these 5 companies are representative for the entire EU-27 market (i.e., they account for the majority of the EU-27 market). Salaries provided are assumed to not include any overhead costs.
4. Monetary values are given in 2022 prices and rounded to the nearest € million, or to the first significant decimal if below a million.

6.5 Economic impacts of a ban

A ban on the use of enzyme products within the scope of the GRA (See **Table 1.2**) will induce significant economic impacts for upstream suppliers, enzyme products, downstream users as well as end-users. Due to time constraints, consultation with actors in the supply chain and derivation of economic impacts and costs throughout the value chain has not been covered. Therefore, the quantitative analysis focuses on impacts on enzyme manufacturers only. The monetised impacts presented in this report should thus be viewed as minimum cost and benefits of a ban. The economic impacts for downstream users are assessed qualitatively, with a few numerical examples (where possible) to illustrate potential order of magnitude of non-quantified effects.

6.5.1 Lost profit to enzyme manufacturers

As explained in Section 5.2, the manufacturers of enzyme products will have limited choices if faced with a ban on their use. The only realistic options will involve reducing production and limiting sales for products outside the scope of the GRA. However, this may not be a feasible long-term strategy. For example, if industrial users (who are not within the scope of the GRA) are unable to sell their enzyme-containing products they will stop purchasing enzymes and thereby further reduce the enzyme market. The drastic reduction in the EU market size will increase competition and likely result in some companies exiting the EU market, as it is not viable to run their production sites under capacity. The costs of decommissioning production sites and other indirect impacts, like possible financial penalties incurred due to breaking supply contracts with downstream users, have not been monetised.

Since it is not possible to reformulation to make enzyme that are not respiratory sensitisers, it follows that the enzyme manufacturers will not incur any costs of substitution. Instead, the main cost at this level in the value chain is believed to be profit lost due to forgone sales of products within the scope of the GRA that are banned.

SEAC has recently published guidance that streamlines the approach to estimating lost profits, which is linked to premature retirements of assets (SEAC, 2021). Assets may be intangible (e.g., R&D and patents) or tangible/physical (e.g., production equipment or a production plant). If a company, production plant or a production line has to shut down (e.g., due to a regulation) the associated assets will no longer generate value. The main assumption behind this methodology is that "*in the short run there is a fixed availability of tangible and intangible assets and in the long run incumbent or rival firms can augment assets by making investments*" (SEAC, 2021). The guidance provides a default time period over which profits lost should be estimated, which is dependent on whether suitable alternatives are generally available (SAGA) or not (no-SAGA). For SAGA cases, 2 years of profits is used to approximate producer surplus losses, whilst a 4-year period is recommended for no-SAGA cases. If a longer time period is to be used (5 years is suggested in the guidance), this must be "*justified by robust supporting evidence*" (SEAC, 2021).

It should, however, be noted that it is deemed unlikely that new assets (after the end of life of the 'old' assets) can be redeployed in equally beneficial or income-generating uses. Hence, it is believed that parts of the losses will remain way beyond the 4-year default period. Albeit likely significant, it is not achievable to quantify the losses associated with deploying resources in less beneficial (second-best options) applications, so a conservative approach with a 4-year period has been used.

As explained in detail in Chapter 4, there are no suitable alternative available for the products covered within this SEA, which means that this is a no-SAGA case. Using the default value of 4 years, as set out in **Table 6.4**, the resulting lost profits amounts to **€1,646 million (PV) over the period 2026-2029 which annualised is €411 million per year**.

Table 6.4: Estimated lost profit to EU-27 enzyme manufacturers from a ban

Enzyme market category	Lost profit over 4 years (2026-2029) undiscounted (€ million)	Lost profit over 4 years (2026-2029) in present value (PV - € million)	Annualised loss in profit (PV- € million/year)
Food	97	78	20
Feed	749	603	151
Technical - detergents	1195	962	240
Technical - all other applications	3	3	1
TOTAL	**2,045**	**1,646**	**411**

Notes:

1. Profits lost are only assumed to occur over 4 years in compliance with (SEAC, 2021).
2. Profit margins differ by enzyme market category and the estimates are based on average profit margins reported across survey responses (n=5). Data from these 5 companies are representative for the entire EU-27 market (i.e. they account for the majority of the EU-27 market). The results have been extrapolated to account for those EU companies that were not surveyed.
3. Values are given in 2022 prices and rounded to the nearest € million.
4. Present value (PV) has been calculated using a 4% discount rate.

6.5.2 Economic costs to downstream users of enzymes

As noted earlier, it was not possible within the timescales available for this study, to quantify and/or monetise all the impacts of a potential ban on enzymes within the scope of the GRA. **Table 6.5** qualitatively summarises a vast

range of economic impacts that have not been quantified in this report. Whilst these impacts have not been monetised, this does not mean they are insignificant. Many of these are substantial costs and should therefore be given the same weight as the quantified costs, when considering net impacts to society.

Table 6.5: Economic impacts of a ban on use of enzymes in certain downstream user products

Enzyme market category	Product affected	Description of impact	Types of economic costs
Food	Use of flour containing enzymes by craft bakers.	Craft bakers would need to reformulate and cease production of products with no enzyme-free alternatives.	• Reformulation costs • Loss of revenue from cease of production
Food	Use of flour containing enzymes by consumers to bake bread.	Producers would need to reformulate product and change instructions on how to use their product (e.g. duration the bread will last). If this is not possible, producers would have to cease production.	• Reformulation costs • Costs associated with redesign and replacement of instructions on packaging • Loss of revenue from cease of production
Food	Use of enzymes by cooks in restaurants to treat meat.	Restaurants would have to cease sales of affected products or use inferior products as they will not have resources to invest in like for like alternatives.	• Restaurants would face loss of revenue if they cannot successfully replace demand for discontinued product
Food	Use of (an) enzyme product(s) in starch factories where workers fall under the definition of professional users (i.e., craft starch factories).	Downstream users would have to cease sales of affected products or use inferior products as they will not have resources to invest in like for like alternatives.	• Loss of revenue from cease of production
Food	Use of (an) enzyme product(s) by craft oil producers.	Craft oil producers would need to reformulate their products or cease production of affected products.	• Reformulation costs • Loss of revenue from cease/halt to production
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft/artisan cheese makers.	Cheese makers would need to reformulate their products leading to inferior products or cease production of affected products.	• Reformulation costs • Loss of revenue from cease/halt to production
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft wineries/breweries.	Downstream users would need to reformulate their products. For many (i.e., wine makers) reformulation would not be possible and would need to cease production of affected products.	• Reformulation costs • Loss of revenue from cease/halt to production
Food	Use of (an) enzyme product(s) as food processing aid(s) by craft fruit juice producers.	Fruit juice producers would need to reformulate their products or cease production of affected products.	• Reformulation costs • Loss of revenue from cease/halt to production
Feed	Use of feed additives by feed millers for the production of animal feeds.	Feed millers would need to reformulate their products (to make up for loss in nutritional value of feed) or cease production of affected products.	• Reformulation costs • Loss of revenue from cease/halt to production

Enzyme market category	Product affected	Description of impact	Types of economic costs
			• Increase in price of feed products
Feed	Use of animal feed with enzymes by farmers.	Feed producers would need to reformulate products with alternatives that maintain nutritional value of feed.	• Reformulation costs
Technical - detergents	Use of detergents containing (an) enzyme(s) by professionals to wash clothes or dishes.	Detergent producers would need to reformulate product and change instructions on how to use product.	• Reformulation costs • Costs associated with redesign and replacement of instructions on packaging
Technical - detergents	Use of detergents containing (an) enzyme(s) by consumers to wash clothes or dishes.	Detergent producers would need to reformulate product and change instructions on how to use product.	• Reformulation costs • Costs associated with redesign and replacement of instructions on packaging
Technical - detergents	Use of cleaning agents containing enzymes by employees of cleaning services for the cleaning of hard surface facilities/sites (e.g., hospitals, corporate facilities, public buildings).	Detergent producers would need to reformulate products. Alternatives would be less effective for certain types of cleaning requirements.	• Reformulation costs • Increase in volume of cleaning agent use for alternative • Increase in labour time to conduct cleaning.
Technical - detergents	Employees at hospital wash medical device with use of enzyme-containing detergents by employees at hospitals for cleaning medical devices.	Detergent producers would need to reformulate products. Alternatives would be less effective for certain types of cleaning requirements.	• Reformulation costs • Increase in volume of cleaning agent use for alternative Increase in labour time to conduct cleaning.
Technical - all other applications	Agricultural waste material conversion to biogas	Biogas sites would need to adapt the technology to stir and agitate more of the raw material to make it usable for microbes.	• Higher energy costs • Less yields • Increased raw material input/resources consumed"
Technical - all other applications	Diagnostic kits containing enzyme(s) used in COVID PCR tests as used at hospital / clinic / COVID centres	No COVID PCR tests as it is not possible to produce COVID / virus diagnostic kits without enzymes	• R&D costs to find alternative(s) • No COVID PCR test which can lead to increased risk of spreading COVID which has proven to have significant economic impacts on businesses and economies
Technical - all other applications	Enzymes are used to diagnosis for many other diseases. Most notable is use by diabetics to test blood sugar for management of blood sugar levels with insulin.	Alternative does not exist. Companies will need to do research on alternative solutions. They would need to seek to reformulate to use an alternative process to fulfil the function of final (formulated) enzyme products	• R&D costs to find alternative(s) • Lost profit from sale of diabetic diagnosis tests • Increase in health costs for people with diabetes

Enzyme market category	Product affected	Description of impact	Types of economic costs
			• Increase in health infrastructure costs due to increase in diabetic related patient admissions
Technical - all other applications	Treatment of water/sewage with enzyme products by employees at sewage/waste treatment centres	Reformulate seeking to use an alternative substance to fulfil the function of final (formulated) enzyme products. However, the efficacy will be compromised.	• Reformulation costs • Increased cost of wastewater treatment due to use of less efficient treatment
Technical - all other applications	Certain cosmetics containing enzymes	Certain cosmetic products will no longer be produced as it is not possible to make without the use of enzymes.	• Lost profit of certain cosmetic products • Unique contribution of enzymes in certain cosmetic products will be lost (consumer loss)
Technical - all other applications	Enzymes in biodegradable food packaging materials	Enzymes are not necessary for biodegradable plastics (not possible to make without the use of enzymes)	• Lost profit from sales of biodegradable plastics
Technical - all other applications	Employees at hospital wash medical device with use of enzyme-containing detergents by employees at hospitals for cleaning medical devices.	There will be a need to reformulate product (including changes in form and functionality) and change instructions on how to use their product (e.g., to compensate for the loss of function provided by final (formulated) enzyme products). Enzymes are commonly used to clean medical devices such as endoscopes. They improve the cleaning of this equipment prior to sterilization.	• Reformulation costs • Possible costs to re-training of staff to ensure clean medical devices, • Increase in the amount of labour time needed to clean medical devices

Notes:

1. Impacts are based on impacts reported in survey responses (n=5). Data from these 5 companies are representative for the entire EU-27 market (i.e., they account for the majority of the EU-27 market).

The economic impacts listed in **Table 6.5** highlight significant impacts to industries that hold serious economic and societal importance to the EU. For example, diagnosis testing for COVID-19 and diabetes would not be possible without the use of enzymes. In June 2022 the EU approved a €2.3 billion COVID-19 recovery plan (European Council, 2022) with the effects of COVID-19 still ever present in European society. Around 32.3 million adults were diagnosed with diabetes in the EU in 2019 (OECD, 2019). The cost of managing diabetes in Europe totalled €149 billion in 2019, representing roughly 9% of EU member states' healthcare budgets (European Parliament, 2019). The associated impacts of a ban on the use of enzymes would contradict the EU's COVID-19 recovery plan, greatly impact its ability to manage the prevalence of diabetes, potentially lead to unnecessary cases of hospitalisation or death and significantly increase the costs of such diseases on European society.

Furthermore, **Box 6.1** shows the value of EU cheese production and internal trade of cheese produced within the EU to provide an example of potential impacts for industries where enzymes cannot be replaced. **Table 6.5** and **Table 6.1** explain that it is not possible to produce cheese to the same qualities (in terms of health, texture, quality

and taste) without enzymes meaning that such industries would face enormous economic losses and potential shutdowns as a result of a ban on enzymes.

Box 6.1: The Importance of Cheese in Europe

The latest available PRODCOM data shows that total cheese production in the EU-27 amounted to roughly €43.5 billion or 15.6 million tonnes in 2020 (PRODCOM, 2022). AMFEP (2022b) note that nine million tonnes of cheese worth €30 billion are consumed in the EU each year.

According to eurostat (2019), Germany accounted for 22% of EU cheese production with France and Italy accounting for 19% and 12%, respectively, in 2017. Roughly half of the EU's cheese production in that year was exported (valuing €20.8 billion), with trade between EU member states accounting for almost 85% of this.

The detergents sector is also heavily impacted by a potential change in scope of the GRA. Whilst they may be impacted by the GRA from the use of products other than enzymes, they are the largest EU market category for enzymes affected by the GRA and are, therefore, directly impacted if there is a ban on the use of enzymes in professional and consumer applications. Ricardo (2022) is a report on behalf of the International Association of Soaps, Detergents and Maintenance Products (A.I.S.E.) which analyses the potential impacts of the Chemicals Strategy for Sustainability. Box 6.2 summarises some of the economic impacts noted in that report related to the GRA.

Box 6.2: Economic impacts on the detergent sector

Table 6.6 below summarises the annualised impacts on selected business and economic indicators for the EU soaps, detergents and maintenance products sector as a result of the changes to the CLP and GRA (this values the impacts of all proposed changes to the CLP and GRA, not just the effects of a restriction on respiratory sensitisers). Ricardo (2022) found that over the period 2023 to 2040:

- Business turnover would be impacted by an average annual loss between €2.4 billion and €6.3 billion,
- Total GVA contribution would be impacted by an average annual loss between €1.4 billion and €4.6 billion,
- Regulatory burdens would create an additional annualised burden between €175 million and €294 million,
- And, total employment would face between 13,300 and 31,700 fewer jobs, on average, compared to the baseline in any given year.

Table 6.6: Annualised impacts on selected business and economic indicators for EU soaps, detergents and maintenance products sector, against the baseline scenario (%)

Business/economic indicators	Scenario 1: Addition of hazard classes to CLP and extension of the GRA	Scenario 2: Faster, 5-year implementation timetable	Scenario 3: Faster implementation timetable with delay on substitution/reformulation
Turnover (first order effects)	Average **€2.4 billion loss per year** compared to baseline	Average **€4.2 billion loss per year** compared to baseline	Average **€6.3 billion loss per year** compared to baseline
Total GVA contribution	Average **€1.4 billion loss**	Average **€2.5 billion loss**	Average **€4.6 billion loss per**

(direct, indirect, induced)	**per year** compared to baseline	**per year** compared to baseline	**year** compared to baseline
Regulatory burden	Additional annualised **burden of €247 million per year**	Additional annualised **burden of €294 million per year**	Additional annualised **burden of €175 million per year**
Total employment contribution (direct, indirect, induced)	**13,300 fewer jobs**, on average, compared to baseline in any given year	**22,700 fewer jobs**, on average, compared to baseline in any given year	**31,700 fewer jobs**, on average, compared to baseline in any given year

Source: Ricardo (2022, pg. xvii)

Note: the quantified impacts measure the full effect of additional hazards introduced under the CLP and the extension of the GRA and not just the costs of a restriction on respiratory sensitisers.

7 Summary and recommendations

The SEA report was prepared for submission to the Commission's contractor to provide evidence on the potential impacts of a possible extension of the GRA under REACH to include substances classified as respiratory sensitisers for European manufacturers, formulators, and downstream users of food, feed and technical enzymes. AMFEP's key recommendation is set out in Box 7.1

Box 7.1: AMFEP recommendation

AMFEP recommends based on the analysis undertaken in this SEA to **provide enzyme product manufacturers (and formulators) with an exemption from a potential ban of enzyme products** resulting from the revised GRA extension. Considering the lack of suitable alternatives to enzymes, combined with significant economic and social costs as well as adverse impacts to human health and the environment of using inferior alternatives, it is believed that a regulatory exemption is justified for enzyme containing products.

The potential ban would affect a broad range of consumer and professional uses of enzyme products. The scale of the effect can vary from significantly reducing product's quality and performance to being removed from the market in the absence of suitable alternatives. Food enzymes which are used as processing aids in various food products (e.g. bread or dairy products) are critical for some processes, such as clotting of milk for cheese production. The EU cheese market alone is estimated to worth €30 billion/year.

Enzymes in feed enhance its digestibility and improve the nutrient availability to give it a higher nutritional value. Enzyme products also make detergents more efficient and sustainable as they provide the compaction and high washing performance at low temperatures.

Around 230,000 tonnes of final formulated enzyme products are either manufactured or imported into the EU, with around 92% of that volume being sold to EU customers. The estimated total value of European enzyme production in 2022 was approximately €2.1billion, with food and technical detergent enzyme products having the largest market shares (33% and 31% respectively). There were 6,700 people directly employed in the EU's enzyme's market, with a further 1,200 indirect jobs supported. Furthermore, the EU leads the global market for enzyme technology. Its estimated R&D spending between 2013-2022 totalled approximately €2.7 billion. If the EU does not maintain this leadership, another regional power (e.g. China or US) will likely take over the global leadership, leaving the EU with a competitive disadvantage (economically, politically and on innovation).

Around 78,500 tonnes per year of manufactured and imported final formulated enzyme products in the EU are within the scope of the GRA (34% of the EU total). The corresponding total value of European enzyme production within the scope of the revised GRA in 2022 was approximately €624 million. For the food category, professional uses would be directly affected, whilst there may be indirect impacts on industrial users if demand fell from professional and consumer applications. In the feed industry, the main actors affected would be professional users, whilst banning the use of enzymes in detergents would mostly impact consumer uses.

An extension of the GRA and the potential ban of enzyme products would be met with two possible responses from enzyme manufacturers (and formulators). The most likely response of manufacturers in the short-term would be to continue producing in the EU and limit their sales to industrial users within the EU and exports outside the EU. In the long-term it is likely that a ban would force them to cease production at EU sites. On the other

hand, downstream users of enzyme products would likely need to reformulate (often using more chemicals and resource intensive processes) and / or cease sales of their products containing enzymes. The latter response is driven by the criticality of enzymes in production of a wide range of products (e.g. detergents, wastewater / sewage treatment, bread and cheese production or diagnostic kits).

A potential ban of enzyme products would induce significant economic impacts for upstream suppliers, downstream users, and end-users. Assuming that the ban would take effect in 2025, it was estimated that enzyme product manufacturers would lose €1,646 million (PV) over the period 2026-2029 (€411 million per year). Though not quantified, it is expected that a ban would cause enzyme downstream uses to bare additional costs such as reformulation costs, increase in raw material used, loss of revenue and higher energy costs.

Furthermore, not using enzyme products would generate a number of environmental and human health impacts in certain downstream user products. For example, these would be greater food wastage due to reduced product shelf life (e.g. bread production), increase in energy consumption and greenhouse gases pollution due to reduced production process efficiency (e.g. less efficient food processing alternatives or substances used in detergents), health hazards from less effective cleaning and inadequate glucose monitoring in diabetes. Around 32.3 million adults were diagnosed with diabetes in the EU in 2019 (OECD, 2019). The cost of managing diabetes in Europe totalled €149 billion in 2019, representing roughly 9% of EU member states' healthcare budgets (European Parliament, 2019).

Reduced production and sales of enzymes within the EU would lead to job losses. It was estimated that the minimum number of jobs at risk would be 1,444 (this includes both direct and indirect employment). These redundancies correspond to the estimated value of temporary unemployment of €315 million (PV).

Finally, a deficit in the supply of enzymes caused by a potential ban would affect the end-users i.e. consumers. Among the potential impacts, there are reduced consumer choice, lower quality of products (incl. lost functionality, reduced durability, and performance) and higher costs associated with increased prices triggered by lower supply and / or more expensive alternatives to enzymes increasing the cost of production.

Therefore, these total costs of a potential ban on enzyme manufacturers were estimated to be at least €700 million per year alone. This is a conservative estimate as it does not include all the impacts which could not have been monetised (such as health, environmental and end-user impacts) or costs to downstream users (e.g. the impacts of a loss of cheese alone is around €30billion/year). All these substantial costs (both quantified and qualitatively assessed) to society should be considered by the Commission contractors when assessing the impacts of the GRA expansion proposal for EU society.

8 References

Amfep, 2008. Amfep Guidance in a Nutshell Classification of enzymes according to the CLP Regulation 1–6.

AMFEP, 2022a. The Essential Role of Enzymes.

AMFEP, 2022b. Enzyme applications [WWW Document]. URL https://amfep.org/about-enzymes/applications/

AMFEP, 2022c. POSITION PAPER: The European Commission's proposal for a Mixture Assessment Factor (MAF) is not appropriate for Enzymes.

AMFEP, 2022d. Benefits of enzymes [WWW Document]. URL https://amfep.org/about-enzymes/benefits/ (accessed 8.10.22).

AMFEP, 2022e. The Essential Role of Enzymes - Reduction of mycotoxin fumonisin in food with enzymes.

AMFEP, 2022f. The Essential Role of Enzymes - Reduction of mycotoxin zearalenone in food with enzymes.

AMFEP, 2022g. AMFEP paper on the essential role of enzymes in the baking industry.

AMFEP, 2022h. AMFEP - Occupational safety [WWW Document].

AMFEP, 2022i. Our members [WWW Document]. URL https://amfep.org/members/

AMFEP, 2022j. Interview with VVA - AMFEP Study supporting the REACH impact assessment – revision of Titles VII and III / extension of GRA.

AMFEP, 2012. Enzymes and criteria of respiratory sensitizers in the 2nd ATP to EU Classification, Labelling and Packaging (CLP) Regulation.

AMFEP, 2008. AMFEP Guidance in a Nutshell Classification of enzymes according to the CLP Regulation 1–6.

AMFEP, n.d. The unintended impact of the REACH revision on Enzymes – and consequences for EU ' s Green Deal Objectives.

AMFEP, A.I.S.E., 2022. ROLE AND IMPORTANCE OF ENZYMES IN CLEANING AND HYGIENE. https://doi.org/10.1136/oem.2005.025304.10

Bano, T., Priyanka, Padmadeo, S.R., 2017. Sustainable Industrial Development through Enzyme Technology: An approach toward cleaner production- a literature review.

Chang, X., Liu, H., Sun, J., Wang, J., Zhao, C., Zhang, W., Zhang, J., Sun, C., 2020. Zearalenone Removal from Corn Oil by an Enzymatic Strategy. Toxins (Basel). 12, 117. https://doi.org/10.3390/toxins12020117

CMS Law-Now, 2022. Significant Consultation on proposed revisions to REACH [WWW Document].

Daxue Consulting, 2020. The enzyme market in China partly driven by the boom of F&B and pharmaceuticals [WWW Document]. URL https://daxueconsulting.com/the-enzyme-market-in-china/#:~:text=According to data from Pacific,growing with the global trend.

De Guzman, D., 2013. BASF to acquire enzymes biz Verenium. Green Chem. Blog.

Debergh, P., Bilsen, V., Velde, E. Van de, 2016. Jobs and growth generated by induStrial biotechnology in europe.

DG GROW, 2022. Online survey on GRA and restrictions and authorisations.

ECHA, 2022a. REACH - What is not a substance? [WWW Document]. URL https://echa.europa.eu/support/substance-identification/what-is-not-a-substance#:~:text=A mixture is a mix or solution of two or more substances. (accessed 8.12.22).

ECHA, 2022b. Substitution to safer chemicals - How to substitute? [WWW Document]. URL https://echa.europa.eu/search-for-alternatives-for-substitution (accessed 8.11.22).

ECHA, 2008. Guidance on Socio-Economic Analysis - Restrictions.

ECHA, n.d. Understanding REACH [WWW Document]. URL https://echa.europa.eu/regulations/reach/understanding-reach (accessed 8.10.22a).

ECHA, n.d. Substances of very high concern (SVHC) [WWW Document]. URL https://echa.europa.eu/chemicals-in-our-life/which-chemicals-are-of-concern/svhc (accessed 8.10.22b).

ECHA, n.d. Understanding CLP [WWW Document]. URL https://echa.europa.eu/regulations/clp/understanding-clp (accessed 8.10.22c).

ECHA, n.d. Harmonised classification and labelling (CLH) [WWW Document]. URL https://echa.europa.eu/regulations/clp/harmonised-classification-and-labelling (accessed 8.10.22d).

ECHA, n.d. Classification of substances and mixtures [WWW Document]. URL https://echa.europa.eu/regulations/clp/classification (accessed 8.10.22e).

EFSA, n.d. Food enzymes [WWW Document]. URL https://www.efsa.europa.eu/en/topics/topic/food-enzymes (accessed 8.10.22).

eftec, 2019. Socio-economic analysis of the impacts of the proposed REACH restriction on intentionally added microplastics on the enzymes sector Final report Association of Manufacturers and Formulators of.

ERC, n.d. Welcome to Enzymes REACH Consortium [WWW Document]. URL http://www.enzymes-reach.org/content/welcome-enzymes-reach-consortium (accessed 8.10.22).

European Commission, 2022. REACH revision under the Chemicals Strategy Overview [WWW Document]. URL https://ec.europa.eu/environment/chemicals/reach/reach_revision_chemical_strategy_en.htm (accessed 8.10.22).

European Commission, 2020. Chemicals Strategy for Sustainability Towards a Toxic-Free Environment.

European Commission, 2019. A European Green Deal [WWW Document]. URL https://ec.europa.eu/info/strategy/priorities-2019-2024/european-green-deal_en (accessed 8.10.22).

European Commission, 2018a. The second REACH Review (REACH REFIT Evaluation) [WWW Document]. URL https://ec.europa.eu/environment/chemicals/reach/review_2017_en.htm (accessed 8.10.22).

European Commission, 2018b. Commission General Report on the operation of REACH and review of certain elements: Conclusions and Actions.

European Commission, n.d. Chemicals - Environment [WWW Document]. URL https://ec.europa.eu/environment/chemicals/index_en.htm (accessed 8.10.22a).

European Commission, n.d. REACH [WWW Document]. URL https://ec.europa.eu/environment/chemicals/reach/reach_en.htm (accessed 8.10.22b).

European Commission, n.d. REACH [WWW Document].

European Commission, n.d. Better Regulation: why and how [WWW Document]. URL https://ec.europa.eu/info/law/law-making-process/planning-and-proposing-law/better-regulation-why-and-how_en (accessed 8.10.22d).

European Commission, DG GROW, 2021. Inception impact assessment: Revision of EU legislation on registration, evaluation, authorisation and restriction of chemicals.

European Council, 2022. COVID-19: the EU's response to the economic fallout [WWW Document]. URL https://www.consilium.europa.eu/en/policies/coronavirus/covid-19-economy/

European Parliament, 2019. Diabetes care in the EU [WWW Document]. URL https://www.europarl.europa.eu/doceo/document/E-9-2020-006356_EN.html#:~:text=The cost of managing diabetes,lives from diabetes-related complications.

European Parliament, European Council, 2008. 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) [WWW Document]. URL https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32008R1272 (accessed 8.10.22).

European Parliament, European Council, 2006. 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).

eurostat, 2019. Where does our cheese come from? [WWW Document]. URL https://ec.europa.eu/eurostat/web/products-eurostat-news/-/EDN-20190119-1

Guerrand, D., 2017. Lipases industrial applications: focus on food and agroindustries. Oilseeds Fats, Crop. Lipids J. https://doi.org/10.1051/ocl/2017031

IFF, 2022. Our Subsidiaries: Legacy Nutrition & Biosciences Subsidiaries [WWW Document]. URL https://www.iff.com/where-we-operate/subsidiaries

Novozymes, 2022a. Frequently asked questions: Enzymes for biocatalysts [WWW Document]. URL https://www.novozymes.com/en/advance-your-business/pharma/pharma-biocatalysts

Novozymes, 2022b. Enzymes for diagnostics [WWW Document]. URL https://biosolutions.novozymes.com/en/diagnostics (accessed 8.12.22).

Novozymes, 2013. Enzymes at work.

OECD, 2021. Guidance on Key Considerations for the Identification and Selection of Safer Chemical Alternatives.

OECD, 2019. Diabetes prevalence [WWW Document]. URL https://www.oecd-ilibrary.org/sites/83231356-

en/index.html?itemId=/content/component/83231356-en#:~:text=About 32.3 million adults were,2019 (IDF%2C 2019).

OECD, 1998. Biotechnology for clean industrial products and processes: Towards industrial sustainability.

Pan, L., Shang, Q.H., Ma, X.K., Wu, Y., Long, S.F., Wang, Q.Q., Piao, X.S., 2017. Coated compound proteases improve nitrogen utilization by decreasing manure nitrogen output for growing pigs fed sorghum soybean meal based diets. Anim. Feed Sci. Technol. 230, 136–142. https://doi.org/10.1016/j.anifeedsci.2017.05.014

PRODCOM, 2022. Sold production, exports and imports by PRODCOM list (NACE Rev. 2) - annual data [WWW Document]. URL https://appsso.eurostat.ec.europa.eu/nui/show.do

Ricardo, 2022. Economic Analysis of the Impacts to the Detergents , Maintenance and Cleaning Products Industry of the Chemicals Strategy for Sustainability.

Sarrouh, B., Santos, T.M., Miyoshi, A., Dias, R., Azevedo, V., 2012. Up-To-Date Insight on Industrial Enzymes Applications and Global Market. J. Bioprocess. Biotech. 4. https://doi.org/10.4172/2155-9821.S4-002

SEAC, 2021. SEAC's approach to assessing changes in producer surplus.

SEAC, 2016. SEAC's Approach For Valuing Job Losses In Restriction Proposals And Applications For Authorisation.

Singh, R.S., Singh, T., Singh, A.K., 2019. Enzymes as Diagnostic Tools, in: Advances in Enzyme Technology. Elsevier, pp. 225–271. https://doi.org/10.1016/B978-0-444-64114-4.00009-1

VVA, 2022. Workshop on the results of the impact assessment of the extension of the generic approach to risk management under the REACH Regulation 27 June 2022 Background paper.

Wood, Ramboll, 2022. 'Targeted' stakeholder consultation - Study supporting the Commission in developing an essential use concept in chemicals legislation.

WWF, 2009. Industrial biotechnology: more than green fuel in a dirty economy? Exploring the transformational potential of industrial biotechnology on the way to a green economy.

Appendix 1 – Volume and value of enzyme products sold by EU Member States (2014-2020)

Appendix Table 1: Sold production quantity (in kg) for 'Enzymes; prepared enzymes (not elsewhere specified or included); excluding rennet and concentrates (PRODCOM Code: 20146470)

Country	2014	2015	2016	2017	2018	2019	2020
Austria	0	0	:	:	0	:	0
Belgium	24,803,532	18,493,832	18,593,291	19,831,830	21,451,435	22,190,463	22,013,610
Bosnia and Herzegovina	0	0	:	0	0	0	0
Bulgaria	:	:	:	:	:	:	:
Croatia	0	0	0	0	0	0	0
Cyprus	0	0	0	0	0	0	0
Czechia	:	:	:	:	169,644	:	:
Denmark	132,245,803	136,170,195	159,225,652	197,452,145	160,783,148	143,870,377	137,786,259
Estonia	0	0	0	0	0	0	:
Finland	53,871,372	56,421,859	59,509,289	57,433,559	64,367,495	62,512,527	62,222,897
France	16,137,975	16,271,210	17,026,400	19,789,985	20,288,867	:	18,943,522
Germany	7,463,649	7,349,304	7,810,932	9,793,501	7,797,815	8,704,815	9,407,702
Greece	13,141	21,300	21,688	32,509	:	:	:
Hungary	0	0	:	0	0	4	0
Iceland	0	0	0	0	0	0	0
Ireland	:	:	:	:	:	:	:
Italy	2,993,000	2,942,000	2,566,000	4,180,000	2,667,000	6,157,000	3,090,000
Latvia	0	:	0	0	0	0	0
Lithuania	9,705	16,056	13,809	9,759	15,470	8,643	10,099
Luxembourg	0	0	0	0	0	0	0
Malta	0	0	0	0	0	0	0
Montenegro	0	0	0	0	0	0	0
Netherlands	:	:	14,155,000	:	:	:	1,152,000
North Macedonia	0	0	0	0	0	0	0
Norway	0	0	0	0	0	0	0
Poland	866,402	1,053,961	999,460	1,110,570	1,264,565	963,687	1,144,417
Portugal	94,371	0	:	647,941	718,342	817,257	781,602
Romania	:	:	:	:	:	:	:

Country	2014	2015	2016	2017	2018	2019	2020
Serbia	0	0	0	0	0	0	0
Slovakia	0	0	0	0	0	0	0
Slovenia	:	:	:	:	:	:	:
Spain	1,086,000	743,000	815,000	738,000	871,000	4,415,000	3,707,000
Sweden	:	:	:	:	:	:	:
Turkey	:	:	:	:	:	:	:
United Kingdom	1,634,886	1,436,728	2,484,618	2,546,536	2,798,338	2,539,126	:
Total (in kg)	**241,219,836**	**240,919,445**	**283,221,139**	**313,566,335**	**283,193,119**	**252,178,899**	**260,259,108**
Total (in tonnes)	**241,220**	**240,919**	**283,221**	**313,566**	**283,193**	**252,179**	**260,259**

Notes: Cells with a colon or ":" indicate that data is not available.

Source: PRODCOM (2020)

Appendix Table 2: Sold production value (in € millions) for 'Enzymes; prepared enzymes (not elsewhere specified or included); excluding rennet and concentrates (PRODCOM Code: 20146470)

Country	2014	2015	2016	2017	2018	2019	2020
Austria	-	-	:	:	-	:	-
Belgium	69	75	75	82	78	80	75
Bosnia and Herzegovina	-	-	:	-	-	-	-
Bulgaria	10	:	12	:	:	:	:
Croatia	-	-	-	-	-	-	-
Cyprus	-	-	-	-	-	-	-
Czechia	:	:	:	:	1	1	1
Denmark	944	1,055	1,067	1,164	1,164	1,171	1,223
Estonia	-	-	-	-	-	-	:
Finland	222	217	230	225	283	278	264
France	140	142	147	165	159	147	159
Germany	141	163	165	179	181	185	192
Greece	1	2	1	1	:	:	:
Hungary	-	-	:	-	-	0	-
Iceland	-	-	-	-	-	-	-
Ireland	:	:	:	:	:	:	5
Italy	25	17	16	27	28	37	41
Latvia	-	:	-	-	-	-	-
Lithuania	22	31	32	25	27	31	121

Country	2014	2015	2016	2017	2018	2019	2020
Luxembourg	-	-	-	-	-	-	-
Malta	-	-	-	-	-	-	-
Montenegro	-	-	-	-	-	-	-
Netherlands	:	:	:	:	:	:	13
North Macedonia	-	-	-	-	-	-	-
Norway	-	-	-	-	-	-	-
Poland	3	:	:	4	5	4	5
Portugal	0	-	:	2	2	2	2
Romania	:	:	:	:	:	:	:
Serbia	-	-	-	-	-	-	-
Slovakia	-	-	-	-	-	-	-
Slovenia	:	:	:	:	:	:	:
Spain	12	2	2	2	2	9	8
Sweden	:	:	:	:	:	:	:
Turkey	:	:	:	:	:	:	:
United Kingdom	55	64	64	60	72	73	:
Total (in € millions)	**1,643**	**1,768**	**1,812**	**1,936**	**2,002**	**2,016**	**2,109**

Notes: Cells with a colon or ":" indicate that data is not available.

Source: PRODCOM (2020)

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