National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Overview of legislation on sensitisers
with focus on consumer products

RIVM Letter report 050013001/2014
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Overzicht van wettelijke kaders op het gebied van sensibiliserende stoffen – met een focus op consumentenproducten

Veel consumentenproducten bevatten stoffen die een allergische reactie kunnen veroorzaken (sensibiliserende stoffen). Dat kan door contact met de huid of als de stoffen worden ingeademd. De sensibiliserende stoffen kunnen in consumentenproducten voorkomen, zoals speelgoed, cosmetica, schoonmaakmiddelen, textiel en sieraden. In opdracht van het ministerie van Volksgezondheid, Welzijn en Sport (VWS) heeft het RIVM geïnventariseerd hoe de productie en het gebruik van allergene stoffen in consumentenproducten in wettelijke kaders is gereguleerd.

Bedrijven die chemische stoffen en mengsels in de handel brengen, zijn verplicht om deze in te delen, te etiketteren en verpakken volgens de criteria van de Verordening Indeling Etikettering en Verpakking (CLP). Dit geldt ook voor stoffen waar mensen allergisch op kunnen reageren. Daarnaast hebben producenten en importeurs van chemische stoffen de verplichting om deze, afhankelijk van de hoeveelheid waarin ze worden geproduceerd, te registreren in verband met de Europese verordening voor de productie en handel van chemische stoffen REACH (Registratie, Evaluatie, Autorisatie en restrictie van Chemische stoffen). Bij de registratie van een chemische stof moeten mogelijke gevaren worden beoordeeld en moet worden aangetoond dat het gebruik van de stof veilig is. Ook biedt REACH overheden de mogelijkheid om zeer gevaarlijke of risicovolle stoffen of toepassingen Europees te beperken of te verbieden.

Daarnaast bestaan er wettelijke kaders voor specifieke productcategorieën, zoals cosmetica, schoonmaakmiddelen en speelgoed. Deze richtlijnen bevatten lijsten met onder andere sensibiliserende stoffen (veelal geurstoffen), die niet aan deze producten mogen worden toegevoegd, of verplicht op het etiket moeten worden vermeld. Het kan ook zijn dat een sensibiliserende stof eerst moet worden beoordeeld voordat het op de markt mag worden toegelaten, zoals bij biociden.

Trefwoorden:
Huid sensibiliserende stoffen, respiratoire sensibiliserende stoffen, wetgeving, contact allergie, contact eczeem

Abstract

Overview of legislation on sensitisers - with focus on consumer products

Many consumer products contain substances (sensitising substances) that can cause allergic reactions. These reactions can occur by contact via skin or via the respiratory tract.
Sensitising substances are present in a wide range of consumer products such as toys, cosmetics, detergents, textiles and jewelry.
RIVM made an inventory, requested by the Ministry of Health, Welfare and Sport (VWS), of the different legal frameworks in which the production and use of sensitising substances in consumer products is regulated.

Companies that place chemical substances and mixtures on the market are obliged to classify, label and package according to the criteria in the Regulation on Classification, Labeling and Packaging (CLP). This also applies to substances that can cause allergic reactions. In addition, producers and importers of chemicals are required under REACH (Registration, Evaluation, Authorisation and restriction of Chemicals), depending on the production volume of the substances, to register their chemicals. An essential part of the registration is the hazard assessment and demonstration of safe use. REACH also offers governments the opportunity to restrict dangerous substances or products in Europe.

There are also legal frameworks for specific product categories, such as cosmetics, detergents and toys. These guidelines contain Annexes listing sensitising substances (mostly fragrances) which may not be added to these products, or must be stated on the label. It is also possible that a sensitising substance needs to be assessed before it is authorised on the market, such as for biocides.

Key words:
Skin sensitisers, respiratory sensitisers, legislation, contact allergy, contact eczema

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Samenvatting

Van een toenemend aantal stoffen (sensibiliserend stoffen) is bekend dat ze een allergische reactie kunnen veroorzaken aan de huid of de luchtwegen. Deze reacties hebben een negatief effect op de volksgezondheid en op gezondheidskosten. Allergene stoffen zoals metalen, geurstoffen, (haar)kleurstoffen, of conserveringsmiddelen kunnen aanwezig zijn in een breed scala aan consumentenproducten.

Om de prevalentie van allergie te verminderen, is een voorstel gemaakt om het gebruik van een groot aantal allergene geurstoffen in cosmetica te beperken (gebaseerd op informatie in een opinie van het Wetenschappelijk Comité voor Consumentenveiligheid (SCCS)).
Als basis voor de discussie over dit voorstel, om de aanwezigheid van meer allergene geurstoffen in cosmetica te beperken, wil het ministerie van Volksgezondheid, Sport en Welzijn (VWS) meer inzicht verkrijgen over de gezondheidswinst van allergene stoffen in verschillende consumentenproducten. Daarnaast wil VWS een overzicht van wetgeving inzake sensibiliserende stoffen. Er bestaan verschillende wettelijke kaders die de veiligheid van producten en chemische stoffen in consumentenproducten reguleren. Dit rapport beoogt een overzicht te geven van deze wetgeving, over hoe de productie en het gebruik van sensibiliserende chemische stoffen in consumentenproducten in verschillende wettelijke kaders gereguleerd is.

- De Richtlijn betreffende Algemene Productveiligheid (“General Product Safety Directive”; GPSD) EC/2001/95 garandeert dat alleen veilige consumentenproducten verkocht worden in de Europese Unie. Het omvat zeer algemeen, fysische, mechanische en chemische risico’s. In de richtlijn zijn geen specifieke eisen opgenomen voor sensibiliserende stoffen.
- De Verordening betreffende Indeling Etikettering en Verpakking (“Classification Labelling and Packaging”; CLP) EC/1272/2008 bepaalt de regels voor de indeling, etikettering en verpakking van chemische stoffen. Er zijn specifieke criteria voor de indeling van chemische stoffen in de gevarencategorie ‘allergenen’ geformuleerd. Voor mengsels die zijn ingedeeld als huid- of luchtweg-allergeen worden algemene concentratielimieten gegeven en voor sommige stoffen een specifieke concentratielimiet. Annex VI van de Verordening bevat onder andere ongeveer 1530 (huid of luchtweg) sensibiliserende stoffen, waarvoor op communautair niveau geharmoniseerde indeling en etikettering is vastgesteld.
- Een van de belangrijkste doelstellingen van de Verordening voor Registratie, Evaluatie, Autorisatie en restrictie van Chemische stoffen (REACH) EC/1907/2006 is het beschermen van de volksgezondheid en het milieu tegen chemische risico’s. REACH verplicht fabrikanten en importeurs hun chemische stoffen te registreren, een tonnage-afhankelijk dossier aan te leveren en geregistreerde toepassingen te beoordelen als veilig. REACH biedt overheden ook de mogelijkheid om dossiers en stoffen te evalueren en om EU-brede maatregelen voor te stellen als dat nodig lijkt. Maatregelen kunnen getroffen worden voor stoffen die geïdentificeerd zijn als ‘zeer zorgwekkend’ (“Substances of

Very High Concern"'; SVHC). SVHC's zullen geleidelijk worden geïdentificeerd en op de zogenaamde kandidatenlijst geplaatst worden en vervolgens geprioriteerd worden voor toevoeging aan de Autorisatie lijst (Annex XIV van REACH) waarna gebruik van deze stoffen onder vergunningsplicht valt. Momenteel staan op de kandidatenlijst drie stoffen, die zijn opgenomen op basis van het feit dat de stof in Europa geharmoniseerd ingedeeld is als luchtweg-allergeen, hiervoor is een gelijkwaardige mate van zorg vastgesteld en heeft de stof als zodanig een SVHC-status. Het prioriteren van stoffen die opgenomen kunnen worden op de Autorisatie-lijst is een lopend proces. De Restrictie-lijst (Annex XVII van REACH) bevat stoffen, waaronder (huid)sensibiliserende stoffen, waarvoor de productie, het gebruik en de verkoop zijn beperkt nadat een risico voor deze stoffen was geïdentificeerd.

- De Cosmetica Verordening ("Cosmetics Regulation"; CR) EC/1223/2009 stelt regels vast die het functioneren van de interne markt en de bescherming van de volksgezondheid op hoog niveau waarborgen. De CR behelst alleen de bescherming van volksgezondheid in relatie tot het gebruik van cosmetica en hygiëneproducten. De CR heeft meerdere bijlagen die positieve lijsten van kleurstoffen, conserveringsmiddelen en UV-filters bevatten. In Bijlage II zijn stoffen opgenomen die verboden zijn in cosmetica, op basis van hun gevaarseigenschappen (zie CLP) waaronder sensibiliserende stoffen. Bijlage III bevat een lijst van stoffen waarvoor het gebruik ervan onderworpen is aan beperkingen. Onder hen zijn 26 allergene geurstoffen die eerder verzameld zijn door de SCCS. De risicobeheersmaatregelen voor deze geurstoffen omvatten dat producten geëtiketteerd moeten worden wanneer de concentratie van de geurstof >0,001% is in leave-on of >0,01% in rinse-off producten.
- De Detergenten Verordening ("Detergents Regulation"; DR) EC/648/2004 is onder andere voornemens, consumenten te beschermen tegen allergene stoffen (bepaalt volgens de CLP criteria) aanwezig in schoonmaakmiddelen. De verordening schrijft specifieke etikettering voor waarmee consumenten geïnformeerd worden over de aanwezigheid van allergene stoffen, bijvoorbeeld bepaalde geurstoffen of conserveringsmiddelen. Bij de etikettering wordt de nomenclatuur van de Cosmetica Verordening gebruikt.
- De Speelgoed Richtlijn ("Toys Directive"; TD) EC/2009/48 heeft als doel kinderen te beschermen tegen risico's veroorzaakt door chemische stoffen in speelgoed. Bijlage II van de TD bevat 55 allergene geurstoffen die niet zijn toegestaan in speelgoed. Ook zijn 11 allergene geurstoffen genoemd, die op het speelgoed moeten worden vermeld indien toegevoegd in concentraties van >100 mg/kg, in het speelgoed.
- De Biocide Verordening ("Biocidal Products Regulation"; BPR) EC/528/2012 zorgt ervoor dat alleen biociden op de markt worden gebracht die veilig zijn voor gebruik. Een actieve stof moet goedgekeurd worden volgens de criteria van de BPR voordat het gebruikt mag worden als biocide product. In de verordening staan geen specifieke voorwaarden vermeld voor het verlenen van autorisatie aan stoffen of producten die sensibiliserend zijn.
- Om in aanmerking te komen voor het EU-milieukeurmerk (EU Ecolabel) EC/66/2010 moet een product voldoen aan een aantal criteria. Voor een paar productgroepen (schoonmaakmiddelen, kleding en doe-het-zelf-

producten) zijn er criteria met betrekking tot de sensibiliserende eigenschappen van de stof.

Kortom, de Europese wetgeving inzake de veiligheid van consumentenproducten bestaat uit een aantal verschillende wettelijke kaders die verschillen van meer generiek (GPSD, REACH/CLP) tot meer specifieke wetgeving (Cosmetica Verordening, Detergenten verordening, Speelgoedrichtlijn). Voor huid en luchtweg-allergene stoffen zijn verboden, beperkingen of eisen tot etikettering zijn aanwezig in verschillende wettelijke kaders.

Summary

An increasing number of substances (sensitisers) are known to cause an allergic reaction of the skin or the respiratory tract. These reactions have negative effects on human health and health care costs. Sensitising substances such as metals, fragrances, (hair) dyes, or preservatives are present in a wide range of consumer products.

To prevent allergic reactions, a proposal is made to restrict the use of a large number of skin sensitising fragrances in cosmetics. The underlying information is reported in an opinion of the Scientific Committee on Consumer Safety (SCCS). As basis for the discussion on these restrictions, the Ministry of Health, Sports and Welfare (VWS) would like to obtain more insight in the health impact of sensitising substances in consumer products and to obtain an overview of legislation on sensitisers. There are several legal frameworks which are applicable to product safety and to chemical substances in consumer products. This current report aims to provide an overview of regulations concerning the production and usage of sensitising chemicals in consumer products.

- The General Product Safety Directive (GPSD) EC/2001/95 ensures that only safe consumer products are sold in the European Union. It covers very generally, physical, mechanical and chemical risks. No specific requirements are included for sensitisers.
- The Regulation on Classification, Labelling and Packaging (CLP) EC/1272/2008 sets the rules for classification and labelling of chemicals. Specific classification criteria are formulated for the hazard category 'sensitisers' for substances. For mixtures, which have been classified as skin or respiratory sensitiser, generic concentration limits of components are given. Some sensitising substances have specific concentration limits. Annex VI lists among others approximately 1530 (skin and respiratory) sensitisers for which harmonised classification and labelling have been established at Community level.
- One of the main aims of the Regulation for Registration, Evaluation, Authorisation and restriction of Chemicals (REACH) EC/1907/2006 is to protect human health and the environment from chemical risks. REACH requires manufacturers and importers to register their chemicals, providing a tonnage dependent dossier and evaluate their registered uses as being safe. REACH also offers authorities the possibility to evaluate dossiers and substances and propose EU wide measures if deemed appropriate. Measures may be taken for substances identified as ´substances' of very high concern' (SVHC). SVHCs will be gradually identified and placed on the so-called candidate list and subsequently prioritised for addition to the Authorisation list (Annex XIV of REACH) after which the use of these substances falls under license requirements. On the candidate list currently three substances are included based on the fact that the substance has an European harmonised classification as respiratory sensitiser, providing an equivalent level of concern and as such an SVHC status. The process for prioritisation for inclusion of substances on the Authorisation list is ongoing. The Restriction list (Annex XVII of REACH) contains substances, among which are some

(skin) sensitisers, for which production, use and marketing are restricted after the identification of an unacceptable risk.

- The Cosmetics Regulation (CR) EC/1223/2009 establishes rules to ensure the functioning of the internal market and a high level of protection of the human health. It only covers the protection of human health in relation to the use of cosmetics and hygiene products. Several Annexes of this Regulation contain positive lists of colorants, preservatives and UV-filters. In Annex II substances are listed which are prohibited in cosmetics, based on their hazardous properties (CLP), amongst them are sensitisers. Annex III contains a list of substances that are subject to restrictions on their use. Amongst them are 26 allergic fragrances compiled by the SCCS. The obligatory risk management measures for these fragrances is that products need to be labelled when the concentration is >0.001% in leave-on and >0.01% in rinse-off products.
- The Detergents Regulation (DR) EC/648/2004 intends, amongst others, to protect consumers against sensitising substances present in detergents (according the provisions of the CLP Regulation). It requires specific labelling to inform consumers about the presence of sensitising substances, such as certain fragrances and preservatives, thereby using nomenclature of the Cosmetic Regulation.
- The Toys Directive (TD) EC/2009/48 intends to protect children against risks caused by chemical substances in toys. In Annex II of the TD 55 allergenic fragrances are listed which are not allowed in toys. In addition, 11 allergenic fragrances are mentioned which shall be listed on the toy if added to a toy, as such, at concentrations exceeding 100 mg/kg in the toy.
- The Biocidal Products Regulation (BPR) EC/528 ensures that only biocidal products that are safe for use are placed on the market To use an active substance as a biocidal product, the active substance must be approved according to the BPR. In the Regulation, no specific conditions are mentioned for granting an authorisation for sensitising substances or products.
- To be eligible for the EU-Ecolabel (ER) EC/66/2010 a product must meet a number of criteria. For a couple of product groups (cleaning agents, clothing and do-it-yourself products), criteria are available in relation to sensitising properties of the substance.

In summary, the European legislation on consumer product safety consists of several different legal frameworks, differing from more generic (GPSD, REACH/CLP) to more specific (Cosmetics Regulation, Detergents Regulation or Toys Directive). Restrictions or labelling requests are present in several legal frameworks for skin and respiratory sensitisers.

1 Introduction

1.1 Background

Research indicates that an increasing number of substances used in consumer products are known to cause sensitisation (causing allergic reactions of skin and respiratory tract). Sensitisation can lead to negative effects on human health and healthcare costs (SCCNFP, 1999).
Sensitisation is caused by exposure to a substance that has the potency to be allergenic. The elicitation reaction, however, which leads to actual complaints, can be triggered by much lower concentrations of that substance. Therefore, there is a movement to restrict these substances in (certain types of) consumer products (such as cosmetics), although different group of products (for example, washing and cleaning agents) may cause the actual sensitisation (SCCNFP, 1999; SCCS, 2012).

To get more insight in the impact of sensitising substances in consumer products, the Dutch Ministry of Health, Sports, and Welfare (VWS) made two requests to RIVM with regard to sensitising substances within the framework of the "Kennisvraag Beleidsadvisering cosmetica en chemische productveiligheid".

First, VWS asked to investigate the relative contribution to the total aggregate exposure for one or two sensitising substances present in cosmetics as well as cleaning agents. This question is raised because there is a proposal within the Cosmetics Regulation to prohibit and/or restrict certain allergenic fragrances (e.g. HICC). However, it is unknown whether exposure to these substances via the use of cosmetics is the largest contribution to the total actual consumer exposure and risk for skin sensitisation.
Therefore, RIVM started a study in which an aggregated exposure estimation is to be performed on an allergen, geraniol, that is frequently used in both cosmetics and cleaning agents, to calculate the relative exposure from both product categories. The results of this study will be published separately at the end of 2014.

Next to the aggregate exposure and risk assessment, VWS asked for an overview of relevant legislation on sensitising substances, which is described in the current report.
In the European Union, in different pieces of legislation several measures are in force to reduce exposure to sensitisers. Prevalence data show that a significant proportion of the population still suffers from contact dermatitis (see chapter 2.1).

1.2 Aim of this report

There are several regulations for ensuring the safety of consumers (Consumer safety website, 2014). This inventory aims to provide insight in implemented risk reduction measures concerning the use of sensitising chemicals in consumer products. This overview facilitates weighting the possible risk management measures when complaints are reported in the population for a sensitising substance in any consumer product. Both skin and respiratory sensitisers are included.

A distinction is made between general legislation for substances and products (REACH Regulation, Classification, Labelling and Packaging Regulation, and General Product Safety Directive) and legislation for specific product categories (Cosmetics Regulation, Toys Directive, Detergents and Biocidal Product Directive).
Not included in this report are product category regulations where sensitisers are not mentioned (e.g. Regulation EU 10/2011 – plastic materials and articles intended to come into contact with food; regulations that do not cover chemical properties, but cover for example machinery safety, and worker legislation).
It is noticed that exposure levels at the workplace for some chemicals can be higher, and might be the cause for the sensitisation. The focus in this report is on legislation on chemicals in non-food consumer products. Therefore, not included are regulations with regard to the worker population. Also, this means food allergy is not included.

1.3 Reading guide

The current overview starts with general information on sensitisers (Chapter 2). In Chapter 3, different legislations relevant for sensitising substances in consumer products are described. For each legislation, a general description of the aim of the legislation is given. Then in more detail, it describes how sensitisers are regulated in the different Regulations and Directives. In Chapter 4, a summary of the report is given.

2 General information on sensitisers

2.1 Allergic reactions related to chemicals

An allergic reaction is a hypersensitivity disorder of the immune system. Allergy occurs when a person's immune system reacts to otherwise harmless substances (Putte et al., 2013; SCCS, 2012).
Contact dermatitis is one of the most occurring skin diseases. Based on few population studies, it can be estimated that the frequency of contact allergy to fragrance ingredients in the general population in Europe is 1-3% (SCCS, 2012). In January 2011, the estimated number of 325,000 people were diagnosed with contact dermatitis, based on the registration of general practitioners in the Netherlands (Nationaal Kompas, 2014). It involved 136.000 men and 189.000 women (16.5 per 1000 men and 22.4 per 1000 women) (Nationaal Kompas, 2014)**.** The actual number of people diagnosed with contact dermatitis is expected to be higher, because not everyone will seek medical care (Nationaal Kompas, 2014). The contribution of contact dermatitis in Western Europe amounts almost 1/5 of the total costs of all allergies (Wijnhoven et al., 2008).
In the context of allergies, sensitisation is the process by which a person becomes, sensitised to a substance (sensitiser) as a consequence of exposure to that substance. Sensitisation might be a slow process by which the person becomes sensitised after relatively longer time of low exposure. It might also result from a single exposure to a higher dose (White et al., 2007). The substance may cause a mild response of the body during first couple of exposures but, as the allergy develops, the response becomes stronger with subsequent repeated exposures. After this allergy has developed, even short exposures to very low concentrations can cause severe reactions (Putte et al., 2013).
There are two types of sensitising substances: skin sensitisers and respiratory sensitisers. A skin sensitiser is a substance that will produce an allergic response following skin contact (dermal route). The allergic skin reaction tends to disappear when exposure to the sensitising agent is eliminated although severe reactions (lesions etc.) can occur (Kimber et al., 2002; Wijnhoven et al., 2008).
A respiratory sensitiser is a substance that will induce hypersensitivity of the airways following inhalation of the substance (inhalatory route). Hypersensitivity means that undesirable reactions are produced by the immune system and these can vary in severity from coughing and wheezing to occupational asthma (Wisnewski, 2001; Wijnhoven et al., 2008).

2.2 Sensitising substances in consumer products

A number of sensitising substances has been identified in a wide range of consumer products. Wijnhoven et al. (2008) made an inventory of the most important product categories that may contain sensitising substances. Five main categories of sensitising substances in consumer products can be distinguished: metals, fragrances, (hair) dyes, preservatives and resins/solvents.
Consumers are exposed to the substances via various consumer products such as cosmetics, toys, clothing, and detergents (Wijnhoven et al., 2008; Bfr report, 2006; Schnuch et al., 2004).

2.3 Legislative aspects of sensitising substances in consumer products

Several legal frameworks exist which are applicable to product safety of and chemical substances in consumer products. Information relevant for sensitisers in consumer products is provided in this report.
A distinction is made between general legislation (GPSD, CLP and REACH) and legislation for specific product categories (Cosmetics Regulation, Toys Directive, Detergents Directive and Biocidal Products Regulation). The general legislation complements the provisions of sector-specific product safety legislation which do not cover certain matter, for instance in relation to producer's obligations and the authorities' powers and tasks.

3 Legislation

In this chapter, we provide an overview of the following Directives and Regulations:

- General Product Safety Directive (GPSD) EC/2001/95
- Regulation on Classification, Labelling and Packaging EC/1272/2008
- Regulation for Registration, Evaluation, Autorisation and Restriction of Chemicals (REACH) EC/1907/2006
- Cosmetics Regulation (CR) EC/1223/2009
- Detergents Regulation (DR) EC/648/2004
- Toys Directive (TD) EC/2009/48
- Biocidal Products Regulation (BPR) EC/528/2012
- EU Ecolabel Regulation (ER) EC/66/2010

The GPSD for product safety applies in a complementary way to the sector-specific product safety legislation. Sector-specific product legislation exists for example for pharmaceuticals, medical devices or cosmetics, fall under separate legislation. Specific rules also exist for the safety of toys, chemicals, electrical equipment, or automotive vehicles. The latter two are not included in this report, because these Directives cover safe use of electrical equipment or automotive vehicles and do not cover safe use of chemicals (ECHA- electrical equipment, 2014).
The Directorate General (DG) Enterprise and Industry is responsible for CLP, TD, DR and partly for REACH. The latter falls also under the responsibility of DG Environment, besides BPR and ER. The DG for Health and Consumers (SANCO) is responsible for the GPSD and CR.

3.1 General Product Safety Directive EC/2001/95

3.1.1 Introduction

The aim of General Product Safety Directive (GPSD) EC/2001/95 is to ensure that only safe consumer products are sold in the European Union (EU): *'producers shall be obliged to place only safe products on the market'* (GPSD, art. 1). The GPSD covers the provisions for consumer products that are not covered by specific sector legislation, for instance in relation to producers' obligations and the authorities' powers and tasks.

The Directive provides a generic definition of a safe product: *'safe product shall mean any product, which under normal or reasonably foreseeable conditions of use including duration and, where applicable, putting into service, installation and maintenance requirements, does not present any risk or only the minimum risks compatible with the product's use, considered to be acceptable and consistent with a high level of protection for the safety and health of persons'*, art.2 of the GPSD.

Products must comply with this definition. If there are no specific national rules, the safety of a product is assessed in accordance with:

- European standards;

- Community technical specifications;
- Codes of good practice;
- The state of the art and the expectations of consumers (GPSD, art. 3 and 4).

The GPSD is implemented in the Dutch "Warenwet", (Warenwet, 2014). Member States of the EU are obliged to enforce the requirements on producers and distributors. They must appoint the authorities in charge of market surveillance and enforcement. The Netherlands Food and Consumer Product Safety Authority (NVWA) are in charge in the Netherlands.
Producers and distributors have the obligation to inform consumers of the risks associated with the products they supply. They must take appropriate measures to prevent or restrict the marketing or use of products posing a serious risk to the health and safety of consumers and of professional users.

In the EU, the information between Member States and the Commission on products posing a serious risk to health and safety is exchanged via the Rapid Exchange of Information System (RAPEX). This system is also used for quick exchange of information on measures taken to prevent or restrict the marketing or use of products posing a serious risk to the health and safety of consumers. It covers products such as clothing, cosmetics or toys with potentially harmful ingredients or quality or even products with technical faults. RAPEX does not include food, pharmaceutical products and drugs. The basis of this alert system lies in the GPSD. Since 1 January 2010, the system also facilitates the rapid exchange of information on products posing a serious risks for professional users or as well as to other public interests protected via the relevant EU legislation (e.g. environment and security (GPSD-website, 2014; RAPEX notifications, 2014; GPSD, art. 5 and 6).

3.1.2 GPSD in relation to sensitisers

The GPSD covers all physical, mechanical and chemical risks. GPSD has no specific requirements for sensitising substances. However, it ensures the safety of all consumer products. There is a role for chemical risks in the Directive, via RAPEX.

In the text box below an example is given of health problems caused by sensitising substances in consumer products whereby a notification of RAPEX has led to a (temporary) European risk management measure.

An illustrative example

Dimethylfumarate (DMF)

DMF is a fungicide used as an anti-mould treatment in shoes, textiles and furniture. In 2007/2008 DMF was found to be a serious risk of inducing (contact) dermatitis (RAPEX notification reports 40 & 52)
The responsible competent national authorities took several recalls and measurements resulting in:

- ban of DMF in seats and footwear (France)
- ban in all products with skin contact (Spain)
- ban in al consumer products (Belgium)

In 2009, based on performed measurements, the European Commission made a decision (2009/251/EC) on those consumer products with > 0.1 mg/kg DMF:
- must not be placed on the market
- must not be made available to consumers
- have to be withdrawn from the market
- have to be recalled from consumers

After 12 months the validity of the DMF ban was extended in 2010 (2010/153/EC) and in 2011 (2011/135/EC).

In 2012, restrictions on the use of DMF are included in Annex XVII of the REACH Regulation. DMF shall not be used in articles or any parts thereof in concentrations greater than 0.1mg/kg. Articles or any parts thereof containing DMF in concentrations greater than 0.1 mg/kg shall not be placed on the market (Commission Regulation (EU) No 412/2012).

3.2 Regulation on Classification, Labelling and Packaging EC/1272/2008

3.2.1 Introduction

CLP (EC/1272/2008) is the Regulation on classification, labelling and packaging of substances and mixtures. It is an implementation of the Globally Harmonised System of Classification and Labelling of Chemicals (GHS)[1]. The Regulation replaces previous EU legislation on classification, labelling and packaging of chemicals (Dangerous Substances Directive 67/548/EEC and the Dangerous Preparations Directive EC/1999/45/EC) although some specific elements are retained.
The aim of this Regulation is to ensure a high level of protection of human health and the environment as well as the free movement of chemical substances, mixtures and certain specific articles, while enhancing competitiveness and innovation (CLP, art. 1). The classification of chemicals is to reflect the type and severity of the intrinsic hazards of a substance or mixture. The CLP regulation sets the rules for classification and labelling of chemicals. It aims to determine whether a substance or mixture displays properties that results into a classification as hazardous. These hazardous properties are communicated in a standardised way including pictograms, warning statement, hazard statement and precautionary statements. CLP itself does not set information requirements (except for determining physical properties) (CLP, art. 8).

Self-classification
Producers and importers itself determine the classification of the substance and mixture. For this, they collect available information, evaluate the adequacy and reliability of the information, review the information against the classification criteria and decide on classification. The information requirements laid down in REACH will however, ensure availability of data (in §3.3 REACH will be described

[1] The GHS is a United Nations system that identifies hazardous chemicals and informs users about the hazards through standard symbols and phrases on the packaging labels and through safety data sheets. It contains classification criteria, hazard symbols and Hazard and Precautionary Statements for labelling, while taking account of elements which are part of the previous EU legislation.

in more detail). Based on the information and tests, a substance or mixture is classified in one or more of the different hazard categories (CLP, art. 3 and 4). Once the substance or mixture is classified the identified hazards should be communicate to other actors in the supply chain, including consumers, via the label and the safety data sheet (CLP, art. 4).

Harmonised classification and labelling
In some cases, the decision on the classification of a substance is taken at Community level. It is mandatory for the suppliers of the respective substance or mixture to apply this harmonised classification and labelling. This process often concerns the most hazardous substances. These are usually carcinogenic, mutagenic, toxic for reproduction or respiratory sensitisers. Member States, manufacturers, importers and downstream users may propose harmonised classification and labelling. Proposals can only be submitted for substances, and not for mixtures (CLP, Annex VI, part 1 and 3). Annex VI lists hazardous substances for which harmonised classification and labelling have been established at Community level (CLP, Annex VI, part 3).

3.2.2 CLP in relation to sensitisers

In this section, the specific classification criteria formulated for the hazard category 'sensitisers' are described based on section 3.4 of the CLP Regulation in line with the Globally Harmonised System (GHS) of classification and labelling. The hazard category 'sensitisers', distinguishes respiratory and skin sensitisers. Criteria for sub-categories are defined (Cat. 1, Sub-cat. 1A and Sub-cat. 1B). Furthermore, criteria for classification are given for substances and mixtures as either respiratory or skin sensitisers are given, see Appendix I for the exact classification criteria (CLP, section 3.4).

3.2.3 Annex VI

Annex VI contains the list of harmonised classifications (CLP, Annex VI). This list is based on proposals submitted by Member State Competent Authorities (MSCA) and industry, assessed by a Committee for Risk Assessment (RAC) and agreed by the MSCAs, the Commission and the European Parliament. Further, there is a register of self-classification of substances by industry as notification of the classification of all hazardous substances to ECHA is required by CLP.
In the study of RPS, the number of substances with harmonised classification of sensitisers is given under the CLP regulation (see Table 1) (Putte et al., 2013).

Table 1. Number of substances with harmonised classification of sensitisers (Category 1) (from Putte et al., 2013, table 5)

Harmonised classification under CLP	Number of substances
Skin Sens. 1	1252
Skin Sens. 1A	10
Skin Sens. 1B	24
Resp. Sens. 1	231
Resp. Sens. 1A	3
Resp. Sens. 1B	12

According to RPS (Putte et al., 2013), the number of skin and respiratory sensitisers, based on the notified self-classification, is much higher compared to the number of sensitisers with harmonised classification (see Table 2).

Table 2. Number of substances with self-classification on sensitisation (Category 1) which have been notified under REACH (from Putte et al., 2013, table 4)

Notified classification under REACH	Number of substances
Skin Sens. 1	10267
Skin Sens. 1A	64
Skin Sens. 1B	136
Resp. Sens. 1	2393
Resp. Sens. 1A	7
Resp. Sens. 1B	25

Some substances that are classified as sensitisers may elicit a response, when present in a mixture in quantities below the generic concentration limits for classification as sensitiser (shown in Appendix 1, table 3). Individuals who are already sensitised to the substance or mixture, might be elicitated when the skin or respiratory sensitiser is present at or above the concentration limits for elicitation as shown in Table 3 (elicitation concentration) (CLP, section 3.4.3.3.2). The concentration limit for elicitation is used for the application of the special labelling requirements of Annex II section 2.8 to protect already sensitised individuals. The label on the packaging shall bear the statement: EUH208 – 'Contains (name of sensitising substance) may produce an allergic reaction' (CLP, Annex II, section 2.8).

Table 3. Concentration limits for elicitation of components of a mixture (from CLP, section 3.4.3.3.2)

Component classified as:	Concentration limits for elicitation		
	Respiratory sensitiser Category 1		Skin sensitiser Category 1
	Solid/liquid	Gas	All physical states
Respiratory sensitiser Category 1	≥ 0,1 % (Note 1)	≥ 0,1 % (Note 1)	
Respiratory sensitiser Sub-category 1A	≥ 0,01 % (Note 1)	≥ 0,01 % (Note 1)	
Respiratory sensitiser Sub-category 1B	≥ 0,1 % (Note 1)	≥ 0,1 % (Note 1)	
Skin sensitiser Category 1			≥ 0,1 % (Note 1)
Skin sensitiser Sub-category 1A			≥ 0,01 % (Note 1)
Skin sensitiser Sub-category 1B			≥ 0,1 % (Note 1)

In the box below, an example is given of a substance, isoeugenol, with no harmonised classification (Annex VI of CLP). As a result products containing isoeugenol are labelled differently.
The Netherlands has the intention to submit a proposal to harmonise the classification for isoeugenol as skin sensitiser Cat. 1A. Harmonised classification

will result in a generic concentration limit ≥0.1% (see Appendix 1, table 13). This will result in uniform classification of substances and mixtures. As a result of the harmonised slassification it is expected that isoeugenol will be used in less consumer products (ECHA website - CLH intentions, 2014).

An illustrative example

Isoeugenol

Isoeugenol is a fragrance and a well-recognised sensitising substance. At present, isoeugenol is not harmonised classified (Annex VI of CLP) and is by the industry often classified as skin sensitiser Cat. 1. Therefore, there is no labeling requirement and Isoeugenol might be present in concentrations >1% (CLP, section 3.4.3.3.2).

Voluntary measures to limit the use of isoeugenol in scented products have been in place since 1980. The International Fragrance Research Association (IFRA) has been issuing recommendations since 1980 for limiting the isoeugenol in finished cosmetics products. At first to a maximum of 2000 pm (0.2%) and from 1998 to 200 ppm (0.02%). The IFRA recommendation has been further reduced to 100 ppm (0.01%) in 2008 for lip products, toys, waxes for mechanical hair remover, deodorants and fragrances bracelets (IFRA, 2009; IFRA, 2011; Rastogi et al., 2008).
Isoeugenol is also listed on Annex III of CR and its presence must be indicated in the list of ingredients when its concentration exceeds:
- 0,001% in leave-on products
- 0,01% in rinse-off products (CR, Annex III)

In addition, isoeugenol shall not be present in toys (TD, Annex II) and when isoeugenol is added at concentrations exceeding 0.01% w/w in detergents, it must be labelled (DR, Annex VII).

The Netherlands has announced the intention to submit a CLH dossier to harmonise the classification for isoeugenol as skin sensitiser Cat. 1A. Expected date of submission is 1 October 2014 (ECHA website - CLH intentions, 2014).

3.3 REACH EC/1907/2006

3.3.1 Introduction

REACH is the Regulation for Registration, Evaluation, Authorisation and Restriction of Chemicals (EC/1907/2006). It entered into force on 1st of June 2007 to streamline and improve the former legislative framework on chemicals in the EU (ECHA-website, 2014).
The main aims of REACH are to ensure a high level of protection of human health and the environment from the risks that can be posed by chemicals, the promotion of alternative test methods, the free circulation of substances on the internal market and enhancing competiveness and innovation (ECHA-website, 2014; REACH, art. 1).

REACH requires industry to generate information on the intrinsic properties of substances, assess these properties, determine D(M)NELs and perform a chemical safety assessment when the substance fulfills certain requirements.

The properties of the substance and the specific conditions for save use of the substance is communicated via the safety data sheet through the supply chain. Manufacturers and importers of substances have a general obligation to submit a registration to the European Chemicals Agency (ECHA) for each substance manufactured or imported in quantities of 1 tonne or more per year per company (legal entity). This obligation applies to substances as such and in mixtures (REACH, art. 6 and 7). A special registration regime applies for certain substances in articles (SVHC).
ECHA and EU Member States will prioritise registered substances for evaluation. There are two types of evaluation under REACH:

1) Dossier evaluation performed by the European Chemicals Agency
2) Substance evaluation performed by a Member State

The CLP regulation sets out the rules for classification and labelling of chemicals (see par. 3.2). Based on the classifications and evaluation of a substance, it might be identified as a substance of very high concern (SVHC) (i.e., carcinogenic, mutagenic or reproduction toxic category 1A or 1B, or of equivalent concern). SVHC's will be gradually identified in the Candidate list and eventually added to the Authorisation list (Annex XIV) of REACH (REACH, Annex XIV; Putte et al., 2013). Substances listed in Annex XIV require authorisation before they can be put on the market or used.
Based on the available information showing a risk, substances can also be restricted or banned for some uses of application (REACH, Annex XVII).
Regarding the purpose of this report, REACH Annex XVII, SVHC list and Authorisation list will be further discussed in relation to sensitisers.

3.3.2 REACH in relation to sensitisers

The assessment of the skin sensitisation potential of substances is among the standard information requirements for substances manufactured or imported in the EU in quantities of one tonne or more (REACH, Annex VII). Therefore, information on skin sensitisation is a mandatory requirement for substances produced or imported with the lowest tonnage level, affecting all chemicals registered under REACH. The assessment of this endpoint comprises two consecutive steps: firstly an assessment of the available human, animal and alternative data and secondly *in vivo* testing.
Animal testing does not need to be conducted in the case there is available information to classify the substance for skin sensitisation. The Local Lymph Node Assay (LLNA) is the first choice method for *in vivo* testing.
The precondition within REACH is that before any new *in vivo* test are carried out to fulfil the information requirements, all available *in vitro* data, *in vivo* data, historical human data, data from valid (Q)SARs and data from structurally related substances shall be assessed (REACH, Annex XI).

3.3.3 Annex XVII Restrictions on the manufacture, placing on the market and use of certain dangerous substances, mixtures and articles

Annex XVII sets out the restrictions on the manufacture, placing on the market and use of certain dangerous chemical substances, mixtures and articles. The Annex contains a list, which are restricted by REACH Regulation.
Annex XVII contains the restrictions of the marketing and use of dangerous substances adopted since 1976 in the framework of Directive 76/769/EEC, as

well as subsequent restrictions adopted under REACH. The revised Annex XVII was adopted on 22 June 2009 (Review of Annexes, 2014).
The Annex XVII contains some restrictions on substances with (skin) sensitising properties. However, the reasons why these substances are included in the Restriction list are not necessary due to their sensitising properties, but often due their CMR properties (Putte et al., 2013).
A restriction can be proposed for a substance inducing sensitisation when it is shown that the current use of the substance results to a risk. Examples for those are the restrictions on nickel, chromium VI and dimethylfumarate (see chapter 3.1.2 for dimethylfumarate). The box below illustrates the background of the restriction on nickel as included in Annex XVII of REACH.

An illustrative example

Nickel

Allergy to nickel-containing products is a frequently occurring problem. A limit of 0.5 µg/cm2/week for the release of nickel from nickel-containing alloys was introduced in Denmark in 1991. In 1994, the so-called Nickel Directive 94/27/EC was adopted in the EU. It became effective in 2001, when the corresponding analytical method became available (Schuur et al., 2008).

The Nickel Directive regulates the use of nickel in jewellery and other products that come into contact with the skin. It imposes limits on the amount of nickel that may be released from jewellery and other products intended to come into direct and prolonged contact with the skin. These limits, known as migration limits are:

- 0.2 ug/cm^2/week for post assemblies which are inserted into pierced ears and other pierced parts of the human body
- 0.5 ug/cm^2/week for other products intended to come into direct and prolonged contact with the skin (REACH, Annex XVII, point 27)

Since 1 June 2009, it has been subsumed into REACH Regulation, specifically item 27 of Annex XVII to that regulation.

3.3.4 SVHC list (Candidate list) and Annex XIV (Authorisation)

In art. 57 of REACH, criteria are defined for identification of substances as Substances of Very High Concern (SVHC), see below.

Substances to be included in Annex XIV
The following substances may be included in Annex XIV in accordance with the procedure laid down in art. 58:
(a) substances meeting the criteria for classification in the hazard class carcinogenicity category 1A or 1B in accordance with section 3.6 of Annex I to CLP;
(b) substances meeting the criteria for classification in the hazard class germ cell mutagenicity category 1A or 1B in accordance with section 3.5 of Annex I to CLP;
(c) substances meeting the criteria for classification in the hazard class reproductive toxicity category 1A or 1B, adverse effects on sexual function and fertility or on development in accordance with section 3.7 of Annex I to CLP;

(d) substances which are persistent, bioaccumulative and toxic in accordance with the criteria set out in Annex XIII of this Regulation;
(e) substances which are very persistent and very bioaccumulative in accordance with the criteria set out in Annex XIII of this Regulation;
(f) substances — such as those having endocrine disrupting properties or those having persistent, bioaccumulative and toxic properties or very persistent and very bioaccumulative properties, which do not fulfil the criteria of points (d) or (e) — for which there is scientific evidence of probable serious effects to human health or the environment which give rise to an equivalent level of concern to those of other substances listed in points (a) to (e) and which are identified on a case-by-case basis in accordance with the procedure set out in art. 59.

Once a substance is identified as SVHC, it is placed on the SVHC-list (Candidate list).
Although many of these substances are included due to their CMR or PBT/vPvB properties, some of them are also known as sensitisers. Sensitisers might be identified and could be included for that reason on the Candidate list as substances of equivalent concern according to art. 57(f) of REACH. They can be identified on a case-by-case basis as substances of very high concern (SVHCs), where there is scientific evidence of probable serious effects to human health or environment, which give rise to an equivalent level of concern to CMR or PBT/vPvB substances (REACH, art. 57). This requires agreement of the Member State Committee of ECHA. Currently 151 substances are on the Candidate list with last update on 16 December 2013 (Candidate list, 2014). Among the dossiers submitted for SVHC identification in August 2012, three entries[2] on this list are found to be classified as respiratory sensitisers under CLP (Candidate list, 2014).
Authorisation list (Annex XIV of REACH) is a list of substances which are prioritised from the Candidate list. The prioritisation is based on the available information on intrinsic properties (irreversible, delayed effect, negative impact, threshold e.g.), uses and volumes of the substances on the EU market. Placing on the market and use of the substances listed on Authorisation list requires an authorisation. Substances placed on the Authorisation list will only be authorised for specific uses if the registrant can demonstrate that the risk from the use of the substance is adequately controlled or that the socio-economic benefits of the substance outweigh risks and no safe alternative exists (REACH, art. 58).

3.3.5 SVHC roadmap-sensitisers

To identify new potential SVHCs, information on a large number of substances needs to be analysed. To achieve this objective, the Commission, with the collaboration of ECHA, drafted a Roadmap, which was discussed with Member States Competent Authorities (MSCA) for REACH. With the Roadmap, the Commission defines a process to identify and assess the following categories of potential SVHCs:

- CMRs (substances that are carcinogenic, mutagenic or toxic for reproduction),
- PBTs (substances that are Persistent, Bioaccumulative or Toxic for the Environment),

- vPvBs (substances that are very Persistent and very Bioaccumulative),
- substances of equivalent concern (such as endocrine disruptors or sensitisers).

The Roadmap describes how to examine the substances that may be one of the above categories, by giving priority to those that have been registered and are not used only as chemical intermediate. The Roadmap aims to improve planning, predictability, communication and to define responsibilities and deliverables (European Commission, 2013).
Several expert groups (PBT and Endocrine Disruptor) and coordination groups (CMR and Sensitisers) focus on substances with specific properties. The groups coordinate the screening activities carried out by Member States or by ECHA and contribute to the development and refinement of screening approaches. The sensitiser coordination group focusses on sensitiser substances that may qualify for SVHC identification based on the criteria in art. 57(f) (Sensitiser Coordination Group, 2014).
ECHA presented a list of potential SVHCs. Member States (voluntary) evaluate this list and add substances on the list they think are potential SVHCs. Among them are sensitising substances (mainly skin sensitisers) which will be evaluated if there is enough "equivalent concern" to propose inclusion on the SVHC list. However, it is expected that respiratory sensitisers will meet more often the criteria of art. 57. At present, the first skin sensitiser to meet the criteria of art. 57(f) for equivalent concern needs to be evaluated (Sensitiser Coordination Group, 2014).

3.4 Cosmetics Regulation EC/1223/2009

3.4.1 Introduction

On 11 July 2013, the Cosmetics Regulation (CR) EC/1223/2009 came into force strengthening the safety of cosmetic products and streamlining the framework for all operators in the sector. The CR, adopted in 2009, replaces Directive EC/76/768 that was adopted in 1976 and has been substantially revised on no less than 7 occasions (CR).
It establishes rules to be complied with by any cosmetic product made available on the market, in order to ensure the functioning of the internal market and a high level of protection of human health (Putte et al., 2013).
The CR covers only cosmetics and hygiene products and not medicinal products, medical devices or biocidal products (CR, art. 1; Wijnhoven et al., 2008). The definition of a cosmetic product is: '*any substance or preparation intended for placing in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or principally to cleaning them, perfuming them or protecting them in order to keep them in good condition, change their appearance or correct body odours*' (CR, art. 1.1).

The main part of the Regulation consists of different Annexes which give, with respect to use in cosmetic products, a list of:

- Annex II substances prohibited in cosmetics; e.g. Carcinogenic, Mutagenic or Reprotoxic substances (CMR substances classified 1A, 1B or 2)

- Annex III substances that are subject to restrictions on their use; such substances might only be permitted for certain types of cosmetics, or in certain concentrations, or subject to warning labels e.g.
- Annex IV allowed colorants
- Annex V allowed preservatives
- Annex VI allowed UV filters

Use in cosmetic products of colorants other than those in Annex IV, preservatives other than those in Annex V, and UV filters other than those in Annex VI, is prohibited (CR).

For the safety assessment of cosmetic ingredients, the European Commission (EC) is assisted by the Scientific Committee on Consumer Safety (SCCS). The SCCS is a scientific committee of DG SANCO with independent scientists and evaluates the safety of a number of cosmetic ingredients (e.g. UV filters, hair dyes, preservatives) and provides opinions on health and safety risks of non-food consumer products (e.g. cosmetic products and their ingredients) and services. SCCS opinions are published in response to a specific request of the European Commission or Member States (SCCS-website, 2014). At the end of the risk assessment process, the opinion is adopted and published. The SCCS can also publish statements on specific topics, at its own initiative. Based on the advice of the SCCS, a draft Regulation for amendment of the Annexes of the Cosmetics Regulation may be proposed by the EC. The Standing Committee on Cosmetic Products with representatives of Member States decides on these amendments (SCCS-website, 2014).

3.4.2 Cosmetic Regulation in relation to sensitisers

Annex II of this Regulation contains a list of 1373 substances which are not allowed in cosmetic products. It mostly includes substances classified as CMR, bust also classified skin and respiratory sensitisers. See for a non-exhaustive list of sensitizing substances Table 4 (Wijnhoven et al., 2008; Putte et al., 2013; CR, Annex II).

Table 4. Non-exhaustive list of sensitizing substances included in Annex II of Cosmetic Regulation (copied from Putte et al. 2013, table 10)

Substance name	***CAS no.***
Alanroot (Inula helenium)	97676-35-2
Allylisothiocyanate	57-06-7
Benzyl cyanide	140-29-4
p-tert-Butylphenol (Wormseed oil)	98-54-4
Diethyl maleate	141-05-9
Dihydrocoumarin (6,7-Dihydrogeraniol)	119-84-6
Dimethyl citraconate	617-54-9
6,10-Dimethyl-3,5,9-undecatrien-2-one (Pseudoionone)	141-10-6
Diphenylamine	122-39-4
Ethyl acrylate	140-88-5
trans-2-Heptenal	18829-55-5
trans-2-Hexenal diethyl acetal	67746-30-9
trans-2-Hexenal dimethyl acetal	18318-83-7
Hydroquinone monoethyl ether (4-Ethoxyphenol)	622-62-8
7-Methoxycoumarin	531-59-9

4-(p-Methoxyphenyl)-3-butene-2-one	943-88-4
1-(p-Methoxyphenyl)-1-penten-3-one	104-27-8
Methyl trans-2-butenoate	623-43-8
7-Methylcoumarin	2445-83-2
5-Methyl-2,3-hexanedione (Acetyl isovaleryl)	13706-86-0
Musk Ambrette (solution only)	83-66-9
4-Phenyl-3-buten-2-one	122-57-6
Verbena oil (Lippia citriodora Kunth)	8024-12-2

Annex III is a list of 265 substances which are allowed for use in cosmetics with restrictions. Amongst them is the list of 26 allergenic fragrances compiled by the SCCS, listed in Table 5 and 6 (SCCNFP, 1999; SCCS, 2012). The restriction for these fragrances is that products need to be labelled (have a declaration limit) when the concentration is > 0.001% in leave-on, and > 0.01% in rinse-off products (SCCNFP, 1999; CR, Annex III). Annex III also contains several sensitising hair dyes for which the conditions of use are a print on the label: "Hair colourants can cause severe allergic reactions. Read and follow instructions".
Regarding sensitisers, it is important to remark that preservatives are only allowed if they are listed in Annex V, part 1, or are allowed with a specific concentration limit as specified in Annex V, part 2 (CR, Annex V). Examples are formaldehyde and paraformaldehyde which are allowed up to 0.2% or 0.1% for oral hygiene products, and forbidden in sprays, and methylchloroisothiozolinone/methylisothiazolinone (MCI/MI) which is not allowed above 15 ppm (Wijnhoven et al., 2008).
In contrast to fragrances, preservatives must always be declared by name on the ingredient labels of cosmetics and detergents.

Table 5. Fragrance chemicals which according to existing knowledge, are most frequently reported and well-recognised consumer allergens (from SCCS, 2012; list A)

Common name	***CAS no.***
Amyl cinnamal	122-40-7
Amylcinnamyl alcohol	101-85-9
Benzyl alcohol	100-51-6
Benzyl salicylate	118-58-1
Cinnamyl alcohol	104-54-1
Cinnamal	104-55-2
Citral	5392-40-5
Coumarin	91-64-5
Eugenol	97-53-0
Geraniol	106-24-1
Hydroxycitronellal	107-75-5
Hydroxymethylpentyl-cyclohexenecarboxaldehyde	31906-04-4
Isoeugenol	97-54-1

Table 6. Fragrance chemicals, which are less frequently reported and thus less documented as consumer allergens (from SCCS, 2012; list B)

Common name	***CAS no.***
Anisyl alcohol	105-13-5
Benzyl benzoate	120-51-4
Benzyl cinnamate	103-41-3
Citronellol	106-22-9
Farnesol	4602-84-0
Hexyl cinnamaldehyde	101-86-0
Lilial	80-54-6
d-Limonene	5989-27-5
Linalool	78-70-6
Methyl heptine carbonate	111-12-6
3-Methyl-4-(2,6,6-trimethyl-2-cyclohexen-1-yl)-3-buten-2-one	127-51-5
Oak moss	90028-68-5
Tree moss	90028-67-4

3.4.3 Opinion and recommendations of the SCCS

In 1991 following an opinion from the Scientific Committee of Non-Food Products (SCNFP), 26 fragrances were identified of which information should be provided to consumers concerning their presence in cosmetic products (SCCNFP, 1999). Declaration limits for these fragrances have been implemented in the Cosmetics Regulation in 2005, which has been shown to be important in the clinical management of patients who are allergic to allergenic fragrances (Utter, 2013).

Recent studies have confirmed that the 26 fragrance allergens, identified by the SCCNFP, are still relevant fragrance allergens for consumers because of their exposure from cosmetic products. Additional exposure to many of these 26 fragrance allergens also occurs from the use of other consumer products, such as detergents, toys, etc. Some of these fragrance substances are also used as preservatives (SCCS, 2012).

Based on additional concerns of the European Commission on the impact of different fragrances in consumer products on human health, the SCCS opinion has been updated with new information and insights in 2012 (SCCS 1459/11). Main conclusion of the SCCS in 2012 is that 82 substances (including the 26 already known fragrance allergens) are identified as established contact allergens in humans, for which a declaration limit should be introduced. Furthermore, 12 chemicals and 8 natural extracts are considered of special concern as they have given rise to at least 100 reported cases of allergenic contact dermatitis in Europe. These substances pose a particularly high risk of sensitisation to the consumer and limitation of exposure would help to protect sensitised consumers from developing allergic contact dermatitis. The SCCS considers that a general threshold of 0.01% (0.8 µg/cm^2) of allergenic fragrances in cosmetic products would limit the problem of fragrance allergy in the consumer significantly. One substance, hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC), was shown to be the cause of allergic contact dermatitis in more than 1500 reported cases since 1999. The number of cases is only those reported in scientific publications, and therefore the actual number of cases is severely under-estimated. According to SCCS, HICC should not be used in consumer products in order to prevent further cases of contact allergy to HICC

and to limit the consequences to those who already have become sensitised. In addition, chloroatranol and atranol, the main sensitising constituents of Evernia prunastri and Evernia furfuracea, should not be present in products for the consumer (SCCS, 2012).

Recommendations of the SCCS:
- refine the QRA method in order to derive more specific concentration limits for the fragrance allergens of concern. Refinement of the QRA should also include a critical analysis of the exposure assessment. The impact of the following issues in the refinement of the QRA should be addressed: aggregate exposure (exposure to more than one source of the same allergen), distribution of products into product categories and leave on versus rins off products.
- ban the three fragrances HICC, atranol and chloroatranol to prevent the development of new allergy cases. These fragrances should be placed on Annex II of the Cosmetics Regulation.
- place twelve fragrance contact allergens of special concern on Annex III of the Cosmetics Regulation, see Table 7. It is recommended that for these fragrances concentration limits will be introduced, if the QRA is able to derive safe exposure levels and no other major sources of exposure (e.g. detergents, toys) exist.

Table 7. Established fragrance contact allergens of special concern (single chemicals only) (SCCS, 2012; table 13-5)

Substance name
Cinnamal
Cinnamyl Alcohol*
Citral
Coumarin
Eugenol*
Farnesol*
Geraniol*
Hydroxycitronellal
Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC)
Isoeugenol*
Limonene (oxidised)
Linalool* (oxidised)

* including their respective esters

3.5 Detergents Regulation EC/648/2004

3.5.1 Introduction

The Detergents Regulation (DR) EC/648/2004 covers the manufacturing, sale and use of detergents. The scope of this Regulation is *'any substance or preparation containing soaps and/or other surfactants intended for washing and cleaning processes. Detergents may be in any form and marketed for or used in household, or institutional or industrial purposes'* (DR, art. 2).

The purpose of this regulation is to: *'establishes rules designed to achieve the free movement of detergents and surfactants for detergents in the internal*

market, while at the same time, ensuring a high degree of protection of the environment and human health,' (DR, art. 1).
Any natural or legal person responsible for placing a detergent or a surfactant for a detergent on the market must comply with this regulation. The Regulation applies to the following: manufacturers/producers of detergents, importers of detergents, any person changing the characteristics of a detergent, any person changing the labelling or packaging of a detergent and packagers working on their own account (DR-website, 2014).
Manufacturers must list on the labelling all components in decreasing order of concentration as well as the address of a website where consumers can obtain the complete list of ingredients (DR-website, 2014).

3.5.2 Detergents Regulation in relation to sensitisers

The DR intends, among others, to protect consumers against sensitising substances present in detergents such as certain fragrances and preservatives. This Regulation requires specific labeling to inform consumers about the presence of sensitising substances in detergents (DR, art. 1; Putte et al., 2013). The nomenclature of the Cosmetics Regulation shall be used, if one of the 26 fragrances (CR, Annex III) is added at concentrations exceeding 0.01% by weight. This should also happen with any other fragrances that will subsequently be added to Annex III of the Cosmetic Regulation (DR, Annex VII).
For healthcare professionals it is possible to obtain from manufacturers full listings of the ingredients in detergents so that they can determine whether there is a causal link between a patient's allergy and a product, which is present in a detergent (DR, art. 9 (3)).

3.6 Toys Directive EC/2009/48

3.6.1 Introduction

In order to ensure a high level of protection of children against risks caused by chemical substances in toys, the use of dangerous substances deserves careful attention. These substances in particular include substances that are classified as carcinogenic, mutagenic or toxic for reproduction under the existing classification system, sensitising substances and certain metals (TD, section 21; Putte et al., 2013).
The Directive on the safety of toys (TD) EC/2009/48 applies to products designed or intended, whether or not exclusively, for use in play by children under 14 years of age (hereinafter referred to as toys) (TD, art. 2). In 2009, the TD came into force and replaces 88/378/EEC. It sets out only the essential safety requirements regarding physical and mechanical properties, flammability, chemical properties, electrical properties, hygiene and radioactivity (TD, section 2). The chemical criteria for substances of this Directive came into force on 23 October 2013.

3.6.2 Toys Directive in relation to sensitisers

Toys shall comply with the relevant Community legislation relating to certain categories of products or to restrictions for certain substances and mixtures (TD, Annex II, part 3, section 1b). Without prejudice to the restrictions, substances that are classified as CMR category 1A, 1B or 2 under CLP shall not be used in

toys (TD, Annex II, part 3, section 3). However, there is no general restriction on the use of substances classified as sensitiser in toys.
In Annex II 55 allergenic fragrances are listed which are not allowed in toys (see Appendix III of this report) (TD, Annex II, part 3, section 11). These allergenic fragrances overlap with the allergenic fragrances listed in Annex III of the CR. In addition, the names of 11 allergenic fragrances are mentioned which shall be listed on the toy (on an affixed label, on the packaging or in an accompanying leaflet) if added to a toy, as such, at concentrations exceeding 100 mg/kg in the toy (TD, Annex II, part 3, section 11 and 12).

3.7 Biocidal Products Regulation EC/528/2012

3.7.1 Introduction

In September 2013, the Biocidial Products Regulation (BPR) (EU) No 528/2012 entered into force to replace Directive 98/8/EC. It aims to provide a high level of protection for humans, animals and the environment.
The scope of this Regulation includes biocidal products and biocides treated articles (BPR, art. 2). Biocidal products contain or generate active substances and are used against harmful organisms such as pests and bacteria. They include household products such as disinfectants, rodenticides, repellents, and insectides. Other biocidal products are used in more industrial applications as wood and material preservatives, anti-fouling paints, and embalming products to avoid damage to natural or manufactured products (BPR-website, 2014). Due to their intrinsic properties and uses, biocidal products may themselves pose human health risks and be harmful to the environment. It is vital therefore to ensure that only biocidal products that are safe for use are placed on the market (BPR-website, 2014). Annex V of the Regulation sets out a list of the types of biocidal products covered (BPR, Annex V).

Authorisation process

The toxicology of new active substances is evaluated before biocidal products containing them are placed on the market (see Appendix II for a decision tree for admission of biocides within the BPR). Producers have the obligation to prepare the risk assessments (BPR, art. 4 and 6).
To apply for a biocidal product authorisation, the active substance must be approved. The active substances are first evaluated. If the active substance is approved at EU level, it will be included in a Community list (known as the Annex I). Under the BPR the subsequent authorisation of a product containing the active substance either takes place at Member (national) State level (single or mutual recognition procedure) or at EU level (central procedure) (Ctgb-website, 2014). The competent authority of the Netherlands is *College voor toelating van gewasbeschermingsmiddelen en biociden* (Ctgb) (Ctgb-website, 2014). When a substance is approved, an additional dossier must be submitted for product authorisation (Ctgb-website, 2014).
ECHA has a facilitating and coordinating role in the authorisation process. It offers ICT support, technical and scientific support to the Member States, guidance and a helpdesk (Ctgb-website, 2014).
Where a product has a biocidal function that is inherent to its cosmetic function, or where that biocidal function is considered to be a secondary claim of a

cosmetic product and is therefore regulated under the CR, that function and the product should remain outside the scope of the BPR (CR, art.2).

3.7.2 Biocidal Product Regulation in relation to sensitisers

In Annex II the requirements for the preparation of the dossier for substances and biocidal products are listed. The data elements, needed to prepare the substance dossier, are considered as the basic data which should in principle, be provided for all active substances. For skin sensitisation, the assessment shall comprise the following consecutive steps:

1. an assessment of the available human, animal and alternative data
2. *in vivo* testing (the Murine Local Lymph Node Assay is the first-choice method)

Step 2 does not need to be conducted if the available information indicates that the substance is classified for skin sensitisation or the substance is a strong acid or base (BPR, Annex II, section 8.3 and 8.4).
Information requirements for authorisation of a biocidal product comprises the consecutive steps mentioned above. Testing on the product/mixture does not need to be conducted if there are valid data available on each of the components (skin or respiratory sensitisers) in the mixture to allow classification of the mixture according to the rules laid down in the CLP regulation (BPR, Annex II, section 8.3 and 8.4).
In the BPR several exclusion criteria referring to intrinsic toxicological properties are mentioned that may lead to non-approval of active substances (art. 5) or for not granting authorisation of biocidal products (art. 19). In a guidance document, options are described how to perform a risk characterisation for skin and respiratory sensitization (ECHA-website: Guidance for health risk assessment, 2013). However, sensitisation is not an exclusion criteria for non-approval of active substances or for authorisation of biocidal products. Therefore, risk assessments may differ on national level.

3.7.3 Currently under discussion

Biocidal products may contain active substances or co-formulants having sensitising properties as long as the risk assessment proves that there is a safe use (for consumers). Under the BPR the Guidance for toxicological risk assessment has been updated. It has been discussed at Technical Meetings and at the Competent Authority (CA) meetings how to perform a local risk assessment, including the assessment of sensitisation. The resulting guidance has been included in the overall Guidance for risk assessment, which was endorsed at the CA in May 2014 (ECHA-website: Guidance for health risk assessment, 2013).
Options on how to perform a risk characterisation for skin and respiratory sensitisation are described in Chapter 4 of the Guidance. The qualitative risk characterisation approach is preferred; however the semi-quantitative and quantitative approaches are also described for potential use depending on the availability of data and taking into account specific limitations (ECHA-website: Guidance for health risk assessment; chapter 4, 2013).
However, further discussion has taken place at EU level. Some Member States are of the opinion that a safe use for consumers may be based on the use of personal protective measures (usually gloves). Other Member States prefer that products that need personal protective measures to ensure a safe use are not to be made available to the general public. Product authorisation procedures are

usually national decisions. As a consequence, different measures are being applied by the different member states. In an attempt for harmonisation, a document was endorsed at the CA meeting in September 2013 making a distinction in products classified as category 1A (not to be placed on the market for general public) or category 1B (to be placed on the market for the general public, irrespective of the need of limited personal protective equipment) (CA-document, 2013). The proposal leaves a lot of room for expert judgement. This might result in national differences: biocidal products with sensitising properties will be allowed in some European Member States, whereas in others they will not be authorised for public use (professional use only).

3.8 EU Ecolabel Regulation EC/66/2010

3.8.1 Introduction

The EU Ecolabel Regulation (ER) EC/66/2010 aims to establish a voluntary Ecolabel award scheme intended to promote products with a reduced environmental impact during their entire life cycle and to provide consumers with science-based information on the environmental impact of products. Voluntary means that manufacturers, importers and retailers can choose to apply for the label for their products. The ER covers a wide range of product groups, from major areas of manufacturing to tourist accommodation services (ER- website, 2014).
The ER lays down the rules for the establishment and application of the voluntary EU Ecolabel scheme (ER, art. 1).
Key experts, in consultation with main stakeholders, develop the criteria for each product group (ER-website, 2014). The criteria for the different product groups are documented in Commission Decisions.

3.8.2 EU Ecolabel Regulation in relation to sensitisers

In this report the focus is on sensitising substances in consumer products, therefore the focus is on the following product groups: Beauty Care, Cleaning up, Clothing and Do-it-yourself see Table 8 (ER-website, 2014).

Table 8. EU Ecolabel criteria in relation to sensitisers (compiled from the ER-website)

Product Group	**Commission decision**	**EU Ecolabel criteria in relation to sensitisers**
Beauty Care	Soaps, shampoos and hair conditioners 2007/506/EC	-
Cleaning up	All-purpose cleaners and sanitary cleaners (2011/383/EU); Detergents for dishwashers (2011/263/EU); Hand dishwashing detergents (2011/382/EU); Laundry detergents (2011/264/EU)	Criteria 3- Excluded or limited substances and mixtures are substances which meets the criteria for classification with the hazard statements in accordance with CLP or substances referred to in art. 57 of REACH Among them are sensitising substances (classification H334 and H317)

Product Group	Commission decision	EU Ecolabel criteria in relation to sensitisers
Clothing	Textile products (2009/567/EC)	A list with potentially sensitising dyes is given which shall not be used in textile products (see Appendix IV of this report)
	Footwear (2009/563/EC)	Classification may be considered according to CLP. No substances or mixtures may be added to the raw materials that are (or might) assigned with the hazard statement H317 (skin sensitiser)
Do-it-yourself	Indoor paints and varnishes (2009/544/EC); Outdoor paints and varnishes (2009/543/EC)	No ingredients that can cause sensitisation by inhalation (R42) (or classified as Respiratory Sensitisation – Cat. I according to CLP) may be used.

3.9 Other national legislations

In the previous paragraphs is described how general and sector specific legislation regulates the production and usage of sensitisers in consumer products in Europe.
Formaldehyde is an example of a sensitising preservative which is regulated in some sector specific legislation. It is listed on Annex V of the CR and is only allowed in cosmetic products with specific concentration limits (CR, Annex V). Formaldehyde is also mentioned as a potentially sensitiser in the Ecolabel criteria (see table 14 of Appendix IV).

For some products, like textile, there is no sector specific legislation and a substance in textile might be regulated by general legislation (like REACH).

However, for some sensitisers national regulations exist, such as for example for formaldehyde in textiles. Table 9 shows that in different countries the regulation on formaldehyde for textiles differs.

Table 9. Existing regulations on formaldehyde for textiles in different countries (copied from Putte et al. 2013, table 20)

Country	Regulations on formaldehyde for textiles	
	Conditions	**Requirements**
Netherlands	direct contact with skin	- Any product containing more than 120 ppm formaldehyde must be labelled "Wash before first use" After washing, these products must not contain more than 120 ppm
Germany	direct contact with skin	Release more than 1500 ppm formaldehyde must bear a label that states: "Contains formaldehyde. Washing this garment is recommended prior to first time use in order to avoid irritation of the skin."

Country	Regulations on formaldehyde for textiles	
	Conditions	**Requirements**
France	For baby products & direct contact with skin	20 ppm
	direct contact with skin	100 ppm
	Not direct contact with skin	400 ppm
US		If a product contains 0.1% or more formaldehyde or can release formaldehyde into the air above 0.1 ppm, then the product label must include the following information, as required by OSHA's Formaldehyde standard, 29 CFR 1910.1048(m)(3): - a statement that the product has formaldehyde in it - the name and address of the manufacturer, importer, or other company responsible for the product a statement that the employer and MSDSs can readily give health hazard information. Additionally, if the product can release formaldehyde into the air above 0.5 ppm, the label must also have the following information: - a list of all product health and safety hazards the phrase "Potential Cancer Hazard".
China	For infants and babies	Less than 20 ppm
	direct contact with skin	Less than 75 ppm
	Not direct contact with skin	Less than 300 ppm

3.10 Overview of European legislations with relevance for sensitisers

In the previous sections is described how the production and use of sensitising substances is regulated in the separate, different legal frameworks, general and sector specific legislation. An overview of the different legislative frameworks and their Annexes relevant for sensitising substances in consumer products is given in Figure 1.

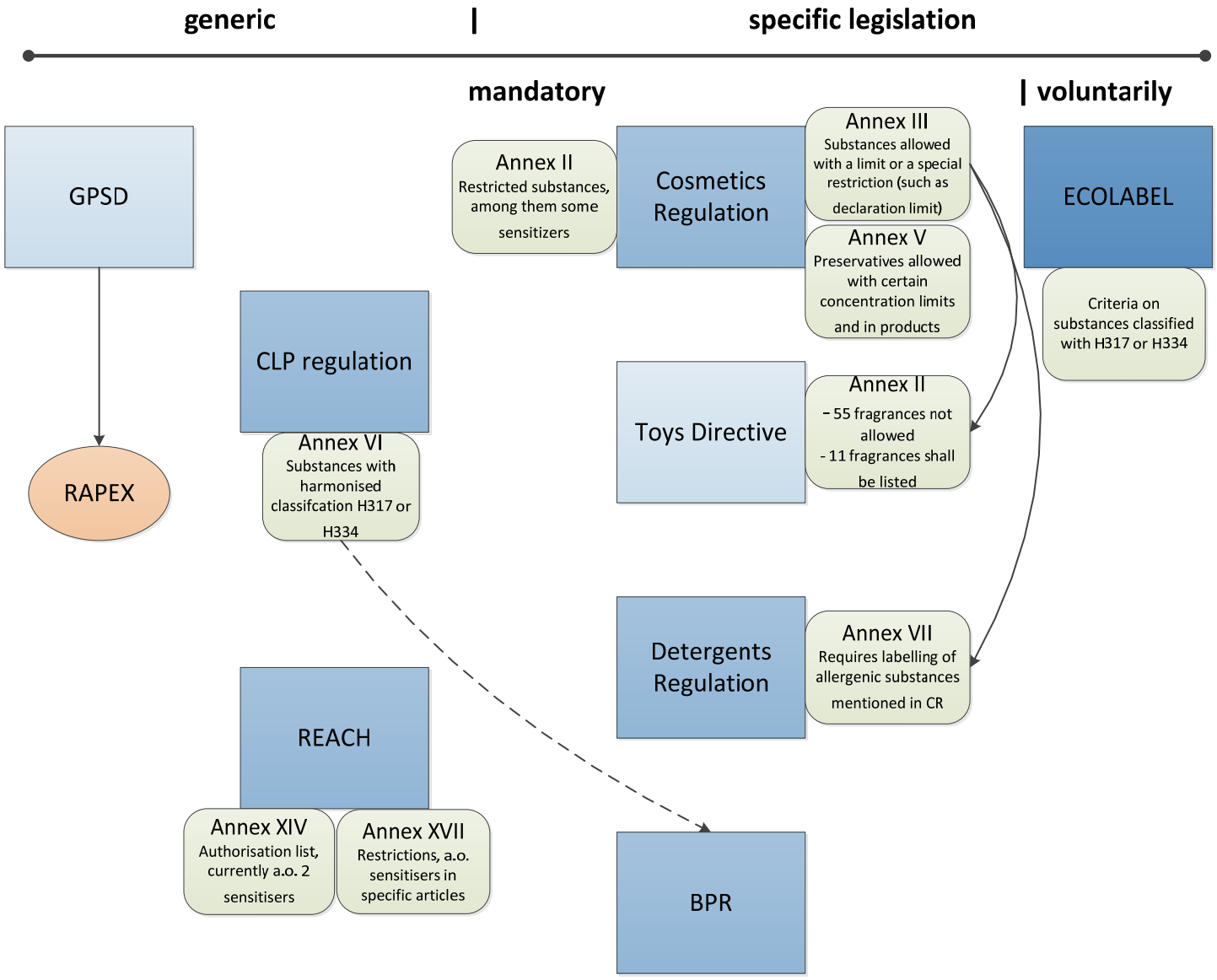

Figure 1. Overview of several European legislation with relevance for sensitisers

4 Overview of the different frameworks

This report provides an overview of regulations concerning the production and usage of sensitizing chemicals in consumer products. European legislation for prevention of adverse health effects of chemicals covers a wide range of product types and exposure situations within different directives. Several risk management options exist to prevent new cases of sensitisation or to reduce complaints caused by exposure to sensitisers from consumer products an overview is given in Table 10.

Products placed on the market in the EU are subject to general safety requirements. These requirements are included in the GPSD which aims at ensuring that only safe consumer products are sold in the EU. The GPSD does not cover for example pharmaceuticals, medical devices or cosmetics, which fall under separate legislation.

Apart from the general provisions, certain categories of products are covered by sector specific legislation and product specific provisions. Specific rules also exist for the safety of toys and chemicals.

Table 10. Overview of legislative frameworks relevant for sensitising substances in consumer products

EU Regulation/Directive	**Directorate General**	**Relevant for product type**	**Application**	**Risk management measure possible for sensitisers**
General Product Safety Directive	Health and Consumers (SANCO)	Consumer products	Products on the EU market	No specific requirements possible, in case of emergencies, with performed risk assessment, enforcement possible
CLP This regulation is based on the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) and is implementing the provisions of the GHS within the EU	Enterprise and Industry	Substances and mixtures	All substances and mixtures placed on the market irrespective of the tonnage level, fall within the scope of classification under CLP and should be evaluated in order to reach a decision as to whether they should be classified or not. All substances subject to REACH are also subject to classification, even those not placed on the market if they are subject to registration or notification	Classify substances as skin or respiratory sensitisers category 1, 1A or 1B
REACH Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals	Enterprise and Industry & Environment	All, except toys, cosmetics, and biocidal products	Skin sensitisation testing is mandatory for all substances manufacture or imported in the EU in quantities of one tone or ore per year (lowest tonnage level)	SVHC candidate list (leading to Annex XIV), probably only relevant for respiratory sensitisers because of demonstration of equivalent concern Restriction (Annex XVII) on presence in specific products, production or use (also applicable for imported articles)

EU Regulation/Directive	Directorate General	Relevant for product type	Application	Risk management measure possible for sensitisers
Cosmetics Regulation	Health and Consumers (SANCO)	Cosmetics	All cosmetic ingredients independent of tonnage level. Skin sensitisation is among the most relevant endpoints for the toxicological profile of cosmetics ingredient (considered to be the endpoint with the highest testing needs for the cosmetic sector). Information requirement for skin sensitisation included in the minimal base set requirement for inclusion of a substance in one of the Annexes of CR	Restriction with certain concentration limit or labelling requirements above certain concentration limits
Detergents Regulation	Enterprise and Industry	Detergents	Any substance or preparation containing soaps and/or other surfactants intended for washing and cleaning processes.	Manufacturers must list on the labelling all components as well as the address of a website where consumers can obtain the complete list of ingredients.
Toys Directive	Enterprise and Industry	Toys	Annex II lists substances not allowed to be used in toys or should be labeled on the toys	Restriction with certain concentration limit or labelling requirements above certain concentration limits

EU Regulation/Directive	Directorate General	Relevant for product type	Application	Risk management measure possible for sensitisers
Biocidal Products Regulation concerning the placing of biocidal products on the market	Environment	Biocidal products	All biocidal products and active substances marketed in the EU independent of tonnage level. Information requirement for skin sensitisation mandatory for both active substances contained in biocidal products and the final product	Approach for sensitisers under discussion, might differ between Member States
EU Ecolabel	Environment	Different product groups	Manufacturers, importers and retailers can voluntary choose to apply for the label for their products	Voluntary. No enforcement possible

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Appendix I. Classification criteria for substances and mixtures

Classification criteria for substances

Where data are not sufficient for sub-categorisation respiratory and skin sensitisers shall be classified in Category 1, based on the criteria in Table 1 for respiratory sensitisers and Table 2 for skin sensitisers (CLP, Part 3.4, table 3.4.1 and 3.4.2).

Where data are sufficient a refined evaluation shall allow the allocation of respiratory or skin sensitisers into sub-category 1A, strong sensitisers, or sub-category 1B for other respiratory or skin sensitisers, see Table 1 (respiratory) and Table 2 (skin) (CLP, Part 3.4). It has to be noted that the concept of sub-categories (1A and 1B) for category 1 sensitisers, which indicates the potency of sensitisers has only been introduced very recently (EU/286/2011).

Classification of respiratory sensitisers is based on human cases and epidemiologic research. At present, there are no recognised and validated animal models for the testing of respiratory hypersensitivity available (CLP, section 3.4.2.1).

Classification of skin sensitisers is based on animal studies, human evidence (positive responses or diagnostic patch test data) and/or epidemiological evidence (CLP, section 3.4.2.2).

Table 11. Hazard category and sub-categories for respiratory sensitisers (from CLP, part 3.4, table 3.4.1)

Category	Criteria
Category 1	Substances shall be classified as respiratory sensitisers (Category 1) where data are not sufficient for sub-categorisation in accordance with the following criteria: (a) if there is evidence in humans that the substance can lead to specific respiratory hypersensitivity; and/or (b) if there are positive results from an appropriate animal test.
Sub-category 1A:	Substances showing a high frequency of occurrence in humans; or a probability of occurrence of a high sensitisation rate in humans based on animal or other tests (1). Severity of reaction may also be considered.
Sub-category 1B:	Substances showing a low to moderate frequency of occurrence in humans; or a probability of occurrence of a low to moderate sensitisation rate in humans based on animal or other tests (1). Severity of reaction may also be considered.

(1) At present, recognised and validated animal models for the testing of respiratory hypersensitivity are not available. Under certain circumstances, data from animal studies may provide valuable information in a weight of evidence assessment.

Table 12. Hazard category and sub-categories for skin sensitisers (from CLP, part 3.4, table 3.4.2)

Category	Criteria
Category 1	Substances shall be classified as skin sensitisers (Category 1) where data are not sufficient for sub-categorisation in accordance with the following criteria: (a) if there is evidence in humans that the substance can lead to sensitisation by skin contact in a substantial number of persons; or (b) if there are positive results from an appropriate animal test (see specific criteria in section 3.4.2.2.4.1).
Sub-category 1A:	Substances showing a high frequency of occurrence in humans and/or a high potency in animals can be presumed to have the potential to produce significant sensitisation in humans. Severity of reaction may also be considered.
Sub-category 1B:	Substances showing a low to moderate frequency of occurrence in humans and/or a low to moderate potency in animals can be presumed to have the potential to produce sensitisation in humans. Severity of reaction may also be considered.

Classification criteria for mixtures

When reliable and good quality evidence from human experience or appropriate studies in experimental animals is available for the mixture, then the mixture can be classified by weight of evidence evaluation of these data. Where the mixture itself has not been tested to determine its sensitising properties, but there are sufficient data on the individual ingredients and similar tested mixtures, these data shall be used (CLP, section 3.4.3). When such data is missing, the classification of the mixture is based on the classification of the components and their concentration. In Table 3 (generic concentration limits), the concentration limits of components of a mixture classified as either respiratory or skin sensitisers that trigger classification of the mixture are given. When at least one ingredient of the mixture is present at or above the appropriate generic concentration limit, the mixture shall be classified as a respiratory or skin sensitiser (CLP, section 3.4, table 3.4.5).
Some sensitising substances have specific concentration limits, see Annex VI of CLP Regulation which apply instead of the generic concentration limits (CLP, Annex VI).

Table 13. Generic concentration limits of components of a mixture classified as either respiratory sensitisers or skin sensitisers that trigger classification of the mixture (from CLP, section 3.4, table 3.4.5)

Component classified as:	Generic concentration limits triggering classification of a mixture as:		
	Respiratory sensitiser Category 1		Skin sensitiser Category 1
	Solid/liquid	Gas	All physical states
Respiratory sensitiser Category 1	≥ 1,0 %	≥ 0,2 %	
Respiratory sensitiser Sub-category 1A	≥ 0,1 %	≥ 0,1 %	
Respiratory sensitiser Sub-category 1B	≥ 1,0 %	≥ 0,2 %	
Skin sensitiser Category 1			≥ 1,0 %
Skin sensitiser Sub-category 1A			≥ 0,1 %
Skin sensitiser Sub-category 1B			≥ 1,0 %

Appendix II. Decision tree admission of biocides within BPR

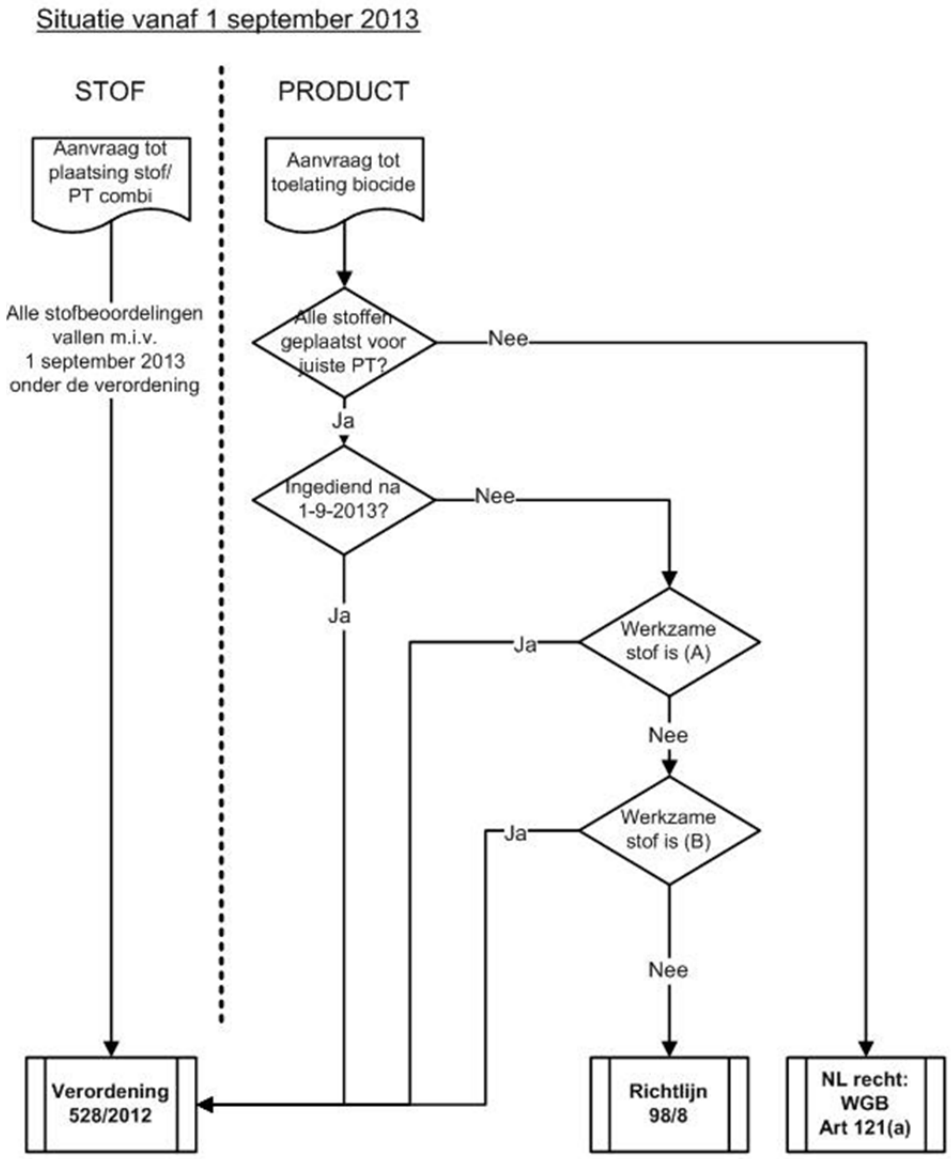

Figure 2. Decision tree admission of biocides within BPR. Specified is how the admission for active biocidal substances and products is regulated after 1 September 2013. Substance (A) are substances with the following hazard properties: CMR 1A or 1B, endocrine disrupting, PBT or vPvB (BPR, art. 5 (1)). Substance (B) is eligible for substitution (BPR, art. 10).
(Beslisboom from Ctgb-website, 2014)

Appendix III. List of allergenic fragrances which toys shall not contain

Table 14. List of allergenic fragrances that toys shall not contain (Annex II of Toys Directive EC/2009/28)

No	Name of the allergenic fragrance	CAS number
(1)	Alanroot oil (Inula helenium)	97676-35-2
(2)	Allylisothiocyanate	57-06-7
(3)	Benzyl cyanide	140-29-4
(4)	4 tert-Butylphenol	98-54-4
(5)	Chenopodium oil	8006-99-3
(6)	Cyclamen alcohol	4756-19-8
(7)	Diethyl maleate	141-05-9
(8)	Dihydrocoumarin	119-84-6
(9)	2,4-Dihydroxy-3-methylbenzaldehyde	6248-20-0
(10)	3,7-Dimethyl-2-octen-1-ol (6,7-Dihydrogeraniol)	40607-48-5
(11)	4,6-Dimethyl-8-tert-butylcoumarin	17874-34-9
(12)	Dimethyl citraconate	617-54-9
(13)	7,11-Dimethyl-4.6,10-dodecatrien-3-one	26651-96-7
(14)	6,10-Dimethyl-3.5,9-undecatrien-2-one	141-10-6
(15)	Diphenylamine	122-39-4
(16)	Ethyl acrylate	140-88-5
(17)	Fig leaf, fresh and preparations	68916-52-9
(18)	trans-2-Heptenal	18829-55-5
(19)	trans-2-Hexenal diethyl acetal	67746-30-9
(20)	trans-2-Hexenal dimethyl acetal	18318-83-7

(21)	Hydroabietyl alcohol	13393-93-6
(22)	4-Ethoxy-phenol	622-62-8
(23)	6-Isopropyl-2-decahydronaphthalenol	34131-99-2
(24)	7-Methoxycoumarin	531-59-9
(25)	4-Methoxyphenol	150-76-5
(26)	4-(p-Methoxyphenyl)-3-butene-2-one	943-88-4
(27)	1-(p-Methoxyphenyl)-1-penten-3-one	104-27-8
(28)	Methyl trans-2-butenoate	623-43-8
(29)	6-Methylcoumarin	92-48-8
(30)	7-Methylcoumarin	2445-83-2
(31)	5-Methyl-2,3-hexanedione	13706-86-0
(32)	Costus root oil (Saussurea lappa Clarke)	8023-88-9
(33)	7-Ethoxy-4-methylcoumarin	87-05-8
(34)	Hexahydrocoumarin	700-82-3
(35)	Peru balsam, crude (Exudation of Myroxylon pereirae (Royle) Klotzsch)	8007-00-9
(36)	2-Pentylidene-cyclohexanone	25677-40-1
(37)	3.6,10-Trimethyl-3.5,9-undecatrien-2-one	1117-41-5
(38)	Verbena oil (Lippia citriodora Kunth)	8024-12-2
(39)	Musk ambrette (4-tert-Butyl-3-methoxy-2,6-dinitrotoluene)	83-66-9
(40)	4-Phenyl-3-buten-2-one	122-57-6
(41)	Amyl cinnamal	122-40-7
(42)	Amylcinnamyl alcohol	101-85-9
(43)	Benzyl alcohol	100-51-6
(44)	Benzyl salicylate	118-58-1
(45)	Cinnamyl alcohol	104-54-1
(46)	Cinnamal	104-55-2
(47)	Citral	5392-40-5
(48)	Coumarin	91-64-5

(49)	Eugenol	97-53-0
(50)	Geraniol	106-24-1
(51)	Hydroxy-citronellal	107-75-5
(52)	Hydroxy-methylpentylcyclohexenecarboxaldehyde	31906-04-4
(53)	Isoeugenol	97-54-1
(54)	Oakmoss extracts	90028-68-5
(55)	Treemoss extracts	90028-67-4

However, the presence of traces of these fragrances shall be allowed provided that such presence is technically unavoidable under good manufacturing practice and does not exceed 100 mg/kg.

In addition, the names of the following allergenic fragrances shall be listed on the toy, on an affixed label, on the packaging or in the accompanying leaflet, if added to a toy, at concentrations exceeding 100mg/kg in the toy or components thereof:

No	Name of the allergenic fragrance	CAS number
(1)	Anisyl alcohol	105-13-5
(2)	Benzyl benzoate	120-51-4
(3)	Benzyl cinnamate	103-41-3
(4)	Citronellol	106-22-9
(5)	Farnesol	4602-84-0
(6)	Hexyl cinnamaldehyde	101-86-0
(7)	Lilial	80-54-6
(8)	d-Limonene	5989-27-5
(9)	Linalool	78-70-6
(10)	Methyl heptine carbonate	111-12-6
(11)	3-methyl-4-(2.6,6-trimethyl-2-cyclohexen-1-yl)-3-buten-2-one	127-51-5

Appendix IV. List of potentially sensitising dyes which shall not be used in Ecolabel textiles

To be eglible for the EU Ecolabel, the following potentially sensitising dyes shall not be used in textile products (Commission Decision EC/2009/567):

- C.I. Disperse Blue 3
- C.I. Disperse Blue 7
- C.I. Disperse Blue 26
- C.I. Disperse Blue 35
- C.I. Disperse Blue 102
- C.I. Disperse Blue 106
- C.I. Disperse Blue 124
- C.I. Disperse Brown 1
- C.I. Disperse Orange 1
- C.I. Disperse Orange 3
- C.I. Disperse Orange 37
- C.I. Disperse Orange 76 (previously designated Orange 37)
- C.I. Disperse Red 1
- C.I. Disperse Red 11
- C.I. Disperse Red 17
- C.I. Disperse Yellow 1
- C.I. Disperse Yellow 9
- C.I. Disperse Yellow 39
- C.I. Disperse Yellow 49

In addition, some other substances which are used in textiles and included in Ecolabel criteria due to other concerns have been also classified as sensitisers or irritants under the existing classification system. Table 15 gives an example of these substances.

Table 15. Other potentially sensitising or/and irritating substances mentioned in Ecolabel criteria (from Putte et al., 2013).

Function group	Substance name	CAS no.	Harmonised classification under CLP related to allergy
Acrylonitrile	acrylonitrile	107-13-1	Skin Sens. 1, H317 Skin Irrit. 2, H315 STOT SE 3, H335
Organic tin compounds Which are restricted under REACH	TBT		Skin Irrit. 2, H315
Pesticides	2,4,5-T	93-76-5	Skin Sens. 1, H317 STOT SE 3, H335
	captafol	2425-06-1	Skin Sens. 1, H317
	Toxaphene	8001-35-2	Skin Irrit. 2, H315 STOT SE 3, H335
	Pentachlorophenol	87-86-5	Skin Irrit. 2, H315 STOT SE 3, H335
Impurities in dyes and pigments	Cobalt	7440-48-4	Skin Sens. 1, H317 Resp. Sens. 1, H334
	Nickel	7440-02-0	Skin Sens. 1, H317
azo dyes which by reductive cleavage of one or more azogroups may release aromatic amines listed	o-aminoazotoluene	97-56-3	Skin Sens. 1, H317
	p-chloroaniline	106-47-8	Skin Sens. 1, H317
	4,4'-diaminobiphenylmethane	101-77-9	Skin Sens. 1, H317
	3,3'-dichlorobenzidine	91-94-1	Skin Sens. 1, H317
	3,3'-dimethyl-4,4'-diaminobiphenylmethane	838-88-0	Skin Sens. 1, H317
	2,4-toluenediamine	95-80-7	Skin Sens. 1, H317
	2,6-xylidine	87-62-7	Skin Irrit. 2, H315 STOT SE 3, H335
dyestuffs classified as CMR	Disperse Blue 1	2475-45-8	Skin Sens. 1, H317 Skin Irrit. 2, H315
	Disperse Orange 11	82-28-0	Skin Sens. 1, H317
	Disperse Yellow 3	2832-40-8	Skin Sens. 1, H317
formaldehyde	formaldehyde	50-00-0	Skin Sens. 1, H317

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