

## The ECETOC Conceptual Framework for Polymer Risk Assessment (CF4Polymers)

Technical Report No. 133-1

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

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DISCLAIMER: This Conceptual Framework reflects current experience and knowledge and shall be adapted, amended and refined as new evidence on polymer risk assessment becomes available

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European Centre for Ecotoxicology and Toxicology of Chemicals

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# The ECETOC Conceptual Framework for Polymer Risk Assessment (CF4Polymers)

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### **SUMMARY**

This Technical Report presents the *Conceptual Framework for Polymer Risk Assessment* (CF4Polymers) developed by the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) Polymers Task Force (TF). Based upon a review of the state-of-the-art polymer grouping and risk assessment (RA), the CF4Polymers provides basic guiding principles to be considered in assessing potential ecological and human health hazards and risks posed by polymer products to facilitate consistency.

The work of the TF was motivated by the versatility and complexity of polymers, that are generally not present as mono-constituent substances, but as complex polymer products consisting of the polymeric substance (polymeric macromolecules), intentionally added substances (IAS; e.g. stabilisers) and non-intentionally added substances (NIAS; e.g. impurities). Further, polymer products can change their form during different life cycle stages. For these reasons, conventional RA approaches for chemicals may need to be modified for polymers.

The CF4Polymers consists of eight steps:

- Step 1: Problem formulation (RA scope and protection goal definition)
- Step 2: Polymer identification
- Step 3: Polymer component strategy
- Step 4: Grouping approach evaluation
- Step 5: Determination of exposure scenarios (first part of exposure assessment)
- Step 6: Exposure characterisation (second part of exposure assessment)
- Step 7: Hazard assessment (hazard identification and characterisation)
- Step 8: Risk characterisation

The sequence of these steps can be adapted as necessary depending on the RA needs and/or data availability. For example, it may be preferable to perform an initial hazard assessment (Step 7) before exposure characterisation (Step 6) and to finalise hazard assessment thereafter, or to determine exposure scenarios (Step 5) already during problem formulation (Step 1).

In developing the CF4Polymers, the TF took account of activities of the Organisation for Economic Cooperation and Development (OECD) related to polymers, of relevant scientific literature and of regulatory documents from the European Union, Australia, Canada, China, Japan, the Philippines, South Korea, and the USA.

Importantly, the CF4Polymers is fully aligned with the internationally agreed paradigm for chemical RA as published by the World Health Organisation – International Programme for Chemical Safety (WHO IPCS). Deviations from the WHO IPCS framework within the CF4Polymers are necessitated by the chemical and physical attributes of polymeric substances and polymer products and their complex markets and uses. These deviations include the introduction of distinct steps for polymer identification and for determining the components of the polymer that shall be included in the RA process:

Polymer identification (Step 2): Directly after problem formulation (Step 1), Step 2 serves to ensure unambiguous and fit-for-purpose identification of the polymer product. This step can be undertaken as an iterative process to identify (1) the polymeric substance including (a) standard chemical descriptors; (b)

commercial identifiers; (c) relevant key parameters; as well as (2) IAS and/or (3) NIAS, as relevant. Depending on the given type of polymeric substance, relevant key parameters can include structural and/or morphological descriptors as well as physico-chemical and screening-level fate properties:

- Structural descriptors include e.g. chemical formula, degree of substitution, tacticity;
- Morphological descriptors include e.g. physical state (e.g. solid liquid), shape (e.g. spherical, fibre, tubular), physical form (e.g. amorphous, crystalline);
- Physico-chemical and screening-level fate properties include e.g. water solubility, n-octanol/water partition coefficient (log Pow), acid dissociation constant (pKa), vapour pressure, degradability.

Polymer component strategy (Step 3): This step serves to determine which components of the polymer product shall be addressed in the further steps of the CF4Polymers, i.e. the polymer product as such; the polymeric substance; specific IAS or NIAS separately; or some or all of the low molecular weight (LMW) components together (i.e. small oligomers, IAS, and NIAS, including unreacted monomers).

The grouping approach evaluation (Step 4) is firmly embedded in the CF4Polymers to ensure that all available data for similar polymer products are taken into account during (Steps 5-7) exposure and hazard assessment. Step 4 follows the general approach for substance grouping and read-across as described by the OECD and the European Chemicals Agency (ECHA). It uses expert knowledge to identify read-across sources thereby serving to avoid unnecessary resource allocation to hazard characterisation, especially animal testing.

With regard to exposure assessment, the broad variety of intended uses and the versatility of polymers throughout the life cycle necessitated separately addressing its two parts, i.e. the determination of exposure scenarios (Step 5) and exposure characterisation (Step 6). These steps are followed by hazard assessment (Step 7) and, finally, risk characterisation (Step 8).

For each of the eight steps of the CF4Polymers, a detailed outline is provided for how it can be completed, accompanied by explanatory notes and illustrative examples. For improved clarity, the Technical Report further includes a comprehensive glossary. The explanatory notes and examples also serve to justify deviations from the conventional RA paradigm. However, specific properties of polymers also provide opportunities to streamline the RA process. For example, the molecular weight (Mw) distribution of a polymer product allows determining if internal bioavailability is likely. If the polymeric substance and/or polymer product are too large to pass through biological membranes, it is not meaningful to conduct higher-tier *in vivo* testing (while testing for local effects on e.g. skin or eyes may still be necessary). Similarly, for LMW components of the polymer product, diffusivity and migration potential from the polymer matrix determine external bioavailability e.g. at the eyes and skin, and internal (systemic) bioavailability (Step 7).

For each step of the CF4Polymers, prevailing knowledge gaps are addressed. For the time being, expert knowledge is required to identify the set of key parameters that are relevant for fit-for-purpose polymer identification (Step 2). This set of key parameters most likely does not only depends on the type of polymer, but also on its intended use(s) and the life cycle stage(s) covered by the problem formulation (Step 1). Presumably, the set of key parameters that is relevant for fit-for-purpose polymer identification also encompasses those key parameters that drive grouping (Step 4) and the data needs for exposure assessment (Steps 5 and 6) as well as hazard assessment (Step 7).

<u>Recommendation 1</u>: Identify sets of structural and/or morphological descriptors as well as physico-chemical and fate properties that are key parameters for different types of polymer products. Further research is merited

to identify which specific properties are the relevant key parameters for fit-for-purpose polymer identification and grouping. Specific key parameters might generally be relevant across different types of polymers, or they might be unique to specific types of polymer products. Knowledge on such key parameters will also facilitate the identification of data needs during exposure and hazard assessment.

Different analytical tools, *in vitro* and *in vivo* test methods, and *in silico* models are available to assess the physical, chemical, fate, ecotoxicological and toxicological properties of chemicals in general. Some of these tools, methods, and models have technical limitations restricting their applicability domain for assessing polymers. These technical limitations can generally be attributed to specific physical or chemical properties of the polymers. For the time being, expert knowledge is required to select the most appropriate tool, method or model to assess a given parameter and to identify potential technical limitations. A detailed review of the applicability of standardised analytical tools, test methods and *in silico* models to assess the physical, chemical, fate, ecotoxicological and toxicological properties of polymers is in preparation by the ECETOC Polymers TF (planned as ECETOC Technical Report (TR) No. 133-2).

<u>Recommendation 2</u>: Consider prevailing technical limitations of available tools, test methods and models for polymer RA. Further, based upon the outcome of the review of the applicability of such tools, methods and models that is being prepared by the ECETOC Polymers TF, further research is merited to contribute to overcoming such technical limitations when assessing polymers and permit standardisation of testing.

The CF4Polymers is founded on a comprehensive review of the state-of-the-art polymer RA. Now, it has to prove itself in practice. The TF is preparing case studies to further evaluate the comprehensiveness and appropriateness of the eight steps of the CF4Polymers, and specifically opportunities for the grouping of polymers (planned as ECETOC TR No. 133-3). These case studies might reveal the need to refine or amend the CF4Polymers. Similarly, as further knowledge on the applicability of the CF4Polymers to support the RA of polymers becomes available, the CF4Polymers should be adapted, as necessary. The flexibility and non-prescriptive nature of the CF4Polymers facilitates timely and straightforward adaptations. An *ad-hoc* committee within ECETOC has been mandated to follow and report such evolution.

<u>Recommendation 3</u>: *Maintain the CF4Polymers as a 'living', flexible framework,* and review and update it in line with emerging knowledge on how it can efficiently and effectively support polymer RA.

In preparing the CF4Polymers, the TF reviewed the regulatory landscape on polymers to identify key elements of polymer RA and to determine if these key elements should, or should not, feed into the CF4Polymers. Important key elements relate to the concept of 'polymers of low concern' (PLC) that has been developed by the US Environmental Protection Agency (US EPA) and several other agencies and was reviewed by the OECD. The PLC concept is generally applied by all jurisdictions reviewed by the TF that have implemented provisions for polymer notification / registration in their chemical legislation. The PLC concept includes specific criteria related to the Mw of the polymeric substance and the proportion of low Mw compounds in the polymer product. Further, PLC exclusion criteria relate to the presence of specific structural alerts, such as reactive or cationic functional groups or specific chemical elements.

While the publicly available dataset to support the PLC concept, or specific PLC criteria / PLC exclusion criteria, is limited, the TF was unable to find any evidence to refute the PLC concept. The TF considers the PLC concept a pragmatic approach to streamline the time and effort for polymer RA. Polymers identified as PLC can generally be considered to exhibit low intrinsic hazard potential. However, this does not allow the reverse conclusion that polymers that are not identified as PLC would *per se* pose a hazard or risk concern. For example, the identification of a specific functional group merely informs on the presence of a structural alert.

This should not by itself lead to the conclusion that the polymer is hazardous, but merely trigger considerations on external and internal bioavailability and lower-tier screening. Only if such screening indicates hazard potential, the TF considers higher-tier *in vivo* testing justifiable. Further, all testing should be selected to reflect the likely mode-of-action (MoA) of the polymer as indicated by the given structural alert.

<u>Recommendation 4</u>: Establish a knowledge base to substantiate the PLC concept and to identify under which conditions the presence of specific structural alerts or physico-chemical properties poses environmental or human health hazard concerns. Particularly, there is only weak evidence that anionic or amphoteric and water absorbing polymers might generally have a relevant hazard potential. Further research is also merited to establish which combinations of properties of a given (type of) polymer truly drive its hazard potential. Such information will also serve to establish an improved scientific foundation for the grouping of polymers.

Polymer water solubility and low Mw should not be misinterpreted as directly related to hazards – they are most probably only modulating factors for aquatic exposure and internal bioavailability. Similarly, the TF was unable to find any evidence that polymer (bio)degradation should be used as PLC exclusion criterion, i.e. that this property by itself indicates a hazard concern. Polymer (bio)degradation is complex, covering physical, chemical, and biological degradation; it can be intended (desirable) or unintended, and this can further depend on the life cycle stage of the polymer. Importantly, assessments surrounding (bio)degradation should consider the duration of (bio)degradation (i.e. half-lives) and the type of evolving breakdown products.

<u>Recommendation 5</u>: Develop environmentally relevant models, methods and/or criteria to assess (bio)degradation to enhance assessments of the RA implications of this property. Such models / criteria should take into account the type of (bio)degradation, its duration (i.e. half-lives), and whether it is intended during the given life cycle stage of the polymer, or not.

In conclusion, to the best of the TF's knowledge, this is the first time that a comprehensive framework for polymer RA, the CF4Polymers, has been put forward that not only addresses the polymeric substance itself, but also potential IAS and NIAS. The present ECETOC TR No. 133-1, the CF4Polymers, is the first of three parts of a Technical Report series that the ECETOC Polymers TF is currently preparing. The other two are:

- 1. A review of the applicability of standardised analytical tools, test methods and *in silico* models to assess the physical, chemical, fate, ecotoxicological and toxicological properties of polymers (planned as ECETOC TR No. 133-2); and
- 2. A selection of case studies addressing different components of polymer grouping and RA to put the CF4Polymers into practice (planned as ECETOC TR No. 133-3).

It is expected that application of the CF4Polymers will contribute to the efficient and effective RA of polymer products. The CF4Polymers has been designed flexibly to accommodate both RA that is conducted for voluntary purposes and to meet regulatory requirements related to chemical and product-specific legislation.

Finally, the CF4Polymers shall be adapted and amended as new evidence on polymer RA becomes available. In this regard, it is anticipated that the outcome of ongoing work of the TF in reviewing the applicability of test methods and preparing case studies will provide important insight to further refine the CF4Polymers. ECETOC has mandated an *ad-hoc* committee to follow-up and report upon developments and evolution in the knowledge, testing and RA related to polymers. It is, therefore, intended that ECETOC will proactively and periodically update the Technical Report No. 133 series to keep abreast of state-of-the-art within this domain.

### 1. INTRODUCTION

Polymers, i.e. macromolecules composed of many monomer units (see Glossary at the end of this Technical Report for definitions of key terms), are widely used in a vast range of applications such as packaging, building and construction, transportation, electrical and electronic equipment, agriculture, as well as in the medical/dental and the sports sectors (ECHA, 2012a). Since polymers frequently have high molecular weight (HMW), which limits their bioavailability, and low reaction potential under environmental conditions, polymers are generally considered 'safer' than substances with lower molecular weight (MW) (OECD, 2009). Therefore, they have been subject to exemptions or reduced regulatory requirements in all jurisdictions worldwide that have implemented a chemical legislation (BIO by Deloitte, 2015). In recent years, however, this pragmatic approach to managing risks associated with polymers is coming under increased scrutiny. Amongst other issues, there is a growing concern on potential hazards resulting from physical effects of solid polymers due to their morphology and the high-volume use of many polymers in combination with their persistence in the environment when present in plastics (Andrady et al., 2009, 2015; Haider et al., 2019).

Against this background, the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) decided that a review of relevant scientific methods and knowledge applicable to the risk assessment (RA) of polymers would be helpful to provide a scientific perspective for the safety assessment of polymers. In April 2018, ECETOC launched the 'ECETOC Polymers Task Force' (TF) that brought together specialists of polymer chemistry, toxicologists, ecotoxicologists and environmental fate modellers (see list of TF members at the end of this Technical Report). The terms of reference of the ECETOC Polymers TF included the development of:

- 1. A conceptual framework for polymer RA, mapping polymer types and their life cycles (Glossary) and associated environmental and human health protection goals; and
- 2. An approach for the grouping of polymers during RA.

This Technical Report summarises the outcome of the work of the ECETOC Polymers TF up until April 2019. The core of the report is the *ECETOC Conceptual Framework for Polymer Risk Assessment (CF4Polymers)* with an integrated step for grouping approach evaluation.

Box 1: Polymer product and its components (see also Glossary for definitions of all key terms)

**Polymer product**: A chemical product with a polymeric substance as main component, and NIAS and sometimes IAS as other components (ECETOC Polymers TF working definition). Polymer products are only in some cases finished articles.

**Polymeric substance (polymeric macromolecules)**: The chemical (co)polymer and possibly present oligomers (both are composed of the same monomeric units) (ECETOC Polymers TF working definition).

Oligomer: Part of the polymeric substance (at the low end of its Mw range). In some contexts, also referred to as NIAS.

Additive, intentionally added substance (IAS): "A substance added to something in small quantities to improve or preserve it." (<u>https://en.oxforddictionaries.com/definition/additive</u>); "A substance which is intentionally added to plastics to achieve a physical or chemical effect during processing of the plastic or in the final material or article; it is intended to be present in the final material or article" (European Commission, 2011).

**Non-intentionally added substance (NIAS)**: "An impurity in the substances used or a reaction intermediate formed during the production process or a decomposition or reaction product" (European Commission, 2011).

**Monomer, unreacted:** Depending on the manufacturing process and intended use of the polymer product, unreacted monomers can either be IAS or NIAS.

In drawing up the CF4Polymers, the TF took into account that:

- Polymers are not mono-constituent substances, but 'polymer products' consisting of the polymeric substance (polymeric macromolecules) and possibly also of intentionally added substances (IAS) and non-intentionally added substances (NIAS) (Box 1, Figure 1, and Glossary). Polymers represent a large range of chemical substances; there is no such thing as 'the (*singular*) polymer'. Notably, while RA activities will most likely focus on synthetic (or semi-synthetic) polymers, the CF4Polymers can potentially also be applied to natural polymers (see Appendix A for further details on the different types of polymers);
- For many polymers in solid form, the physical properties of the polymer matrix determine if low Mw (LMW) components (i.e. small oligomers, IAS, and NIAS, including unreacted monomers) of the polymer product are encapsulated therein or might migrate / diffuse therefrom, thereby becoming physically available (Glossary);
- There are often many actors in the value chain (Glossary) of polymer products (and articles containing polymer products) that modify the chemistry and morphology of the product that is placed on the market.



Figure 1: Components and aspects of polymer products covered by the CF4Polymers

<u>Footnote to Figure 1</u>: This illustrative Figure is not to scale, i.e. neither scales nor font size are indications of quantities or sizes of the components of the polymer product. Polymer macromolecules pertain to the molecular weight (Mw) distribution upper range); whereas oligomers pertain to the Mw distribution lower range. Intentionally added substances (IAS) include, e.g., antioxidants, UV filters, surfactants, plasticisers, processing aids, solvents. Non-intentionally added substances (NIAS) include, e.g., impurities, contaminants, degradation / decomposition products of the polymer, of raw materials or of additives. Depending on the polymer product, oligomers can be regarded to be either part of the polymeric substance or NIAS; and unreacted monomers can be regarded to be IAS or NIAS.

Some conventional approaches to chemical RA need to be adapted to appropriately address these attributes, and this is reflected in the CF4Polymers.

As starting point for the development of the CF4Polymers, the TF reviewed:

- Available definitions for (different forms of) polymers and information on the versatility and complexity of polymers;
- The chemical legislation and related guidance, as relevant for polymer RA, adopted in the European Union (EU) in the context of *Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals* (REACH; EP and Council, 2006) as well as in Australia, Canada, China, Japan, the Philippines, South Korea, and the USA;
- Product-specific legislation of relevance for polymer products e.g.
  - *Regulation (EC) No 1935/2004 on materials and articles intended to come into contact with food* ('Food Contact Materials (FCMs) Regulation'; EP and Council, 2004a);
  - Regulation (EC) No 648/2004 on detergents ('Detergents Regulation'; EP and Council, 2004b);
  - *Regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food* ('Regulation on Plastics in Contact with Food'; European Commission, 2011);
  - Regulation (EU) 2017/745 on medical devices (EP and Council, 2017);
- Test Guidelines (TGs) and Guidance Documents adopted by the Organisation for Economic Cooperation and Development (OECD) or the US Environmental Protection Agency (US EPA) as well as technical reports and standards from the International Standardisation Organisation (ISO) or national standards institutes.

This information was evaluated to identify components of current RA approaches that could (or could not) be applied to polymers in general or to specific types of polymers. Further, the TF aimed at identifying knowledge gaps preventing applicability of conventional RA approaches, or the proposed CF4Polymers, to all types and forms of polymers, and at making suggestions for how such knowledge gaps could be addressed e.g. by future ECETOC work or within the European Chemical Industry Council (Cefic) Long-range Research Initiative (LRI).

The complexity and versatility of polymers necessitated a delineation of the scope of the TF work, and of the CF4Polymers.

# All components of the **polymer product**, **i.e. the polymeric substance**, **IAS and NIAS**, are considered in the CF4Polymers (Figure 1).

'Non-intentionally added substances' (NIAS; Glossary) are, for example, impurities that may appear in the polymer product during the polymerisation reaction or during decomposition. The term NIAS was introduced in the Regulation on Plastics in Contact with Food (European Commission, 2011) in the context of food packaging. However, NIAS also occur in non-plastic / non-polymer FCMs (Geueke, 2018) as well as in polymers and non-polymers used for other purposes than as FCMs. For specific polymer products, the composition and structure of oligomers (that are generally considered part of the polymeric substance) may be modified during production. In such cases, it may be more appropriate to consider oligomers as NIAS (Geueke, 2018).

Additives are intentionally added substances (IAS; Glossary) as also defined in the Regulation on Plastics in Contact with Food (European Commission, 2011). Often, additives form an integral part of the complex polymer mixture, e.g. they are added to impart different physico-chemical properties upon the polymer product. In the EU, additives, as distinct chemicals, are covered by the REACH Regulation (EP and Council, 2006) as any other substance. Hence, they may only be used in the polymer product if the respective applicable RA provisions implemented under REACH have been met. Further, additives are often addressed in use-specific legislation e.g. in the Regulation on Plastics in Contact with Food (European Commission, 2011).

The CF4Polymers also considers **specific life cycle stages of polymer products** and their associated routes of exposure e.g. their down-the-drain release from consumer products and removal in wastewater treatment plants (WWTPs). However, the CF4Polymers does not address comprehensive life cycle sustainability assessments (Guinée, 2016), which would include considerations beyond product RA, e.g. related to the global environmental impact of the use of raw materials and energy during polymer production. As for any other compound, assessing the global environmental impact of polymer products considers relevant aspects related to their production, use, and end-of-life stage. The form of the polymer product at its end-of-life stage not only depends on the physical and chemical characteristics of the 'as produced' polymer, but also on its intended use(s). The same polymer can be used in many different applications or for a broad variety of different purposes leading to different end-of-life transformations. As a result, the comprehensive life cycle sustainability assessment of a polymer can be highly complex and include considerations outside the scope of the CF4Polymers.

The TF work took account of the ECETOC Technical Report *Challenges and limitations associated with aquatic toxicity and bioaccumulation studies for sparingly soluble and manufactured particulate substances* (ECETOC, 2018); as well as work of the ECETOC Nanomaterials TF that drew up a *Decision-making framework for the grouping and testing of nanomaterials* (Arts et al., 2015, 2016). The specific considerations related to nanomaterial RA presented therein are generally also applicable to nano-sized polymers. Therefore, the ECETOC polymers TF excluded **nano-sized polymers** from the scope of its work.

Finally, the TF work excluded considerations on **environmental pollution by plastics or microplastics** (Glossary and Box 2). While the ongoing policy activities regarding plastics and microplastics waste also motivated the establishment of the ECETOC Polymers TF, these policy activities include societal aspects, such as waste management and littering behaviour. By contrast, the TF work is exclusively science-based, i.e. to establish the state-of-the-art ecological and human health RA of polymers. Notwithstanding, it is expected that application of the CF4Polymers will facilitate the establishment of a scientific foundation to address the environmental and human health impact of plastics waste and microplastics.

Against this background, this ECETOC Technical Report (TR) No. 133-1 is structured as follows:

- Section 2 informs on regulatory definitions of polymers and related terms.
- Section 3 presents and discusses the eight steps of the CF4Polymers.
- **Section 4** provides an overview on key elements of polymer regulation implemented in different jurisdictions showing how these key elements have been addressed in the CF4Polymers.
- Section 5 presents conclusions and recommendations.

As two further parts of this Technical Report series, the ECETOC Polymers TF is currently preparing a review on the applicability or technical limitations of internationally accepted analytical tools, test methods, and *in silico* models (that were developed to assess the physical, chemical, fate, and (eco)toxicological properties of chemical substances in general) for the assessment of polymers (planned as ECETOC TR No. 133-2), and a set of case studies to corroborate the outline of the CF4Polymers and/or to identify the need to amend parts of it, as necessary (planned as ECETOC TR No. 133-3).

#### Box 2: Public debate and policy activities regarding plastic and microplastics waste

Polymers and plastics are closely interlinked in the public perception. While plastics are a specific type of material based on synthetic polymers (Glossary), this distinction is often not fully understood by laypeople, or even scientists. For example, discussions on *'what is the difference between a polymer and a plastic?'* can be found in internet fora e.g. in ResearchGate<sup>1</sup> or Quora<sup>2</sup>. In Quora, the answer begins with: *'They mean the same thing in common parlance...'*<sup>2</sup>. By contrast, although all plastics are polymers, not all polymers are plastics.

The high-volume use of many polymers used in plastics in combination with their release and persistence in the environment when present in plastics (Andrady et al., 2009, 2015; Haider et al., 2019) have fuelled a public debate on the environmental impact of waste plastics and potential uptake of breakdown products by humans and wildlife (e.g. *'Plastic now pollutes every corner of the earth'* (McKie, 2016); *'The plastics crisis is more urgent than you know'* (Vidal, 2018); plastic waste is seen as a *'global challenge'*<sup>3</sup> or *'key societal challenge'*<sup>4</sup>). The concerns related to the release of plastics into the environment are being taken up by policy makers and regulators.

In the USA, the *Microbead Free Waters Act* prohibiting the manufacture, packaging and distribution of rinse-off cosmetics and non-prescription drugs containing plastic microbeads was adopted in 2015 (US Government, 2015).

In the EU, the European Commission published a *European Strategy for Plastics in a Circular Economy* (European Commission, 2018a). In January 2019, the European Chemicals Agency (ECHA) submitted a proposal for an EU-wide restriction for intentionally added microplastics (ECHA, 2019a). Therein, it is stated: *"The term 'microplastic' is not consistency* [presumably: 'consistently'] *defined, but is typically considered to refer to small, usually microscopic, solid particles made of a synthetic polymer"* (ECHA, 2019a). Earlier, ECHA defined microplastics as *"synthetic, water-insoluble polymer items smaller than 5 mm, which are considered to be of particular concern for the aquatic environment"* (ECHA, 2019a). Discussions on how to scope the ECHA (2019a) restriction appropriately are ongoing at the time of publication of this Technical Report.

<sup>&</sup>lt;sup>1</sup><u>https://www.researchgate.net/post/what is the difference between a polymer and a plastic</u> <u>Note</u>: Throughout the Technical Report, all websites were accessed in March and April 2019.

<sup>&</sup>lt;sup>2</sup> <u>https://www.quora.com/What-is-the-difference-between-polymers-and-plastic</u>

<sup>&</sup>lt;sup>3</sup> <u>https://microbiologysociety.org/news/society-news/plastic-waste-a-global-challenge-and-an-opportunity.html</u>

<sup>&</sup>lt;sup>4</sup> <u>http://www.plasticsinsociety.global/the-plastics-challenge</u>

### 2. REGULATORY DEFINITIONS OF POLYMERS AND RELATED TERMS

Polymers can be defined from a chemical perspective (i.e. macromolecules composed of a series of interconnected, repeating units), or from a regulatory perspective. In preparation of Section 3, presenting the CF4Polymers, this Section 2 introduces regulatory definitions for polymers and related terms formulated by the OECD and within the EU REACH Regulation (EP and Council, 2006). A sound understanding of these definitions is an essential starting point for all deliberations on polymer RA, to understand the complexity of polymeric substances and polymer products and to substantiate deviations from the standard RA paradigm as it has been described by the World Health Organisation – International Programme on Chemical Safety (WHO IPCS, 2004, 2010). Supplementing this section, Appendix A (*Complexity and versatility of polymers*) provides further details on the chemistry, manufacture, processing and use of polymers.

The focus on OECD and EU REACH definitions in this section is motivated by the central role of the OECD in drawing up definitions for polymers and related terms as well as by the ongoing European Commission activities related to polymer regulation. Notwithstanding, many non-EU jurisdictions have made significant contributions to the establishment of procedures to ensure polymer safety, and the TF has considered these contributions in drawing up the CF4Polymers. This is further explored in Section 4 (*Key elements of international polymer regulation*) and in Appendix B (*Regulatory landscape on polymers*) that summarises the polymer RA provisions implemented in Australia, Canada, China, Japan, the Philippines, South Korea, the USA and the EU. These summaries relate to the respective chemical legislation, whereas legislation related to e.g. specific consumer uses (e.g. medical devices, FCMs, cosmetics) or occupational safety are not addressed.

The OECD, within its Expert Group on Polymer Definitions established in 1990, has drawn up definitions for polymers and related key terms; <u>http://www.oecd.org/env/ehs/oecddefinitionofpolymer.htm</u>:

"A <u>polymer</u> means a substance consisting of molecules characterized by the sequence of one or more types of monomer units and comprising a simple weight majority of molecules containing at least three monomer units which are covalently bound to at least one other monomer unit or other reactant and consists of less than a simple weight majority of molecules of the same molecular weight. Such molecules must be distributed over a range of molecular weights wherein differences in the molecular weight are primarily attributable to differences in the number of monomer units. In the context of this definition a 'monomer unit' means the reacted form of a monomer in a polymer."

"<u>Sequence</u>: means that the monomer units under consideration are covalently bound to one another and form a continuous string within the molecule, uninterrupted by units other than monomer units.

<u>Monomer</u>: means a molecule which is capable of forming covalent bonds with two or more like or unlike molecules under the conditions of the relevant polymer-forming reaction used for the particular process.

<u>Other reactant</u>: means a molecule linked to one or more sequences of monomer units but which, under the relevant reaction conditions used for the particular process, cannot become a repeating unit in the polymer structure."

Hence, the OECD definition for polymer reflects the TF's working definition for 'polymeric substance' since it does not refer to additives or NIAS.

Legally implemented definitions for polymers are generally founded on these OECD definitions.

In the EU, a definition for polymer is included in Article 3(5) of the REACH Regulation (EP and Council, 2006): "Polymer: means a substance consisting of molecules characterised by the sequence of one or more types of monomer units. Such molecules must be distributed over a range of Mw's wherein differences in the Mw are primarily attributable to differences in the number of monomer units. A polymer comprises the following:

- a. A simple weight majority of molecules containing at least three monomer units which are covalently bound to at least one other monomer unit or another reactant;
- b. Less than a simple weight majority of molecules of the same Mw.

In the context of this definition a 'monomer unit' means the reacted form of a monomer substance in a polymer."

Further, Article 3(6) of the REACH Regulation defines a monomer as "a substance which is capable of forming covalent bonds with a sequence of additional like or unlike molecules under the conditions of the relevant polymer-forming reaction used for the particular process."

The European Chemicals Agency (ECHA) *Guidance for monomers and polymers* provides further explanations on the REACH definition of polymer (ECHA, 2012a):

"In accordance with REACH (Article 3(5)), a polymer is defined as a substance meeting the following criteria:

- a. Over 50 percent of the weight for that substance consists of polymer molecules [...]; and,
- b. The amount of polymer molecules presenting the same molecular weight must be less than 50 weight percent of the substance."

ECHA (2012a) explains that "a monomer unit means the reacted form of a monomer substance in a polymer (for the identification of the monomeric unit(s) in the chemical structure of the polymer the mechanism of polymer formation may, for instance, be taken into consideration)".

With respect to "sequence" and "other reactants", ECHA (2012a) provides definitions that are similar to, but not identical with, the corresponding OECD definitions (see above).

"A 'sequence' is a continuous string of monomer units within the molecule that are covalently bonded to one another and are uninterrupted by units other than monomer units. This continuous string of monomer units can possibly follow any network within the polymer structure" (ECHA, 2012a).

"'Other reactant' refers to a molecule that can be linked to one or more sequences of monomer units but which cannot be regarded as a monomer under the relevant reaction conditions used for the polymer formation process" (ECHA, 2012a).

ECHA (2012a) defines 'unreacted monomers' as "the quantities of a monomer substance that do not react during the polymerisation reaction and remain in the composition of a polymer" and highlights that "unreacted monomers in a polymer are also constituents of that polymer".

ECHA (2012a) also provides details on additives, stabilisers and impurities: A polymer (as any other substance defined in Article 3(1) of the REACH Regulation) can also contain "any additive necessary to preserve its stability and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition"; and: "Stabilisers and impurities are considered to be part of the substance and do not have to be registered separately. Stabilisers include, for example, heat stabilisers, anti-oxidants (both useful during extrusion) and light stabilisers (e.g. for preservation during use). Impurities are unintended constituents of the polymer such as catalysts residues" (ECHA, 2012a).

Finally, ECHA (2012a) explains under which conditions polymers should be considered mixtures or articles: "Substances may also be added to improve the performance of the polymer even though they are not necessary for preserving the stability of the polymer. Indeed, substances are commonly added to a polymer for the purpose of adjusting or improving the appearance and/or the physico-chemical properties of the polymeric material. Examples of such substances include pigments, lubricants, thickeners, antistatic agents, antifogging agents, nucleating agents and flame retardants. When a polymeric material contains such substances, it should be considered as a mixture or an article, as the case may be [...]. For such substances normal registration requirements apply."

Hence, ECHA, in its guidance document, uses the term polymer in a different meaning than the OECD since it explicitly also includes some types of additives and impurities.

### 2.1 ECETOC Polymers TF appraisal of existing definition for polymers

This brief overview of OECD and EU REACH definitions for polymers shows that the term polymer is sometimes used to refer to the polymeric substance and sometimes to refer to the polymer product. Notwithstanding, these definitions include a range of Mw's for any given polymer. This highlights that polymer products are not mono-constituent substances. Some components of the polymer products (IAS) may be well characterised, whereas others (NIAS) may not be. All components of the polymer product, that can further change during different life cycle stages, should be considered during polymer RA as far as necessary. Due to the complexity of polymer value chains and life cycles, this can be challenging. For example, for solid polymers, the polymer matrix determines the migration and diffusion behaviour of small oligomers, IAS and NIAS embedded therein, and hence how exposure to these LMW compounds can occur. The CF4Polymers has been designed to address these complexities.

To improve the clarity of the CF4Polymers, the Glossary at the end of this Technical Report provides a comprehensive list of relevant definitions. As far as possible, the TF selected agreed definitions as published e.g. by the WHO IPCS, the OECD, the US EPA, the European Commission or ECHA. However, for specific terms (e.g. polymer product), the TF identified the need to draw up new definitions to address the specific purpose of polymer RA. These 'TF working definitions' have been formulated to stand in line with agreed definitions for related terms.

### 3. ECETOC CONCEPTUAL FRAMEWORK FOR POLYMER RISK ASSESSMENT (CF4POLYMERS)

This section outlines the eight steps of the *ECETOC Conceptual Framework for Polymer Risk Assessment* (CF4Polymers; Figure 2) presenting basic guiding principles to be considered in assessing risks posed by polymer products to facilitate consistency. The steps of the CF4Polymers adhere to the scientific principles of the internationally agreed framework for chemical RA published by the WHO IPCS (2004, 2010); Box 3.

#### Box 3: Risk assessment (RA) and risk management according to the WHO IPCS framework

<u>Risk assessment (RA):</u> "A process intended to calculate or estimate the risk to a given target organism, system, or (sub)population, including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system" (WHO IPCS, 2004). The RA process, that should be preceded by <u>problem formulation</u> and <u>substance identification</u>, includes the following four steps (WHO IPCS, 2010):

<u>Step 1 - Hazard identification</u>: "The identification of the type and nature of adverse effects that an agent has an inherent capacity to cause in an organism, system, or (sub)population. Hazard identification is the first stage in hazard assessment" (WHO IPCS, 2004).

<u>Step 2 - Hazard characterisation (dose-response assessment)</u>: "The qualitative and, wherever possible, quantitative description of the inherent property of an agent or situation having the potential to cause adverse effects. This should, where possible, include a dose-response assessment and its attendant uncertainties. Hazard characterization is the second stage in the process of hazard assessment" (WHO IPCS, 2004).</u>

<u>Step 3 - Exposure assessment</u>: "The process of estimating or measuring the magnitude, frequency, and duration of exposure to an agent, along with the number and characteristics of the population exposed. Ideally, it describes the sources, pathways, routes, and the uncertainties in the assessment" (WHO IPCS, 2004).

<u>Step 4 - Risk characterisation</u>: "The qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of occurrence of known and potential adverse effects of an agent in a given organism, system, or (sub)population, under defined exposure conditions" (WHO IPCS, 2004).

<u>Risk management:</u> "Decision-making process involving considerations of political, social, economic, and technical factors with relevant risk assessment information relating to a hazard so as to develop, analyse, and compare regulatory and non-regulatory options and to select and implement appropriate regulatory response to that hazard. Risk management comprises three elements: risk evaluation; emission and exposure control; and risk monitoring" (WHO IPCS, 2004).



#### Figure 2: The eight steps of the CF4Polymers

<u>Footnote to Figure 2:</u> The CF4Polymers has been designed flexibly. This also implies that the sequence of the eight steps can be adapted depending on the specific RA needs and/or data availability.

Further to being aligned with the WHO IPCS framework for chemical RA, the CF4Polymers also recognises the specific attributes and properties of polymer products that must be considered during RA. In this regard, the CF4Polymers takes into account the relevant work undertaken on the level of the OECD e.g. as published in the *Data analysis of the identification of correlations between polymer characteristics and potential for health or ecotoxicological concern* (OECD, 2009). Ten years ago, this document reviewed scientific criteria for how to identify a polymer's potential for (eco)toxicological concern, and its general outline has been confirmed in

practice. However, the OECD (2009) did not lay out a strategy for polymer RA. The CF4Polymers is intended to contribute to closing this gap.

Additionally, the specific needs for polymer RA addressed in the CF4Polymers, that are founded on the complexity and versatility of polymer products, takes advantage of experiences gained in assessing non-polymeric multi-constituent substances and 'substances of unknown or variable composition, complex reaction products and biological materials' (UVCBs; Glossary). Further, the CF4Polymer considers key elements of polymer RA implemented in different jurisdictions world-wide (Section 4).

Based on these underpinnings, the CF4Polymers is generally compatible with polymer RA procedures implemented in different jurisdictions both within the respective chemical legislation and product-specific legislation e.g. related to cosmetics products or packaging. As such, the CF4Polymers can also be taken into account in emerging regulations. Notably, while the CF4Polymers lays out a state-of-the-art framework for the RA of polymers, it is not prescriptive. The CF4Polymers has been designed to be flexible. It describes how polymer RA can be undertaken, regardless of the underlying motivation and/or legal requirements. Thereby, the CF4Polymers can both be applied in voluntary and in regulatory settings. There may be regulatory settings requiring more or less knowledge than outlined in the CF4Polymers. Evidently, such regulatory requirements supersede if the RA is conducted to fulfil the respective legal obligations. In such cases, the CF4Polymers may provide insight that facilitates adaptations of traditional testing approaches implemented in current legislation.

As with many non-polymeric substances, a single polymeric substance and/or polymer product can be used for a variety of different purposes. Therefore, the problem formulation (i.e. RA scope) and information needs may vary based on the specific stage of the value chain / life cycle of the polymer. For example, the evaluation of the safety of a cooking dish does not need to consider the safe occupational handling of the polymer pellets after polymerisation at the chemical plant. This adds complexity to hazard assessment (i.e. hazard identification and characterisation) and exposure characterisation. All such issues are considered in the CF4Polymers as relevant for the polymer product under investigation to ensure that it provides an accurate estimation of the risk potential in a given scenario.

Further, the CF4Polymers has been designed pragmatically by not only addressing the complexity and versatility of polymers, but also outlining options to streamline the RA to the given information needs. In this regard, two principles are incorporated in the CF4Polymers:

(1) Reliance on structural and morphological descriptors as well as physico-chemical and fate properties of the polymer to inform the scope and extent of environmental and human health exposure characterisation and hazard assessment that is sufficient for the RA of the given polymer product. Specific properties of polymers, such as HMW impairing systemic uptake, allow identifying reduced potential for systemic toxicological concern without resource-intensive vertebrate animal testing. Similarly, specific structural alerts (e.g. reactive functional groups (RFGs)) of the polymer allow identifying its likely mode-of-action (MoA; Sonich-Mullin et al., 2001; Boobis et al., 2009; Fenner-Crisp and Dellarco, 2016). Within the CF4Polymers such information is used to select relevant (eco)toxicological endpoints and test methods for hazard identification and characterisation.

(2) Grouping of polymers to ensure that all available relevant data (also on similar polymers) are exploited; and new data are only generated when truly relevant and indispensable for RA.

Thereby, the CF4Polymers has been designed to ensure that resources are used efficiently in protecting humans and the environment from unacceptable effects arising from exposure to polymer products while at the same time reducing vertebrate animal testing needs to the maximum extent possible. As such, application

of the CF4Polymers also serves the mandate to replace, reduce, and refine animal testing (Russell and Burch, 1959) that has been implemented in *Directive 63/2010/EU on the protection of animals used for scientific purposes* (EP and Council, 2010), in the *US Federal Collaboration Toxicity Testing in the 21<sup>st</sup> Century* (Tox21; Choudhuri et al., 2018); as well as in the OECD Testing of Chemicals Programme (<u>http://www.oecd.org/chemicalsafety/testing/animal-welfare.htm</u>).

Importantly, while the CF4Polymers has been designed to reflect the current science of polymer RA, due to the complexity of the polymer life cycle and evolving science surrounding polymer RA, it may require future modification to adapt to new information and/or to reflect experience gained from its application.

The eight steps of the CF4Polymers are presented in detail below. Each step is structured to present (1) a concise outline of the step; (2) explanatory notes; (3) illustrative examples; and (4) knowledge gaps.

Potential differences to the RA of small mono-constituent substances, as well as particularities of polymers that need to be considered during polymer RA, are discussed. Such particularities can also affect the applicability and/or applicability domain of internationally accepted analytical tools, *in vitro* and *in vivo* test methods and *in silico* models for polymer identification, exposure and hazard assessment. Since this topic is addressed in detail in the review under preparation by the ECETOC Polymers TF (planned as ECETOC TR No. 133-2), it is only briefly referred to in this Technical Report.

The flexibility of the CF4Polymers also implies that the sequence of its eight steps can be adapted depending on the specific RA needs and/or data availability. Step 1 addresses the problem formulation (RA scope definition and protection goal definition), Step 2 polymer identification, and Step 3 the polymer component strategy. These three steps are closely linked and will generally be addressed in parallel. Notwithstanding, their specific order can also be changed as necessary. Directly after these initial steps of the RA, Step 4 encompasses identifying the potential for grouping. Thereby, all available data for similar polymers are taken into account during the subsequent exposure and hazard assessment. Steps 5 and 6 relate to exposure assessment (i.e. Step 5 – determination of exposure scenarios and Step 6 – exposure characterisation) and Step 7 – hazard assessment. Depending on the given RA needs, it can be more appropriate to determine exposure scenarios (Step 5) already during problem formulation (Step 1); to refine exposure characterisation (Step 6) after an initial completion of the hazard assessment (Step 7); or to first assess hazard and then characterise exposure (e.g. when the hazard profile is well-known, this will serve to streamline the RA process). Finally, Step 8 completes the RA by addressing risk characterisation.

### 3.1 Step 1: Problem formulation

#### Step 1: Problem formulation

The Step 1 problem formulation includes RA scope definition and protection goal definition.

Identify:

- The life cycle stage(s) and intended uses of the polymer product that shall be covered (e.g. industrial, professional, consumer uses).
- Define the protection goal, i.e. the type of risk assessed and the acceptable level of risk for the environment and/or human health; define target population (e.g. individual, population, subpopulation).

- Determine if only intrinsic or also physical hazards are within scope of the RA.
- Parts of the RA that can be set aside because out of scope.

#### **3.1.1** Step 1: Problem formulation – explanatory notes

The problem formulation includes identifying the product and use perspective of the RA, i.e. the uses and life cycle stage(s) of the polymer that lie within the scope of the RA and those that are out of scope of the RA, the protection goal, and whether intrinsic and/or physical hazards are within the scope.

While Step 5 (determination of exposure scenarios) extensively addresses how the given life cycle stage affects exposure potential, the initial considerations on intended uses during Step 1 allow streamlining the subsequent steps thereby ensuring that time and resources are used efficiently.

The protection goal depends on the intended uses and/or the scope of the applicable legal framework. It can relate to e.g. product liability, occupational, consumer or patient safety as well as environmental protection (Hunter and Fewtrell, 2001). The acceptability of a risk depends on the available scientific data as well as social, economic, and political factors, and the perceived benefits arising from exposure to the given substance (WHO IPCS, 2004). While the protection goal definition can be more complex for polymer products than for many mono-constituent substances, it is not inherently different from the protection goal definition for non-polymers. The protection goal definition can include pre-defining margins-of-safety, i.e. safe levels of use of the given polymer product, taking into account its intended uses.

#### **3.1.2** Step 1: Problem formulation – examples

Any given polymer product can have only one single use, few uses, or a large variety of uses. Further, the specific life stage(s) of relevance for the given RA process can vary even for the same polymer product.

The assessment of a food additive polymer may have a defined RA scope limited to consumer exposure to the polymer product. In this case, assessment of the safe handling of the polymer upon manufacture and formulation would be out of scope.

The RA scope for a polyolefin product may include environmental and human health RA for different uses and life stages of the polymer product including extrusion after polymerisation, use as waste bags, and disposal. Further, the RA scope might include unintended uses (e.g. contact with food or littering) and/or modifications of the polymer product downstream of manufacturing (e.g. addition of specific additives, thermal decomposition during processing). The RA scope might also include occupational exposure to raw materials and/or raw products. If a similar polymer is being used as a component in multilayer FCMs, the RA scope might be confined to the life cycle stages of the food packaging after the films or pellets have been converted to articles and to the resulting consumer exposure via article use.

Polymer products used very widely, such as polyethylene glycols, require a stringent scoping of the RA process to ensure that it is manageable. For example, different high-purity polyethylene glycol products with Mw ranging from 400 Da to 8000 Da can be used as film coating agents in food supplement products for adults (e.g. vitamins, minerals). The RA could be focused solely on workplace safety and the risk imposed to target

consumer groups upon oral uptake of the food supplement. Thereby, the RA scope would exclude e.g. unintended exposure to infants.

For surfactant or conditioning polymers found in personal care products, depending on the actor in the value chain, i.e. if the RA is performed by a downstream actor (e.g. manufacturer of an end-use product), the RA scope may be defined to address consumer exposure during intended use of the products as well as potential environmental risks based on rinse-off or leave-on emission scenarios. By comparison, for the very same polymer, another, broader RA scope (e.g. defined by the formulator of the raw material) may include manufacture, formulation at customer sites, and consumer exposure to / associated environmental releases from different product types other than or in addition to personal care – if relevant for the RA scope, and as far as the respective information is available to the manufacturer, an issue that is not unique to polymer RA.

An important consideration during Step 1 (problem formulation) is to include all relevant exposure routes and, in doing so, to consider whether any of the intended uses are likely to generate significant amounts of respirable aerosols and to determine and document if those aerosols are included in the RA scope, or if they are being addressed by other RA processes.

The following example shows that specific polymer products are often regulated by different legislation – with different information requirements. Often, one polymer product is marketed in a number of jurisdictions. Even in one jurisdiction, several product regulations can apply. For example, a polymer with sole intended use in personal care products that shall be sold in the EU, Canada, and China will have to comply with the EU REACH and Cosmetics Regulations, the Canadian chemical legislation, the Chinese chemical and cosmetics legislation, and possibly further legislation e.g. related to workplace and transport safety. Finally, specific components of polymer products, such as biocides, may be subject to other regulations than the polymer itself. (Appendix B provides a summary of some of the regional chemicals regulations as applicable to polymers.)

An example for an overall environmental protection goal for polymers is to not have significant and widespread risk of adverse effects on those environmental compartment(s) that the polymer is most likely to be found in. For example, the environmental protection goal for a water-soluble polymer is to minimise the risk of a significant negative effect on natural biodegradation and engineered processes in WWTPs and to protect against adverse environmental effects upon discharge via treated or untreated wastewater and sludge to the environment.

### 3.1.3 Step 1: Problem formulation – knowledge gaps

The TF did not identify any polymer-specific knowledge gaps regarding Step 1 of the CF4Polymers. While the problem formulation can be more complex for polymer products than for many mono-constituent substances, it is not inherently different from the problem formulation for such non-polymers.

### **3.2** Step 2: Polymer identification

#### Step 2: Identification of the polymer

To ensure a fit-for-purpose identification of the polymer, use expert knowledge to select those key parameters from the list below that are relevant for the polymer at the given life cycle stage(s) (Step 1).

#### Step 2.1: Identification of the polymeric substance

#### Standard chemical descriptors

- CAS name and number and/or other relevant names and numbers (e.g. EC number, INCI name);
- Chemical name (and synonyms); monomer units and other reactants (qualitative and quantitative (e.g. monomer ratios)).

#### Commercial identifiers

Trade names, descriptors for market types (e.g. extrusion polymers, casting polymers, sheet polymers).

#### Structural and morphological descriptors and/or physical, and chemical properties

Depending on the type of polymer under investigation, relevant key parameters may be structural and/or morphological descriptors as well as physico-chemical and screening-level fate properties (no order of properties is inferred):

- <u>Structural descriptors</u> include e.g. chemical formula, degree of substitution, tacticity, Mw, Mw distribution (polydispersity), number average molecular weight (NAMW), and RFG(s) (see Section 4.3 for further details on RFGs);
- <u>Morphological descriptors</u> include e.g. physical state at ambient temperature and pressure (solid, liquid), shape (e.g. spherical, fibre, tubular), physical form (e.g. amorphous, crystalline);
- <u>Physico-chemical properties</u> include e.g. water solubility, n-octanol/water partition coefficient (log Pow), acid dissociation constant (pKa), net charge (under conditions that are relevant for ecological and human health hazard assessment), vapour pressure, viscosity / melt-flow index / glass transition temperature, density, degradability.

Step 2.2: Identification of additives, if relevant

- CAS name and number;
- Relative concentration.

Step 2.3: Identification of NIAS, if relevant

- Substance identification, relative concentration, Mw.

#### 3.2.1 Step 2: Polymer identification – explanatory notes

The identification of the polymer under investigation is a crucial starting point for RA, and it is also important to substantiate grouping and read-across. In conventional RA frameworks, substance identification is typically part of the hazard identification step. Due to the complexity of polymer identification, it is assigned a distinct step in the CF4Polymers. Polymer identification shall be as detailed as necessary for the given scope (fit-forpurpose), and it can be undertaken as an iterative process to identify (1) the polymeric substance including (a) standard chemical descriptors; (b) commercial identifiers; (c) relevant key parameters; as well as (2) IAS and/or (3) NIAS, if relevant.

In all jurisdictions, the identification of a polymer for notification / registration and inventory listing is based upon the chemical composition of its principal monomers. This is reflected in the Chemical Abstract Service (CAS; <u>https://www.cas.org</u>) nomenclature and numbering (and/or European Community (EC) numbering, the International Nomenclature Cosmetic Ingredient (INCI) nomenclature, etc.). The standard CAS naming system for polymers refers to the monomers, naming each along with the suffix/prefix 'polymer of' or 'polymer with' and further takes into account some information on the polymer manufacture process.

Therefore, a wide range of polymers that vary in terms of unreacted monomers, physical form, physical state, Mw and range, chemical reactivity, etc., can carry the same CAS name and number (and hence ultimately also the same notification / registration status). *Vice versa*, the same final polymer composition can have multiple CAS numbers depending on how the polymer has been produced and/or registered with the CAS. This approach fails to recognise specific structural, morphological, physico-chemical or fate aspects of the polymer that may impact its RA process.

To ensure unambiguous and fit-for-purpose polymer identification, Step 2.1 of the CF4Polymers includes determination of all structural and/or morphological descriptors as well as physico-chemical and fate properties of the polymeric substance that are relevant for the RA scope defined in Step 1 (problem formulation). Expert knowledge is required to select these key parameters that are not only pivotal for polymer identification (Step 2), but also for informing the grouping approach evaluation (Step 4); and the ecological and human health hazard assessments (Step 7).

Different key parameters may be relevant during different life cycle stage(s) of the polymer, as covered by the problem formulation (Step 1). Similarly, the extent of information describing the composition can vary among the different life cycle stages. Acquisition of information appropriate to address a scenario of interest is a fundamental challenge in any RA but can prove particularly complex in the polymer value chain.

Further, polymer identification should not only address the polymeric substance itself, but also its other components, i.e. IAS and NIAS, as relevant and practicable.

### 3.2.2 Step 2: Polymer identification – examples

Due to the complex nature of polymer products combined with analytical challenges and confidential business information barriers, it is often not possible to obtain all information that would be desirable for polymer identification. However, depending on the RA scope defined in Step 1 (i.e. the life cycle stages and intended uses under evaluation), often only selected structural, morphological, physico-chemical and screening-level fate parameters will be necessary for fit-for-purpose polymer identification. For example, where hazard data matching the foreseen uses are already available on the polymer product, or exposure is minimal, knowledge of monomer ratios, reactant levels and some other parameters will not be necessary for RA.

Strategic decisions can also be taken with respect to the type and quality of the available data. For example, it is impossible to accurately determine the Mw of HMW, insoluble polymers. Therefore, analytical experts often only determine the Mw distribution of the soluble fraction of the polymer (that is highly dependent on

the chosen analytical tools and the solvent used). Frequently, proxies for Mw, such as viscosity or melt flow index, are used to distinguish between different Mw ranges of the same polymer type. For example, a linear polydimethoxysiloxane with a viscosity of 100,000 cSt has a number average Mw (NAMW) of approximately 74,000 Da (ECETOC, 2011a). Due to this very high NAMW, full Mw distribution data for this polymer (or other polymers having similar viscosity ranges) are not relevant for most uses.

Examples for polymers that change identity throughout the value chain are reactive polymers containing e.g. isocyanate groups or allyl groups. Such polymers are supplied to be further polymerised or 'cured' triggered by contact with other reagents, humidity or heat to take variable forms e.g. when used in window sealants, isolation foams, or industrial adhesives. During the RA of such polymers, different stages in the value chain imply that different substance identities need to be taken into account.

For uses including the intentional generation of aerosols, information on aerosol size distributions is important. These are dependent on the formulation in which the polymer shall be included and on the aerosol generation method. This information is used to determine if any relevant portion of respirable aerosol will be generated. For example, hair fixative pump sprays do not contain any significant respirable portion, while propellant-based can sprays often, but not always, contain respirable aerosol concentrations warranting assessment of pulmonary effects.

### **3.2.3** Step 2: Polymer identification – knowledge gaps

Different analytical tools and *in silico* models are available to assess the physico-chemical and screening-level fate properties of chemical substances in general. Some of these tools and models have technical limitations with respect to the assessment of polymers, which again depend on their physico-chemical and fate properties. Just as expert knowledge is required to identify the key parameters for polymer identification that also drive grouping (Step 4) and hazard assessment (Step 7), expert knowledge is required to select the most appropriate analytical tools to assess these parameters and potential technical limitations of such tools. The detailed review of the applicability of standardised tools, methods and models (planned as ECETOC TR 133-2) will include suggestions for how to address the identity of specific types of polymers.

### **3.3** Step 3: Polymer component strategy

#### Step 3: Polymer component strategy

Based on decisions taken in Step 1 on the RA scope and protection goal, and information acquired in Step 2 on the identity of relevant components, Step 3 serves to decide on those components of the polymer product that shall be addressed in the further steps of the CF4Polymers, i.e.

- the polymer product as such, i.e. including its LMW components (i.e. small oligomers, IAS, and NIAS);

- the polymeric substance;

- specific IAS and/or NIAS, separately;
- or some or all of the LMW components together (i.e. small oligomers, IAS, and NIAS).

### **3.3.1** Step 3: Polymer component strategy – explanatory notes

Step 3 serves to decide on the components of the polymer product to be addressed in the further steps of the CF4Polymers.

For dermal and oral contact, the HMW components, which make up the bulk of many polymer products, are generally expected to be relatively inert (unless RFGs of concern, cationic groups, heavy metals, or specific physical attributes are present) and to have low or no bioavailability (Step 7 – hazard assessment). Therefore, LMW components (i.e. small oligomers, IAS, NIAS) often drive the hazard assessment and RA process. In such cases, it is more precise and protective to base the polymer product RA on data from the LMW components.

Despite this, in case of significant inhalation exposure (e.g. to polymers in dust or aerosolised form), pulmonary toxicity may necessitate further consideration.

In cases where lower Mw polymer products and/or the polymeric substance are expected to drive the risk due to hazard properties and/or higher exposure, an assessment of minor components may be unnecessary.

Whenever such prior knowledge is not available, all components of the polymer product should be taken forward into the next steps of the CF4Polymers, where they can be assessed separately or by the 'whole mixture approach' (SCHER, SCENIHR, SCCS, 2012; OECD, 2018; see also Glossary).

Additives in polymer products include, but are not necessarily limited to, solvents, antioxidants, UV-stabilisers, plasticisers, residual reactants and unreacted monomers, polymer production aids and catalysts, surfactants, and biocides (ILSI, 2015). These substances are specifically added during polymer production and have a specific function either during manufacturing, processing, or in the final product. In the EU, additives in plastic materials and articles intended to come into contact with food are generally listed and controlled by the Regulation on Plastics in Contact with Food (European Commission, 2011) and have specific or generic migration limits listed in Annex I of this Regulation (the Union list of authorised substances that can be used in the manufacture of the plastic layers of food contact plastic materials and articles). Hence, it can generally be expected that their risk to humans is managed. Further, additives on their own will often have completed RA following the respective chemical legislation implemented in the given jurisdiction.

Additives can also be added to polymers with the intention of chemically or physically altering a specific aspect of the polymers (e.g. oxo-additives or plasticisers). Where such alterations affect the hazard potential of the polymers, it can be necessary to assess the polymeric substance and such additives together, i.e. to assess the polymer product.

**NIAS** include (1) impurities arising e.g. from raw materials or additives used during polymer manufacture; (2) newly formed compounds e.g. reaction products formed from common ingredients under certain conditions; (3) contaminants e.g. when using recycled materials during polymer manufacture; (4) substances originating from degradation processes when polymers are submitted to e.g. high temperatures, irradiation for sterilisation, thermo-mechanical processes; and (5) substances originating from the degradation of additives e.g. due to microwave heating (Nerin et al., 2013). Various procedural parameters can impact the generation of NIAS including reaction time and temperature, and the types of catalysts, lubricants, and cleaning agents used.

While **oligomers** are generally considered to be part of the polymeric substance at the low end of its Mw range, for specific polymer products, the composition and structure of oligomers may be modified during

production. In such cases, it may be more appropriate to consider oligomers as NIAS (Geueke, 2018). Depending on the type of polymer product, **unreacted monomers**, if present, can either be IAS or NIAS.

The presence of NIAS can be carefully controlled during the manufacture of e.g. polymer products intended for sensitive applications to ensure optimised efficiency of production and control of hazard potential (Araújo et al., 2004). Accordingly, the most relevant NIAS should be known on account of the manufacturer's, compounder's or converter's knowledge of the polymer product, its manufacture process and use. However, this information may not be readily accessible.

### **3.3.2** Step 3: Polymer component strategy – examples

Examples for polymer products which represent 'simple mixtures' i.e. where influence of the polymer matrix is not relevant, are surfactant polymer products or certain emulsion polymers used in coatings. For such polymer products, all components are typically subject to an initial assessment. However, those components (polymeric or not) that are of low hazard or where hazards are irrelevant at low concentrations (such as irritation) may not need to be pursued in further detail in (Step 6) exposure characterisation and (Step 7) hazard assessment.

Other polymer products, e.g. resin intermediates or isocyanate prepolymers, are intended to be reacted further in the value chain and contain free monomers as main components. In those cases, the already known hazards of the monomer will often drive the RA so that the properties of the polymeric substance become insignificant and can be set aside from further consideration. This again demonstrates the iterative nature of polymer RA and the effectiveness of a flexible approach.

On the other hand, a multitude of solid polymer products are of HMW and lack solubility and systemic bioavailability. Examples are polymers forming articles (e.g. the case of a laptop, a door handle, parts within a car motor or a syringe). In such cases, the polymer component strategy will focus on determining if the use type included in the RA scope during Step 1 (problem formulation) combined with the product composition triggers a concern for potential leaching of LMW components with subsequent relevant exposure. If so, the further RA will focus on the LMW components.

### **3.3.3 Step 3: Polymer component strategy – knowledge gaps**

The TF did not identify any specific knowledge gaps for Step 3 - polymer component strategy. If in doubt about the relevance of a given component, it will be taken further along in the RA.

### **3.4** Step 4: Grouping approach evaluation

#### Step 4: Grouping approach evaluation

The grouping approach evaluation aims at identifying read-across sources and serves to avoid unnecessary resource allocation to hazard characterisation, especially with regard to animal testing. Step 4 can be skipped

if sufficient hazard information is readily available to assess the uses and components in scope for the whole polymer product.

#### Step 4.1: Use expert judgement to identify key parameters

Collect information on structural and morphological descriptors, physico-chemical properties and screeninglevel fate data of the polymer product under investigation and of other polymer products with similar structure and/or composition; and/or of the IAS / NIAS and similar substances, if applicable (Step 3 – polymer component strategy).

Depending on the type of polymer that is being evaluated (and of its form in the given life cycle stage), different combinations of the parameters listed in Step 4.2 (and possibly further parameters) might be key in driving hazard potential (see also Steps 2 and 7) and therefore relevant for grouping. Similarly, the set of key parameters may depend upon the (eco)toxicological endpoint(s) for which read-across shall be applied (Steps 4.3 and 4.4).

#### Step 4.2: Use expert judgement to determine polymer similarity (i.e. potential for grouping)

- Same (or similar) monomer units? Homopolymer or copolymer? Same or similar polymer backbone? Is there cross-linking, and what is the degree of substitution?
- Same form of polymer (e.g. crystalline, amorphous, blended, sheet, pellet)? Same morphology?
- Same chemical elements? Are heavy metals present?
- Same Mw range, i.e. < 1,000 Da; 1,000-10,000 Da; > 10,000 Da?
- Similar partitioning in water / solvents? Which environmental compartment is relevant? Which partitioning behaviour is relevant?
- Same or similar composition and proportion of LMW components (< 500 and < 1,000 Da)?
- Same RFGs? Similar charge density, i.e. functional group equivalent weight (FGEW) above or below 1,000 Da / above or below 5,000 Da?
- Similar cationic density, i.e. FGEW above or below 5,000 Da?
- Similar water solubility / water insolubility?
- Similar surface tension?
- For insoluble polymers: Same or similar particle shape and size, density, agglomeration, zeta-potential?
- Same or similar screening-level fate properties? Same or similar breakdown products?
- If IAS / NIAS are focus of RA: Identify substances with structural and/or biological similarities.

Step 4.3: Define hypothesis for grouping and read-across and determine relevant approach

- For example, the polymer of interest has the same type of physico-chemical interaction with target structures, adverse effect(s), or the same molecular initiating event / MoA relevant for a given (eco)toxicological endpoint, as structurally similar polymer(s).
- Determine if the analogue or category approach shall be applied for grouping (see Box 4 and Glossary).

#### Step 4.4: Identify available ecotoxicity, fate and toxicity data

 For the (eco)toxicological endpoint(s) that is/are relevant for the hypothesis for grouping: Identify bioavailability and available ecotoxicity, fate and toxicity data for the polymer of interest and the structurally similar polymer(s) (and/or of the IAS / NIAS and similar substances, if applicable, depending on the polymer component strategy), and evaluate relevance and quality of the available data for source polymer.

- Identify data gaps.

#### Step 4.5: Use expert judgement to justify grouping and to fill data gaps by read-across

For each hypothesised MoA (Step 4.3):

- Refer to the physico-chemical and fate key parameters selected in Step 4.1 to describe the similarities and dissimilarities of the polymers included in the grouping approach evaluation.
- Describe how differences in these key parameters contribute to constant patterns in the changing of the (ecotoxicological and/or toxicological) properties across the group.
- Use this information to justify opportunities to fill data gaps by read-across.

#### **3.4.1** Step 4: Grouping approach evaluation – explanatory notes

Step 4 of the CF4Polymers, grouping approach evaluation, includes the identification of structurally and/or biologically similar polymers (or IAS / NIAS, if applicable) for which data are available that are potentially relevant for read-across. This approach follows the general approach for substance grouping and read-across as described in the OECD Guidance Document on grouping of chemicals (OECD, 2014) and the ECHA Read-Across Assessment Framework (ECHA, 2017a); see Box 4 for definitions.

#### Box 4: Definitions for grouping and read-across

<u>Grouping (of chemicals</u>) is defined as the general approach for considering more than one chemical at the same time. It can include formation of a chemical category or identification of chemical analogue(s) with the aim of filling data gaps as appropriate (OECD, 2014).

<u>Read-across</u>: As explained in the ECHA Read-Across Assessment Framework (ECHA, 2017a), under the REACH Regulation, read-across is a technique for predicting endpoint information for the target substance by using available data from the same endpoint from the source substance(s). The read-across approach encompasses (i) elements addressing the structural similarity; (ii) a read-across hypothesis; (iii) a read-across justification; and (iv) the prediction of the property (properties) of the target substance(s) (ECHA, 2017a).

<u>The analogue approach</u> is employed between a few, very structurally similar substances for which it is not possible to establish a trend or a regular pattern.

<u>The category approach</u> is employed between several substances that are grouped together based on defined structural similarity for one or more (toxicological or other) properties. Predictions are made within the group for the target substance(s) based on the observed regular pattern (adapted from ECHA (2017a); see also Laroche et al. (2018)).

The identification of structural and/or biological similarity (and hence polymer grouping and read-across) should be based on an understanding of the fundamental relationship between key parameters of relevance for the given type of polymer (at the given life cycle stage(s)) and may also include a certain biological aspect (e.g. bioavailability and/or a specific (eco)toxicological endpoint). As applicable, such key parameters can

include structural and/or morphological descriptors as well as physico-chemical and screening-level fate properties (see Section 3.2.1) and may inform on environmental and human health hazard potential.

Finally, the potential utility of available human data should not be overlooked, especially when animal data are likely to be scarce for a given type of polymer. For example, polymers with long-standing use in consumer products, food packaging and/or medical devices are expected to have a history of safe use and so would not be expected to cause e.g. skin irritation (ECETOC, 2009).

### **3.4.2** Step 4: Grouping approach evaluation – examples

Prior work exists on group RAs of carboxylate polymers used in laundry or cleaning applications (HERA, 2014). Similarly, it seems justified to group various types of cationic polymers (polyquaterniums) because the cationic charge drives aquatic hazards across a broad range of polymers (Cumming, 2008). Within those two examples, while the main monomeric units or pendant functional groups are generally the same, the diversity arises from variations in Mw and ratio of monomeric units or the degree of substitution with functional groups.

The case studies evaluating the available physico-chemical, fate and effects data on several variants of these types of polymers under preparation by the ECETOC Polymers TF (planned as ECETOC TR No. 133-3) shall serve to demonstrate trends and similarities within the polymer sub-sets and the potential for grouping based on polymer key parameters. As relevant, the findings from the case studies shall also be used to derive more generalised guiding principles for polymer grouping and to identify which (combinations of) physical, chemical and/or fate parameters can be considered key parameters for these (or other) types of polymers.

### 3.4.3 Step 4: Grouping approach evaluation – knowledge gaps

As compared to mono-constituent substances that are often data rich, there are generally very limited publicly available data linking hazard information with sufficient polymer identity information. Therefore, it is challenging to develop evidence-based grouping schemes for the multitude of types of polymers, and more work will be necessary, respecting confidential business information. Hence, Step 4 of the CF4Polymers as it is currently described focuses on expert judgement to identify those key parameters driving the molecular initiating events / MoAs and hazard potential of the polymer of interest at the given life cycle stage and to identify similarity, i.e. to assign different polymers to one group. It is expected that the case studies that the TF is currently preparing (see Section 3.4.2) will reveal opportunities and/or needs to refine and amend Step 4 in its current form. A major challenge will be to describe the different levels of knowledge required with respect to molecular initiating events, MoAs, or adverse effects to enable efficient read-across. For example, there is wide acceptance for a read-across hypothesis that any product with pH 2 will most probably be an irritant or that alkylating substances may be DNA-reactive. However, such generalised knowledge is not yet established for many other physico-chemical or structural features.

### **3.5** Step 5: Determination of exposure scenarios

#### Step 5: Determination of exposure scenarios

Step 5 takes into account the life cycle stage(s) of the polymer product identified in Step 1. The results of Step 5 determine which exposures and hazards should be characterised in Steps 6 and 7 to meet the given RA scope defined in Step 1 (problem formulation).

The substances to be addressed in Steps 5.1 and 5.2 will depend on the decisions made in Step 3 (polymer component strategy).

#### Step 5.1: Ecological exposure scenarios

- Describe form of the polymer product in the relevant life cycle stage(s) (e.g. solid, dissolved, aerosolised).
- Consider structural and/or morphological descriptors as well as physico-chemical and screening-level fate properties relevant to polymer product (e.g. Mw, partitioning coefficients, solubility, compound diffusivity) supporting the identification of ecological receptors (e.g. aquatic or sediment organisms).
- Identify source of exposure and ecological receptor(s).
- Describe relevant environmental compartments.
- Identify duration / time frame of exposure.
- Are aggregate exposures relevant?

#### Step 5.2: Human exposure scenarios

- Describe form of the polymer product in the relevant life cycle stages (e.g. solid, dissolved, aerosolised).
- Consider structural and/or morphological descriptors as well as physico-chemical properties relevant to polymer product supporting the identification of relevant human populations.
- Identify relevant human populations (e.g. workers in production sites, professionals using finished products, consumers), specific population groups (e.g. infants, adults, aged persons) further considering specific preconditions for exposure, if relevant (e.g. pregnancy, life-style habits).
- Relevant routes of exposure include oral, dermal, and/or inhalation routes (see <u>Note 1</u> below).
- Identify duration / time frame of exposure.
- Are aggregate exposures relevant?

<u>Note 1</u>: The CF4Polymers was not developed with medicinal applications in mind (e.g. intravenous, subcutaneous routes of application, implantation of medical devices). Therefore, it might be applicable for some cases of medicinal applications, whereas it might not be applicable for others.

#### 3.5.1 Step 5: Determination of exposure scenarios – explanatory notes

Step 5 (determination of exposure scenarios) is the first of two steps related to exposure assessment (Box 5). Step 6 is the second step related to exposure assessment, i.e. exposure characterisation (also called exposure estimation).

#### Box 5: Definitions related to exposure scenarios

Aggregate exposures: Exposures to the same substance from multiple pathways and routes (adapted from OECD (2018)).

**Ecological receptor:** "Includes any living organisms other than humans, the habitat which supports such organisms, or natural resources which could be adversely affected by environmental contaminations resulting by a release at or migration from a site. Typical receptor categories may be (1) wider-ranging ecological receptors that may frequent the affected property and use less mobile receptors (e.g., plants, soil invertebrates, small rodents) as a food source, (2) benthic invertebrates within waters in a region"; <u>http://www.eugris.info/FurtherDescription.asp?e=34&Ca=2&Cy=0&T=Receptor</u>

**Exposure assessment:** "The process of estimating or measuring the magnitude, frequency, and duration of exposure to an agent, along with the number and characteristics of the population exposed. Ideally, it describes the sources, pathways, routes, and the uncertainties in the assessment." (WHO IPCS, 2004)

**Exposure scenario:** "A combination of facts, assumptions, and inferences that define a <u>discrete situation</u> where potential exposures may occur. These may include the source, the exposed population, the time frame of exposure, microenvironment(s), and activities. Scenarios are often created to aid exposure assessors in estimating exposure." (WHO IPCS (2004); see Glossary for further definitions for 'exposure scenario')

**Microenvironment:** "Surroundings that can be treated as homogeneous or well characterized in the concentrations of an agent (e.g., home, office, automobile, kitchen, store). This term is generally used for estimating inhalation exposures." (WHO IPCS, 2004)

**Use and exposure category:** "An exposure scenario covering a <u>wide range of processes or uses</u>, where the processes or uses are communicated, as a minimum, in terms of the brief general description of use." (EP and Council, 2006; Art. 3(38))

The determination of exposure scenarios (or use and exposure categories) should address the complexity and versatility of polymers. Just as stands true for many non-polymeric engineered or natural substances, many polymers are ubiquitous in modern society (Namazi, 2017). Therefore, one single polymer product can have a large variety of different types of uses, and exposure to some polymers can be prolonged. Similarly, end-of-life release into the environment can take a number of routes.

The determination of relevant exposure scenarios to a polymer product includes consideration of its use, frequency of use and of its different life cycle stages. Multiple exposure scenarios can apply to one polymer product, and a variety of ecological receptor(s), different human populations as well as different routes of exposure may have to be considered during polymer RA. Notwithstanding, while the determination of exposure scenarios can be more complex for polymer products than for many mono-constituent substances, it is not inherently different from the general approach for such non-polymers. Use codes (e.g. the use descriptor system published by ECHA (2015a) with standardised descriptors for life cycles stages, sectors of use, chemical products categories, process categories, environmental release categories (ERCs) / specific environmental release categories (SpERCs), article categories, and technical functions) enhance comprehensiveness on the description of exposure scenarios and facilitate communication within the value chain and with authorities (ECHA, 2015a).

A very distinct feature of exposure assessment for solid polymers, in contrast to that for many solid nonpolymeric substances, is that the majority of exposure scenarios (if not all) will deal with the evaluation of exposure resulting from releases of LMW compounds from the solid polymer matrices, i.e. they will be focused on the (industrial, professional, or consumer) service life of the finished articles.

**Environmental compartments** to consider in determining exposure scenarios include (1) soil, (2) sediment (freshwater and marine), (3) water (freshwater and marine), and (4) the atmosphere (WHO IPCS, 2010).

Further, potential exposure via food-chain accumulation and exposure to the microbiological organisms present in WWTPs should be considered (EP and Council 2006). The relevant environmental compartment can be identified based upon use and emission data (taking into account the polymer's life cycle stage), physico-chemical key parameters and screening-level fate properties. For example, for some hydrophobic polymers, the soil and/or sediment compartment can be relevant.

The identification of ecological receptors considers that soil, sediment, and water species can be exposed to different application types of the polymer via e.g. consumer down-the-drain products or intentional agricultural applications. Hence, there may be multiple sources of exposure for a given type of polymer. Soil exposure may be direct (by spraying on fields) or indirect (sewage sludge application). For soil exposure from land application of biosolids, regional differences in sewage sludge disposal procedures and agricultural practices need to be considered. Sediment exposure can occur when polymers enter receiving water bodies in effluent (dissolved phase or sorbed to solids) that partition onto sediment or undergo settlement in the non-adsorbed form. Aquatic species can be exposed to breakdown products of polymers that are poorly or only moderately soluble in aqueous media if they degrade into water-soluble substances.

Potentially relevant **human exposures** include (1) occupational exposure during polymer manufacture (focusing on the polymer product and polymeric substance) and processing with potential for dermal and inhalation exposure; (2) professional exposure with potential for dermal and inhalation exposure; and (3) consumer exposure, with the following potential routes of exposure: dermal (e.g. household products, cosmetics, glues, paints); inhalation (e.g. household products, cosmetics, glues, paints); inhalation (e.g. household products, cosmetics, glues, paints); and oral (e.g. mouth/lip cosmetics, excipients, food additives). Further, humans can be exposed indirectly via the environment, and both humans and the environment can be exposed to LMW components migrating from solid polymer matrices.

If **exposures** to one polymer can occur from multiple sources, aggregate RA may be necessary (OECD, 2018).

#### **3.5.2** Step 5: Determination of exposure scenarios – examples

As has been extensively addressed in the examples to Step 1 (problem formulation), challenges in determining exposure scenarios for polymers relate to complexities regarding the supply chain and intended uses of the polymer product. The following examples further demonstrate the enormous value of exposure and use scenarios for steering exposure characterisation and hazard assessment.

For polymers used in offshore oil fields, relevant exposure scenarios relate to workers and marine species. By comparison, for window sealant polymers after curing, the exposure scenario relates to dermal occupational exposure, but not to relevant environmental exposures. For polymer products used in infant food packaging, typical food contact exposure scenarios are relevant, and additionally specific exposure considerations related to infant populations. A polymer used as excipient in injection solutions has a very use-specific exposure scenario, while the same polymer type when used in shampoos has relevant exposure scenarios related to dermal exposure of consumers and the aquatic environment.

### 3.5.3 Step 5: Determination of exposure scenarios – knowledge gaps

While the determination of exposure scenarios can be more complex for polymer products than for many non-polymers, the TF did not identify any polymer-specific knowledge gaps regarding this step of the CF4Polymers.

### **3.6** Step 6: Exposure characterisation

#### Step 6: Exposure characterisation

Step 6 is performed for the polymer product as such or for those components of the polymer product identified as in scope during Step 1 (problem formulation) and Step 3 (polymer component strategy).

Step 6 may also consider breakdown products of the polymer, if relevant.

It can be necessary to refine Step 6 after an initial passage of Step 7 (hazard assessment).

Based upon the exposure scenarios determined in Step 5:

- Estimate release / emission (via modelling and/or testing, as applicable) to determine physical availability. For LMW components, this includes addressing the potential to migrate from the polymer matrix.
- Assess fate (via modelling and/or testing, as applicable) and exposure pathways.
- Define exposure metrics for environmental, occupational, and consumer exposure, respectively (e.g. daily or lifetime exposure, duration of employment).
- Estimate exposure levels (via modelling and/or testing, as applicable): Establish quantity released into the environment corresponding to relevant life cycle stage taking into account ERCs or SpERCs; or use default value related to process.
- Conclude on exposure assessment (i.e. determination of exposure scenarios and exposure characterisation) and identify prevailing data gaps.

#### **3.6.1** Step 6: Exposure characterisation – explanatory notes

Step 6 involves quantifying the exposure levels of the ecological receptor(s) and/or relevant human population (Step 5) to the life cycle stage(s) of the polymer under the conditions of its intended use (Step 1) taking into account relevant routes of exposure (Step 5). As identified during Step 3 (polymer component strategy), Step 6 can be performed on the polymer product as such, i.e. including its LMW components, and/or on isolated components (polymeric substance, IAS, NIAS, or combinations thereof), as applicable.

Accordingly, exposure characterisation for polymer products can be relatively simple where, comparable to mono-constituent substances, no other relevant components are present or in scope of the RA. In other cases, comparable to mixtures of small chemicals, multiple components will have to be assessed separately for exposure, as their different concentrations and properties (e.g. polarity, solubility, vapour pressure, biodegradability) may result in different exposure quantities. The one aspect where quantitative exposure characterisation (mainly of minor components melted into solid polymer products) may require polymer-specific consideration are effects of the polymer matrix on release of LMW components (see below).
In few cases, exposure monitoring data may be available for the uses and components of interest, for example occupational air monitoring or WWTP effluent concentrations. In other cases, exposure is described easily via typical use, for example the inclusion level and typical use level of a skin cream. In most cases, however, the key step in exposure characterisation will be the selection of appropriate conceptional or computational models. The type of model will depend on the use type and physico-chemical properties of the components to be assessed. It may become necessary to apply different exposure estimation models for the polymeric substance as compared to the LMW components of a polymer product, and consideration of ERCs (ECHA, 2015a) or specific SpERCs (e.g. as published by the European Crop Protection Association (ECPA, 2017)) during polymer exposure characterisation is presented and discussed in the planned review of methods and models ECETOC TR No. 133-2.

#### Box 6: Definitions for key terms related to exposure characterisation

**Emission estimation (estimation of release):** "Estimation of the amounts of the substance released to the different environmental compartments during all activities carried out by the manufacturer or importer and all identified uses, and an identification of the likely routes by which humans and the environment are exposed to the substance." (EP and Council, 2006; Annex I, 4.2)

**Exposure characterisation (exposure estimation):** *"The exposure estimation entails three elements: (1) emission estimation; (2) assessment of chemical fate and pathways; and (3) estimation of exposure levels."* (EP and Council, 2006; Annex I, 5.2.1)

**Exposure level:** The (predicted) concentration to which a (sup-)population may be exposed under a given exposure scenario related to the life cycle of the polymer under evaluation. For instance, this exposure level will be compared to the derived-no-effect level in order to establish if safe use is attained with respect to the exposure above which humans should not be exposed. (TF working definition, using information from EP and Council (2006); Annex I, 1.0.1)

**Exposure pathway:** "The course an agent takes from the source to the receptor." (US EPA, 2016)

**Fate:** "Pattern of distribution of an agent, its derivatives, or metabolites in an organism, system, compartment, or (sub)population of concern as a result of transport, partitioning, transformation, or degradation." (WHO IPCS, 2004)

As such, exposure characterisation (i.e. exposure quantification) addresses external exposure (Box 6) or physical availability. Just as stands true for many non-polymeric substances, the external exposure might be much higher than the internal exposure, i.e. the concentration of the substance that is taken up systemically and ends up reaching the relevant target organs (Laroche et al., 2018). In Step 7 (hazard assessment), Section 3.7.1.1 further discusses the relationship between physical availability, external and internal bioavailability.

The physical availability of (and hence potential exposure to) **LMW compounds** (i.e. small oligomers, IAS, and NIAS, including unreacted monomers) present in the polymer product is dependent upon its form. Polymer products can be soluble in water and/or different media, suspended, and solid. Indeed, the same polymer product can be produced in soluble, suspended and solid form. Further, some polymer products can change their form and properties during processing and use, for example when heated or when in prolonged contact with water, oils or solvents. These changes may include water/solvent absorption (swelling) or in extreme cases transformation to a gel-like state resulting in the loss of form. Accordingly, the polymer matrix can also change depending on the life cycle stage of the polymer product.

Water-soluble polymers generally act as true mixtures in aqueous compartments, and do not show significant matrix effects. For solid polymers, migration / leaching and diffusivity from the polymer matrix are rate-

limiting parameters for the physical availability of LMW compounds, and hence also for their external or internal bioavailability. Generally, solid polymers frame the LMW compounds into their matrix. In many cases, only those LMW compounds present in the external surface layer of solid polymers (representing only a very small fraction of the total composition of the polymer product) can potentially migrate from the polymer matrix (PlasticsEurope, 2014). This has been recognised for many years as was shown by the derogation from labelling implemented for alloys, polymers and elastomers in the previous Dangerous Substances Directive (Council, 1967) that has been maintained in *Regulation (EC) 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures* (EP and Council, 2008) (see Appendix B, 2.1.3).

The examples also show that the migration potential of LMW compounds can be affected by various intrinsic factors (e.g. water solubility, size of the polymer product and/or article, and hence surface area to volume ratio). Further, external factors (e.g. contact media, temperature and ultraviolet light) and aging of the polymer can affect the migration of LMW compounds. The blooming (Glossary) of additives from the polymer matrix has been described as a special form of migration of additives from the polymer matrix onto the surface of the polymer product (Nouman et al., 2017). In this Technical Report, migration is considered to include blooming.

Diffusivity (that follows Fick's law of diffusion (Fick, 1855)) describes how fast a substance moves within the matrix towards the surface. Diffusion depends on the Mw (small molecules move more freely within the polymer matrix than larger ones); temperature (which enhances diffusion via the Arrhenius effect (Arrhenius, 1896)); and the activation energy or Ap\* coefficient (a parameter describing the diffusion behaviour of the migrant within the specific polymer matrix). In soft and/or flexible polymers (e.g. low-density polyethylene), a high Ap\* reflects the relatively easy movement of LMW compounds within the polymer. By comparison, more rigid polymers (e.g. polyesters, acrylonitrile butadiene styrene and polystyrene) have lower Ap\* values reflecting lower mobility (Hoekstra et al., 2015; Welle and Franz, 2010). LMW compound diffusion plays no role for short contact times to these rigid polymers such as under conditions of repeat use of articles (Welle and Franz, 2018).

The migration of LMW compounds can occur both during polymer manufacture and use, and possibly to different extents for different life cycle stages. Some LMW compounds are loosely bound in the polymer product, some are entrapped within the polymer matrix, resulting in reduced potential for physical availability. When the matrix of such solid polymers is intact, exposure may nevertheless arise via diffusion and partitioning from the polymer surface to the contact medium. However, when the polymer structure breaks down, LMW compound release into the (aqueous) environment can be augmented. For water-absorbing polymers, hydration of the polymer surface can occur with resulting expansion of the polymer matrix, increased partitioning and diffusivity and/or migration of LMW compounds.

For comprehensive exposure assessment, the 'strength' with which LMW compounds are bound into the polymer matrix, both during use and at the end-of-life (whether disposed directly into the environment or via WWTPs), should be clearly understood. However, generally, LMW compounds only make up a minor fraction of the polymer product, leading to very low exposures even if released from the matrix.

Particularly for **additives**, the potential mechanism for release from the polymer product should be considered during polymer exposure characterisation since this aspect might not have been considered during RA of these substances under the respective chemical legislation. The impact of migration and diffusivity on the physical availability, and hence release and exposure potential, of additives is being considered in the ongoing *Plastic Additives Initiative* (ECHA, 2019b) that has been launched under the *EU Strategy for Plastics in the Circular* 

*Economy* (European Commission, 2018a). This initiative includes several hundred hazardous substances identified during the REACH registration procedure, with tonnage bands above 100 tonnes/year, and potential intended uses as additives in plastics. The initiative aims at comparing the relative release potential of additives in plastics. Release potential is defined as "*a result of diffusion-speed through the plastic matrix and partitioning from plastic surface to the contact medium*", and it is driven by molecular volume, diffusivity, relative affinity of the additive to the matrix, and temperature. Mw is used as a proxy for molecular volume and a threshold of < 600 Da has been set to identify LMW compounds that can migrate from plastics (ECHA, 2019b)<sup>5</sup>.

With respect to **human exposure characterisation** (and subsequent hazard assessment), if LMW components are unable to migrate from the polymer matrix to any relevant extent, the oral and dermal routes of exposure or systemic toxicity upon inhalation are unlikely to be of relevance for these compounds. In cases where minor components of polymer products are assumed to become physically available, the hazard assessment should be conducted on the components as such. Typically, any toxicity studies performed on complex mixtures will deliver less precise information on minor components. For situations where NIAS cannot be fully characterised or synthesised, screening approaches applying quantitative structure-activity relationships, thresholds of toxicological concern, or *in vitro* assays should be employed where available and relevant to the components and endpoint(s) of interest (ILSI, 2015). Existing guidance regarding the assessment of articles or other solid substances such as metals, and relevant guidance on non-polymeric formulated products, can also be consulted during polymer exposure characterisation (e.g. US EPA, 2007a; ECHA, 2015b, 2017b). This is further explored in the case studies on polymer RA planned as ECETOC TR No. 133-3.

With respect to ecological exposure characterisation (and subsequent hazard assessment), polymers with sorptive properties (e.g. cationic polymers) are likely to partition to sludge, soils and sediments after release into the environment (Step 5 – determination of exposure scenarios). In this case, their physical availability and extractability, such as desorption from the matrix over time and resulting external / internal bioavailability, needs to be characterised. It cannot be excluded that some types of polymers may form bound, non-extractable residues (NER) over time. Bound NER are compounds which tend to remain irreversibly sorbed in the environment in the form of parent substance, metabolite(s), or bound to organic matter (humus). By contrast, the dissolved fraction and the fraction that is readily extractable with aqueous phase and weak organic solvent mixtures is characterised as bioavailable. Therefore, the formation of NER reduces (bio)availability significantly (Führ et al., 1998). The TF is unaware of relevant scientific literature specifically addressing if / how specific types of polymers might form bound NER over time. However, the ECETOC Technical Report Development of interim guidance for the inclusion of non-extractable residues in the risk assessment of chemicals (ECETOC, 2013a) provides general guidance for how NER can be assessed in the context of RA. The nature of the type of binding process can be clarified by a sequence of matrix altering extraction methods (from soft to harsh) and sophisticated analytical techniques. To provide a realistic picture of the level of adsorption, the extraction methods must not substantially change or destroy the compounds themselves or the structure of the matrix.

<sup>&</sup>lt;sup>5</sup> see also <u>https://echa.europa.eu/comparing-relative-release-potential#table</u> and <u>https://echa.europa.eu/-/high-volume-plastic-additives-mapped?\_cldee=dXJzdWxhLnNhdWVyQHNhdWVydWcuZGU%3d&recipientid=lead-ed1702cfc0e0e71180fa005056952b31-b467fe2116ef48c59c66f5e8534b6a6a&esid=2f92d803-6b3a-e911-810a-005056952b31.</u>

## 3.6.2 Step 6: Exposure characterisation – examples

#### 3.6.2.1 Environmental exposure characterisation - examples

If used in cleaning products that go down the drain, the physico-chemical properties of polymers will drive their partitioning behaviour in environmental compartments in addition to information on the biodegradation potential in WWTPs. Considerations on solubility and the presence of RFGs may inform on the partitioning potential of polymers between the solid and aqueous compartments. Generally, water-insoluble polymers will partition to soil, suspended particles, sediments, and sludge, while soluble and/or dispersible polymers may remain (at least partially) in water.

If the partitioning behaviour can be characterised with experimental data or predicted with modelling, this insight should be used to guide selection of the appropriate fate and ecotoxicological studies. For example, performing studies to inform on the most relevant compartments (e.g. soil compartment directly via spray applications or indirectly via sewage sludge applications; or sediment compartment) can reduce the complexities and logistical challenges related to the testing of poorly soluble materials and the resulting data interpretation (e.g. physical effects versus intrinsic toxicity).

Polymers used in bags used for the collection of organic waste or single-use tableware have a specific route of exposure as they will be handled with organic waste by composting and subsequently applied to land. Knowledge on the conditions of use help tailor the testing needs to the soil compartment.

Some basic physical and chemical properties, such as log P, may not be relevant and even appropriate to describe polymers that are complex mixtures. This issue becomes apparent when considering available models to estimate environmental exposure. An in-depth appraisal of such model applicability is included in the planned ECETOC TR No. 133-2.

#### 3.6.2.2 Human exposure characterisation - examples

When polymers are for example used as co-formulants of food supplements, characterisation of consumer exposure is straightforward since it should be restricted to oral exposure based on label recommendations. Iterations of assessment may include consideration of systemic exposure and health-based guidance values based on internal exposure metrics. For dermal and oral cosmetic applications of polymers, the *European Commission Scientific Committee on Consumer Safety Notes of guidance for the testing of cosmetic ingredients and their safety evaluation* (SCCS, 2018) include default amounts of daily use of personal care products. In combination with the inclusion level of the polymer product in the cosmetic, these default amounts can be used for simple worst-case external exposure estimates. For food contact exposure assessments, typically only the components migrating into food are assessed, based on experimental migration simulation or computational modelling. Plastic compounders blending e.g. hazardous additives into polymers can use leaching experiments or migration models to characterise dermal exposure of workers and exposure of environmental species to LMW components. Pulmonary exposure to polymer products which are intended to be aerosolised can be assessed based on measured aerosol particle size distributions combined with aerosol exposure models or measurements (Delmaar and Bremmer, 2009; Steiling et al., 2014, 2018).

## **3.6.3** Step 6: Exposure characterisation – knowledge gaps

Knowledge gaps with respect to exposure characterisation during polymer RA relate to the applicability of available test methods and models for exposure characterisation, which were generally developed for non-polymers. The review of the applicability of test methods and *in silico* models for polymer RA (planned as ECETOC TR No. 133-2) also includes an evaluation of methods and models for exposure characterisation.

An important aspect to consider when assessing the end-of-life release of polymer products, LMW compounds (or non-polymers) into the environment is the time span of exposure. It is one of the determinants of the amount of substance emitted to the environment. The most often used approach for LMW compounds is steady-state modelling. However, this approach yields exposure concentrations that occur when environmental removal rates equal the emission rates. This may correspond to unrealistically long-lasting exposure scenarios and result in overly conservative exposure estimates. Research work is merited to address such limitations of currently available models.

As necessary, new environmentally relevant models, test methods and/or criteria to assess (bio)degradation should be developed to enhance assessments of the RA implications of this property. Such models / criteria should take into account the type of (bio)degradation, its duration (i.e. half-lives), and whether it is intended during the given life cycle stage of the polymer, or not.

## **3.7** Step 7: Hazard assessment

#### Step 7: Hazard assessment (i.e. hazard identification and characterisation)

Step 7 is performed for the given life cycle stage of the polymer (Step 1), simulating the relevant ecological receptor(s) and exposed human population (Step 5).

Polymer hazard assessment should be science-driven. The identification of data needs should consider relevant life cycle stages and intended uses of the polymer product, the environmental or human target population to be protected, exposure characterisation, and relevant (eco)toxicological endpoints, taking into account the key parameters and potentially relevant MoAs identified in Steps 2 and 4, respectively.

As determined during Step 3 (polymer component strategy), Step 7 is performed for the polymer product (i.e. including its LMW compounds), for the polymeric substance, and/or for all or selected NIAS or IAS, as relevant. Further, Step 7 may consider the hazard potential of breakdown products of the polymer, if relevant.

Step 6 (exposure characterisation) may have to be revisited and refined using initial results from Step 7, which would then be completed after the reiteration of Step 6.

#### Step 7.1: Derive ecological hazard descriptors (Figure 3)

- Identify structural and/or morphological descriptors as well as physico-chemical properties that are relevant for ecological hazard assessment and that may indicate relevant endpoints and/or potential molecular initiating events / MoAs (e.g. Mw distribution, water solubility, surface tension, cationicity, RFGs, heavy metals).
- Identify relevant screening-level fate and partitioning properties (e.g. (bio)degradation, bioaccumulation, adsorption to sludge or soil).

- Identify available *in vitro* and *in vivo* ecotoxicity data and dose-response relationships, including predicted no-effect concentrations, effect concentrations in terms of degree of effect (EC<sub>x</sub>), benchmark dose levels; or use suitable *in silico* tools and/or read-across procedures (see Step 4).
- Consolidate all available relevant data within a weight-of-evidence (WoE) evaluation.
- If necessary: Define testing needs in accordance with the defined RA scope (Step 1); perform testing and repeat WoE evaluation.

Step 7.2: Derive human health hazard descriptors (Figures 3 and 4)

- Identify structural and/or morphological descriptors as well as physico-chemical properties that are relevant for human health hazard assessment and that may indicate relevant endpoints and/or potential molecular initiating events / MoAs.
- Assess external and internal (systemic) bioavailability (toxicokinetics).
- Assess reactivity potential (RFGs and/or cationicity) preferably using in vitro assays.
- Identify available *in vitro* and *in vivo* toxicity data and dose-response relationships, including no- or lowestobserved adverse effects concentrations / levels, EC<sub>x</sub> (or similar), benchmark dose levels.
- Consolidate all available relevant data within a WoE evaluation.
- If necessary: Define testing needs in accordance with the defined RA scope (Step 1); perform testing and repeat WoE evaluation.

### **3.7.1** Step 7: Hazard assessment – explanatory notes

Step 7 (hazard assessment) includes both hazard identification and hazard characterisation (Glossary). It involves identifying and characterising the potential hazards of the life cycle stage(s) of the polymer (Step 1) towards the ecological receptor(s) and/or human populations taking into account relevant routes of exposure (Step 5). As identified during Step 3 (polymer component strategy), Step 7 can be performed on the polymer product (i.e. including its LMW components), and/or on all or selected IAS or NIAS, as relevant. As typical for chemical hazard assessment, Step 7 focuses on intrinsic toxicity and physical effects of polymer products as chemical substances. By comparison, the CF4Polymers does not address the physical effects caused by finished articles.

Step 7 considers specific structural and/or morphological descriptors as well as physico-chemical and screening-level fate properties of the polymer that are relevant to streamline (eco)toxicity data needs. Most likely, these properties are concordant with the key parameters used in Step 4 (grouping approach evaluation) to substantiate polymer similarity and to inform on a likely MoA. Consideration of the structural, morphological, physico-chemical and fate key parameters and likely MoA serves to ensure that all newly generated data are truly relevant for hazard assessment and RA (Figure 3).





Figure 3: Workflow: Step 7 – polymer hazard assessment, embedded in the other steps of the CF4Polymers

Due to the versatility and complexity of polymer products, of their different life cycle stages and intended uses, streamlining data needs by scientific relevance is of utmost importance to ensure that time and resources are used efficiently and that no unnecessary vertebrate animal testing is performed as mandated e.g. by the EU animal protection legislation (EP and Council, 2010). By contrast, 'tick-box testing', i.e. addressing lists of ecotoxicological and toxicological endpoints without consideration of their scientific relevance, would run the risk of performing vertebrate animal testing that is not indispensable and of yielding an abundance of data that are irrelevant for polymer hazard assessment or RA.

Notably, polymer classification and labelling e.g. under the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS; United Nations, 2017) or the corresponding legislation implemented in the given jurisdiction, as a tool to formalise hazard identification and communication are suitable for polymers but are not specifically addressed in the CF4Polymers. Cefic and PlasticsEurope (2014) and PlasticsEurope (2014) provide guidance on aspects of hazard classification of polymeric mixtures under *Regulation (EC) 1272/2008 on classification, labelling and packaging of substances and mixtures* (EP and Council, 2008).

### 3.7.1.1 The role of bioavailability in ecological and human health hazard assessment

**Bioavailability** characterisation is of utmost importance for ecological and human health hazard assessment of polymers. The WHO IPCS has defined bioavailability as "the rate and extent to which an agent can be absorbed by an organism and is available for metabolism or interaction with biologically significant receptors. Bioavailability involves both release from a medium (if present) and absorption by an organism" (WHO IPCS, 2004).

Hence, the WHO IPCS definition indicates that bioavailability can either result from *"release from a medium"* or from *"absorption by an organism"*. Release from a medium links to physical availability and exposure characterisation and can be use- or life cycle-dependent.

To ensure unambiguous usage of the term bioavailability, the ECETOC Polymers TF distinguishes between (1) physical availability, addressed in Step 6 - exposure characterisation; (2) external bioavailability; and (3) internal (systemic) bioavailability and has drawn up the following working definitions (see also Glossary):

- **Physical availability** means that one or more individual components of the polymer product are released from the polymer matrix e.g. by migration / leaching. (Physical availability can be prevented e.g. by encapsulation (Störmer et al., 2017).)
- External bioavailability describes the condition that some HMW polymers that are too large to cross biological barriers might nevertheless exert local toxicity in tissues (e.g. skin, eyes, respiratory tract). This toxicity may well be due to LMW components (i.e. small oligomers, IAS, and NIAS, including unreacted monomers) that migrate under conditions of contact to the transitional fluid (e.g. sweat, tears, saliva), thereby being available to be absorbed and exert their toxic effect. The specific mechanisms by which such effects can occur remain to be determined.
- **Internal (systemic) bioavailability** means that the polymer product is absorbed into the blood stream by an organism thereby becoming systemically available and potentially causing systemic effects.

Notably, this distinction does not consider routes of exposure other than the oral, dermal or inhalation routes, e.g. implantation of medical devices containing polymer products, or intramuscular, intravenous or subcutaneous administration. Assessing the internal bioavailability of polymer products or their components

upon such (medical) routes of exposure requires special considerations beyond the scope of this Technical Report.

As explored in further detail below, the internal bioavailability of a polymer is determined by its size (Mw) as well as its charge, and further physical properties, including solubility and partitioning in water and/or biological media, and physical state.

### **3.7.1.2** Ecological hazard assessment

It is highly important that ecological hazard assessment is performed on species that are relevant to the environmental compartment(s) of exposure (Figure 3). Depending on the use of the polymer product of interest, the testing strategy may focus on relevant species among freshwater, marine water, their respective sediment, the soil and/or air compartments. Ecological hazard screening assessment is often limited to testing of freshwater species, but the water compartment may not necessarily be relevant for the polymer product of interest.

Beyond the route of exposure and the potential for (bio)degradation, physico-chemical descriptors (Step 2.1) will further inform on the relevance and suitability of the testing approach. The potential presence of RFGs (and their further assessment, see Section 3.7.1.3) as well as specific factors that can affect the ecological hazard potential of polymers include the potential hazards associated with breakdown products (Section 4.5), water solubility (Section 4.6), cationicity (Section 4.7), surface activity (section 4.8) and indirect effects.

For smaller polymers, increased water solubility typically increases physical availability and hence the potential for external bioavailability. By contrast, very large polymers will still not be systemically available even if highly soluble but can nevertheless be bioavailable externally and hence potentially elicit local effects. Indeed, local effects, e.g. at fish gills, can be physical effects caused by polymers that are too large to become systemically available (OECD, 2019).

### 3.7.1.3 Human health hazard assessment

Figure 4 provides a flow chart for human health hazard assessment. It is applicable to the polymer product itself or to physically available LMW components.

Exposure routes (Step 5), physical availability (Step 6), and **external / internal bioavailability** (Section 3.7.1.1) should be the very first consideration when designing the human health hazard assessment procedure and when identifying necessary and/or relevant test methods. For those components of the polymer product that can become physically available, the next step includes determining if only external bioavailability or also internal bioavailability are of relevance: If a polymer product is not capable of crossing biological membranes, systemic toxicity by the oral and dermal routes of exposure or upon inhalation exposure as well as genotoxicity are unlikely to be of relevance. In such cases, hazard assessment should focus on assessments for potential local effects (e.g. skin and eye irritation, skin sensitisation, pulmonary effects).



Figure 4: Workflow: Polymer human health hazard assessment

#### Footnote to Figure 4: This workflow can be applied to the polymer product or to physically available LMW components.

Similarly, Annex 2 (polymeric additives) of the European Food Safety Authority (EFSA) Panel on Food Contact Materials, Enzymes, Flavourings, and Processing Aids (CEF) Note for guidance for the preparation of an application for the safety assessment of a substance to be used in plastic food contact materials (EFSA Panel on CEF, 2017) highlight the pivotal role of bioavailability for the RA of LMW compounds:

"Components with a molecular mass above 1,000 Dalton (Da) are very unlikely to be absorbed by the gastrointestinal tract and thus are not considered to present a toxicological risk. The value of 1,000 Da was chosen because it takes into account the effect of the shape of the molecule, which has an important influence on the likelihood of absorption of substances in the molecular mass range 600-1,000 Da. Below 600 Da, most substances are absorbed and the rate of absorption is determined by factors other than size and shape of the molecule. Since only the fraction of the polymeric additive with molecular mass below 1,000 Da is regarded as toxicologically relevant, a distinction has been made between polymeric additives with a weight averaged molecular mass (Mw) below 1,000 Da and those with Mw above 1,000 Da. For polymeric additives with Mw above 1,000 Da, the fraction with molecular mass below 1,000 Da case-by-case consideration of the specification will determine whether further data are required..."

The TF is unaware of any scientific evidence to support setting the threshold for LMW compound bioavailability at 600 Da, as undertaken by the EFSA Panel on CEF, as opposed to 500 Da, as indicated in the polymer of low

concern (PLC) concept (see Section 4.1). Indeed, as compared to these regulatory thresholds for the Mw of LMW compounds of polymers, more recent evidence suggests that for harder plastics with higher glass transition temperatures, LMW compounds with Mw as low as 200 Da have low diffusivity from FCMs and hence low physical availability (Brandsch, 2017) and resulting potential for external and/or internal bioavailability.

For **polymeric substances** that can become externally and/or internally bioavailable, the presence of RFGs, and their functional group equivalent weight (FGEW) should be addressed (Section 4.3). As further explored in Section 4.3, RFGs constitute structural alerts, but do not *per se* indicate hazard potential. Therefore, the identification of RFGs should be followed up by lower-tier screening together with an evaluation of all available data for the given polymer and similar ones as well as *in silico* modelling as applicable. Only if the lower-tier screening indicates hazard potential, the TF considers higher-tier *in vivo* testing justifiable. The identification of RFGs also serves to hypothesise a MoA (see also Step 4) and hence to identify relevant toxicological endpoints and applicable test methods. If more than one RFG is present, the polymer can generally be assessed on the basis of the most harmful RFG (NICNAS, 2019a).

Only in few cases of polymers with relevant systemic bioavailability under specific use types (e.g. excipients, food additives, orally applied cosmetics), repeated dose toxicity data will be required for RA. For such polymers, assessments of the potential impact of body fluids on decomposition and the potential bioavailability of breakdown products might also be relevant. If inhalation exposure is relevant, the potential for pulmonary effects has to be addressed (Figure 4). This is the case when aerosols with respirable particle sizes are generated, typically upon intentional generation of propellant-based sprays or when fine dusts are handled in workplaces. Effects typically observed in polymer aerosol studies are unspecific pulmonary overload effects with non-reactive polymers or local respiratory tract irritation with reactive polymers. By contrast, few polymer types can evoke specific pulmonary toxicity (ECETOC, 1997; Warheit et al., 2001).

Following the polymer component strategy (Step 3), and provided that Step 6 indicated potential exposure to **LMW compounds** (i.e. small oligomers, IAS, and NIAS, including unreacted monomers), Step 7 may include hazard identification and characterisation of the LMW compounds present in the polymer product. Indeed, often, such LMW compounds drive the requirements for polymer hazard assessment.

Finally, Lithner et al. (2011) and Groh et al. (2019) have based polymer hazard characterisation on the hazards of the **monomers** rather than those of the polymer itself. Thereby, polymers that include monomers that are classified as e.g. carcinogenic, mutagenic or toxic to reproduction in accordance with the GHS (United Nations, 2017) are suggested as posing the highest potential harm (Lithner et al., 2011; Groh et al., 2019), and RA focusses on the concentration of unreacted monomers. However, this approach fails to recognise the true potential for exposure to such monomer(s) or other chemical and structural aspects that are specific for polymer RA, so that it is irrelevant for the majority of polymers and polymer products. Typically, the hazards of monomers are driven by their reactive groups, but those cease to exist in the polymers. The monomer units in polymers typically lack reactivity and are expected to have a different, mostly less hazardous toxicity profile. In situations where a polymer is only produced and handled in mixtures with hazard-triggering concentrations of unreacted monomers and exposure to the polymer on its own is unlikely, hazard characterisation of the polymer itself is not informative for RA or handling of the product. As compared to the approach followed by Lithner et al. and Groh et al., the CF4Polymers is designed to ensure that all aspects of polymer hazard characterisation and exposure assessment are considered during RA in an integrated approach.

## **3.7.2** Step 7: Hazard assessment – examples

Dusty particulate polymers (e.g. produced by suspension or solution polymerisation with subsequent drying to remove the liquid phase) may represent a dust explosion hazard and inhalation risk to workers. Hazard can be assessed by read-across to similar polymers for which data are available, or by testing. (European and American standards are available to instruct on dust explosion testing<sup>6</sup>.) The need for *in vitro* or *in vivo* inhalation hazard assessment of dusty particulate polymers or polymers used in sprays depends upon their potential for respiration or inhalation, as indicated by specific physical and chemical properties, e.g. the aerodynamic size of the particles (see also Section 3.7.1).

Polymers that have pendent RFGs, IAS or NIAS with allergenic potential might represent a handling risk upon dermal contact and/or inhalation. Skin sensitisation hazard assessment can follow conventional testing approaches adapted to the physical form under likely conditions of use.

Polymeric surfactants should be tested *in vitro* for skin and eye irritation potential if the intended uses result in relevant dermal exposure, for example when they are used in toilet cleaners. By contrast, polymeric substances may also have to be assessed for systemic effects and genotoxicity if oral exposure occurs and/or if they are likely to become systemically available, for example when used in kitchen surface cleaning products.

The ecological hazard assessment of such polymeric surfactants (e.g. toilet cleaners and/or kitchen surface cleaning products) should consider that these products are most likely released down-the-drain with resulting potential exposure to the aquatic compartment. Accordingly, the screening assessment can focus on the characterisation of acute effects on aquatic species. The subsequent higher-tier assessment may be extended to chronic endpoints on a case-by-case basis as indicated by the outcome of the lower-tier screening.

By contrast, the assessment of aquatic hazards elicited by less soluble polymers with potential release downthe-drain merits an in-depth review to characterise the likelihood of exposure of the aquatic compartment following wastewater treatment, as well as the relevance of the outcome of the aquatic toxicity testing to support RA. Technically, poorly soluble polymers can be tested on aquatic systems, however they pose logistical and technical challenges regarding the dosing in the aqueous medium used in the test systems (ECETOC, 2018). For example, a hazard assessment associated with the preparation of the water-soluble (water-accommodated) fraction may only be representative of the soluble fraction of the polymer product.

Polymers with other routes of primary exposure may still be screened for environmental hazards in aquatic species if the test method is appropriate. In the case of a polymer used in a plant protection product, testing aligned with the route of exposure (soil) is nevertheless not typically carried out on the polymer itself, but rather on the formulated product that includes the polymer. When the routes of primary exposure do not include aquatic systems and/or aquatic screening is not technically representative or appropriate, a review of the level of adsorption may inform on the route of exposure to soil species (oral, dermal) and associated representative species to select for testing (plant versus earthworm).

The following example further highlights the need to perform polymer hazard assessment in its 'as used and as disposed' form. The polymer under investigation is only used in an aqueous, oily dispersion (e.g. for the encapsulation of an oily liquid). During manufacture, this polymer is also only present in aqueous dispersion

<sup>&</sup>lt;sup>6</sup> <u>http://www.dustexplosion.info/standards.htm</u>.

and never isolated as a fine powder. After use, i.e. at disposal, it is also only present in dispersion or as a component of a mixture of damp solids (e.g. sewage sludge). Hence, this polymer will not be present as a powdery solid during any of its life cycle stages. For such a polymer, human health hazard assessment should address potential local effects at the eyes and/or skin and in the gastrointestinal tract, as well as potential systemic uptake upon oral exposure, provided that the use scenarios identified oral exposure routes and the polymer is assumed to be systemically available. By contrast, inhalation toxicity testing for respirable dusts is not relevant for such a polymer that is only present in aqueous oily dispersion.

## **3.7.3** Step 7: Hazard assessment – knowledge gaps

Standard test methods to identify hazards (and to determine physico-chemical characteristics) have been developed specifically for non-polymers. Often, the test method addressing the (eco)toxicological endpoint of relevance for the given RA can be adapted for the testing of the polymer of interest. Notwithstanding, for some polymers, technical limitations can impair test method performance or reduce the reliability of test results, particularly for the clarification of intrinsic hazard effects and physical-related effects, the sum of which result in an overall observed adverse effect (ECETOC, 2018). To date a standardised set of test methods specifically designed to address the complexity of polymer hazard assessment, including allowable adaptations under pre-defined criteria, is unavailable. The development of such a testing strategy will enhance the efficiency of polymer hazard assessment while ensuring a high-quality RA. It is expected that the critical review of the applicability of standard test methods for polymer RA that is in preparation by the ECETOC Polymers TF (planned as ECETOC TR No. 133-2) will contribute to meeting this goal.

Below, specific research needs related to ecological and human health hazard assessment are presented in further detail. Importantly, some of these research needs are not polymer-specific but reflect an ongoing shift in the focus of RA strategies for all types of substances. For example, integrated testing strategies for hazard characterisation, including *in silico* and *in vitro* steps as lower tiers, and higher-tier *in vivo* studies only as needed, are under development and require validation for different types of substances (OECD, 2016).

With regard to ecological hazard assessment, specific research work is merited to evaluate the environmental relevance of methods to measure, analyse and interpret indirect physical effects of natural and manmade materials on the environment. This includes the identification of means to distinguish between direct test material-induced effects and indirect physical effects as well as the identification of representative test organisms for each environmental compartment that allow identifying potential hazards (ECETOC, 2018). Furthermore, gaining knowledge on the polymer attributes that drive ecotoxicity (e.g. RFGs; size and shape for particulates) would support the development of *in silico* approaches for the ecological hazard assessment of polymers.

Screening approaches to characterise the fate of polymers are currently limited to adsorption / desorption studies in soil and sludge and biodegradation assays, and the applicability domains of these assays mainly include soluble polymers of LMW. Due to the size (HMW) and limited bioavailability of most polymers and the associated longer timeframes expected for mineralisation, it is critical to characterise the environmental compartment where exposure is most relevant.

Accordingly, research activities related to ecological hazard assessment should focus on approaches that promote a more comprehensive understanding of the potential environmental fate and transport of polymers. This includes:

- The identification of physical and chemical properties relevant for the prediction (modelling) of partition coefficients; and
- The development of laboratory screening assays supporting these in silico assessments.

With regard to human health hazard assessment, since potential for systemic effects will mostly be irrelevant for polymers, research activities should focus on developing and/or validating *in vitro* methods to assess local effects elicited by polymers (e.g. eye and skin irritation, skin sensitisation, and local pulmonary effects). Such test methods should also allow evaluation of how polymers biodegrade in the lung or are cleared therefrom. Research is ongoing to develop organotypic *in vitro* models for pulmonary effects (see e.g. Hiemstra et al., 2018). It will be highly useful to validate such models for different types of polymers, as for other materials.

Just as stands true for ecological hazard assessment, further research is also merited in the context of human health hazard assessment to develop and validate adaptations to test methods or *in silico* models to distinguish between test-material induced direct effects and polymer-unspecific physical effects.

Importantly, future research should aim at enhancing a mechanistic understanding for how the presence of specific RFGs might affect the hazard potential of polymers. In order to assure that the identification of structural (chemical) alerts only leads to higher-tier *in vivo* testing if truly indispensable, such research activities should include the following topics:

- Establish if the available *in chemico / in vitro* methods for skin and eye irritation and skin sensitisation also deliver acceptable results for polymers containing RFGs (e.g. by case studies and/or validation exercises) or if these methods require adaptations for the testing of polymers.
- As necessary, develop and validate new *in vitro* assays to allow predicting the biological activity of specific RFGs.
- Establish the suitability of *in vitro* cytotoxicity assays to distinguish between polymers where present RFGs are sufficiently abundant and exposed to evoke local effects – or not. If such screening assays yield negative results for a polymer containing RFGs, it should not be necessary to run the battery of *in chemico / in vitro* assays for irritation and sensitisation.

## 3.8 Step 8: Risk characterisation

#### Step 8: Risk characterisation

- Compare hazard(s) to exposure(s) to generate quantitative estimates of risk for the combinations of components, use scenarios and hazard endpoints which had been defined to be in scope. Conclude on the overall risk from use of the product in scope.

- Qualitatively describe level of confidence, uncertainties and assumptions. Describe conditions under which the risk assessment outcome applies.

- Evaluate risk management measures (which may already be in place) and their impact on the risk characterisation.
- Refine risk characterisation of use scenarios as needed and possible (which may include the need to revisit exposure and hazard assessment).
- Formulate testing proposal to address unanswered concerns, if uncertainty remains.

## **3.8.1** Step 8: Risk characterisation – explanatory notes

While the risk characterisation for polymers can be more complex for polymer products than for many monoconstituent substances, it is not inherently different from the risk characterisation procedure for such nonpolymers. Below, relevant key terms are defined.

**Risk characterisation** is *"the qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of occurrence of known and potential adverse effects of an agent in a given organism, system, or (sub)population, under defined exposure conditions"* (WHO IPCS, 2004).

**Uncertainty** refers to *"imperfect knowledge concerning the present or future state of an organism, system, or (sub)population under consideration"* (WHO IPCS, 2004).

The uncertainty assessment should include reflections on what was defined as out of scope of the RA, and document the conditionality of the RA, i.e. under which conditions it applies. For example, when a polymer product was assessed for risks from use as adhesive in car manufacture, the assessment outcome may not be applicable to uses as tile adhesives. The application of conservative safety factors to (eco)toxicological endpoints to derive predicted no-effect concentrations and derived no-effect levels is a regulatory approach to take into account cross-species sensitivity differences, thus reducing uncertainty. Typically, the higher the tier of the available test is, the lower the uncertainty and, therefore, the lower the applicable safety factor.

Risk characterisation is the final step of RA, and its outcome can then be used e.g. to identify the need for specific risk management measures (see also Box 3).

### **3.8.2** Step 8: Risk characterisation – knowledge gaps

The TF did not identify any polymer-specific knowledge gaps regarding Step 8 of the CF4Polymers.

# 4. KEY ELEMENTS OF INTERNATIONAL POLYMER REGULATION

The TF reviewed the regulatory landscape on polymers, evaluating how polymers are covered by the chemical legislations implemented in the EU, Australia, Canada, China, Japan, the Philippines, South Korea, and the USA (Appendix B). This review had a focus on identifying key elements of polymer RA and determining if they should, or should not, feed into the CF4Polymers.

Further details on the regulatory landscape on polymers up until 2015 in these jurisdictions as well as in New Zealand, Taiwan, and the State of California, and relevant information for Switzerland, Mexico, and Turkey are provided in BIO by Deloitte (2015).

Generally, all jurisdictions follow the OECD definition of a polymer to identify if a substance is a polymer. Notably, the OECD definition relates to 'polymeric substances' as defined by the ECETOC Polymers TF (Section 2). Therefore, the respective provisions could be inferred to apply only to polymeric substances, i.e. excluding IAS and NIAS. However, many polymer products do include IAS or NIAS, and often their properties drive the overall hazard of the polymer products. Therefore, the CF4Polymers explicitly distinguishes between polymer product and polymeric substance and addresses all components of the polymer product in the RA process.

In the EU, polymers are exempt from registration and evaluation under Article 2(9) of the REACH Regulation (EP and Council, 2006). (By reverse conclusion, they are not exempt from restriction or authorisation.) The monomers from which a polymer is formed must be registered (REACH Article 6(3)). Notwithstanding, the REACH Regulation does not exclude the future possibility of a requirement to register polymers – nor that the full exemption could become permanent (Box 7).

#### Box 7: REACH provisions and the future possibility of a requirement to register polymers

Article 138(2) of the REACH Regulation has laid down that "the Commission may present legislative proposals as soon as a practicable and cost-efficient way of selecting polymers for registration on the basis of sound technical and valid scientific criteria can be established, and after publishing a report on the following (1) the risk of polymers in comparison with other substances; (2) the need, if any, to register certain types of polymer, taking account of competitiveness and innovation on the one hand and the protection of human health and the environment on the other".

To date, two such reports have been published, i.e. one prepared by Risk & Policy Analysts Ltd. (RPA, 2012) and one prepared by BioIntelligence by Deloitte (BIO by Deloitte, 2015). The European Commission summarises the outcomes of these two reports as follows: "While the first study from 2012 provided a first overview on the EU polymer market and an analysis of risk assessment options based on current requirements as well as increased requirements, the second study completed in 2015 evaluated two possible complementary registration systems for polymers, (1) grouping of similar polymers and (2) criteria for Polymers of Low Concern (PLC) for which no or lighter registration obligations would apply" (European Commission, 2018b).

As a follow-up to these two reports, in April 2018, the European Commission published a call for tenders for *Scientific* and technical support for the development of criteria to identify and group polymers of concern for registration / evaluation under REACH and their impact assessment (European Commission, 2018b). The tenderer was asked to propose criteria to characterise 'polymers of concern' and justify the selected criteria; to propose solutions for their grouping as well as registration requirements under REACH; and to estimate the potential risks posed by such 'polymers of concern' in comparison to other chemicals based on available scientific evidence on their hazards and exposure (European Commission, 2018b).

As compared to the legal situation in the EU, all reviewed non-EU jurisdictions have implemented specific provisions for the notification / registration of new polymers in their chemical legislation. New polymers can be exempt from notification / registration if they fulfil the criteria for PLC (Section 4.1). Further, in some jurisdictions, 'similar polymers' may be notified / registered together thereby reducing regulatory efforts and expenditure. Specifically, "USA, Australia and Canada allow submission of a single registration for similar polymers, under the names 'consolidated notice', 'group assessment' and 'consolidated notification', respectively" (BIO by Deloitte, 2015).

If new polymers are not included in one of these two categories, they generally have to be notified / registered as standard substances in the non-EU jurisdictions. However, many jurisdictions apply increased low volume exemption limits for polymers (generally between < 100 kg/year and < 10 tonnes/year). Thereby, higher tonnage band thresholds apply for the manufacture or import of polymers than for non-polymers before the respective notification / registration requirements apply<sup>7</sup>.

To distinguish between new and existing polymers, generally, the 2% rule (US EPA, 2019b; Glossary) applies. The 2% rule states that monomers and reactants that make up more than 2 weight% of the polymer contribute to its chemical identity. Thus, if an existing polymer is modified by adding more than 2 weight% of new (i.e. not yet notified / registered) monomers or reactants, it must be considered as new polymer, and hence be submitted to notification / registration. Further, in Canada and Australia, existing polymers may be subject to regulatory requirements if so requested by the Competent Authority (BIO by Deloitte, 2015).

Polymers are also regulated (directly or indirectly via the monomers) by their use in specific products, such as FCMs, medical devices, cosmetics, pharmaceuticals, construction materials, and toys. Such legislation is being considered in the case studies that the TF is currently preparing (planned as ECETOC TR. No. 133-3).

Below, specific topics of relevance for the regulation of polymers are presented in further detail, each followed by the TF's appraisal of the scientific evidence to support considering this aspect during polymer RA:

- Section 4.1: The PLC concept in general;
- Section 4.2: Mw distribution and proportion of LMW compounds;
- Section 4.3: The presence of RFGs;
- Section 4.4: The presence of specific chemical elements (e.g. fluorine atoms);
- Section 4.5: (Bio)degradation, decomposition and depolymerisation;
- Section 4.6: Water solubility and extractability;
- Section 4.7: Cationicity;
- Section 4.8: Surface activity and anionicity / amphotericity;
- Section 4.9: Water-absorption.

<sup>&</sup>lt;sup>7</sup><u>https://www.chemsafetypro.com/Topics/Registration/Comparison of Small Volume Exemption for New Chemical</u> <u>Substance\_Registrations.html</u>

# 4.1 Polymer of low concern (PLC) concept in general

Polymers of low concern (PLCs) are "those deemed to have insignificant environmental and human health impacts. Therefore, these polymers should have reduced regulatory requirements" (OECD, 2009).

The OECD document *Data analysis of the identification of correlations between polymer characteristics and potential for health or ecotoxicological concern* (OECD, 2009) presents the outcome of a systematic analysis of the PLC concept using data for 205 polymers collated from Australia, Canada, Japan, South Korea and the USA. The analysis aimed at identifying correlations between specific polymer characteristics and potential for environmental or human health hazard (OECD, 2009). The OECD Expert Group on Polymers highlighted that the limited database of only 205 polymers impaired the analysis since many types ('classes') of polymers were only represented by a few polymers. Further, data were of *"variable quality"*. Therefore, *"examination of specific effects was not possible"* and *"trends were not clearly observed between polymer class and any observed toxicity"* (OECD, 2009). In spite of these limitations, the OECD Expert Group on Polymers did not find any evidence to refute the PLC concept. It concluded that *"this initial analysis has provided scientific evidence that builds confidence in the PLC criteria (where sufficient data were available)"* (OECD, 2009).

All non-EU jurisdictions considered in this Technical Report make use of the PLC concept in their polymer regulations (Appendix B). The actual information requirements for the notification / registration of a polymer depend upon whether it is considered a PLC, or not. PLC generally only require evidence that they meet the respective PLC criteria (together with a description of the manufacturing process, intended uses, safety data sheets, etc.).

Generally, polymers are considered PLC if they meet specific criteria related to Mw and the proportion of LMW compounds (Section 4.2) and if they do not meet specific PLC exclusion criteria. These PLC exclusion criteria vary between different jurisdictions, but generally address the presence of pre-defined RFGs (Section 4.3) or chemical elements (Section 4.4), polymer (bio)degradation (Section 4.5) and/or water solubility (Section 4.6), and cationicity (Section 4.7). Finally, in some jurisdictions (e.g. Australia, Canada, USA), polyesters that are made up only of prescribed reactants are considered PLC (Appendix B, 2.2.2, 2.3.2, 2.8.2).

Notably, while the present Technical Report was being finalised in April 2019, the *Australian National Industrial Chemicals Notification and Assessment Scheme* (NICNAS) implemented new provisions, with immediate effect, exempting PLC from notification and expanding its prior PLC criteria (Appendix B, 2.2.1 and 2.2.2).

The OECD website on the definition of polymer presents the following PLC criteria or PLC exclusion criteria; <u>http://www.oecd.org/env/ehs/oecddefinitionofpolymer.htm</u>:

- "Concerning Mw: the range of 1,000 10,000 NAMW was agreed as a range within which the concern value was likely to lie.
- Concerning Mw of LMW compounds giving rise to concern: the agreement was Mw below 1,000.
- Concerning percentage of LMW compounds of concern: no agreement.
- Concerning functional groups: only one value, applicable to epoxy and anhydride groups was mentioned (it was 1 reactive group in 20 monomer units); no general conclusion was reached.
- Metal content: no value agreed.
- Extractivity in water: 10 mg/L was seen as acceptable, provided that test conditions were standardized.
- Cationic charge density: the 5,000 equivalent weight value was accepted (as defined by EPA: not more than one cationic charge in 5000 monomer units)."

## 4.1.1 ECETOC Polymers TF appraisal of the PLC concept in general

The TF recognises, as did OECD (2009), that the OECD analysis of the PLC concept is limited by the available database. In spite of these shortcomings, the spectrum of criteria addressed in the OECD document formed a useful starting point for drawing up the CF4Polymers. Importantly, the OECD analysis yielded no evidence to refute the PLC concept, that further has been implemented in different non-EU jurisdictions for many years, or even decades, without indications to disprove its validity. For example, it was included in the Australian Industrial Chemicals (Notification and Assessment) Regulations 1990 (Australian Government, 1990), and 29 years later, in April 2019, NICNAS re-confirmed the relevance of the PLC concept by exempting PLC from notification and expanding its prior PLC criteria (see above, Section 4.1).

The TF found no published scientific evidence that the assumption that most polymers are of low concern would be wrong. The TF is further unaware of any comprehensive database, either publicly available or within industry, that would facilitate a profound scientific analysis of the performance of individual PLC criteria, PLC exclusion criteria, or the PLC concept as such.

In summary, the TF is not aware of any scientific evidence that polymers meeting the PLC criteria would exhibit environmental or human health hazards, or for rejecting the PLC concept. The TF considers the PLC concept a pragmatic approach to streamline the time and effort for polymer RA. It is practicable and cost effective, and it stands in line with the requirement to replace, reduce, and refine animal testing (Russell and Burch, 1959).

Importantly, however, while polymers identified as PLC can generally be considered to exhibit low intrinsic hazard potential, this does not allow the reverse conclusion that polymers that are not identified as PLC would *per se* pose a hazard or risk concern. The PLC concept has been implemented for regulatory purposes. As such, it is a conservative approach, as also highlighted by the above summary of the OECD (2009) analysis. The human health or environmental hazard potential of polymers that do not meet all PLC criteria has to be determined on a case-by-case basis. Indeed, many, if not most, non-PLC polymers are also non-hazardous and/or do not pose any risk upon foreseeable use conditions (Reinert and Carbone, 2008), just as many polymers have histories of long-standing safe consumer uses.

## 4.2 Molecular weight distribution and proportion of LMW compounds

In the OECD data analysis (OECD, 2009), polymers with certain characteristics – foremost Mw distribution and proportion of LMW compounds – were recognised as presenting minimal if any risk to human health and the environment: "One of the most striking findings related to the NAMW of a polymer; the lower the NAMW, the higher the potential for health or ecotoxicological concern. Similar results were obtained when the contents of low molecular weight, oligomeric species were investigated – the higher the content, the more likely a polymer was to display concern" (OECD, 2009). Notably, OECD (2009) does not report evaluating this outcome for confounders, e.g. the potential over-representation of reactive or surface-active polymers in the LMW polymers. Hence, it is unclear if this specific conclusion can be applied to all types of polymers.

In all jurisdictions that have implemented the PLC concept in their chemical legislation, polymers can generally only qualify for PLC status if their NAMW is ≥ 1000 Da. Additionally, polymers with NAMW between 1,000 and 10,000 Da can only be considered for PLC status if the content of oligomers is:

- < 10% components with Mw < 500 Da; and
- < 25% components with Mw < 1,000 Da.

Further, many jurisdictions (e.g. Australia, Canada, China, South Korea and the USA) have implemented additional restrictions for the proportion of oligomers that may be present in polymers with > 10,000 Da NAMW (i.e. < 2% components with Mw < 500 Da and < 5% components with Mw < 1,000 Da) in order for them to be considered PLC.

# 4.2.1 ECETOC Polymers TF appraisal of 'Mw distribution' and 'proportion of LMW compounds' as PLC criteria

The thresholds for NAMW of the polymeric substance and for the size and proportion of LMW compounds relate to the polymer's / LMW compound's potential to become systemically (internally) bioavailable and the permissible proportion of such compounds (see Section 3.7.1.1 for further details on the role of bioavailability in ecological and human health hazard assessment). The lowest Mw referred to in the PLC criteria is 500 Da, for the LMW components of the polymer product. This threshold relates to one parameter of the 'Lipinski rule of 5' that "predicts that poor absorption or permeation is more likely when there are more than 5 H-bond donors, 10 H-bond acceptors, the Mw is > 500 and the calculated Log P is greater than 5" (Lipinski et al., 2001). (By comparison, for polymeric substances the lower threshold is set at 1,000 Da.)

Notwithstanding, these thresholds should not be interpreted to imply that LMW compounds or LMW polymeric substances are hazardous, merely that they may have internal bioavailability. Further, identifying LMW compounds by their Mw and relative proportion alone disregards the impact of diffusivity and migration from the polymer matrix on their release potential, and hence hazard potential (see Section 3.7.1). This is because gel permeation chromatography to determine LMW content is typically performed with strong organic solvents to solubilise LMW structures. The LMW content determined with such methods will for many polymers not reflect the fraction becoming physically available under environmental conditions.

In conclusion, for LMW polymers and polymer products with proportions of LMW compounds that exceed the PLC thresholds <u>and</u> that can migrate / diffuse from the polymer matrix, the hazard potential needs to be followed up beginning with lower-tier screening.

## 4.3 Reactive functional groups (RFGs)

In the US EPA Polymer Exemption Manual (US EPA, 1997), a reactive functional group (RFG) is defined as "an atom or associated group of atoms in a chemical substance that is intended or can be reasonably anticipated to undergo facile chemical reaction".

As an outcome of the OECD (2009) analysis, three RFGs were identified as indicating increased human health concern (i.e. amino groups, epoxide groups, and unsubstituted positions ortho- to a phenolic hydroxyl) and one RFG as indicating increased ecotoxicological concern (i.e. amino groups). The OECD Expert Group on Polymers noted that the database was insufficient to allow identifying further RFGs (OECD, 2009).

RFGs are generally divided into three categories – low, moderate and high concern – to reflect their relative reactivity. Table 1 presents a collection of RFGs as listed in the Australian, Canadian, and US chemical legislation and guidance (Australian Government, 1990; NICNAS, 2019b; Canada, 2005a, b; US EPA, 1997; see also Appendix B). Notably, this list does not claim comprehensiveness, and the listed RFGs merely constitute structural alerts, but do not *per se* indicate hazard potential. The hazard potential of polymers containing RFGs depends upon e.g. the type of RFG(s), their relative proportion, and their specific location on the repeating units of the polymer.

Accordingly, RFGs should not only be identified, but additionally their 'functional group equivalent weight' (FGEW) should be calculated. The FGEW of resident RFGs is the weight of the polymer that contains one equivalent weight (one mole) of this particular functional group (Canada, 2005a). Consequently, large FGEW values represent polymers having relatively few functional groups (Canada, 2005a). Methods for calculating the FGEW have been published in the *US EPA Polymer Exemption Guidance Manual* (US EPA, 1997; therein Section 5.3); in the *Canadian Guidelines for the Notification and Testing of New Substances: Chemicals and Polymers* (Canada, 2005a; therein Section 3.4.1.5); and on the NICNAS website (NICNAS, 2019b). All FGEW calculations take into account if the polymer is linear or branched and further address e.g. the location of the RFGs on structural repeating units, or if various RFGs in a polymer arise from multiple monomers (US EPA, 1997; Canada, 2005a; Australian Government, 1990; NICNAS, 2019b).

The number of RFGs present in a polymer may determine whether it meets the respective PLC criteria, or not. For example, in accordance with US EPA (1997), polymers containing moderate- or high-concern RFGs can be PLC if each RFG has a FGEW of  $\geq$  1000 Da and  $\geq$  5000 Da, respectively (Table 1). In addition, some RFGs (e.g. carboxylic esters, ethers, amides, urethanes, sulfones and the nitro groups) are not considered to pose moderate or high concern if they have not been modified to enhance reactivity (US EPA, 1997). Similar provisions have been implemented in Canada (Canada, 2005a, b) and Australia (Australian Government, 1990).

As explained by NICNAS (2019b), if a polymer does not meet the cut-off for moderate or high concern RFGs included in the PLC criteria, it can still be considered to be of low concern if sufficient additional information is provided to negate the concern. Such additional information can include relevant toxicological data for the polymer or a suitable analogue. For example, if a polymer contains sulfonyl halide RFGs with a FGEW < 5000 Da, it would not be eligible to be a PLC since sulfonyl halides are potential sensitisers. However, if toxicological tests on this polymer or on a suitable analogue show that the polymer is unlikely to be a sensitiser, NICNAS may still accept it for notification as a PLC (NICNAS, 2019b).

| Concern                  | Low  | Moderate   | High  |
|--------------------------|--|--|---|
| Definition               | Lack reactivity, or low adverse reactivity in a biological setting   | Evidence for biological reactivity, but effects not sufficiently severe to<br>be of high concern<br>Sufficient evidence to establish that RFG is of moderate concern   | Evidence for adverse effects in humans or conclusive evidence<br>of severe effects in animals<br>Where there is no, insufficient, or contradictory information on<br>an RFG, it can be assigned as being of high concern until new<br>evidence enable reappraisal   |
| FGEW<br>threshold<br>[a] | No threshold   | PLC threshold > 1000 Da  | PLC threshold > 5000 Da   |
|                          | In the USA, cut-off limits for combinations of functional groups have also been implemented, and it must be checked if more than one RFG is present in the polymer (Table 2 on p. 16 of US EPA, 1997).   |  |   |
| Examples                 | Aliphatic hydroxyl<br>Blocked isocyanates (including<br>ketoxime blocked isocyanates)<br>Butenedioic acid<br>Carboxylic acid<br>Conjugated olefinic groups (if<br>contained in naturally-occurring<br>fats, oil and carboxylic acids)<br>Halogens (except reactive benzylic<br>or allylic halides)<br>Thiols<br>Unconjugated nitrile<br>Unconjugated olefinic considered<br>ordinary | Acid anhydrides<br>Acid halides<br>Aldehydes<br>Alkoxysilanes bearing alkoxy-groups > C <sub>2</sub> -alkoxysilanes<br>Allyl ethers<br>Conjugates olefinic groups (except those contained in naturally-<br>occurring fats, oils and carboxylic acids)<br>Cyanates<br>Epoxides<br>Hemiacetals<br>Imines (ketimines and aldimines)<br>Methylol-amides<br>Methylol-amines<br>Methylol-ureas<br>Unsubstituted positions ortho and para to phenolic hydroxyl<br>Canada Phase 2 [b]: Structural features, such as ethylene glycol,<br>amines or maleic acid anhydrides, which may be associated with | Alkoxysilanes with alkoxy of C <sub>1</sub> - or C <sub>2</sub> -alkoxysilanes<br>Alpha lactones<br>Amines<br>Aziridines<br>Beta lactones<br>Carbodi-imides<br>Halosilanes<br>Hydrazines<br>Hydrosilanes (as per NICNAS in April 2019 [a])<br>Isocyanates<br>Isothiocyanates<br>Partially hydrolysed acrylamides<br>Pendant acrylates<br>Pendant methacrylates<br>Vinyl sulfones or analogous compounds<br>Other RFGs not in low or moderate concern groups |

#### Table 1. Definitions and examples for reactive functional groups (RFGs) of low, moderate, and high concern

Footnote to Table 1: Table 1 does not claim comprehensiveness. For compliance with the regulatory processes, the respective effective legislation and guidance should be consulted.

[a] As implemented in US EPA (1997); Canada (2005a, b); NICNAS (2019b, c). While the present Technical Report was being finalised in April 2019, NICNAS published expansions to the PLC criteria with immediate effect. Amongst other issues, the lists of moderate- and high-concern RFGs were aligned with those used in USA and Canada; <a href="https://www.nicnas.gov.au/New-scheme-1-July-2020/Early-commencement-whats-already-changed-for-importers-and-manufacturers#criteria">https://www.nicnas.gov.au/New-scheme-1-July-2020/Early-commencement-whats-already-changed-for-importers-and-manufacturers#criteria</a>. In this update of the PLC criteria, NICNAS further lists azo groups, disulfides, and trithiocarbonates as high-concern RFGs.

[b] Final Screening Assessment for the Second Phase of Polymer Rapid Screening (Canada, 2018b); see also <u>https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/second-polymer-rapid-screening.html</u>.

## 4.3.1 ECETOC Polymers TF appraisal of 'presence of RFGs' as PLC exclusion criterion

The TF is unaware of any published scientific studies assessing if and when polymers containing specific RFGs elicit hazardous effects, or not. A comprehensive database would be required for such a profound scientific analysis of the hazard potential of RFG-containing polymers (see also Section 4.1.1).

The identification that a specific structural alert is present on a polymer should not *per se* lead to the conclusion that it is hazardous, but merely trigger lower-tier screening using e.g. read-across, *in vitro* assays, *in silico* tools; algae and/or invertebrates, as applicable. If the structural alert is not present on the polymeric substance in a form that it can be presented biologically, there should be no hazard concern. Only if the lower-tier screening (together with an evaluation of all available data for the given polymer and similar ones, as applicable) indicates hazard potential, the TF considers higher-tier *in vivo* testing justifiable. Further, all *in vitro* and *in vivo* testing should be selected to reflect the likely relevant endpoint / molecular initiating event / MoA of the polymer as indicated by the respective RFG(s).

The TF considers the calculation of FGEWs to be a pragmatic approach to pre-select if a polymer containing RFGs should be screened for hazard potential. Notwithstanding, again, the TF is unaware of any scientific evidence underlying the FGEW thresholds of 1,000 Da and 5,000 Da for moderate- and high-concern RFGs, respectively, or the need to consider further parameters (in addition to polymer structure, location of the RFGs, etc.) in calculating FGEWs.

## 4.4 Presence of specific chemical elements

In different jurisdictions, the presence of specific elements in the polymer has been implemented as PLC exclusion criterion. For example, Section 4.2.2 of the *US EPA Polymer Exemption Guidance Manual* (US EPA, 1997) states that a polymer that shall be considered a PLC (and therefore be exempt from the requirement to undergo the full pre-manufacture notification (PMN) review process):

"must contain as an integral part of its composition at least two of the atomic elements of carbon, hydrogen, nitrogen, oxygen, sulfur, or silicon (C, H, N, O, S, Si). In addition to the six elements listed above, only certain other elements are permitted either as counterions or as an integral part of the polymer. These additional elements are as follows: fluorine, chlorine, bromine and iodine (F, Cl, Br and I) when covalently bonded to carbon, and the monatomic counterions chloride, bromide, and iodide (Cl<sup>-</sup>, Br and I<sup>-</sup>). The fluoride anion, (F<sup>-</sup>) is not permitted... Other permitted monatomic cations are sodium, magnesium, aluminum, potassium, and calcium (Na<sup>+</sup>, Mg<sup>2+</sup>, Al<sup>3+</sup>, K<sup>+</sup> and Ca<sup>2+</sup>). Allowed at less than 0.20 weight% total (in any combination) are the atomic elements lithium, boron, phosphorus, titanium, manganese, iron, nickel, copper, zinc, tin and zirconium (Li, B, P, Ti, Mn, Fe, Ni, Cu, Zn, Sn, and Zr). No other elements are permitted, except as impurities."

Similar provisions have been implemented in Canada (Canada, 2005a, b) and Australia (Australian Government, 1990).

# 4.4.1 ECETOC Polymers TF appraisal of 'presence of specific chemical elements' as PLC exclusion criterion

While the presence of specific elements (e.g. heavy metals) either as counterions or as an integral part of the polymer generally exempts a polymer from being a PLC, the TF is of the opinion that, just as stands true for the presence of RFGs, the chemical composition of the polymeric substance should not *per se* be taken as indicating hazard potential. Instead, this should be taken as trigger for concern that needs to be followed by lower-tier screening (using e.g. read-across, *in vitro* assays, *in silico* tools; algae and/or invertebrates, as applicable) if no data are available.

Further, the TF is unaware of scientific reviews addressing the circumstances under which polymeric substances containing specific chemical elements are, or are not, hazardous. Again, this topic merits further investigation to allow substantiating this PLC exclusion criterion, or amending it as necessary.

## **4.4.2** Presence of fluorine atoms

Fluoropolymers are polymers containing fluorine atoms in their chemical structures. They are called perfluoropolymers, when all hydrogen atoms in the analogous hydrocarbon polymers structures are replaced by fluorine atoms, and partially fluorinated polymers, when both hydrogen and fluorine atoms are present, possibly along with additional elements (Teng, 2012).

Fluoropolymers are a sub-group of the per- and polyfluoroalkyl substances (PFAS) (Henry et al., 2018). PFAS, and specifically perfluorooctane sulfonate and perfluorooctanoic acid, have become a matter of regulatory and public concern due to their poor biodegradation resulting in environmental bioaccumulation and ultimately human health concerns (Kotthoff et al., 2015; CDC, 2017). The OECD has dedicated a portal to per- and polyfluorinated substances focusing specifically on PFAS "*in order to support a global transition towards safer alternatives*"; http://www.oecd.org/chemicalsafety/portal-perfluorinated-chemicals/.

Since 2010, the US EPA no longer generally considers fluoropolymers as not presenting an unreasonable risk and amended the polymer exemption rule accordingly (US EPA, 2010). Polymers containing specific perfluoroalkyl moieties are not eligible for PLC exemption from the PMN review process (US EPA, 2019a). In Japan, fluoro groups are designated as RFGs preventing a polymer from being a PLC.

# 4.4.3 ECETOC Polymers TF appraisal of 'presence of fluorine atoms' as PLC exclusion criterion

ECETOC and its member companies are dedicated to protecting humans and the environment from unwanted effects elicited by chemicals. At the same time, the ECETOC Polymers TF is unaware of scientific evidence to justify generally assigning fluoropolymers the same level of regulatory concern as other PFAS chemicals. The family of fluoropolymers covers a wide range of different types of polymers that do not necessarily pose any hazard concern. This is exemplified by a comprehensive review of stable, HMW fluoropolymers without other functional groups showing that these fluoropolymers meet all PLC criteria (Henry et al., 2018):

"Fluoropolymers, high Mw polymers, have unique properties that constitute a distinct class within the PFAS group. Fluoropolymers have thermal, chemical, photochemical, hydrolytic, oxidative, and biological stability.

They have negligible residual monomer and oligomer content and low to no leachables. Fluoropolymers are practically insoluble in water and not subject to long-range transport. With a Mw well over 100,000 Da, fluoropolymers cannot cross the cell membrane. Fluoropolymers are not bioavailable or bioaccumulative, as evidenced by toxicology studies on PTFE [...] Clinical studies of patients receiving permanently implanted PTFE cardiovascular medical devices demonstrate no chronic toxicity or carcinogenicity and no reproductive, developmental, or endocrine toxicity. [...] fluoropolymers satisfy widely accepted assessment criteria to be considered as PLC. [...] Grouping fluoropolymers with all classes of PFAS for 'read across' or structure–activity relationship assessment is not scientifically appropriate" (Henry et al., 2018).

This example shows that the hazard potential of fluoropolymers needs to be assessed on a case-by-case basis taking into account all relevant physical, chemical, and fate properties. In addition, further investigations are merited to evaluate if the hazard potential of fluoropolymers that do pose concern is truly driven by the fluorogroups present on the polymeric substance, or rather by other more reactive, surfactant-type groups.

# 4.5 (Bio)degradation, decomposition, depolymerisation

In accordance with Section 4.2.3 of the US EPA Polymer Exemption Manual (US EPA, 1997), a polymer is not eligible for PLC exemption from the PMN review process if it is "designed or reasonably anticipated to substantially degrade, decompose, or depolymerize including those polymers that could substantially decompose after manufacture and use, even though they are not actually intended to do so".

Degradation, decomposition, or depolymerisation are defined as: "A type of chemical change in which a polymeric substance breaks down into simpler, smaller weight substances as the result of (for example) oxidation, hydrolysis, heat, sunlight, attack by solvents or microbial action" (US EPA, 1997).

Similar provisions have been implemented in Canada (Canada, 2005a, b). Canada (2005a) further generally requests providing data from the ready biodegradability test. (The applicability of this test method for the assessment of polymers is being addressed in the planned ECETOC TR 133-2.)

In NICNAS (2019b), it is stated:

"A PLC must be a polymer that is stable under the conditions in which it is used.

A polymer is not eligible to be a PLC if it readily breaks down by any process under the conditions in which it is used throughout its lifecycle. This includes break down by any process where the polymeric substance readily breaks down into simpler, smaller weight substances as the result of, but not limited to, oxidation, hydrolysis, heat, sunlight, attack by solvents or microbial action.

Examples of polymers that would not meet this criterion include those that:

- are designed to be pyrolysed or burnt during normal use;
- are explosive;
- substantially biodegrade in the environment (for example, starch);
- are hydrolytically unstable ( $t_{1/2} < 12$  hours).

Note: A polymer may still be eligible as a PLC despite its potential to readily break down in the environment if under the conditions in which it is used substantial degradation would not be expected to occur. For example,

polymers used in cements, adhesives, hot melts, and extrusion molding would be eligible as a PLC as the polymer would be expected to be protected from environmental degradation."

By contrast, Section 4.2.3 of US EPA (1997) does not specify any timeframe for (bio)degradation, i.e. any threshold (half-life) below which a (bio)degradable polymer would still be eligible for the PLC exemption from the PMN review process. However, in Section 7 of the US EPA manual (Common questions and answers), questions 9-16 relate to polymer degradation, and questions 9, 11 and 12 include considerations on timeframes:

"9. What is the time frame for "polymers that do not degrade, decompose or depolymerize?" Does EPA want us to synthesize polymers that bioaccumulate in the environment? Does the term "degrade" apply to biodegradation or other degradation in waste treatment systems? - This restriction is essentially unchanged from the 1984 polymer exemption. While EPA recognizes in principle the beneficial effects of biodegradability, it commented in the discussion section of that rule that the Agency "...has little experience reviewing the mechanism by which breakdown may occur, the decomposition products that may result, and the potential uses of such polymers. ... Because of the complexity of review necessary for many of these polymers and the lack of EPA review experience, the Agency did not believe that an expedited review period was sufficient to adequately characterise risk." The Agency acknowledged in that discussion that essentially all polymers degrade or decompose to a limited degree over time. It gave as examples the normal fate of polymers in landfills and the weathering of paint, and specifically stated that the exclusion was not intended to address such degradation. Substantial biodegradation in a waste treatment system would render a polymer ineligible for the exemption."

"11. Starch is a polymer that readily degrades in the environment. If it were not listed on the TSCA Inventory, would starch be eligible for the exemption? - No; polymers that readily degrade are excluded from the exemption."

"12. What does the Agency mean by "substantially" in the phrase "substantially degrade..."? Does this refer to any specific conditions (e.g., sunlight, water, low pressure) or under normal environmental conditions? - By "substantially," the Agency means considerably; meaningfully; to a significantly large extent. The restriction refers to polymers that undergo considerable degradation, under normally anticipated conditions of use or disposal, and in a reasonable length of time."

## 4.5.1 ECETOC Polymers TF appraisal of '(bio)degradation' as PLC exclusion criterion

The TF considers that the provisions of the US EPA Polymer Exemption Manual (US EPA, 1997), including the further information provided in the questions and answers section do not serve to clarify how potential concerns related to polymer (bio)degradation should be addressed. The answer to question 9 indicates that the provisions from Section 4.2.3 of US EPA (1997), that generally exclude all (bio)degradable polymers from being PLC, are founded on a lack of review experience. The answer to question 11 states that the US EPA does not consider starch a PLC. Above all, the answer to question 12 does not provide further clarity: The asked for term 'substantial' – which would need to be clearly defined – is explained by equally unspecific terms, i.e. 'considerable', 'meaningful', and 'significantly large extent', none of which are defined. In conclusion, US EPA (1997) does not specify a threshold above which (bio)degradation should be assessed as 'considerable', as 'not readily', or as not occurring in a 'reasonable length of time', it does not specify the appropriate duration of

biodegradation studies, and it further does not distinguish between intended and unintended (bio)degradation.

While the recent update of the NICNAS PLC website does include one threshold (i.e. a half-life of < 12 hours for hydrolysis), these NICNAS provisions remain unspecific for (bio)degradation by other processes. Also, the TF considers the exemptions from the PLC exclusion related to conditions of use under which substantial degradation would not be expected to occur to be difficult to apply from a chemical management perspective since many polymers have broad spectra of uses.

The TF is of the opinion that polymers that can (bio)degrade should not *per se* be considered as posing a hazard concern. Polymer (bio)degradation is complex, and this complexity needs to be addressed during polymer RA.

First, all considerations on polymer (bio)degradation should distinguish between physical degradation (induced by heat, irradiation, etc.), chemical degradation (induced by the presence of specific acids, bases, or oxidative agents, etc.), hydrolytic and biological degradation (induced by the presence of specific microorganisms) (Doyle et al., 1982; Leja and Lewandowicz, 2010).

Second, it should be considered if (bio)degradation is intentional or unintentional and at which life cycle stage of the polymer it might occur. Some polymers are specifically designed to intentionally (physically, chemically, or biologically) degrade at a certain life cycle stage, and some are manufactured to be resistant to physical, chemical, and/or biological degradation. Other polymers can exhibit unintended physical degradation under certain environmental conditions (increased temperature, etc.) and/or with increasing age; or they intentionally biodegrade during end-of-life stages, e.g. during waste disposal. Indeed, biodegradation during waste disposal is a desirable trait – to prevent long-term exposure.

Third, for polymers that (bio)degrade either during intended uses or during disposal, the timeframe of (bio)degradation, the type and quantity of resulting breakdown products, as well as their fate, needs to be considered on a case-by-case basis. A broad spectrum of breakdown products can result from polymer (bio)degradation, many of which do not pose fate or hazard concerns, and in general, polymers do not degrade into their monomeric units. Polymers intended for biodegradation can also show full mineralisation.

This overview underlines the complexity of polymer (bio)degradation. Polymer (bio)degradation should be assessed on a case-by-case basis taking into account the relevant life cycle stage included in the RA scope, whether (bio)degradation is intentional or not, the timeframe of (bio)degradation, and the type, quantity, fate and hazard potential of breakdown products.

Understanding the (bio)degradation of any polymer in the environmental compartments of concern is critical to an environmental exposure evaluation. Some polymers are known to be completely mineralised in the environment after use. If polymers do break down in the environment but do not completely mineralise, it is important to understand the degradation products and evaluate their safety.

## 4.6 Water solubility and extractability

In the OECD data analysis, polymer <u>water solubility</u> ranging from 10 to 10,000 mg/L was identified as indicating increased human health concern (OECD, 2009). Similarly, the OECD website (<u>http://www.oecd.org/env/ehs/oecddefinitionofpolymer.htm</u>) refers to <u>extractability in water</u> as PLC

criterion, stating "10 mg/L was seen as acceptable, provided that test conditions were standardized" (see Section 4.1). These two statements highlight the need to define water solubility and related terms (Box 8).

#### Box 8: Definitions for water solubility and related terms

Dispersion: The distribution of a solid material in a suspending medium (adapted from Arts et al., 2015).

**Dissolution rate:** As compared to solubility, the dissolution rate is a kinetic parameter describing the time-dependent dissolution of a material in water (or other solvents) (adapted from Arts et al., 2015).

**Emulsion:** A mixture of two or more liquids where one is present as microscopic, or ultramicroscopic droplets distributed throughout the other (adapted from <u>https://www.britannica.com/science/emulsion-chemistry</u>).

**Hydrolysis**: A chemical process of decomposition involving the splitting of a bond and the addition of the hydrogen cation and the hydroxide anion of water; <u>https://www.merriam-webster.com/dictionary/hydrolysis</u>.

**Surface activity**: The alteration of properties and especially lowering of the tension at the surface of contact between phases (adapted from <u>https://www.merriam-webster.com/dictionary/surface-active</u>).

**Swelling**: The process of absorbing water. A water-absorbing polymer is capable of absorbing its weight in water (US EPA, 1997); see Section 4.9 of the present Technical Report.

Water availability: The capacity of forming stable emulsions or dispersions (EC, 2009); see also definitions for emulsion and dispersion.

Water extractability / extractivity: The preferable extraction of some molecules in water leaving others remaining within the bulk substance (adapted from EC (2009).

**Water solubility**: The saturation mass concentration of a substance in water at a given temperature (OECD, 1995); the maximum mass of a material that is found in molecularly dissolved state in a given volume of water containing a particulate material under specific conditions (adapted from Arts et al., 2015).

Usually, polymer water solubility decreases with increasing Mw and/or decreasing concentration of RFGs (Cefic and PlasticsEurope, 2014). In many jurisdictions, polymers with significant solubility in water are viewed as having higher potential for environmental concern than insoluble ones e.g. due to the increased physical availability of potentially hazardous LMW components (OECD, 2009). On the other hand, water solubility may be a pre-requisite for biodegradability of a polymer and therefore one aspect to consider in addressing polymer (bio)degradation and decomposition (Section 4.5).

In the *Canadian New Substances Notification Regulations (Chemicals and Polymers)* (NSNR (C&P); Canada, 2005b), Schedules 10 and 11 (relating to the information requirements for non-PLC polymers with production volumes of at least 10,000 kg; see Appendix B, 2.3.1, of the present Technical Report) require that polymer water extractability is measured. If the measured water extractability exceeds 2%, the hydrolysis rate of the polymer should be determined as a function of pH and the products of the hydrolysis identified, as applicable (Canada, 2005b).

With respect to this threshold, Environment Canada (EC, 2009) explains that "polymers with less than 2% water extractability are generally considered of low bioavailability in the aquatic environment, which is a factor in determining the risk the substance may pose to human health and the Canadian environment."

Environment Canada (EC, 2009), referring to OECD TG 120 (*Solution / extraction behaviour of polymers in water*), highlight the distinction between solubility and extractability:

"Ideally, an aqueous polymer solution would be described as a uniform distribution of a macromolecular solute in water. In practice, an aqueous polymer system is not necessarily representative of the initial polymer, because water can preferentially extract some molecules, leaving others remaining within the polymer bulk.

Dissolution of polymers generally involves the following steps:

- a. **Permeation/diffusion of water molecules into the polymer bulk:** The process of dissolving a polymer begins with water molecules permeating its surface.
- b. **Swelling of the polymer bulk:** The swelling starts at the surface and, if water molecules are able to penetrate further, continues into the bulk of the polymer.
- c. **Detachment of molecules from the polymer bulk:** During the process of swelling, some low-molecularweight molecules may detach from the bulk and diffuse into the water phase. However, if the polymer is cross-linked, the swelling may only result in a gel formation."

# 4.6.1 ECETOC Polymers TF appraisal of 'water solubility / extractability' as modifying factors for polymer hazard assessment

While systemic bioavailability will typically be low for highly hydrophilic molecules, water solubility and extractability are closely linked to physical availability and external bioavailability to aquatic species (Section 3.7.1.1). Water solubility or water extractability of a polymer cannot be interpreted to imply that the polymer is hazardous, merely that relevant exposure to aquatic species is more likely (especially if the aquatic compartment is identified for potential exposure). Notwithstanding, a lack of water solubility /extractability can mitigate aquatic hazard potential of polymers containing RFGs or cationic groups, as also reflected in e.g. the US EPA PLC criteria (Section 4.7).

## 4.7 Cationicity

Cationic polymers have "one or more monomer units that are covalently bound and bear a net positive charge" (Canada, 2005b). Nitrogen groups (e.g. quaternary nitrogen atoms (Jaeger et al., 2010)) are the most common cause of cationicity in polymers, and available data show that aquatic toxicity is related to the charge density of the polymer (US EPA, 2015). Dissolved cationic polymers are extremely polar, not volatile, not chelatable and not extensively filterable (Norberg-King et al. (2005); citing Rowland et al. (2000)).

Generally, all non-EU jurisdictions have implemented a PLC exclusion criterion for cationic polymers (and/or polymers likely to become cationic at specific pH values). This is justified by concerns for aquatic toxicity, e.g. *"cationic polymers and polymers reasonably anticipated to become cationic in a natural aquatic environment are not eligible as PLCs. The main concern is their toxicity towards aquatic organisms such as fish and algae"* (NICNAS, 2019b).

Specific cationic polymers may nevertheless meet the criteria for PLC. For example, in the US EPA Polymer Exemption Manual (US EPA, 1997) these are:

- "Cationic or potentially cationic polymers that are solids, are neither water soluble nor dispersible in water, are only to be used in the solid phase, and are not excluded from exemption by other factors; and
- Cationic or potentially cationic polymers with low cationic density (the percent of cationic or potentially cationic species with respect to the overall weight of polymer) which would not be excluded from the exemption by other factors.

For a polymer to be considered to have low cationic density, the concentration of cationic functional groups is limited to a FGEW of  $\geq$  5,000 Da."

Similar provisions have been implemented in Australian Government (1990) and Canada (2005b).

## 4.7.1 ECETOC Polymers TF appraisal of 'cationicity' as PLC exclusion criterion

For water-soluble or dispersible cationic polymers or polymers that are not only used in the solid phase, the TF considers the calculation of FGEWs for cationic density to be a pragmatic approach to pre-select if the polymer should be screened for hazard potential. Notwithstanding, again, the TF is unaware of the scientific evidence underlying the < 5,000 Da FGEW threshold for high cationic density or of any comprehensive scientific review addressing under which circumstances cationic polymers undercutting the FGEW threshold are, or are not, hazardous.

If the FGEW for cationic density of a water-soluble or dispersible polymer undercuts the 5,000 Da FGEW threshold, the TF is of the opinion that, just as stands true for the presence of RFGs (Section 4.3) or specific chemical elements (Section 4.4), this should not *per se* be taken as indicating aquatic toxicity (or any other toxicity). Instead, cationic density with FGEW < 5,000 Da should be taken as a trigger to initiate lower-tier screening if no data are available.

In summary, the (eco)toxicological impact of cationic polymers merits further investigation. An ongoing Cefic LRI project aims at improving the understanding of the specific physico-chemical properties of these materials that will (or will not) result in a concern for aquatic toxicity (Box 9).

Box 9: Cefic LRI project Improved Aquatic Toxicity and Assessment of Polymers (ITAP)

http://cefic-lri.org/projects/eco-46-improved-aquatic-testing-and-assessment-of-cationic-polymers-itap/

The Cefic LRI project ECO46 entitled *Improved Aquatic Toxicity and Assessment of Polymers (ITAP)* is aiming at improving the aquatic toxicity testing and eventual RA of cationic polymers. The project focuses on a group of closely related model cationic polymers, that are widely used in industry, to determine if these model cationic polymers continue the trends established in quantitative structure-activity relationships of higher nitrogen-containing polymers. This shall serve to generalise physico-chemical and (eco)toxicological patterns. The ITAP project will also add and build to the knowledge base of aquatic effects data by studying algae, cyanobacteria, *Daphnia magna* and fish embryo toxicity. Other key deliverables are to provide recommendations on methods to appropriately monitor bioavailability, and on mitigation factors to be used for deriving aquatic predicted no-effect concentrations (PNECs) from tests run with well-characterised river water or organic carbon amendments.

# 4.8 Surface activity and anionicity / amphotericity

Surface-active polymers, or polymeric surfactants, can be built as graft copolymers with hydrophobic chains grafted to a hydrophilic backbone or *vice versa*, or as block copolymers with alternating hydrophilic and hydrophobic segments (Kronberg et al., 2014).

In accordance with Article 6(2) of the EU Detergents Regulation (EP and Council, 2004b), a surfactant is defined as "any organic substance and/or preparation used in detergents, which has surface-active properties and which consists of one or more hydrophilic and one or more hydrophobic groups of such a nature and size that it is capable of reducing the surface tension of water, and of forming spreading or adsorption monolayers at the water- air interface, and of forming emulsions and/or microemulsions and/or micelles, and of adsorption at water-solid interfaces".

Environment Canada (EC, 2009) describes the physical properties of surface-active polymers: "In some cases, surface-active polymers can form colloidal dispersions (solid polymers) or emulsions (liquid polymers). The size of the dispersed particles is generally between 1 nm and 1  $\mu$ m in diameter. Although some colloidal dispersions are inherently stable, polymer dispersions often need to be stabilized. Providing water extractability data is not necessary for surface-active polymers and polymers formulated in water and marketed as such, since they will be assumed to be completely water-available."

In the US EPA Interpretative Assistance Document for the Assessment of Polymers (US EPA, 2013), surface activity and non-ionicity / ionicity (anionicity and amphotericity) are jointly addressed in establishing levels of concern for aquatic hazard potential. Nonionic polymers are generally considered to be of low concern for aquatic hazard, due to negligible water solubility, except for "nonionic polymers that have monomers blocked in such a way as to use the polymer as a surfactant or dispersant, which may cause toxicity to aquatic organisms" (US EPA, 2013).

Further, US EPA (2013) describes the environmental hazard concerns for anionic polymers:

"Anionic polymers – Polyanionic polymers with NAMW > 1,000 that are soluble or dispersible in water may pose a concern for direct or indirect toxicity. These polymers are further divided into 2 subclasses: Poly (aromatic acids) and Poly(aliphatic acids).

Poly(aromatic acids) – These chemicals are usually poly(aromatic sulfate/carboxylate) [presumably, 'sulfate' should read 'sulfonate'] structures and generally are of moderate hazard concern to aquatic organisms, with acute  $LC_{50}/EC_{50}$  values between 1 mg/L and 100 mg/L, depending upon the exact structure of the polymer. Monomers associated with toxicity include: carboxylated sulfonated diphenolsulfones, sulfonated phenols, sulfonated cresols, sulfonated diphenylsulfones, and sulfonated diphenylethers. Monomers usually associated with low aquatic toxicity concern include: sulfonated naphthalene and sulfonated benzene. The toxicity of this type of polymer appears to be moderate and not affected by water hardness...

Poly (aliphatic acids) – This type of polymer is made up of repeating carboxylic acid, sulfonic acid, and/or phosphinic acid monomers. At pH 7 this polymer type generally exhibits low toxicity toward fish and daphnid, with  $LC_{50}$  values >100 mg/L. However, there may be toxicity hazard concerns for green algae; toxicity to algae is believed to arise from chelation of nutrients. The toxicity of this type of polymer can be assumed to be low for fish and daphnid... The toxicity is highly dependent on the structure of the polymer, with space between repeating acid units and addition of non-chelating groups affecting toxicity... Water hardness has been shown to mitigate the toxicity of poly (aliphatic acid) polymers to green algae..."

With respect to amphoteric polymers, US EPA (2013) writes:

"These polymers contain both positive and negative charges in the same polymer. The toxicity of these polymers is dependent on cation-to-anion ratio and the overall cationic charge density. Toxicity increases with cationic charge density and, when charge density is constant, increases with cation-to-anion ratio. The toxicity of these polymers may be reduced by a toxicity reduction factor calculated for each endpoint... If a polymer has a structure similar to that of amphoteric surfactants, the toxicity of the polymer may be assessed based on information available for such surfactants."

Finally, US EPA (2013) describes how polymer ionicity can affect environmental fate properties. For cationic, amphoteric, and nonionic polymers, it is stated that they will generally absorb strongly to soil and sediment, whereas for anionic polymers, it is stated that they usually have low sorption to soil, but that, due to large size and weight parameters, they may still have low mobility in soil.

# 4.8.1 ECETOC Polymers TF appraisal of 'surface activity' and/or 'anionicity / amphotericity' as potential elements for polymer hazard assessment

The evidence for generally higher hazard potential of anionic polymers is weak. For example, polycarboxylates are a group of anionic polymers of low hazard. Hazardous anionic polymers often have surfactant properties according to the experience of the TF. Hence, it might be hypothesised that surface activity is a more precise alert than presence of anionic groups. This is an area where further analyses of datasets will be helpful.

The aquatic concerns related to polymeric surfactants should be assessed on a case-by-case basis (Lechuga et al., 2016). With respect to human health hazard assessment, the potential for local or systemic toxicity of polymeric surfactants may not be driven by the degree of surface activity alone, but by the presence of specific RFGs (Matsuda et al., 2009), physico-chemical properties and chain length. Some surface-active polymers show good ocular tolerance regardless of the concentration and emulsifying properties (Baydoun et al., 2004). Just as stands true for non-polymeric surfactants, the eye or skin irritation potential of surface-active polymers has to be assessed on a case-by-case basis. In the context of the EU Detergents Regulation (EP and Council, 2004b), the "international trade tariff value" of 45 mN/m reduction in surface tension was chosen to identify surfactants in general (European Commission, 2018c). Research work is merited to evaluate if this regulatory threshold would qualify as a criterion to distinguish potentially eye / skin irritating surfactant polymers from PLC.

## 4.9 Water-absorption

As defined in the US EPA Polymer Exemption Guidance Manual (US EPA, 1997), a water-absorbing (swellable) polymer is "a polymeric substance that is capable of absorbing its weight of water." In accordance with Section 4.2.5 of US EPA (1997), water-absorbing polymers with NAMW  $\geq$  10,000 Da are excluded from the PMN exemption.

The US EPA applies polymer swellability, in combination with (in)solubility and HMW (> 10,000 Da), as key parameters to assign polymers to one of three categories with different levels of inhalation toxicity concern;

https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/high-molecularweight-polymers-new:

**1. Soluble HMW polymers:** "As these are expected to rapidly clear the respiratory tract and not cause pulmonary overloading, no additional testing is required beyond the proof of solubility and those endpoints required to meet other regulatory requirements (e.g. depending on exposure, functional groups, etc.)."

**2. Insoluble, non-swellable HMW polymers:** "Although exempt from TSCA notification, if a company chooses to submit a PMN and the polymer meets specific exposure criteria, the US EPA may require inhalation toxicity testing or additional personal protective equipment. Attention will also be given to the presence of ultrafine particles."

**3. Insoluble, swellable HMW polymers:** "Especially if the polymer absorbs its own weight or more in water, it is not eligible for the polymer exemption, but is subject to full PMN submission, with emphasis on inhalation exposure and risk."

Hence, the highest concern for inhalation toxicity potential is assigned to insoluble, swellable HMW polymers. On the above- mentioned US EPA website, it is stated: "*This concern is based on a study (designated TSCA 8(e)-0668) which reported irreversible lung damage with inhalation of respirable particles of water-insoluble polymers (toner in copy machines) of Mw 70,000 Da or greater*".

The US EPA website provides no details on the animal species or strain used in this study, or on the applied dosage, exposure period, parameters addressed, histopathological findings, etc. The website also does not provide any reference details allowing to retrace the study. A Google search for *"TSCA 8(e)-0668"* conducted in February 2019 revealed three study summaries with the numbering *"TSCA Section 8(E) .... -0668)"* presented in Cheremisinoff (1994). All three summaries refer to *'Xerox 9000-type* photocopying toner' as test material.

<u>1. Chronic inhalation study, June 1987, Fischer 344 rats, aerosol concentrations 1.0, 4.0, 16.0 mg/m<sup>3</sup></u>: "No unusual histopathological findings except the 16 mg/m<sup>3</sup> group showed increase in collagen, possibly result of artefact associated with thickly cut histologic sections, and increased lung weight, retention of test material, and retardation of alveolar macrophage mediated clearance. Toner material used enriched ten-fold in respirable size particles with respect to commercially available toner material" (Cheremisinoff, 1994).

<u>2. Sub-chronic inhalation study, June 1987, Fischer 344 rats, 1.0, 4.0, 16.0, 64.0 mg/m<sup>3</sup>: "Increase in lung</u> weight observed at 16 and 64 mg/m<sup>3</sup> dose levels. At 64 mg/m<sup>3</sup>, food consumption in both male and female rats slightly decreased, but body weight not affected. Dose-related increase in particle-laden alveolar macrophages. Thickening of alveolar walls observed in high exposure groups. ...maximum lung burden for which macrophage-mediated lung clearance not significantly impaired exceeded 64 mg/m<sup>3</sup> exposure level" (Cheremisinoff, 1994).

<u>3. December 1989, no study details (possibly concatenation of results from above two studies)</u>: "Absence of systemic or upper respiratory system toxicity, coupled with changes in lungs or lymph nodes in chronic toner inhalation study in rats showed respiratory system target organ and pulmonary changes attributed to 'lung overloading', a generic response of respiratory system to excessive amounts of dust retained in lungs for prolonged interval. Exposure at high level resulted in exceeding lung overloading with chronic and persistent inflammatory response in rat lung. Exposure at low level resulted in below lung overloading transient and reversible inflammatory response in rat lung" (Cheremisinoff, 1994).

In addition to the reference to the study designated TSCA 8(e)-0668, the above-mentioned US EPA website refers to four *"other references"*. The TF has evaluated their contents in view of informing on the hazard concerns for polymers that are insoluble and water-absorbing and HMW.

<u>1. Morrow et al. (1991)</u>: This is a review on pulmonary overload in rats and the derivation of occupational exposure limits for dusts, without evident focus on polymers, HMW, or substance swellability.

<u>2. Muhle et al. (1991)</u>: This is publication of a chronic inhalation study of a special Xerox 9000 type xerographic toner (0, 1.0, 4.0, 16.0 mg/m<sup>3</sup>). TiO<sub>2</sub> (5 mg/m<sup>3</sup>) and crystalline SiO<sub>2</sub> (1 mg/m<sup>3</sup>) were used as negative and positive controls: "*The incidence of primary lung tumors was comparable among the three toner-exposed groups and the TiO<sub>2</sub>-exposed, and air-only controls, as well as consistent with historical background levels. A mild to moderate degree of lung fibrosis was observed in 92% of the rats in the toner high-exposure group, and a minimal to mild degree of fibrosis was noted in 22% of the animals in the toner middle-exposure group. The pulmonary changes in the toner high-exposure group were smaller in magnitude than those found in the crystalline silica-exposed group. The comparative fibrogenic potency of TiO<sub>2</sub>, toner, and SiO<sub>2</sub> was estimated to be 1:5:418 using a dosimetric model and assuming a common mechanistic basis. There were no pulmonary changes of any type at the toner low-exposure level, which is most relevant in regard to potential human exposures. The lung alterations in the toner high-exposure group are interpreted in terms of "lung overloading," a generic response of the respiratory system to saturation of its detoxification capacity..." (Muhle et al., 1991).* 

<u>3. Bellmann et al. (1991):</u> This article refers to the same study (design) as Muhle et al. (1991) and describes measurement of pulmonary retention of toner and control materials after 3-24 months of exposure: *"The quantity of all three materials retained in the lungs and lung-associated lymph nodes increased with exposure duration and level. The final pulmonary burdens of toner at the three exposure levels were 0.22, 1.73, and 15.6 mg/lung, respectively. Alveolar clearance of both tracers was substantially impaired at the toner high-exposure level, and moderately slowed at the toner middle-exposure level. The excessive quantity of toner retained and the substantially retarded clearance in the toner high-exposure group are indicative of 'lung overloading'."* 

<u>4. Mermelstein et al. (1992)</u>: This is an abstract from a presentation held at the 1992 US Society of Toxicology Meeting. The online database of the proceedings from these meetings only begins in 2003 (<u>https://www.toxicology.org/application/ToxicologistDB/index.aspx</u>). Therefore, the TF is unable to retrace the details of this abstract (or the underlying study).

At the very bottom of the above-mentioned US EPA website it is further stated that concerns regarding swellable polymers are based on a study on polyacrylate absorbents (numbered TSCA 8(e)-1795) which indicated that "*HMW polyacrylate polymers caused lung neoplasms in animal studies*".

Since the US EPA website provides no further details on this study, the following search query was conducted in the US National Library of Medicine – National Institutes of Health database PubMed (<u>https://www.ncbi.nlm.nih.gov/pubmed/</u>): "polyacrylate polymer (lung OR pulmonary) (tumor OR tumour OR cancer OR \*carcinom\*)". This search yielded three retrievals on 5 March 2019. None of these articles addressed the *in vivo* inhalation toxicity potential (or *in vitro* cellular toxicity) of polyacrylate polymers. However, a Google search using the phrase "polyacrylate polymers caused lung neoplasms in animal studies" retrieved a research article by Warheit et al. (2001).

<u>Warheit et al. (2001)</u> reported that 2-year application of 0.2 and 0.8 mg/m<sup>3</sup> polyacrylate dust resulted in a 3.6% and 30% incidence of lung tumours, respectively. Since polyacrylate polymers are generally not respirable (**Warheit et al. refer to < 0.1% respirable material**), the polyacrylate material "*was ground into particles of approximately 2 µm for these studies*". Warheit et al. indicated that this was a study from the Institute for

Polyacrylate Absorbents. A Google search for "TSCA 8(e)-1795" also yielded a reference to a chronic inhalation study on polyacrylate polymers submitted by the Institute for Polyacrylate Absorbents<sup>8</sup>.

# 4.9.1 ECETOC Polymer TF appraisal of special provisions related to insoluble, swellable, HMW polymers:

The TF is of the opinion that neither the statements on the US EPA website, nor the scientific studies retrieved provide strong evidence for how polymer solubility/insolubility, swellability, or HMW (let alone a combination of these parameters) correlate with the inhalation toxicity potential of polymers. The studies assessing the photocopying toner demonstrate substance-unspecific physical overload reactions. Such reactions are generally observed in rats upon long-term exposure to high aerosol concentrations of poorly soluble particles, regardless of the swellability of the particles – but conditional to their inhalability (as shown in the study by Warheit et al., 2001). The human health relevance of pulmonary overload conditions observed in rats has been questioned (ECETOC, 2013b).

Since the US EPA website does not provide clear references for the 'TSCA 8(e)-0668' studies, the TF is unable to establish with certainty that the studies reported by Cheremisinoff (1994) are indeed the studies referred to on the above-mentioned US EPA website. Notwithstanding, as also indicated on the US EPA website, a single test material was applied in these studies, i.e. 'Xerox 9000-type photocopying toner'. The powder of this toner contains approx. 90% random copolymer with a Mw of approx. 70,000 Da (composed of 58% styrene and 42% 1-butylmethacrylate) and approx. 10% high purity, medium colour furnace type carbon black (Muhle et al., 1991). Concordantly, the US EPA website refers to a 'toner in copy machines' as having been assessed. Hence, these studies merely inform on the pulmonary hazard potential of an **article (mixture) containing polymers**. Any observed effects might also be caused by its further component, i.e. carbon black. With decreasing primary particle size (and hence increasing surface area), carbon black can elicit pulmonary overload conditions in rats (Arts et al., 2016).

Similarly, the TF is unable to establish with certainty that the chronic inhalation toxicity study assessing polyacrylate polymers published by Warheit et al. (2001) is indeed the study referred to on the US EPA website. Interestingly, in this study, the polyacrylate polymers could only be applied to the rats via inhalation after test material grinding since the native material contained below 0.1% respirable material. Hence, under foreseeable conditions of use, these polymers would not pose a respiratory toxicity concern.

The CF4Polymers fully addresses the need to consider the pulmonary toxicity potential of respirable aerosols deriving from polymer products (see Step 1 – problem formulation; Step 2 – polymer identification; and Step 5 – determination of exposure scenarios). At the same time, the TF is unaware of scientific evidence to substantiate if and how polymer swellability, as such, or in combination with HMW, might contribute to pulmonary overload conditions in the rat. The studies referred to on the US EPA website apparently also do

<sup>&</sup>lt;sup>8</sup><u>https://books.google.de/books?id=s0MxCgAAQBAJ&pg=PA136&lpg=PA136&dq=TSCA+8(e)-</u>

<sup>&</sup>lt;u>1795&source=bl&ots=YXcQoWtDHm&sig=ACfU3U19DORb7NYjKYQWdbjRQggwu9piZQ&hl=en&sa=X&ved=2ahUKEwjEyvGom-3gAhWC26QKHSLPAFMQ6AEwBHoECAMQAQ#v=onepage&q=TSCA%208(e)-1795&f=false</u>

not specifically address this topic, but generally address pulmonary overload conditions. The TF concludes that the database is insufficient to establish a general respiratory or inhalation concern for HMW, insoluble and swellable polymers. Furthermore, significant exposure to respirable aerosols of polymers (or non-polymers) typically requires intentional generation of such aerosols by dedicated devices, or a high degree of dustiness paired with fine powder life stages. It would be highly ineffective to base a general PLC scheme exclusion on a rarely occurring specific exposure type.
# 5. CONCLUSIONS AND RECOMMENDATIONS

In this Technical Report, the ECETOC Polymers TF has presented the *ECETOC Conceptual Framework for Polymer Risk Assessment* (CF4Polymers) with an integrated step for grouping approach evaluation. The CF4Polymers provides basic guiding principles to be considered in assessing risks posed by polymer products to facilitate consistency. It is based upon a comprehensive review of relevant scientific literature, of OECD activities related to polymers, and of legislative and regulatory documents from the EU, Australia, Canada, China, Japan, the Philippines, South Korea, and the USA.

Importantly, the CF4Polymers is aligned with the internationally agreed paradigm for chemical RA as published by the WHO IPCS (2004, 2010). Indeed, within the CF4Polymers, Step 1 (problem formulation), Steps 5 and 6 (exposure assessment, i.e. determination of exposure scenarios and exposure characterisation), Step 7 (hazard assessment, i.e. hazard identification and hazard characterisation) as well as Step 8 (risk characterisation) are identical with the steps of the framework for chemical RA developed by the WHO IPCS. Deviations from the WHO IPCS framework within the CF4Polymers are necessitated by the chemical and physical attributes of polymeric substances and polymer products and their complex markets and uses. These deviations include the introduction of a distinct step for polymer identification (Step 2) and for determining the polymer component strategy (Step 3). These two steps are required for fit-for-purpose identification of the polymer product and to ensure that all relevant components of the polymer product are addressed during RA. Further, the broad variety of intended uses and the versatility of polymers throughout the life cycle necessitated addressing the two parts of exposure assessment separately, i.e. the determination of exposure scenarios (Step 5) and exposure characterisation (Step 6).

The sequence of the steps of the CF4Polymers can be adapted as necessary depending on the RA needs and/or data availability. Overall, the CF4Polymers is flexible and it is not prescriptive. It can be applied in voluntary settings and for regulatory purposes. Due to its flexibility and non-prescriptive format, the CF4Polymers is compliant with polymer RA procedures implemented in different jurisdictions world-wide both within the respective chemical legislation and product-specific legislation, and as such can also be taken into account in emerging regulations.

For each of the eight steps of the CF4Polymers, a detailed outline has been provided in this Technical Report for how it can be completed, accompanied by explanatory notes and illustrative examples and a comprehensive glossary providing definitions for all relevant terms. Further, for each step, prevailing knowledge gaps are addressed. For the time being, expert knowledge is required to identify the set of key parameters that are relevant for fit-for-purpose polymer identification (Step 2). This set of key parameters most likely not only depends on the type of polymer, but also on its intended use(s) and the life cycle stage(s) covered by the problem formulation (Step 1). Presumably, the set of key parameters that is relevant for fitfor-purpose polymer identification also encompasses those key parameters that drive grouping, i.e. the identification of structural and biological similarity and hence also of a common MoA (Step 4), and the data needs for exposure assessment (Steps 5 and 6) and hazard assessment (Step 7).

Depending on the type of polymer under investigation, relevant key parameters may be structural and/or morphological descriptors as well as physico-chemical and screening-level fate properties:

- Structural descriptors include e.g. chemical formula, degree of substitution, tacticity;
- Morphological descriptors include e.g. physical state, shape, physical form;

• Physico-chemical and screening-level fate properties include e.g. water solubility, vapour pressure, acid dissociation constant (pK<sub>a</sub>), n-octanol/water partition coefficient (log P<sub>ow</sub>), degradability.

<u>Recommendation 1</u>: *Identify sets of structural and/or morphological descriptors as well as physico-chemical and fate properties that are key parameters for different types of polymer products*. Further research is merited to identify which specific properties are the relevant key parameters for fit-for-purpose polymer identification and grouping. Specific key parameters might generally be relevant across different types of polymers, or they might be unique to specific types of polymer products. Knowledge on such key parameters will also facilitate the identification of data needs during exposure and hazard assessment.

Different analytical tools, *in vitro* and *in vivo* test methods, and *in silico* models are available to assess the physical, chemical, fate, ecotoxicological and toxicological properties of chemicals in general. Some of these tools, methods, and models have technical limitations restricting their applicability domain for assessing polymers. These technical limitations can generally be attributed to specific physical or chemical properties of the polymers. For the time being, expert knowledge is required to select the most appropriate tool, method or model to assess a given parameter and to identify potential technical limitations. A detailed review of the applicability of standardised tools, methods and models to assess the different properties of polymers is in preparation by the ECETOC Polymers TF (planned as ECETOC TR No. 133-2).

<u>Recommendation 2</u>: Consider prevailing technical limitations of available tools, test methods and models for polymer RA. Further, based upon the outcome of the review of the applicability of such tools, methods and models that is being prepared by the ECETOC Polymers TF, further research is merited to contribute to overcoming such technical limitations when assessing polymers.

The CF4Polymers is founded on a comprehensive review of the state-of-the-art polymer RA. Now, it has to prove itself in practice. The TF is preparing case studies to further evaluate the comprehensiveness and appropriateness of the eight steps of the CF4Polymers and to identify specific opportunities for the grouping of polymers (planned as ECETOC TR No. 133-3). These case studies might reveal the need to refine or amend the CF4Polymers. Similarly, as further knowledge on the applicability of the CF4Polymers to support the RA of polymers becomes available, the CF4Polymers should be adapted, as necessary. The flexibility and non-prescriptive nature of the CF4Polymers facilitates timely and straightforward adaptations. An *ad-hoc* committee within ECETOC has been mandated to follow and report such evolution.

<u>Recommendation 3</u>: *Maintain the CF4Polymers as a 'living', flexible framework,* and review and update it in line with emerging knowledge on how it can efficiently and effectively support polymer RA.

In preparing the CF4Polymers, the TF reviewed the regulatory landscape on polymers to identify key elements of polymer RA and to determine if these key elements should, or should not, feed into the CF4Polymers. Important key elements relate to the PLC concept that has been developed by the US EPA and several other agencies and was reviewed by the OECD. The PLC concept is generally applied by all jurisdictions reviewed by the TF that have implemented provisions for polymer notification / registration in their chemical legislation. The PLC concept includes specific criteria related to the Mw of the polymeric substance and the proportion of LMW compounds in the polymer product. Further, PLC exclusion criteria relate to the presence of specific structural alerts, such as functional groups or specific chemical elements.

While the publicly available dataset to support the PLC concept, or specific PLC criteria / PLC exclusion criteria, is limited, the TF was unable to find any evidence to refute the PLC concept. The TF considers the PLC concept a pragmatic approach to streamline the time and effort for polymer RA. Polymers identified as PLC can

generally be considered to exhibit low intrinsic hazard potential. However, this does not allow the reverse conclusion that polymers that are not identified as PLC would *per se* pose a hazard or risk concern. For example, the identification of a specific functional group merely informs on the presence of a specific structural alert. This should not by itself lead to the conclusion that the polymer is hazardous, but merely trigger considerations on external and internal bioavailability and lower-tier screening. Only if such screening indicates hazard potential, the TF considers higher-tier *in vivo* testing justifiable. Further, all testing should be selected to reflect the likely MoA of the polymer as indicated by the respective structural alert.

<u>Recommendation 4</u>: Establish a knowledge base to substantiate the PLC concept and to identify under which conditions the presence of specific structural alerts or physico-chemical properties poses environmental or human health hazard concerns. Particularly, there is only weak evidence that anionic or amphoteric and water absorbing polymers might generally have a relevant hazard potential. Further research is also merited to establish which combinations of properties of a given (type of) polymer truly drive its hazard potential. Such information will also serve to establish an improved scientific foundation for the grouping of polymers.

Specifically, water solubility and low Mw should not be misinterpreted as directly related to hazards – they are most probably only modulating factors for aquatic exposure and internal bioavailability. Similarly, the TF was unable to find any evidence that polymer (bio)degradation should be used as PLC exclusion criterion, i.e. that this property by itself indicates a hazard concern. Polymer (bio)degradation is complex, covering physical, chemical, and biological degradation; it can be intended (desirable) or unintended, and this can further depend on the life cycle stage of the polymer. Importantly, assessments surrounding (bio)degradation should consider the duration (i.e. half-lives) and the type of evolving breakdown products.

<u>Recommendation 5</u>: Develop environmentally relevant models, methods and/or criteria to assess (bio)degradation to enhance assessments of the RA implications of this property. Such models / criteria should take into account the type of (bio)degradation, its duration (i.e. half-lives), and whether it is intended during the given life cycle stage of the polymer, or not.

In conclusion, to the best of the TF's knowledge, this is the first time that a comprehensive framework for polymer RA, i.e. the CF4Polymers, has been put forward that not only addresses the polymeric substance itself, but also potential additives and NIAS. The present ECETOC TR No. 133-1, the CF4Polymers, is the first of three parts that the ECETOC Polymers TF is currently preparing with the other two being:

- 1. A review of the applicability of standardised analytical tools, test methods and *in silico* models to assess the physical, chemical, fate and ecotoxicological and toxicological properties of polymers (planned as ECETOC TR No. 133-2); and
- 2. A selection of case studies addressing different components of polymer grouping and RA to put the CF4Polymers into practice (planned as ECETOC TR No. 133-3).

It is expected that application of the CF4Polymers will contribute to the efficient and effective RA of polymer products be it conducted for voluntary purposes or to meet regulatory requirements related to chemical and product-specific legislation. The CF4Polymers shall be adapted and amended as new evidence on polymer RA becomes available. In this regard, it is anticipated that the outcome of ongoing work of the TF in reviewing the applicability of test methods and preparing case studies will provide important insight to further refine the CF4Polymers. ECETOC has mandated an *ad-hoc* committee to follow-up upon developments and evolution in the knowledge, testing and RA related to polymers. It is, therefore, intended that ECETOC will proactively and periodically update the Technical Report No. 133 series to keep abreast of state-of-the-art within this domain.

# GLOSSARY

### 2% rule (or polymer exemption rule):

Initially developed as part of the TSCA polymer exemption (US EPA, 2019b), the 2% rule states that "a polymer is not eligible for exemption [from PMN] if it contains at > 2 weight% monomers and/or reactants that are not included on the TSCA Inventory; manufactured under an applicable TSCA §5 exemption, excluded from exemption, or a non-isolated intermediate. Monomers and reactants at > 2% make up the 'chemical identity' of the polymer. For an exempt polymer, monomers and reactants at  $\leq$  2 weight% are not considered part of the 'chemical identity' of the polymer." (US EPA, 2019b)

"A polymer is not considered as new if it is manufactured by modifying the formulation of an existing one by adding existing reactants, none of which constitutes more than 2 weight% of the polymer." (https://www.chemsafetypro.com/Topics/Review/polymer\_registration\_in\_EU\_USA\_China\_Japan\_Korea\_Ta\_iwan\_Philippines.html)

### Additive:

"A substance added to something in small quantities to improve or preserve it." (<u>https://en.oxforddictionaries.com/definition/additive</u>)

"A substance which is intentionally added to plastics to achieve a physical or chemical effect during processing of the plastic or in the final material or article; it is intended to be present in the final material or article." (European Commission, 2011)

Aggregate exposures: Exposures to the same substance from multiple pathways and routes (adapted from OECD (2018))

**Article:** "An object which during production is given a special shape, surface or design which determines its function to a greater degree than does its chemical composition." (EP and Council, 2006; Article 3(3))

**Bioaccumulation:** Similar to bioconcentration (see definition) but relates to all routes of exposure e.g. via food, sediment, etc. (van Leeuwen and Vermeire, 2007).

**Bioavailability:** "The rate and extent to which an agent can be absorbed by an organism and is available for metabolism or interaction with biologically significant receptors. Bioavailability involves both release from a medium (if present) and absorption by an organism." (WHO IPCS, 2004)

- **Physical availability** of components of the polymer product: As an aspect of exposure characterisation, this involves release from the polymer matrix e.g. by migration / leaching; and can be prevented e.g. by encapsulation of the product. (ECETOC Polymers TF working definition)
- External bioavailability describes the condition that some HMW polymers that are too large to cross biological barriers might nevertheless exert local toxicity in tissues (e.g. skin, eyes, respiratory tract). This toxicity may well be due to LMW components (i.e. small oligomers, IAS, and NIAS, including unreacted monomers) that migrate under conditions of contact to the transitional fluid (e.g. sweat, tears, saliva), thereby being available to be absorbed and exert their toxic effect. The specific mechanisms by which such effects can occur remain to be determined. (ECETOC Polymers TF working definition)
- Internal (systemic) bioavailability means that the polymer product is absorbed into the blood stream by an organism thereby becoming systemically available and potentially causing systemic effects. (ECETOC Polymers TF working definition)

**Bioconcentration:** The net accumulation of a chemical by an organism as a result of uptake directly from its surrounding physical environment only through respiratory or dermal surfaces (Burkhard et al., 2011).

**Biodegradability:** *"The ability of a material to decompose after interactions with biological elements"* (Goswami and O'Haire, 2016).

**Biodegradation:** "The process by which organic substances are decomposed by micro-organisms (mainly aerobic bacteria) into simpler substances such as carbon dioxide, water and ammonia." (OECD Glossary of Statistical Terms; <u>https://stats.oecd.org/glossary/detail.asp?ID=203</u>); see also definition for degradation.

**Blooming:** Special form of migration of additives from polymer matrix onto the surface of the polymer product. (ECETOC Polymers TF working definition)

**Breakdown product / degradation product**: "A metabolite / a chemical derived from a parent molecule that has been altered e.g. by heat, light, or enzymes." (<u>https://medical-dictionary.thefreedictionary.com/Breakdown+Product</u>)

**Cationic density:** The percent of cationic or potentially cationic species with respect to the overall weight of polymer. (US EPA, 1997)

**Cationic polymer**: A polymer that has "one or more monomer units that are covalently bound and bear a net positive charge" (Canada, 2005b).

**Copolymer**: A polymer composed of at least two repetition units.

**Degradation, decomposition, or depolymerisation:** "A type of chemical change in which a polymeric substance breaks down into simpler, smaller weight substances as the result of (for example) oxidation, hydrolysis, heat, sunlight, attack by solvents or microbial action." (US EPA, 1997)

- **Physical degradation,** induced by e.g. heat, irradiation;
- **Chemical degradation**, induced by e.g. the presence of specific acids, bases, or oxidative agents, as applicable;
- **Biological degradation** (biodegradation), induced by specific microorganisms. (adapted from Doyle et al. (1982))

**Dendrimer:** Highly branched, star-shaped macromolecules with nanometre-scale dimensions, and they are defined by three components: a central core, an interior dendritic structure (the branches), and an exterior surface with functional surface groups (<u>https://www.sigmaaldrich.com/materials-science/material-science-products.html?TablePage=16375655</u>)

Dispersion: The distribution of a solid material in a suspending medium. (adapted from Arts et al., 2015)

**Dissolution rate:** As compared to water solubility (see definition), the dissolution rate is a kinetic parameter describing the time-dependent dissolution of a material in water (or other solvents). (adapted from Arts et al., 2015)

Ecological receptor: "Any living organisms other than humans, the habitat which supports such organisms, or natural resources which could be adversely affected by environmental contaminations resulting by a release at or migration from a site. Typical receptor categories may be (1) wider-ranging ecological receptors that may frequent the affected property and use less mobile receptors (e.g., plants, soil invertebrates, small rodents) as food source, (2) benthic invertebrates within waters in region." а а (http://www.eugris.info/FurtherDescription.asp?e=34&Ca=2&Cy=0&T=Receptor)

**Emission estimation / characterisation:** "Estimation of the amounts of the substance released to the different environmental compartments during all activities carried out by the manufacturer or importer and all identified uses, and an identification of the likely routes by which humans and the environment are exposed to the substance." (EP and Council, 2006; Annex I (4.2))

**Emulsion:** A mixture of two or more liquids where one is present as microscopic, or ultramicroscopic droplets distributed throughout the other (adapted from <u>https://www.britannica.com/science/emulsion-chemistry</u>).

**Environmental fate**: "The result/outcome of the chemical or biological pollutant after it has been released into the natural environment. The fate depends upon the specific characteristics of the chemical and the physical and biological forces which may act upon that chemical, such as heat, water or soil microorganisms." (TOXMAP Glossary of Terms; <u>https://definedterm.com/environmental\_fate/294507</u>)

**Exposure assessment:** "The process of estimating or measuring the magnitude, frequency, and duration of exposure to an agent, along with the number and characteristics of the population exposed. Ideally, it describes the sources, pathways, routes, and the uncertainties in the assessment." (WHO IPCS, 2004)

**Exposure estimation:** *"The exposure estimation entails three elements: (1) emission estimation; (2) assessment of chemical fate and pathways; and (3) estimation of exposure levels."* (EP and Council, 2006; Annex I (5.2.1))

**Exposure level:** The concentration or predicted concentration to which a population or sub-population may be exposed under a given exposure scenario related to the life cycle of the polymer under evaluation. For instance, this exposure level will be compared to the derived-no-effect level in order to establish if safe use is attained with respect to the exposure above which humans should not be exposed. (TF working definition, using information from EP and Council, 2006; Annex I (1.0.1))

**Exposure pathway:** "The course an agent takes from the source to the receptor." (US EPA, 2016)

### Exposure scenario:

<u>WHO IPCS</u>: "A combination of facts, assumptions, and inferences that define a <u>discrete situation</u> where potential exposures may occur. These may include the source, the exposed population, the time frame of exposure, microenvironment(s), and activities. Scenarios are often created to aid exposure assessors in estimating exposure." (WHO IPCS, 2004)

<u>OECD</u>: "A set of conditions or assumptions about sources, exposure pathways, amount or concentrations of agent(s)involved, and exposed organism, system or (sub) population (i.e. numbers, characteristics, habits) used to aid in the evaluation and quantification of exposure(s) in a given situation." (OECD, 2003)

<u>REACH Article 3(37)</u>: "The set of conditions, including operational conditions and risk management measures, that describe how the substance is manufactured or used during its life-cycle and how the manufacturer or importer controls, or recommends downstream users to control, exposures of humans and the environment. These exposure scenarios may cover one specific process or use or several processes or uses as appropriate." (EP and Council, 2006)

**Functional group equivalent weight (FGEW):** The FGEW of resident cationic or reactive functional groups is the weight of the polymer that contains one equivalent weight (one mole) of a particular functional group. (Canada, 2005a)

**Grouping (of chemicals**): The general approach for considering more than one chemical at the same time. It can include formation of a chemical category or identification of chemical analogue(s) with the aim of filling data gaps as appropriate. (OECD, 2014)

**Hazard identification**: "The identification of the type and nature of adverse effects that an agent has an inherent capacity to cause in an organism, system, or (sub)population. Hazard identification is the first stage in hazard assessment." (WHO IPCS, 2004)

**Hazard characterisation (dose-response assessment):** "The qualitative and, wherever possible, quantitative description of the inherent property of an agent or situation having the potential to cause adverse effects. This should, where possible, include a dose-response assessment and its attendant uncertainties. Hazard characterization is the second stage in the process of hazard assessment." (WHO IPCS, 2004)

**Hydrolysis**: A chemical process of decomposition involving the splitting of a bond and the addition of the hydrogen cation and the hydroxide anion of water. (<u>https://www.merriam-webster.com/dictionary/hydrolysis</u>)

Intentionally added substance (IAS): see definition for 'additive'.

**Life cycle (of a product):** The entire lifespan of a product, i.e. all stages from raw material extraction through materials processing, manufacturing, distribution, use, repair and maintenance, and eventual disposal or recycling. (adapted from ICCA, 2016)

LMW (low molecular weight) compound / LMW component: Small oligomers, IAS, and NIAS, including unreacted monomers.

**Macromolecule:** "A molecule of high relative molecular mass, the structure of which essentially comprises the multiple repetitions of units derived, actually or conceptually, from molecules of low relative molecular mass." (IUPAC, 1997)

**Microenvironment:** "Surroundings that can be treated as homogeneous or well characterized in the concentrations of an agent (e.g., home, office, automobile, kitchen, store). This term is generally used for estimating inhalation exposures." (WHO IPCS, 2004)

### Microplastic:

"Synthetic, water-insoluble polymer items smaller than 5 mm, which are considered to be of particular concern for the aquatic environment." (ECHA, 2018)

"Typically considered to refer to small, usually microscopic, solid particles made of a synthetic polymer." (ECHA, 2019a)

**Mixture:** "A mix or solution of two or more substances. Under the EU chemicals legislation, mixtures are not considered substances." (<u>https://echa.europa.eu/support/substance-identification/what-is-not-a-substance</u>)

**Mode-of-action (MoA)**: The biologically plausible sequence of substance-specific key events, starting with exposure and proceeding through the interaction of the substance or its metabolites with a cell, through functional and anatomical changes leading to an observed effect supported by robust experimental observations and mechanistic data (Sonich-Mullin et al., 2001; Boobis et al., 2009; Fenner-Crisp and Dellarco, 2016).

### Monomer:

<u>OECD</u>: "A molecule which is capable of forming covalent bonds with two or more like or unlike molecules under the conditions of the relevant polymer-forming reaction used for the particular process." (http://www.oecd.org/env/ehs/oecddefinitionofpolymer.htm)

<u>REACH (Article 3(6))</u>: "A substance which is capable of forming covalent bonds with a sequence of additional like or unlike molecules under the conditions of the relevant polymer-forming reaction used for the particular process." (EP and Council, 2006)

**Monomer unit:** "The reacted form of a monomer substance in a polymer (for the identification of the monomeric unit(s) in the chemical structure of the polymer the mechanism of polymer formation may, for instance, be taken into consideration)." (ECHA, 2012a)

**Monomer, unreacted (residual):** *"The quantities of a monomer substance that do not react during the polymerisation reaction and remain in the composition of a polymer... unreacted monomers in a polymer are also constituents of that polymer"* (ECHA, 2012a)

**Multi-constituent substance:** A substance with more than one constituent, with each main constituent encompassing  $\geq$  10 weight%, but < 80 weight%; each main constituent is completely identified by IUPAC name, and typical minimum and maximum concentrations of each constituent are reported in the composition. The generic name format for a multi-constituent substance is "reaction mass of [main constituent 1] and [main constituent 2] and ..." (ECHA, 2012b)

**Non-extractable residues (NER)**: Compounds which tend to remain irreversibly sorbed in the environment in the form of parent substance, metabolite(s), or bound to organic matter (humus). (adapted from ECETOC, 2013a)

**Non-intentionally added substance (NIAS)**: "An impurity in the substances used or a reaction intermediate formed during the production process or a decomposition or reaction product." (European Commission, 2011)

**Number average molecular weight (NAMW):** "The arithmetic average (mean) of the Mw's of all molecules in a polymer." (US EPA, 1997)

**Oligomer:** "A compound of relatively low molecular weight (Mw) containing up to five monomer units"; <u>https://www.collinsdictionary.com/dictionary/english/oligomer</u>

### Other reactant:

"A molecule linked to one or more sequences of monomer units but which, under the relevant reaction conditions used for the particular process, cannot become a repeating unit in the polymer structure." (http://www.oecd.org/env/ehs/oecddefinitionofpolymer.htm)

"A molecule that can be linked to one or more sequences of monomer units but which cannot be regarded as a monomer under the relevant reaction conditions used for the polymer formation process." (ECHA (2012a); p. 10)

**Plastic:** "A synthetic material made from a wide range of organic polymers such as polyethylene, polyvinyl chloride, nylon, etc., that can be moulded into shape while soft, and then set into a rigid or slightly elastic form." (https://en.oxforddictionaries.com/definition/plastic)

### Polymer:

<u>IUPAC:</u> "Substances composed of macromolecules, very large molecules with molecular weights ranging from a few thousand to as high as millions of grams/mole." (<u>https://iupac.org/polymer-edu/what-are-polymers</u>)

OECD: "A polymer means a substance consisting of molecules characterized by the sequence of one or more types of monomer units and comprising a simple weight majority of molecules containing at least three monomer units which are covalently bound to at least one other monomer unit or other reactant and consists of less than a simple weight majority of molecules of the same molecular weight. Such molecules must be distributed over a range of molecular weights wherein differences in the molecular weight are primarily attributable to differences in the number of monomer units. In the context of this definition a 'monomer unit' the means reacted form of а monomer in а polymer," (http://www.oecd.org/env/ehs/oecddefinitionofpolymer.htm)

<u>REACH (Article 3(5)):</u> "A substance consisting of molecules characterised by the sequence of one or more types of monomer units. Such molecules must be distributed over a range of Mw's wherein differences in the Mw are primarily attributable to differences in the number of monomer units. A polymer comprises the following:

- a) a simple weight majority of molecules containing at least three monomer units which are covalently bound to at least one other monomer unit or another reactant;
- b) less than a simple weight majority of molecules of the same Mw.

In the context of this definition a 'monomer unit' means the reacted form of a monomer substance in a polymer." (EP and Council, 2006)

**Polymer backbone**: "The main chain of a polymer, i.e. that linear chain to which all other chains, long or short or both, may be regarded as being pendant. Note: Where two or more chains could equally be considered to be the main chain, that one is selected which leads to the simplest representation of the molecule" (IUPAC, 1997).

**Polymer of low concern (PLC):** "Those deemed to have insignificant environmental and human health impacts. Therefore, these polymers should have reduced regulatory requirements." (OECD, 2009)

**Polymer product:** A chemical product with a polymeric substance as main component, and NIAS and sometimes IAS as other components. (ECETOC Polymers TF working definition). Polymer products are only in some cases finished articles.

**Polymer matrix**: The continuous phase in multi-constituent or multi-phase (composite) systems (adapted from: Wang et al. (2011))

**Polymeric substance (polymeric macromolecules)**: The chemical (co)polymer and possibly present oligomers. (ECETOC Polymers TF working definition)

**Product:** An article, preparation (mixture), or substance, that is manufactured, formulated or refined for further processing or sale. In this context polymers can be regarded as "specialty products" in that they have unique characteristics and/or brand identification. (ECETOC Polymers TF working definition)

<u>Note:</u> In the REACH Regulation (EP and Council, 2006), the term 'product' is not defined. In the EU Cosmetic Products Regulation (EP and Council, 2009), 'cosmetic product' is defined as "any substance or mixture".

**Reactive functional group (RFG):** *"An atom or associated group of atoms in a chemical substance that is intended or can be reasonably anticipated to undergo facile chemical reaction."* (US EPA, 1997; NICNAS, 2019b)

**Read-across:** A technique for predicting endpoint information for the target substance by using available data from the same endpoint from the source substance(s). The read-across approach encompasses (i) elements addressing the structural similarity; (ii) a read-across hypothesis; (iii) a read-across justification; and (iv) the prediction of the property (properties) of the target substance(s). (ECHA, 2017a)

**Risk assessment (RA):** "A process intended to calculate or estimate the risk to a given target organism, system, or (sub)population, including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system" (WHO IPCS, 2004). The RA process includes the four steps, i.e. (1) hazard identification) and (2) hazard characterisation (together: hazard assessment); (3) exposure assessment; (4) risk characterisation (adapted from WHO IPCS, 2004).

**Risk characterisation:** *"The qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of occurrence of known and potential adverse effects of an agent in a given organism, system, or (sub)population, under defined exposure conditions"* (WHO IPCS, 2004).

**Risk management**: "Decision-making process involving considerations of political, social, economic, and technical factors with relevant risk assessment information relating to a hazard so as to develop, analyse, and compare regulatory and non-regulatory options and to select and implement appropriate regulatory response to that hazard. Risk management comprises three elements: risk evaluation; emission and exposure control; and risk monitoring" (WHO IPCS, 2004).

### Sequence:

"Means that the monomer units under consideration are covalently bound to one another and form a continuous string within the molecule, uninterrupted by units other than monomer units." (http://www.oecd.org/env/ehs/oecddefinitionofpolymer.htm)

"A continuous string of monomer units within the molecule that are covalently bonded to one another and are uninterrupted by units other than monomer units. This continuous string of monomer units can possibly follow any network within the polymer structure." (ECHA (2012a); p. 10)

Supply chain: See value chain.

**Surface activity**: The alteration of properties and especially lowering of the tension at the surface of contact between phases (adapted from Merriam-Webster Dictionary; <u>https://www.merriam-webster.com/dictionary/surface-active</u>)

**Surfactant**: "any organic substance and/or preparation used in detergents, which has surface-active properties and which consists of one or more hydrophilic and one or more hydrophobic groups of such a nature and size that it is capable of reducing the surface tension of water, and of forming spreading or adsorption monolayers at the water- air interface, and of forming emulsions and/or microemulsions and/or micelles, and of adsorption at water-solid interfaces". (EP and Council, 2004b)

Swelling: The process of absorbing water. (US EPA, 1997; see also definition for water-absorbing polymer)

**UVCB (substances of unknown or variable composition, complex reaction products or biological materials)**: "A substance that cannot be sufficiently identified by its chemical composition, because (1) the number of constituents is relatively large and/or (2) the composition is, to a significant part, unknown and/or (3) the variability of composition is relatively large or poorly predictable." (ECHA, 2012c)

**Value chain:** "The full range of activities – including design, production, marketing and distribution – businesses conduct to bring a product or service from conception to delivery. For companies that produce goods, the value chain starts with the raw materials used to make their products, and consists of everything added before the product is sold to consumers." (Harrison, 2018)

**Water-absorbing polymer:** *"A polymeric substance that is capable of absorbing its weight of water."* (US EPA, 1997)

**Water availability:** The capacity of forming stable emulsions or dispersions (EC, 2009); see also definitions for emulsion and dispersion.

**Water extractability / extractivity**: The preferable extraction of some molecules in water leaving others remaining within the bulk substance. (adapted from EC (2009)

### Water solubility:

The saturation mass concentration of a substance in water at a given temperature. (OECD, 1995)

The maximum mass of a material that is found in molecularly dissolved state in a given volume of water containing a particulate material under specific conditions. (adapted from Arts et al., 2015)

**Whole mixture approach**: "The whole mixture approach to combined exposure assessment considers a group of substances as if they were a single unit, with the assumption and limitation that the components and concentrations of the mixture do not vary significantly across individuals, over time, or between exposure routes, and that toxicity studies are conducted on the whole mixture." (OECD (2018) citing NAS (2008); US EPA (2007b); and ECETOC (2011b))

# **ABBREVIATIONS**

| AICS            | Australian Inventory of Chemical Substances                                    |  |  |
|-----------------|--|--|--|
| AISE            | International Association for Soaps, Detergents and Maintenance Products       |  |  |
| BIO             | BioIntelligence by Deloitte  |  |  |
| CAS             | Chemical Abstract Service  |  |  |
| CDC             | Centers for Disease Control and Prevention (USA)                               |  |  |
| CEF             | Food Contact Materials, Enzymes, Flavourings, and Processing Aids (EFSA Panel) |  |  |
| Cefic           | European Chemical Industry Council   |  |  |
| CEPA            | Canadian Environmental Protection Act  |  |  |
| CF4Polymers     | Conceptual Framework for Polymer Risk Assessment                               |  |  |
| CSCL            | Chemical Substance Control Law (Japan)   |  |  |
| Da              | Dalton (g/mol)   |  |  |
| DENR            | Department of Environment and Natural Resources (Philippines)                  |  |  |
| DMF             | Dimethylformamide  |  |  |
| DOC             | Dissolved oxygen concentration (Japan)   |  |  |
| DSL             | Domestic substances list (Canada)  |  |  |
| EC              | Environment Canada / European Community (depending on context)                 |  |  |
| ECB             | European Chemicals Bureau  |  |  |
| ECCC            | Environment and Climate Change Canada  |  |  |
| ECETOC          | European Centre for Ecotoxicology and Toxicology of Chemicals                  |  |  |
| ECHA            | European Chemicals Agency  |  |  |
| ECPA            | European Crop Protection Association   |  |  |
| EC <sub>x</sub> | Effect concentration in terms of degree of effect (x)                          |  |  |
| EINECS          | European Inventory of Existing Commercial Chemical Substances                  |  |  |
| ERC             | Environmental release category   |  |  |
| EU              | European Union   |  |  |
| FCM             | Food contact material  |  |  |
| FGEW            | Functional group equivalent weight   |  |  |
| GHS             | Globally Harmonised System for Classification and Labelling of Substances      |  |  |
| GPC             | Gel permeation chromatography  |  |  |
| НС              | Health Canada  |  |  |

| HERA       | Human and Environmental Risk Assessment (project; AISE and Cefic)                |  |
|------------|--|--|
| HMW        | High molecular weight  |  |
| IAS        | Intentionally added substances   |  |
| IC(NA)     | Industrial Chemicals (Notification and Assessment) Act (Australia)               |  |
| IECSC      | Inventory of Existing Chemical Substances Produced or Imported in China          |  |
| ILSI       | International Life Sciences Institute  |  |
| IMAP       | Inventory for Multi-tiered Assessment and Prioritisation (NICNAS, Australia)     |  |
| INCI       | International Nomenclature Cosmetic Ingredient                                   |  |
| ISO        | International Standardisation Organisation                                       |  |
| ITAP       | Improved Aquatic Toxicity and Assessment of Polymers (Cefic LRI project)         |  |
| IUPAC      | International Union of Pure and Applied Chemistry                                |  |
| KOPTRI     | Korean Polymer Testing and Research Institute                                    |  |
| LMW        | Low molecular weight   |  |
| LRI        | Long-range research initiative   |  |
| METI       | Ministry of Economy, Trade and Industry (Japan)                                  |  |
| MoA        | Mode-of-action   |  |
| Mw         | Molecular weight   |  |
| NAMW       | Number average molecular weight  |  |
| NAS        | National Academy of Science  |  |
| NER        | Non-extractable residue  |  |
| NDSL       | Non-domestic substances list (Canada)  |  |
| NIAS       | Non-intentionally added substances   |  |
| NICNAS     | National Industrial Chemicals Notification and Assessment Scheme (Australia)     |  |
| NSNR (C&P) | New Substances Notification Regulations (Chemicals and Polymers) (Canada)        |  |
| OECD       | Organisation for Economic Co-operation and Development                           |  |
| PAC        | Priority action chemical (Japan)   |  |
| PEC        | Predicted environmental concentration; PFAS: Per- and polyfluoroalkyl substances |  |
| PFS        | Polymer Flow Scheme (Japan)  |  |
| PICCS      | Philippine Inventory of Chemicals and Chemical Substances                        |  |
| PLC        | Polymer of low concern   |  |
| PMMA       | Polymethyl methacrylate  |  |

| PMN      | Pre-manufacture notification   |  |
|----------|--|--|
| PMPIN    | Polymers and PLCs from Pre-Manufacture and Pre-Importation Notification (Philippines)            |  |
| PNEC     | Predicted no effect concentration  |  |
| PTFE     | Polytetrafluoroethylene  |  |
| RA       | Risk assessment  |  |
| REACH    | Registration, Evaluation, Authorisation and Restriction of Chemicals                             |  |
| RFG      | Reactive functional group  |  |
| RPA      | Risk & Policy Analysts Ltd   |  |
| RQ       | Risk quotient  |  |
| RRR      | Reduced regulatory requirements (Canada)   |  |
| SpERC    | Specific environmental release category  |  |
| TF       | Task Force   |  |
| TG       | Test guideline   |  |
| THF      | Tetrahydrofuran  |  |
| TR       | Technical Report   |  |
| TSCA     | Toxic Substances Control ACT (USA)   |  |
| US EPA   | United States Environmental Protection Agency  |  |
| UVCB     | Substance of unknown or variable composition, complex reaction products and biological materials |  |
| WHO IPCS | World Health Organisation – International Programme on Chemical Safety                           |  |
| WoE      | Weight-of-evidence   |  |
| WWTP     | Waste water treatment plant  |  |

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#### <u>Note 2:</u> This Bibliography also includes the references from Appendix A and B.

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# APPENDIX A: COMPLEXITY AND VERSATILITY OF POLYMERS

## **1.1 Polymer chemistry and polymerisation process**

Chemically, the term <u>polymer</u> (Greek: *poly* = many, *meros* = parts) refers to macromolecules composed of the concatenation many repetition units, which are joined together to create chains by covalent chemical liaison. (Ullmann's, 2016; see Box A-1 for history of polymers). The original, unconnected compounds are called <u>monomers</u>, i.e. substances containing a functional group able to form chemical bonds with other monomers or other chemical groups (Glossary).

In forming polymers, monomers can be connected in linear chains, branched chains, or more complicated structures, with each type of chain having specific properties and molecular size. These complex chains can be organised or not.

### Box A-1: History of polymers

Adapted from: Feldman (2008); Morawetz (2014); NRC (1994); Ullmann's (2016); Sivaram (2017); <a href="https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/">https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/</a>; <a href="https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/">https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/</a>; <a href="https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/">https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/</a>; <a href="https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/">https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/</a>; <a href="https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/">https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/</a>; <a href="https://www.icis.com/explore/resources/news/2018/">https://www.icis.com/explore/resources/news/2008/05/12/9122056/history-of-the-synthetic-rubber-industry/</a>; <a href="https://www.icis.com/explore/resources/news/2018/">https://www.icis.com/explore/resources/news/2018/</a>; <a href="https://www.icis.com/explore/resources/news/2018/">https://www.icis.com/explore/resources/news/2018/</a>; <a href="https://www.icis.com/explore/resources/news/2018/">https://www.icis.com/explore/resources/news/2018/</a>; <a href="https://www.icis.com/explore/resources/news/2018/">https://www.icis.com/explore/resources/news/2018/</a>; <a href="https://www.icis.com/explore/resources/news/2018/">https://www.icis.com/explore/resources/news/2018/</a>; <a href="https://www.icis.com/explore/resources/news/2018/">https://www.icis.com/ex

Polymer science is a recent science. The very first polymers used by man occur in nature, and they were and are still being used without further chemical transformation (e.g. cellulose for paper and cardboard, natural waxes, starches). Natural polymers are extracted as such and not subject to any chemical modification. Some examples for natural polymers are presented in Table A-1. The most abundant natural organic polymer is cellulose, an important structural component of the primary cell wall of green plants, that is constituted of glucose repetition units (Figure A-1). Cellulose is mainly used industrially to produce paperboard and paper.

With the introduction of the chemical modification of natural polymers with retention of their chain structures, more processable materials appeared, e.g. cellulose acetates from cellulose. These modified materials are called semi-synthetic materials. The first semi-synthetic polymer was based on nitrocellulose and was produced by Parkes in 1862 and Hyatt in 1866 by adding camphor to nitrocellulose. By 1900, this material was used for movie films.

Approximately 1897, Galalith ("*pierre de lait*") was produced in Germany by reacting casein (a milk protein) with formaldehyde. The first synthetic thermoset polymer (a phenol formaldehyde), known as Bakelite, was obtained in 1907 by Baekeland through the polycondensation of phenol with formaldehyde. Bakelite was commercialised in 1909–1910, and this event is considered to be the beginning of the 'synthetic plastic era' and of the plastic industry, although the semi-synthetic cellulose nitrate had been known and in use for some time.

The idea of macromolecule (main principle of the polymers) was defined by Herman Staudinger in the early 1920s. H. Staudinger published evidence that polymers are covalently bonded molecules of high Mw formed by the linking together of smaller molecules, and he was awarded the Nobel Prize of Chemistry for his work on polymers in 1953. Staudinger's theory opposed the conventional theories on organic molecules that were divided into 'crystalloids' and 'colloids' at that time. The meaning of the term polymers has evolved from its inception by Hermann Staudinger up until the present time.

In the 1930s, the industrial production of polymers was taken up by the German chemical and pharmaceutical conglomerate 'IG Farben' and DuPont industries. In the 1950s, Carothers and Florys discovered that a polymer is composed of high Mw covalent structures (> 100 000 Da). This discovery was a milestone initiating the industrial development of synthetic polymers. Table A-2 presents examples of synthetic monomers and associated polymers.

| Monomer                | Polymer                            |
|------------------------|------------------------------------|
| Monosaccharide (sugar) | Glycogen, polysaccharide-cellulose |
| Fatty acid             | Triglyceride                       |
| Phenolic structures    | Lignin                             |
| Sterol esters          | Lanolin                            |

Table A-1: Examples of natural monomers and associated polymers



*Figure A-1: Chemical structure of cellulose* (adapted from: <u>https://en.m.wikipedia.org/wiki/File:Cellulose</u> <u>Sessel.svg;</u> public domain file, ineligible for copyright)

| Table A-2: Examples of s | synthetic monomers and | associated polymers | (used in plastics) |
|--------------------------|------------------------|---------------------|--------------------|
|--------------------------|------------------------|---------------------|--------------------|

| Main Monomers   | Polymers  | Indicative EU<br>tonnage band<br>(million tpy) |
|---|---|--|
| Propylene<br>CH <sub>3</sub><br>I<br>CH <sub>2</sub> =CH            | Polypropylene (PP)<br>$CH_3$<br>I<br>$+CH_2-CH_2$   |  |
| Ethylene<br>CH <sub>2</sub> =CH <sub>2</sub>                        | High Density Polyethylene (HDPE)<br>$(CH_2-CH_2)_n$   | > 5  |
| Ethylene<br>CH <sub>2</sub> =CH <sub>2</sub>                        | Low Density Polyethylene (LDPE)<br>$+ CH_2 - CH_2 +_n$  |  |
| Vinyl Chloride<br>Cl<br>H<br>$CH_2=CH$                              | Polyvinyl Chloride (PVC)<br>(CI)<br>$(CH_2 - CH)$   |  |
| Diisocyanate Polyols<br>$O=C=N-O-CH_2-O-N=C=O$<br>$HO-CH_2-CH_2-OH$ | Polyurethane (PUR)<br>O $OH$ $H$ $O$ $H$  |  |
| Terephthalic Acid   | Polyethylene Terephthalate (PET)<br>$\begin{pmatrix} O \\ O \end{pmatrix} - \begin{pmatrix} O \\ O \end{pmatrix} - \begin{pmatrix} O \\ O \end{pmatrix} - \begin{pmatrix} O \\ O \end{pmatrix}_{n}$ | 1-5  |

| Main Monomers   | Polymers   | Indicative EU<br>tonnage band<br>(million tpy) |
|---|--|--|
| Styrene<br>I<br>CH <sub>2</sub> =CH   | Polystyrene PS<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$   |  |
| Styrene   | Expandable Polystyrene EPS<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$<br>$\downarrow$   |  |
| Styrene Butadiene Acrylonitrile<br>CN<br>$H_2$ =CH CH <sub>2</sub> =CH—CH=CH <sub>2</sub> CH <sub>2</sub> =CH | Styrenic Copolymer (ABS / SAN)<br>$(+ CH_2 - CH + (CH_2 - CH + CH_2) - (CH_2 - CH + (CH_2 - CH_2)))$   | 1-5  |
| Dicarboxylic Acid + Diamine<br>O O<br>II II<br>$HO-C-R_{n}-C-OH + H_{2}N-R_{m}-NH_{2}$                        | Polyamide (Pa <sub>m,n+2</sub> )<br>O O<br>$(\Pi = \Pi = \Pi + C - NH - R_m - NH)_k$   |  |
| Bisphenol A<br>$CH_3$<br>HO - O - C - O - OH<br>I - O - OH<br>$CH_3$  | Polycarbonate (PC)<br>$(\circ - \bigcirc - \begin{matrix} CH_3 & O \\ - \begin{matrix} CH_3 & O \\ - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \end{matrix} - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} - \end{matrix} - \end{matrix} - \end{matrix} - \end{matrix} - \end{matrix} - \begin{matrix} O \\ - \end{matrix} -$ | < 1  |

Footnote to Table A-2: Tpy: Tonnes per year

The International Union of Pure and Applied Chemistry (IUPAC) defines polymers as "*substances composed of macromolecules, very large molecules with molecular weights ranging from a few thousand to as high as millions of grams/mole*" (<u>https://iupac.org/polymer-edu/what-are-polymers/</u>). IUPAC clearly states that polymers and macromolecules are not the same (IUPAC, 2012).

The IUPAC definition of a <u>macromolecule</u> is: "A molecule of high relative molecular mass, the structure of which essentially comprises the multiple repetitions of units derived, actually or conceptually, from molecules of low relative molecular mass" (IUPAC, 1997). (In essence, macromolecules have one specific defined structure, whereas polymers are a mixture of multiple related macromolecules.)

The three main processes for the manufacture of synthetic polymers are condensation polymerisation, polyaddition (such as free radical polymerisation) and ring-opening polymerisation (Box A-2).

#### Box A-2: Polymer manufacturing processes

Polycondensation is one of the most known techniques used to synthesise polymers from bifunctional and polyfunctional monomers, accompanied by the elimination of LMW compounds (NIAS, e.g. water, alcohols, and hydrogen halides). The reason for the name of this process derives originally from the elimination of a molecule of water from reactants at each polymerisation step. Polycondensation may be applied to multifunctional units to produce thermoset polymers. A classic example of polycondensation leading to thermoset polymers is the copolymerisation between phenol and formaldehyde (Conley and Bieron, 1962).

Polyethylene, polypropylene, and polyvinyl chloride are common types of plastics made by chain polymerisation. They are used extensively in packaging and are the primary component of four of the plastics that the US Society of the Plastics Industry Inc. specifically labelled with a recycling code (<u>https://plastics.americanchemistry.com/Plastic-Packaging-Resin-Identification-Codes/</u>).

Some reactions of ring-opening polymerisation can be considered as a chain polymerisation (addition of monomer to a growing chain end) but many reactions are more complicated and involve, e.g. activated monomers. Lactones such as lactide or caprolactones are typical monomers that can be polymerised by ring-opening polymerisation. Particularly, ring-opening polymerisation has proved to be a useful synthetic route to technologically interesting polymers with very specific, and controllable properties (e.g. refractive index), for preparing synthetic variants to naturally occurring polymers (e.g. chitin) or to optimise biodegradable polymers for agricultural, medicinal and pharmaceutical applications (Nuyken and Pask, 2013).

Polyesters, such as polylactide, can be produced by different routes / mechanisms. The main differences then are the process conditions (e.g. temperature, pressure, solvents, catalysts), and the polydispersity of the resultant polymer.

The supply chain linked to polymer production is one of the most complex in the chemical industry. It does not only involve the raw materials needed for the polymer itself (monomer, solvent, catalyst), but also a broad variety of additives required for the stability of the matrix or specific to the application of the end-products (thermoplastics, thermosets, etc.). One of the main parameters that might affect not only the polymerisation process, but also polymer RA, is the purity profile of the monomers, catalysts, or solvents.

In determining the purity profile of polymers, the information available from the suppliers throughout the supply chain is critical. Due to the complexity of polymers, numerous suppliers can be involved in delivering the substances necessary for the polymerisation process. It can be challenging to track the exact composition of each substance entering in the manufacturing process or the finishing of the article to be used.

Further, depending on the manufacturing process, impurities (NIAS) can be introduced into a polymer that may also be of concern for human and environmental RA. Impurities can also affect the efficiency of either the catalyst, or the initiation, propagation and termination steps of the polymerisation reaction, potentially leading to poor polymerisation rate or broader polydispersity, leading to rejection of the produced material.

## **1.2 Polymer types and uses**

The information in this section was taken from IUPAC (2008);<a href="http://polymerdatabase.com/polymer%20chemistry/A%20index.html">http://polymerdatabase.com/polymer%20chemistry/A%20index.html</a> and<a href="https://www.cmu.edu/gelfand/education/k12-teachers/polymers/natural-synthetic-polymers/">http://www.cmu.edu/gelfand/education/k12-teachers/polymers/</a>.

Due to their versatility and complexity, polymers cannot be sorted by a unique set of parameters. Instead, they can be sorted according to their origin, or on account of specific physico-chemical properties.

Sorting polymers by their origin distinguishes between natural, synthetic and semi-synthetic polymers.

*Natural polymers* are present in nature. They are extracted as such and not subject to any chemical modification. Examples include cellulose in cotton or wood, carrageenan, silk, keratin, rubber and hair (Table A-1). The most abundant natural organic polymer is cellulose which is constituted of glucose repetition units. Cellulose, comprised of repeating monomer units of glucose (Figure A-1), is an important structural component of e.g. the primary cell wall of green plants. As such, cellulose is a renewable commodity. Its main industrial use includes the production of paperboard, paper and a broad range of construction materials.

Semi-synthetic polymers are derived from naturally occurring polymers by chemically modifying them. For example, the natural cellulose can be acetylated with acetic anhydride in the presence of sulphuric acid to form cellulose diacetate polymers which are used in making thread, films, glasses, etc. Other examples include vulcanised rubber used in the manufacture of tyres; and cellulose nitrate (gun cotton) used in the manufacture of explosives.

*Synthetic polymers* are created by man. Currently, most polymers used industrially are synthesised chemically from synthetic monomers from petroleum oil; however, progress in biotechnology is stimulating the production of bio-based synthetic monomers. Synthetic polymers derived from petroleum oil include polyamides (nylon), polyethylene glycols, polyester, polytetrafluoroethylene (PTFE; Teflon), polyvinyl chloride, polystyrene, polyacrylonitrile, and polymethyl methacrylate (PMMA; Box A-3) (Table A-2).

### Box A-3: Versatility and complexity of polymers: The example of PMMA

Synthetic polymers are manufactured for the physical and chemical properties that they impart on products. Since these properties can be achieved using a combination of monomers and other reactants, their chemical composition and structure may be very varied. For example, PMMA has the structural formula  $[CH_2C(CH_3)(CO_2CH_3)]_n$  and is comprised of repeating methyl methacrylate (methacrylic acid methyl ester) monomer units. It is assigned the single CAS number 9011-14-7. PMMA is manufactured in many different forms including thermoplastic sheets (i.e. acrylic or acrylic glass), bead or extrusion polymers for moulding into articles like vehicle lights, or suspension or solution resins to be used in the manufacture of inks and coatings etc. The Mw and physical form of PMMA varies greatly depending upon the manufacturing conditions and intended application. Therefore, the conventional descriptor used by the CAS is insufficient to describe the varied forms of the polymers placed on the market. Further, the substances used to aid the polymerisation process and added to stabilise the polymer and enable its processing, as well as the polymerisation process itself, will vary between different polymers and manufacturers.

Synthetic polymers are used in a myriad of different applications including:

- Active pharmaceutical ingredients: Cholesterol binders, laxatives;
- Aeronautic: Aerospace components in the aeroplane cabin;
- Automotive: Air induction systems, seals, sound isolation, seats, airbags;
- Construction: Sealants, adhesives, coatings, insulation, concrete additives, pipes, window profiles, roofing, waterproofing membranes, etc.;
- Electronics: Computers, phones, etc.;
- Energy: Solar panels, windmills;
- Excipients;
- Food additives: Thickeners, coatings, surfactants;
- Health care: Parts of simple medical devices (e.g. infusion bags) to more complex medical devices which replace parts of the human body (e.g. artificial hips or hands);
- Oil and gas: Compressor rings, back-up seal rings;

- Packaging: Plastics, elastomers, adhesives;
- Personal care: Stabiliser of cosmetic formulation or surfactants in detergents, etc.;
- Water treatment: Flocculation agents, filtration aids, disinfectants, ion exchange resins, osmosis membranes.

The economic impact of polymer production and use is highlighted by the following figures (Cefic, 2018):

- EU total chemical sales in 2017 (542 billion €), of which 20.5% related to polymers;
- Extra-EU chemical exports in 2017: 18% polymers; extra-EU imports 2017: 21%.

Of the 20.5% EU total chemical sales in 2017 that related to polymers, the vast majority appertained to the plastics industry (Cefic, 2018). In 2017, the European plastic industry had a turnover of 355 billion € and gave direct employment to more than 1.5 million people in Europe, in close to 60,000 companies, many of which small and medium enterprises (PlasticsEurope, 2018). High production volume polymers include PMMA, PTFE, polyamides (nylon), polyimides, poly vinyl acetates, thermoplastic elastomers, different resins, polyurethanes, synthetic rubbers, and silicones (RPA, 2012).

In addition to sorting by origin, polymers can be sorted by different physico-chemical properties:

<u>Type of repetition units</u>: A *homopolymer* is composed of one single repetition unit. A *copolymer* is composed of at least two repetition units (Figure A-2). In *random copolymers*, the sequence of repeat units is completely random (<u>http://polymerdatabase.com/polymer%20chemistry/Ideal%20Copolymers.html</u>). *Block copolymers* consist of "two or more strands (blocks) of different polymers chemically attached to each other" (<u>http://polymerdatabase.com/polymer%20chemistry/Block%20Copolymers.html</u>).



Figure A-2: Homopolymer versus copolymer: A: Example of homopolymer (polyethylene); B: Example of copolymer (poly(ethylene-vinyl) acetate block polymer

<u>Polymer backbone</u>: Synthetic polymers derived from petroleum oil present an *organic, carbon-based* backbone, but e.g. silicones have *inorganic, non-carbon-based* backbones composed of alternating silicon and oxygen atoms (with organic, carbon-containing side groups attached to the silicon atoms).

<u>Organisation of the monomers:</u> (1) *Crystalline polymers* only have organised monomer chains; (2) *amorphous polymers* only have unorganised monomer chains; (3) *semi-crystalline polymers* have both organised and unorganised monomer chains.

Distribution of the repetition units: Linear, branched or cross-linked polymers (Table A-3).



Table A-3: Distribution of repetition groups determining polymer structure

Footnote to Table A-3: R: Repetition group; C: Crosslinking group (can also be the Repetition group)

In this regard, *dendrimers* are highly branched, star-shaped macromolecules with nanometre-scale dimensions, and they are defined by three components: a central core, an interior dendritic structure (the branches), and an exterior surface with functional surface groups; <u>https://www.sigmaaldrich.com/materials-science/material-science-products.html?TablePage=16375655</u>.

<u>Molecular size</u>: Polymers can range from e.g. soft paraffin (C16-C40) with a Mw < 500 Da (Luyt and Krupa, 2008) to polyethylene ultra-high (CAS No. 9002-88-4) with a Mw distribution ranging from 3-6 Million Da.

<u>Physical form at ambient temperature</u>: Polymers can be liquids or solids.

<u>Tacticity (relative stereochemistry of adjacent chiral centres)</u>: (1) *Isotactic polymers*: All substituents of the macromolecular chain are on the same side; (2) *syndiotactic polymers*: Substituent groups are on both sides of the chain (Figure A-3); (3) *atactic polymers*: Random distribution of the substituents along the macromolecule chain; see also <u>https://www.compositespress.com/wikicomposites/polymer/</u>.

Molecular forces: Synthetic polymers can be elastomers, thermoplastics, or thermosets.

- Elastomers are characterised by high mean Mw, low cross linking and low glass transition temperature. Accordingly, elastomers are easily and highly deformable, and they can support high deformation when submitted to a constraint before breaking. Before being submitted to a constraint, elastomers are only composed by unorganised macromolecular chains.
- *Thermoplastics* ('plastics') can be repeatedly moulded or extruded into various solid forms and retain their defined form in the intended applications (or during use);
- *Thermosets* can be changed into a substantially infusible product when cured by heat, by crosslinking by reaction of functional groups, or by radiation. Thermosets retain their defined form in the intended applications (or during use).



Figure A-3: Top panel: Isotactic polymer. Bottom panel: Syndiotactic polymer

Hence, thermoplastics and thermosets differ by their thermal properties (Table A-4). The name plastics refers to their easy processability and shaping (Greek: *plastein* = to form, to shape). Some polymers are raw materials for plastics; they become plastics only after processing. The same polymers may be used as plastics or as fibres, paints, rubbers, coatings, adhesives, thickeners, surfactants, and ion-exchange membranes. Typically, plastics contain additives that are needed to enhance their stability and to modify their properties.

| Characteristics                             | Thermoplastics   | Thermosets  |
|---|--|---|
| Behaviour with<br>increasing<br>temperature | Softening<br>Deformation<br>Decrease viscosity                                     | Crosslinking which involve hardening, insolubility and infusibility |
| Behaviour with<br>decreasing<br>temperature | Hardening  | No modification   |
| Reshaping possible                          | Yes, by temperature cycle (increase – decrease)                                    | No, the shape obtained after temperature increase is irreversible   |
| Main characteristics                        | Two important temperatures:<br>Glass transition temperature<br>Melting temperature | One important temperature:<br>Melting temperature                   |

During manufacture, properties of polymers are engineered by varying the molecular architecture or the formulation, combining them with different materials in multicomponent and multiphase systems. This further adds to the complexity and versatility of polymers.

The IUPAC *Compendium of Polymer Terminology and Nomenclature* (IUPAC, 2008) includes recommendations to harmonise and unify the definitions and terminology used for polymers. These recommendations are continuously reviewed (<u>https://IUPAC.org</u>).

## **APPENDIX B: REGULATORY LANDSCAPE ON POLYMERS**

Appendix B outlines legal provisions of relevance for polymer RA implemented in the EU, Australia, Canada, China, Japan, the Philippines, South Korea, and the USA. As applicable for the given jurisdiction, the focus of the summaries lies on (1) legislation relevant for the registration or notification, and hence also hazard and risk assessment of new chemicals; (2) provisions on PLC; (3) programmes for the assessment of 'existing' polymers; (4) schemes for the environmental assessment of polymers.

<u>Note</u>: The information provided in this Appendix serves to provide an overview on the regulatory landscape on polymers. For compliance with the regulatory processes, the respective effective legislation and guidance should be consulted.

## 2.1 European Union

### **2.1.1 EU legislation of relevance for polymers prior to REACH**

Polymers were not reportable for the *European Inventory of Existing Commercial Chemical Substances* (EINECS) listing substances deemed to be on the European Community market between 1 January 1971 and 18 September 1981. Only in 1992, new polymers (containing > 2% of a monomer not on EINECS) became subject to notification following Article 12 of Council Directive 92/32/EEC (Council, 1992), i.e. the 7<sup>th</sup> amendment of the Dangerous Substances Directive (Council, 1967). Reduced testing requirements were implemented for polymers with high Mw, low water solubility, and low monomer or oligomer content (European Commission, 1993). Further, a 'family approach' to notification was permitted for polymers having the same CAS number, but varying Mw or relative monomer ratio.

Before the 7<sup>th</sup> amendment of Directive 67/548/EEC (Council, 1967) was adopted in 1992 (Council, 1992), the EU definition for polymers differed from the OECD definition. Upon implementation of the 7<sup>th</sup> amendment (Council, 1992), a number of substances which had been considered to be polymers under EINECS were no longer considered as such. These substances were called no-longer polymers and mainly included alkoxylated substances; oligomeric reaction products; oligomers from one monomer only; dimers and trimers; polymer-like substances containing  $\geq$  50 weight% of species with the same Mw (ECB, 2007). When the REACH Regulation entered into force, the no-longer polymers had to be registered as phase-in substances in accordance with Article 12 of the REACH Regulation (EP and Council, 2006).

### **2.1.2 Polymers under the REACH Regulation**

Polymers are exempt from registration and evaluation as per Article 2(9) of the REACH Regulation (EP and Council, 2006): *"The provisions of Titles II and VI shall not apply to polymers."* Title II relates to the registration of substances, and Title VI to their evaluation. By reverse conclusion, polymers are not exempt from restriction or authorisation. Also, monomers must be registered in accordance with Article 6(3) of the REACH Regulation:

"Any manufacturer or importer of a polymer shall submit a registration to the Agency for the monomer substance(s) or any other substance(s), that have not already been registered by an actor up the supply chain, if both the following conditions are met:

- a. the polymer consists of 2 % weight by weight or more of such monomer substance(s) or other substance(s) in the form of monomeric units and chemically bound substance(s);
- b. the total quantity of such monomer substance(s) or other substance(s) makes up 1 tonne or more per year."

Further, Article 138(2) of the REACH Regulation (EP and Council, 2006) has laid down that "the Commission may present legislative proposals as soon as a practicable and cost-efficient way of selecting polymers for registration on the basis of sound technical and valid scientific criteria can be established, and after publishing a report on the following (1) the risk of polymers in comparison with other substances; (2) the need, if any, to register certain types of polymer, taking account of competitiveness and innovation on the one hand and the protection of human health and the environment on the other".

Since the implementation of REACH, two reports have been published in accordance with the above-quoted Article 138(2) of the REACH Regulation, i.e. RPA (2012) and BIO by Deloitte (2015); see Box 7 in Section 4 of the present Technical Report.

### 2.1.3 Derogation from labelling implemented for polymers

The influence of the physical form of the polymer and of its matrix on physical availability have been recognised for many years, as was shown by the derogation from labelling implemented for alloys, polymers, and elastomers in the previous Dangerous Substances Directive 67/548/EEC (Council, 1967); Annex VI *General classification and labelling requirements for dangerous substances and* preparations; Section 9.3 *Alloys, preparations containing polymers, preparations containing elastomers*).

The Dangerous Substances Directive (Council, 1967) has been replaced by Regulation (EC) 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures (EP and Council, 2008). Therein, the derogation from labelling implemented for alloys, polymers and elastomers has been maintained: Section 1.3.4 of Annex I of the CLP Regulation relates to *Metals in massive form, alloys, mixtures containing polymers, mixtures containing elastomers*. Section 1.3.4.1 reads: "*Metals in massive form, alloys, mixtures containing polymers, mixtures containing elastomers*. Section 1.3.4.1 reads: "*Metals in massive form, alloys, mixtures containing polymers and mixtures containing elastomers do not require a label according to this Annex, if they do not present a hazard to human health by inhalation, ingestion or contact with skin or to the aquatic environment in the form in which they are placed on the market, although classified as hazardous in accordance with the criteria of this Annex."* 

By comparison in the REACH Regulation (Annex II), polymers are not explicitly mentioned when referring to these derogations from labelling: "Safety data sheets are also required for certain special substances and preparations (e.g. metals in massive form, alloys, compressed gases, etc.) listed in chapters 8 and 9 of Annex VI to Directive 67/548/EEC, for which there are labelling derogations" (EP and Council, 2006).

Presumably, the reason that polymers are not explicitly referred to in Annex II of the REACH Regulation is that they are generally exempt from registration and evaluation under REACH. The derogation from labelling implemented in the CLP Regulation shows that the European Commission continues to consider lack of bioavailability an essential determinant for the lack of hazard concerns.

### 2.1.4 ECHA Board of Appeal decision related to polymers

In 2016, ECHA published a decision on substance evaluation for the monomer 'phenol, 4-nonyl-branched, CAS No 84852-15-3' pursuant to Article 46(19) of the REACH Regulation (ECHA, 2016). Specifically, ECHA requested additional information on endpoints related to environmental impact; tonnages, environmental toxicity, impurity concentrations and exposure scenarios. The registrant appealed against this decision.

On 6 June 2018, ECHA's Board of Appeal released their decision (ECHA Board of Appeal, 2018) specifying that in some cases, ECHA can ask REACH registrants of monomers to provide additional information on the substance, as an unreacted impurity in, or degradation products of, polymers. However, ECHA can only request this additional information as part of the evaluation process. Therefore, it does not have to be provided within the registration dossier. Hence, the Board of Appeal rejected a general requirement for monomer suppliers to provide data from their downstream users. However, monomer suppliers are required to provide information on the 'typical' concentration of the registered substance as unreacted impurity in polymers and on its potential formation from the polymers during environmental degradation, in order to justify waiving of exposure scenario information for the substance as polymer breakdown product and as component of paints during their service life.

## 2.2 Australia

### **2.2.1** Polymer notification under the Australian IC(NA) Act

Figure B-1 presents the decision-making process for the notification of polymers implemented in Australia.

In Australia, polymer RA is regulated in the *Industrial Chemicals (Notification and Assessment) Act* (IC(NA) Act; Australian Government (1989)) and the ensuing IC(NA) Regulations (Australian Government, 1990). The provisions of the IC(NA) Act are executed within the *National Industrial Chemicals Notification and Assessment Scheme (NICNAS)*.

The IC(NA) Act distinguishes between existing and new substances. All new chemicals (including polymers) are subject to – either limited or standard – notification:

"Limited notifications are for chemicals fitting one of these categories:

- Small-volume chemicals, biopolymers, and LMW synthetic polymers (NAMW < 1000 Da) that is, chemicals to be imported or manufactured at a rate of up to 1 tonne/12-month period;
- Site-limited chemicals, biopolymers, and LMW synthetic polymers (NAMW < 1000 Da) that is, chemicals restricted to their manufacturing site and manufactured at a rate of not more than 10 tonnes/12-month period;
- Synthetic polymers with NAMW > 1000 Da that do not meet the PLC criteria.

Standard notifications are for chemicals, biopolymers and LMW synthetic polymers (NAMW < 1000 Da) imported or manufactured at greater than 1 tonne/year that do not fulfil the requirements of any other category"; <u>https://www.nicnas.gov.au/notify-your-chemical/types-of-assessments/assessment-certificatecategories/standard-or-limited-notifications</u>.



Figure B-1: Decision-making process for the notification of a polymer implemented in Australia

<u>Footnote to Figure B-1</u>: Flow-chart serves illustrative purposes only. For compliance with the regulatory process, the effective legislation and guidance should be consulted. <u>Colour legend</u>: Purple oval: 'Point of entry'; red oval: Standard notification requirements; green oval: Reduced notification requirements. <u>Abbreviations</u>: FGEW: Functional group equivalent weight (Da); NAMW: Number average molecular weight (Da); PLC: Polymer of low concern.

These provisions include the term 'biopolymer'. For the term 'biochemical' (and hence 'biopolymer'), the following definition has been proposed: "A chemical, including a polymer, that is directly produced by living or once-living cells or cellular components or a derivative or modification of a chemical referred to in paragraph (a) in which the original chemical remains substantially intact"; https://www.nicnas.gov.au/reforms/consultation-paper-5/defined-terms.

Part D of the Schedule to the IC(NA) Act describes 'matters to be dealt with' in polymer notification statements. These are the weight% of the total ingredients, the NAMW of the polymer, the weight% of LMW components upon introduction represented by each residual monomer and of LMW components < 500 Da and < 1,000 Da,
respectively; information about all products resulting from the degradation, decomposition or depolymerisation of the polymer and on the natural loss of monomers, additives and impurities from the polymer.

The Australian Government is currently drafting new **Industrial Chemicals (General) Rules 2018** setting out the details for the regulation of the import and manufacture of industrial chemicals under the new Australian Industrial Chemicals Introduction Scheme. Thereby, introductions of new chemicals will be either exempted or reported, and the classification of introduced new chemicals will be based on RA and categorised according to hazard and exposure bands. Although the majority of the NICNAS reforms will only enter into force in July 2020, on account of 'early regulatory changes' that came into force in April 2019 – i.e. while the present Technical Report was being finalised, PLC are now exempt from NICNAS notification (https://www.nicnas.gov.au/notify-your-chemical/chemicals-exempt-from-notification). Further, the PLC criteria have been expanded (see update at end of Section 2.2.2 below).

### 2.2.2 PLC concept implemented under the NICNAS New Chemicals Program

Section 5 of the IC(NA) Act and IC(NA) Regulation 4 introduce the concept of PLC. Complex rules apply to determine if a polymer is a PLC based upon high NAMW, relative mass of small molecules, and the presence of RFGs. Further, polyesters can be PLC if they are made up only of prescribed reactants. A flowchart to establish if a polymer is a PLC is provided in NICNAS (2019b).

The PLC criteria are closely linked to the eligibility for a low volume chemical permit as the overview below shows that summarises information from <a href="https://www.nicnas.gov.au/notify-your-chemical/types-of-assessments/permit-categories/low-volume-chemical-permit">https://www.nicnas.gov.au/notify-your-chemical/types-of-assessments/permit-categories/low-volume-chemical-permit</a>. Where notification of a polymer is required, a low volume chemical permit allows a chemical to be introduced onto the Australian market at a maximum quantity of 100 kg/year, or 1,000 kg where certain criteria are met, for a maximum of 3 years.

### Exemption of low hazardous criteria for chemicals (including polymers) with NAMW < 1,000 Da

Due to the resulting environmental or human health concerns, chemicals whose production volumes exceeds 100 kg/year are <u>not</u> eligible for a low volume chemical permit if they are (1) likely to be persistent and/or bioaccumulative, or have breakdown products with these characteristics; (2) covered by data requirements for notification of new chemical substances containing a perfluorinated carbon chain; members of a chemical class with an 'exposure standard' (e.g. occupational exposure limit).

### Polymers with NAMW ≤ 1,000 Da can meet the low hazardous criteria, if they have:

- < 10 mass% of molecules with Mw < 500 Da;
- < 25 mass% of molecules with Mw < 1,000 Da;
- A low charge density, i.e. they are:
  - $\circ$  Not cationic / not likely to become cationic in an aquatic environment with pH > 4 and < 9; OR
  - A solid that is not soluble or dispersible in water and is to be used only in its solid phase; OR
  - (For a polymer that includes 1 or more cationic groups): The total combined FGEW of any cationic group is at least 5000 Da; AND
- These polymers must not have certain hazard classifications as per 'Approved Criteria' (Australian Government, 2004) or GHS hazard categories (United Nations, 2017).

### Polymers with NAMW $\geq$ 10,000 Da can meet the low hazardous criteria, if they have:

• < 2% components with Mw < 500 Da and < 5% components with Mw < 1,000 Da.

### New PLC criteria as per April 2019

While the present Technical Report was being finalised, the following expansions to the PLC criteria were published; <u>https://www.nicnas.gov.au/New-scheme-1-July-2020/Early-commencement-whats-already-changed-for-importers-and-manufacturers#criteria</u>:

- Removal of the Mw specification for polyesters;
- Addition of chemicals to the prescribed reactants list for polyesters;
- Alignment of Mw boundaries with those used in USA;
- Alignment of the moderate and high concern functional groups with those used in USA and Canada;
- Restrictions on perfluorinated polymers so they cannot be PLCs.

Further, PLC are now generally exempt from NICNAS notification.

### 2.2.3 The Australian IMAP framework for the assessment of existing chemicals

To accelerate the assessment and prioritisation of existing chemicals on the Australian Inventory of Chemical Substances (AICS), in 2012, NICNAS has implemented the *Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework* (Australian Government, 2013). Therein, chemicals are assessed following a staged approach (NICNAS, 2019c, d). In IMAP Stage 1, an approach was developed for identifying polymers with RFGs consistent with the PLC approach implemented for new chemicals (see above). Of the approx. 3,000 existing chemicals addressed in Stage 1, 43 polymers were identified as being of low concern to human health (<u>https://www.nicnas.gov.au/chemical-information/imap-assessments/how-chemicals-are-assessed/Low-concern-polymers</u>). Only those polymers identified as having additional concerns were prioritised as higher risk chemicals requiring RA.

In Stage 2, around 6,000 unassessed polymers are being reviewed to identify polymers that are PLC and therefore of low priority for environmental and / or human health safety assessment (NICNAS, 2019c). As per 22 January 2019, the IMAP Stage 2 PLC list includes 1,941 polymers identified by CAS name and number (NICNAS, 2019c).

Polymers posing potential concern for either environmental or human health safety are submitted to the NICNAS polymer assessment methodology (NICNAS, 2019a). This methodology follows a tiered approach, with the assessment effort increasing with each tier, while the number of polymers requiring assessment decreases.

Below, the 3 Tiers of the NICNAS polymer assessment methodology are summarised focussing on environmental assessment. Generally, the classical paradigm for chemical RA is followed (hazard evaluation, exposure evaluation, risk characterisation). Further, processes are in place to prioritise the assessment of polymers based on exposure, polymer charge / functionality and stability. Polymers progress through the 3 Tiers until the polymer is either found to pose no unreasonable risk to the environment, or RM measures can be implemented to prevent unreasonable risks to the environment.

### Tier 1: Hazard evaluation

Tier 1 includes high-throughput assessment against predefined criteria e.g. to identify PLC, to prioritise higherrisk polymers. Under the IMAP Framework, all synthetic polymers are considered persistent and not bioaccumulative, i.e. as meeting the equivalent of an aquatic half-life > 2 months and a BCF/ BAF  $\leq$  2000 (NICNAS, 2019a).

Tier 1 toxicity assessment is based on available information on the constituent monomer to determine potential for the polymer and constituent monomers to have environmental hazard characteristics, potential degradation to environmentally hazardous substances and the ability of the polymer to sequester essential nutrients. Polymers that are considered to have high environmental hazards are prioritised for Tier 2 assessment (Table B-1).

Table B-1: Prioritisation of polymers for environmental RA implemented under the NICNAS IMAP Framework (Australian Government, 2013)

| Priority for<br>environmental risk<br>assessment | Polymer characteristics  |
|--|--|
| Low  | Non-ionic in the environment<br>Unmodified natural polymer, not cationic   |
| Moderate   | Degradable synthetic polymer<br>Structure is a mix of natural biodegradable components and synthetic components<br>Indirectly toxic to algae due to sequestration of nutrients |
| High [a]   | Cationic in the environment<br>Polymer degradation products are persistent, bioaccumulative and toxic or very persistent and very<br>bioaccumulative                           |

<u>Footnote to Table B-1</u>: [a] Polymers with high priority for environmental risk assessment are automatically prioritised for Tier 2 assessment.

### Tier 2: Exposure evaluation

Polymers identified to have a high concern use pattern, such as direct application to water bodies, are prioritised for further assessment within Tier 2 using specific exposure models. For other polymers, predicted environmental concentrations (PECs) are calculated using standard exposure scenarios and industry volume derived from available, surrogate, or default exposure information.

#### Tier 3: Risk characterisation

Tier 3.1: Risk quotients (RQ) are determined for low environmental hazard polymers to assess risk. The RQ is calculated by dividing the PEC by a conservative PNEC which is set for low environmental hazard polymers as a group. If RQ < 1, the calculation is validated by confirming the polymer indeed has the expected Tier 1 low environmental hazard characteristics. When confirmed, the polymer is considered a PLC. Otherwise, for RQ  $\geq$  1, or if the polymer does not have all the low hazard characteristics, the polymer is prioritised for Tier 2 assessment.

For polymers in the moderate environment hazard category, a rule-based approach is used to determine whether a RQ can be calculated at Tier 1 based on a conservative PNEC, or whether high tiered models are needed to assess risk.

Tier 3.2: A refined risk characterisation approach is taken for polymers using more sophisticated models for exposure and hazard evaluation, including options to mitigate exposure and toxicity. Polymer degradation products may also be assessed for potential environmental hazards and risks.

## 2.3 Canada

### **2.3.1** Polymers under the Canadian New Substances Notification Regulations

Figure B-2 presents the decision-making process for the notification of polymers implemented in Canada.

Generally, the *Canadian Environmental Protection Act* (CEPA; Canada, 1999) governs the assessment and management of chemicals. For new chemicals and polymers, provisions on the notification and uptake into national inventories (the Domestic Substance List (DSL) or the Non-domestic Substance List (NDSL); Box A-5) are included in the *New Substances Notification Regulations (Chemicals and Polymers)* (NSNR(C&P); Canada, 2005b) and the subsequent *Guidelines for the Notification and Testing of New Substances: Chemicals and Polymers* (Canada, 2005a).

### Box A-5: The Canadian Domestic Substances List (DSL) and Non-Domestic Substances List (NDSL)

The DSL is an inventory of approximately 23,000 substances manufactured in, imported into or used in Canada on a commercial scale, and it is based on substances present in Canada, under certain conditions, between January 1, 1984 and December 31, 1986; <u>https://www.canada.ca/en/environment-climate-change/services/canadian-environmental-protection-act-registry/substances-list/domestic.html</u>.

The NDSL is based on the US EPA TSCA chemical substances inventory for 1985, and contains more than 58,000 entries. Substances that are not on the DSL but are listed on the NDSL are subject to lesser information requirements. Since 1995, the NDSL has undergone annual revisions; <u>https://www.canada.ca/en/environment-climate-change/services/canadian-environmental-protection-act-registry/substances-list/non-domestic.html</u>.

Different notification types have been implemented as Schedules (Annexes) to the NSNR(C&P) (Canada, 2005b), precising information requirements in relation to tonnage and presence on either the DSL or the NDSL. Schedules of relevance for polymers are:

- <u>Schedule 3</u>: Information respecting polymers and biopolymers that are research and development substances, contained site-limited intermediate substances or contained export-only substances;
- <u>Schedule 9</u>: Reduced Regulatory Requirement (RRR) polymers and other polymers and biopolymers (import/manufacture volume < 1000 kg/year);
- <u>Schedule 10</u>: Polymers and biopolymers on the NDSL or all of whose reactants are on the DSL or NDSL (import/manufacture volume < 10,000 kg/year);
- <u>Schedule 11</u>: Other polymers and biopolymers not on the NDSL (import/manufacture volume < 10,000 kg/year).



Figure B-2: Decision-making process for the notification of a polymer implemented in Canada

<u>Footnote to Figure B-2</u>: Flow-chart serves illustrative purposes only. For compliance with the regulatory process, the effective legislation and guidance should be consulted. See text for explanations of Schedules. <u>Colour legend</u>: Purple oval: 'Point of entry'; red oval: Standard notification requirements; green oval: Reduced notification requirements. <u>Abbreviations</u>: DSL: Domestic substances list; FGEW: Functional group equivalent weight; Mn: Number average molecular weight (Da), NDSL: Non-domestic substances list; R&D: Research and development; RRR: Reduced regulatory requirement.

The information requirements for each Schedule are outlined in Appendix 4 ('Schedules under the Regulation') of the Guidelines for the Notification and Testing of New Substances: Chemicals and Polymers (Canada, 2005a).

Further, Environment Canada (EC; now: Environment and Climate Change Canada (ECCC)) and Health Canada (HC) developed a tailored approach to address the complexity of information gathering and assessment activities for polymers, i.e. the "Approach under the Canadian Environmental Protection Act, 1999 to address polymers on the DSL that were identified as priorities during categorisation" (EC and HC, 2014).

## 2.3.2 PLC in Canada: Reduced regulatory requirements (RRR) polymers

Section 9 of the NSNR(C&P) (Canada, 2005b) and Section 3.4.1.3 of the *Guidelines for the Notification and Testing of New Substances: Chemicals and Polymers* (Canada, 2005a) define RRR polymers. The definition is comparable to the definition for PLC implemented in other jurisdictions, i.e.:

"...Polymers with a high NAMW that have a limited percentage of LMW components (< 1000 Da), are chemically stable and do not contain certain reactive or cationic moieties.

An RRR polymer is one of the following:

a) A polymer that... [does not meet specific criteria for cationicity and reactivity, see below] and that has a NAMW > 10 000 Da, with < 2% of its components having Mw < 500 Da and <5% of its components having Mw < 1000 Da;

b) a polymer that... [does not meet specific criteria for cationicity and reactivity, see below] and that has a NAMW > 1000 Da and  $\leq$  10 000 Da, with < 10% of its components having Mw < 500 Da and < 25% of its components having Mw < 1000 Da; or

c) a polymer that is a polyester manufactured solely from reactants listed in Schedule 8 or an anhydrous form of those reactants, other than the reactants or their anhydrous forms that include both 1-butanol and fumaric or maleic acid" (Canada, 2005a).

In accordance with Section 3.4.1.5 of the Guidelines (Canada, 2005a), the fulfilment of specific criteria for cationicity and reactivity is determined by calculating the FGEW of resident cationic or reactive functional groups, i.e. the weight of the polymer that contains one equivalent weight (one mole) of a particular functional group. This Section 3.4.1.5 also lists various types of functional group distributions within a polymer and provides equations to calculation FGEW for each type. Further, a PLC cannot have elements other than carbon, hydrogen, nitrogen, oxygen, silicon, sulphur, fluorine, chlorine, bromine or iodine covalently bound to carbon.

## 2.3.3 Existing polymers under the Canadian Chemicals Management Plan

The Chemicals Management Plan is a Government of Canada initiative aimed at reducing risks posed by chemicals. Within the Chemicals Management Plan, the potential health and ecological risks associated with existing polymers are being assessed and managed; <u>https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan.html</u>.

Based upon an DSL inventory update initiated in 2012, of 603 polymers that had not previously been addressed under CEPA (Canada, 1999), 267 polymers were identified as having been in commerce in Canada in 2011 above the reporting threshold of 1,000 kg. Further information gathering was deemed necessary for these polymers. By contrast, 336 polymers were identified as not meeting this threshold, and a rapid screening approach was applied for these; <u>https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan/initiatives/polymer-rapid-screening-approach.html</u>.

In April 2018, the *Final Screening Assessment for the Second Phase of Polymer Rapid Screening* was released (Canada, 2018; see also <u>https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/second-polymer-rapid-screening.html</u>). Out of the 336 polymers considered:

• 283 polymers did not meet the definition for 'toxicity' set out in Section 64 of CEPA (Canada, 1999);

- 2 polymers met the broad classification of nonylphenol ethoxylates so that they were considered already sufficiently addressed through the 2001 *Priority Substances List Assessment of Nonylphenol and its Ethoxylates;*
- 51 polymers were identified for further assessment:
  - o 29 polymers due to ecological considerations;
  - 19 polymers due to human health considerations
  - 3 polymers due to both ecological and human health considerations.

The screening of the 336 polymers for further assessment encompassed the following four steps, as described in the *"Second Phase of Polymer Rapid Screening: Results of the Screening Assessment"*, jointly published by ECCC and HC (ECCC and HC, 2018).

### Step 1: Identification of polymers with import and/or manufacturing volume > 1,000 kg/year

Polymers with import and/or manufacture volumes less than 1,000 kg/year are not likely to be of ecological concern. This is consistent with the notifying trigger quantity of 1,000 kg for polymers under Section 7 of the NSNR (C&P), as well as experience gained in the first phase of the polymer rapid screening, which did not identify risk potential for any of the polymers (1,000 kg/year maximum) based on results of steps 2, 3, or 4.

### Step 2: Identification of polymers with water extractability > 2 weight%

Water extractability > 2 weight% indicates that the polymer may be more bioavailable to aquatic organisms. The increased potential for exposure to aquatic organisms may present higher ecological risk. This is consistent with the approach taken by the Canadian New Substances program.

A polymer is considered to have water extractability > 2 weight% if it contains one or more functional groups that could increase water extractability. In addition, polymers that are formulated in water and polymers that form a stable emulsion in water are considered to have water extractability > 2 weight%.

#### Step 3: Identification of polymers with RFGs

Polymers containing RFGs may be of increased ecological concern and require further screening. Therefore, they will continue to Step 4, unless available information indicates that they are not of ecological concern. Also, if there is ecological information indicating that a polymer without RFGs may be of ecological concern, it will continue to Step 4.

#### Step 4: Aquatic exposure scenarios

This final step of the rapid screening involves applying environmental release scenarios to estimate environmental exposure. Two generic aquatic exposure scenarios were applied to identify potential concerns near the point of discharge of a polymer into the environment. These scenarios involve comparing conservative estimates of exposure in receiving waters (PEC) with an effects threshold (PNEC) in order to evaluate whether a polymer is likely to cause harm to the local aquatic environment (see ECCC and HC (2018), for an illustration of the ecological exposure estimation approaches applied in the Canadian 'polymer rapid screening' programme).



Figure B-3: Decision-making process for the notification of a polymer implemented in China

<u>Footnote to Figure B-3</u>: Flow-chart serves illustrative purposes only. For compliance with the regulatory process, the effective legislation and guidance should be consulted. <u>Colour legend</u>: Purple oval: 'Point of entry'; red oval: Standard notification requirements; green oval: Reduced notification requirements. <u>Abbreviations</u>: IECSC: Inventory of Existing Chemical Substances Produced or Imported in China; Mw: Molecular weight; tpy: Tonnes per year.

## 2.4 China

Figure B-3 presents the decision-making process for the notification of a polymer implemented in China.

Under China's new chemical legislation, polymers that are not on the Inventory of Existing Chemical Substances Produced or Imported in China (IECSC) are regarded as new substances. The notification to the Chemical Registration Centre shall be done in accordance with the regulation requirement. The manufacture in China and import into China may only begin after the notification certificate is approved by the Chemical Registration Centre. For manufacture in China, the notification applicant shall be the manufacturer of the polymer. For importation into China, the notification applicant either shall be the importer or exporter. If overseas companies are exporters, they may appoint a local Chinese agent to apply for the notification.

Polymers in China can be subject to different notification types:

**Simplified notification - special case**: If all monomers > 2 weight% used during polymer manufacture are already listed on IECSC; or if the polymer meets the rules of PLC (that are very similar to the US EPA PLC criteria; Yang and Wen, 2011).

**Simplified notification - basic case**: If either the 2% rule or the PLC criteria are not met and the expected tonnage is < 1 tonne/year.

Standard notification (without the need of chemical safety report): If either the 2% rule or the PLC criteria are not met and the expected tonnage is > 1 tonne/year.

**Standard notification with reduced data (health and environmental toxicity data not required)**: For PLC that are intended to be listed on the IECSC five years after approval of the notification.

## 2.5 Japan

## **2.5.1** Notification of new and existing chemicals in Japan

Figure B-4 presents the decision-making process for the notification of a polymer implemented in Japan.

In Japan, substances are covered by the Chemical Substances Control Law (CSCL), and new substances additionally by the Industrial Safety and Health Law<sup>9</sup>. Generally, new polymers have to be notified, but exemptions have been implemented for e.g. inorganic polymers, block and graft polymers of which all units are included in the New Chemical Substances Inventory, and for copolymers that do not contain more than 1% of a new chemical, or 2% of an existing chemical<sup>6</sup>.

<sup>&</sup>lt;sup>9</sup> <u>https://www.chemsafetypro.com/Topics/Japan/Overview\_of\_Chemical\_Regulations\_in\_Japan.html</u> <u>https://www.chemsafetypro.com/Topics/Japan/Japan\_New\_Substance\_Notification\_CSCL\_ISHL.html</u> and <u>https://chemicalwatch.com/24516/regulating-polymers</u>.



Figure B-4: Decision-making process for the notification of a polymer implemented in Japan

<u>Footnote to Figure B-4</u>: Flow-chart serves illustrative purposes only. For compliance with the regulatory process, the effective legislation and guidance should be consulted. See text for details on the PFS test. <u>Colour legend</u>: Purple oval: 'Point of entry'; red oval: Standard notification requirements; green oval: Reduced notification requirements. <u>Abbreviations</u>: % w/w: Weight percentage; CSCL: Chemical Substances Control Law; ENCS: Existing and New Chemical Substances; NAMW: Number average molecular weight; PFS: Polymer flow scheme; PLC: Polymer of low concern; tpy: Tonnes per year.

## 2.5.2 Japanese Polymer Flow Scheme (PFS) test and identification of PLS

If polymers are imported or manufactured at volumes exceeding 1 tonne/year, they have to be submitted to the Polymer Flow Scheme (PFS) test that aims at assessing the stability of a polymer and at identifying its breakdown products (METI, 2015); <u>https://www.scas.co.jp/en/services/regulatoryscience/application-japan/chemical-substances-japan/polymer-kashinho.html.</u>

Thereby, Japan is one of only two countries (the other being South Korea) which require a specific endpoint for polymer assessment. The premise of the PFS test is to ensure that only polymers, or their breakdown products, that have low hazard to human health and the environment and which will not pass through a biological membrane are considered as PLC.

The PFS test measures changes in Mw distribution, infrared spectra, and dissolved oxygen concentration (DOC). The protocol of the PFS test has been recently revised to simplify it while maintaining the standards for identifying concerns. The DOC change limit of < 5ppm with corresponding weight change of < 2% has been changed to < 1% DOC change, or weight change of < 2% where the DOC is not applicable. Further, 2 of the 5 solvents originally required for solubility testing (i.e. n-octanol and n-heptane) have been abandoned so that now only water, THF and DMF have to be used as solvents. Finally, clarification was provided on testing that had to be completed in Good Laboratory Practice-compliant laboratories, or not.

The PFS criteria are similar to the PLC criteria adopted under the Japanese CSCL. If the new polymer meets the criteria below, it is evaluated as not being hazardous under the CSCL, and no additional data or evaluations are required for such PLC (METI, 2015):

- NAMW ≥ 1,000 Da;
- Stable at pH 1.2, 4, 7,9 (< 2% weight change) and unaffected by heat and light;
- Polymer is not cationic and does not contain metals other than Na, Mg, K, Ca;
- Insoluble in water, tetrahydrofuran (THF), or dimethylformamide (DMF); OR
- For polymers that are soluble in water, THF, or DMF:
  - ≤ 1% oligomer content (Mw < 1,000 Da); OR
  - > 1% oligomer content, but no concern for bioaccumulation.

Further, PLC in Japan may not contain specific RFGs, i.e. C-C double bond (excluding conjugated double bond in a ring), C-C triple bond, C-N double bond, C-N triple bond, aziridyl, phenolic hydroxyl, sulfonic acid, epoxy, fluoro, amino or hydrazine (METI, 2015).

### 2.5.3 Japanese provisions applying to existing polymers

Polymers not meeting the PFS / PLC criteria undergo a screening process for Priority Action Chemicals (PAC), just like other substances (MoE Japan, undated). However, polymers which are not biodegradable or bioaccumulative and which are manufactured or imported at < 10 tonnes/year can take advantage of low volume exemption, even if they do not pass the PFS test. Toxicity and eco-toxicity tests are required for any polymer which is potentially hazardous to human health or to the environment (i.e. neither PLC nor low volume) when completing a normal notification. Currently, specific guidance to submit non-PLC / non-PFS polymers to the PAC screening process is unavailable. Therefore, they are assessed in the same manner as non-polymers, i.e. for environmental safety assessment (MoE Japan, undated):

- 1. Score 1-5 for toxicity by using algae / Daphnia and fish acute or chronic toxicity data;
- 2. Score 1-5 for exposure depending on the total usage volume in Japan;
- 3. The overall scores are applied to assign substances into specific 'boxes' of the CSCL matrix; thereby substances can be (1) categorised as PAC; (2) placed in a holding pattern; or (3) for substances of lower concern based on specific effects and exposure scenarios, designated as PAC.

## 2.6 Philippines

In the Philippines, chemicals are regulated under the Toxic Substances and Hazardous and Nuclear Waste Control Act of 1990 (Republic Act No. 6969; Philippines DENR, 2017; Mendoza, 2018). Further, the Philippines Department of Environment and Natural Resources (DENR) Administrative Order No. 20, approved in 1992, contains Implementing Rules and Regulations of the Republic Act 6969. While polymers are generally exempt from the Philippine Pre-Manufacture and Pre-Importation Notification (PMPIN) requirements, applicants have to file for an exemption certificate. A polymer is only eligible for this exemption if (1) all of its monomers are already listed on the Philippine Inventory of Chemicals and Chemical Substances (PICCS); or (2) if it contains less than 2 weight% of monomers/reactants (including cross linking, chain transfer agents, and postpolymerisation reactants not on the PICCS; or (3) if  $\geq$  2 monomers or a new polymer are already included in the definition of another polymer on the PICSS (Mendoza, 2018).

In late 2017, the DENR released a draft Circular for public commenting (Philippines DENR, 2017) that aims at providing further guidance on polymers that are considered to be PLC or of low risk to human health and the environment and which can therefore be exempted from the PMPIN process. Specific definitions of cationic polymer, FGEW, gel permeation chromatography (GPC), infrared spectroscopy, Mw monomer, new monomer, reactant, oligomer and polymer were given in this Circular.

In the Philippines, polymers are considered PLC if they meet one of two conditions:

- NAMW ≥ 10,000 Da; < 5% of oligomers with Mw < 1,000 Da and < 2% of oligomers with Mw < 500 Da; and, for cationic polymers, FGEW > 5000 Da; OR
- NAMW ≥ 1,000 Da and < 10,000 Da, < 25% of oligomers with Mw < 1,000 Da and < 10% of oligomers with Mw < 500 Da, and no RFGs in excess of 2 weight%.</li>

Importers and manufacturers must submit a duly notarised and accomplished polymer exemption form along with substance identification information, use(s) of the polymer and safety data sheet of the isolated polymer. A 100% composition breakdown including the CAS numbers of monomers and other reactants must be included. Test data to prove that the polymer meets the PLC criteria (e.g. Mw information obtained by GPC), must also be included. All polymers previously granted exemption are not subject to the new policy. Exempt polymers are not listed on PICCS (Mendoza, 2018).

## 2.7 South Korea

Figure B-5 presents the decision-making process for the registration of a polymer implemented under the so-called 'Korea REACH' (see below).



Figure B-5: Decision-making process for the registration of a polymer implemented in South Korea

<u>Footnote to Figure B-5</u>: Flow-chart serves illustrative purposes only. For compliance with the regulatory process, the effective legislation and guidance should be consulted. <u>Colour legend</u>: Purple oval: 'Point of entry'; red oval: Standard registration requirements; green oval: Reduced registration requirements. <u>Abbreviation</u>: NAMW: Number average molecular weight.

The information provided below has been derived from Kim (2015), Underwriters Laboratories (2017); and <a href="https://www.chemsafetypro.com/Topics/Korea/Introduction to Korean Chemicals Control Act.html">https://www.chemsafetypro.com/Topics/Korea/Introduction to Korean Chemicals Control Act.html</a>.

In South Korea, chemicals are regulated by the *Korean Chemicals Control Act* and the *Act on the Registration and Evaluation of Chemicals* (the 'Korea REACH') that were both adopted in 2013 and came into force in 2015. Generally, new polymers require registration albeit with reduced information requirements. PLC are exempt from registration provided that a PLC exemption with proof of eligibility is submitted.

Together with Japan (see above), South Korea is one of two countries where a specific test is required for polymers. This test is often referred to as the KOPTRI test after the Korean Polymer Testing and Research Institute (http://www.polymer.co.kr/main.do; website in Korean only) where it is usually completed. The KOPTRI test assesses the stability of a polymer following exposure to a range of pH values (OECD TG 120).

The following PLC exemption criteria have been implemented in Korea REACH:

- 1. NAMW  $\geq$ 10,000 Da, of which NAMW < 1,000 Da at < 5% and NAMW < 500 Da at < 2%; OR
- 2. NAMW 1,000-10,000 Da, of which NAMW < 1,000 Da at < 25% and NAMW < 500 Da at < 10%.

Further, PLC exclusions apply for:

- 1. Cationic polymers (unless used only in solid state, and not soluble or dispersed in water);
- 2. NAMW < 10,000 Da in which unreacted monomers corresponding any one of the following are present in an amount of ≥ 0.1 weight%:
  - (a) Hazardous chemicals;
  - (b) Priority control substances;
  - (c) New chemicals (new chemicals are excluded which are registered with completion of hazard evaluation for more than 1 tonne/year).

## 2.8 USA

## 2.8.1 Polymer pre-manufacture notification under the amended US Toxic Substances Control Act

Figure B-6 presents the decision-making process for the notification of a polymer implemented in the USA.

In the USA, chemicals are regulated under the *Toxic Substances Control Act (TSCA) as amended by the Frank R. Lautenberg Chemical Safety Act of the 21<sup>st</sup> Century* (US Government, 2016). Generally, a PMN has to be submitted prior to manufacture or import of a new substance, which must include information on chemical identity, production volume, by-products, use, environmental release, disposal practice, human exposure and existing test data<sup>10</sup>.

Further, the US EPA maintains a list of manufactured or imported substances, i.e. the TSCA Chemical Substances Inventory<sup>11</sup>. As of July 2018, 48 of the 92 substances assessed under the new TSCA and found to be *Chemicals Determined Not Likely to Present an Unreasonable Risk Following Pre-Manufacture Notification Review* were polymers (US EPA, 2019c).

<sup>&</sup>lt;sup>10</sup> <u>https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/filing-pre-manufacture-notice-epa</u>

<sup>&</sup>lt;sup>11</sup> <u>https://www.epa.gov/tsca-inventory/about-tsca-chemical-substance-inventory</u>



Figure B-6: Decision-making process for the notification of a polymer implemented in the USA

<u>Footnote to Figure B-6</u>: Flow-chart serves illustrative purposes only. For compliance with the regulatory process, the effective legislation and guidance should be consulted. <u>Colour legend</u>: Purple oval: 'Point of entry'; red oval: Standard notification requirements; green oval: Reduced notification requirements. <u>Abbreviations</u>: FGEW: Functional group equivalent weight; NAMW: Number average molecular weight; PLC: Polymer of low concern; PMN: Premanufacture notification.

Notably, as compared to the 'old TSCA', the 'new TSCA' includes an option to request / submit PMNs for PLCs (that is very similar to the Canadian 'RRR' polymers; see Appendix B, 5.3.2). PLCs are listed on the Inventory with 'PE-flags' indicating that they are only considered 'listed' when they meet the PLC criteria<sup>12</sup>:

- PE1: The polymer has NAMW ≥ 1,000 Da and < 10,000 Da and is exempt under the 1995 polymer exemption rule. The < 500 Da oligomer content is < 10 weight% and < 25 weight% for < 1,000 Da.
- PE2: The polymer has NAMW ≥ 10,000 Da and is exempt under the 1995 polymer exemption rule. The < 500 Da oligomer content is < 2 weight% and < 5 weight% for < 1,000 Da.
- PE3: The polymer is a polyester that is exempt under the 1995 polymer exemption rule. It is made only from monomers and reactants included in a specified list that comprises one of the eligibility criteria for the 1995 polymer exemption rule.

Further, four new chemical categories related to lung effects have been introduced under the new TSCA. Three of these categories impact polymers, i.e. general surfactants, polycationic substances, and insoluble polymer lung overload. The fourth category refers to 'water-proofing agents' (Henry, 2017). Under the old TSCA, the US EPA already expressed concerns for the inhalation toxicity potential of water-insoluble HMW polymers (Section 4.9 of the present Technical Report).

## **2.8.2** Polymer exemption from premanufacture notification (PLC)

New polymers can be exempt from the obligation to submit a PMN (corresponding to PLC) if they do not *"present an unreasonable risk of injury to human health and the environment"* (US EPA, 1997). Generally, the exemption from PMN applies to polymers that meet the following conditions:

- NAMW  $\geq$  1,000 Da and < 10,000 Da; < 10% oligomer with Mw < 500 Da and < 25% oligomer with Mw < 1,000 Da; OR
  - NAMW ≥ 10,000 Da; < 2% oligomer with Mw < 500 Da and < 5% oligomer with Mw < 1,000 Da; AND
- No RFGs; OR only low-concern functional groups; OR has FGEW above threshold levels for moderateand high-concern functional groups.

Cationic polymers and potentially cationic polymers can be exempt from the obligation to submit a PMN if they are solid and not soluble or dispersible in water and used only in the solid phase; OR if they have low cationic density (i.e. their FGEW is  $\geq$  5,000 Da).

Polyesters are considered not likely to present an unreasonable risk as long as they are manufactured from a list of approved reactants. In the *US EPA Polymer Exemption Guidance Manual* (US EPA, 1997), Table 3 (exemption (e)(3) monomer and reactant list) presents a 'polyester list' for TSCA following substance proposal by industry and review of level of concern to human health and the environment. The assumption is that polyesters will eventually degrade to the monomer units so that only the monomer toxicity is relevant for RA. Although the US EPA estimated that the new chemical substance would be very persistent, this did not indicate a likelihood that the substances would present an unreasonable risk, given that they have low potential for bioaccumulation, low human health concern, and low environmental hazard.

<sup>&</sup>lt;sup>12</sup> <u>https://www.epa.gov/tsca-inventory/how-access-tsca-inventory</u>

Polymer exemptions from PMN are generally not granted for:

- Cationic polymers and potentially cationic polymers (unless they fulfil the above-mentioned criteria);
- Polymers containing medium- or high-concern RFGs above the prescribed FGEWs;
- Polymers that can substantially degrade, decompose, or depolymerise;
- Polymers that contain specific chemical elements other than the ones allowed for in accordance with Section 4.2.2 of US EPA (1997).
- Polymers prepared from > 2 weight% monomers and other reactants other than those on the TSCA Chemical Substance Inventory;
- Polymers containing as an integral part of their composition, except as impurities, certain perfluoroalkyl moieties consisting of a CF<sub>3</sub>- or longer chain length;
- Water-absorbing polymers with NAMW  $\geq$  10,000 Da.

By contrast, as per 1997, polymers containing < 32% carbon; polymers manufactured from reactants containing halogen atoms or cyano groups; and biopolymers are no longer generally excluded from the polymer exemption.

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