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

Definition of serious risk within RAPEX notifications

RIVM Letter Report 090013001/2013
S.W.P. Wijnhoven | P.J.C.M. Janssen | A.G. Schuur

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

Definition of serious risk within RAPEX notifications

RIVM letter report 090013001/2013
S.W.P. Wijnhoven | P.J.C.M. Janssen | A.G. Schuur

Colofon

© RIVM 2013
Parts of this publication may be reproduced, provided acknowledgement is given to the 'National Institute for Public Health and the Environment', along with the title and year of publication.

Susan Wijnhoven, RIVM-SIR
Paul Janssen, RIVM-SIR
Gerlienke Schuur, RIVM-SIR

Contact:
Gerlienke Schuur
Veiligheid Stoffen en Producten
gerlienke.schuur@rivm.nl

This investigation has been performed by order and for the account of the Dutch Food and Consumer Product Safety Authority, within the framework of "kennisvraag 9.1.3 Consumentenblootstelling en –risico's consumentenproducten" (2012/2013)".

Abstract

Definition of 'serious risk' within RAPEX notifications

The European Union has a notification system for Member States to exchange information on the safety of consumer products. The purpose of this so-called RAPEX-system (Rapid Alert System for Non-Food Products) is to be able to quickly recall products from the market. A risk may be caused by a mechanic defect or by a chemical substance in the product. Three categories of risk are defined: low, moderate and serious. In practice, Member States interpret the concept of 'serious risk' differently for risks caused by chemical substances. Due to this, the risk of the use of these products is often not correctly defined and reported as 'serious'.

The Dutch Food and Product Safety Authority (NVWA) is responsible for the Dutch notifications in RAPEX. NVWA asked RIVM to map out this problem and come up with possible solutions. It turns out that substances and products are notified for two reasons. Firstly, when a legal concentration limit of a substance is exceeded, and secondly, when health complaints caused by a product are reported. When a concentration limit is exceeded, it does not necessarily mean that there is a serious risk. Concentration limits are not always quantitatively based on a specific effect of the substance, but sometimes set at 0.1% to restrict the use of hazardous substances.

RIVM provides some solutions to remove the differences in interpretation.
A possible way would be adapt the definition of 'serious risk' specifically for risks of chemical substances. In addition, drawing up guidance for risk assessments for chemicals within RAPEX would be another approach. Finally, the RAPEX notification could be extended with a justification, such as exceeding a legal concentration limit or health complaints.

Keywords:
serious risk, consumer, product safety, RAPEX notification

Rapport in het kort

Definitie van 'serious risk' in Europees meldingssysteem voor veiligheid producten (RAPEX)

De Europese Unie beschikt over een meldingssysteem, waarmee lidstaten informatie kunnen uitwisselen over de veiligheid van consumentenproducten. Het doel van dit zogeheten RAPEX-systeem (Rapid Alert System for Non-Food Products) is om producten die een ernstig risico vormen voor de volksgezondheid snel van de Europese markt te kunnen halen. Een risico kan een gevolg zijn van een mechanisch defect of van een chemische stof in het product. Er zijn drie categorieën risico's: laag, matig en ernstig (*serious risk*). In de praktijk blijken lidstaten de definitie van serious risk voor risico's veroorzaakt door chemische stoffen verschillend te interpreteren. Hierdoor wordt het risico van het gebruik van deze producten vaak ten onrechte als ernstig bestempeld en gemeld.

Voor Nederland verzorgt de Nederlandse Voedsel en Warenautoriteit (NVWA) de RAPEX-meldingen. De NVWA heeft het RIVM gevraagd om dit probleem in kaart te brengen en mogelijke oplossingen aan te reiken. Het blijkt dat stoffen en producten bij RAPEX om twee redenen worden gemeld. Ten eerste als een wettelijke concentratielimiet van een stof wordt overschreden, en ten tweede als een product klachten veroorzaakt. Als een concentratielimiet wordt overschreden, hoeft er echter niet altijd sprake te zijn van een ernstig risico. Dat komt omdat normen niet altijd gebaseerd zijn op een specifiek effect van een schadelijke stof, maar bijvoorbeeld ook vanuit een basale wens om het gebruik van een stof te beperken.

Het RIVM reikt enkele oplossingen aan om de verschillen in interpretatie weg te nemen. Een mogelijkheid is de definitie van serious risk aan te passen door deze specifiek op te stellen voor chemische risico's. Ook kan worden verduidelijkt hoe een risicobeoordeling voor chemische stoffen het beste binnen RAPEX kan worden uitgevoerd, bijvoorbeeld door daar een leidraad voor op te stellen. Als laatste zou bij een RAPEX-melding toegevoegd kunnen worden waar de risicobeoordeling op is gebaseerd (normoverschrijding of klacht), zodat de reden voor de melding duidelijk wordt.

Trefwoorden: RAPEX, GSPD, serious risk, productveiligheid, consument

Contents

Summary

The European Union has a notification system for Member States to quickly exchange information on the safety of consumer products. The purpose of this so-called RAPEX-system (Rapid Alert System for Non-Food Products) is to recall products from the market. The Dutch Food and Product Safety Authority (NVWA) has encountered a problem in the past few years with the definition and the implementation of the concept of 'serious risk' as used within the EU Rapid Alert system (RAPEX). More specifically, for chemical risks no clear definition of 'serious risk' exists, with the consequence that 'serious risk' is interpreted differently by different EU Member States using RAPEX.

The new RAPEX guidelines (2010) indicate that before deciding on 'serious risk', a risk assessment should be performed. The risk assessment method as provided in Appendix 5 to the new RAPEX-guidelines, deals with a wide range of risks. The guidelines provided on chemical risks are of a very general nature and do not specify criteria for 'serious risk' due to chemical exposures resulting from consumer product use. As is noted also in the same Appendix, non-compliance with standards or concentration limit values does not automatically mean that the product presents a 'serious risk'. Thus, an additional risk assessment with clear definition of criteria is needed.
The present report explores the issue of how to deal with the definition of 'serious risk' for chemical exposure due to consumer product use within the RAPEX framework.

'Serious risk' for chemicals in consumer products within RAPEX has not (yet) been clearly defined. The term 'serious' as a qualifier to risk is difficult to interpret within the accepted framework of risk assessment for chemicals.

In practice, RAPEX notifications based on chemical risks occur according to three different scenarios:
1. A concentration limit/limit value is exceeded (with a factor of 2 to x-fold).
2. A substance in a product results in actual complaints or incidents.
3. A substance in a product poses (or probably poses) a concern but there is no limit value available.

In the first situation, risk assessment may show that there actually is no serious risk or even no risk at all in terms of risk assessment. Concentration limits in consumer products frequently are not health-based limits, but are set for risk management reasons. An example is the case of 0.1% for CMRs in preparations for consumers. It is a matter of definition whether this exceedance is considered a 'serious risk'.

According to the RAPEX guidelines, in any case of notification, a risk assessment should be performed. However, specific guidance on how to perform this risk assessment is not given in the guidelines, only reference is made to the SCCS notes of guidance and the REACH guidance.
Various issues of concern regarding this risk assessment are discussed, such as:
- How to assess the, in most cases incidental (acute or short-term), exposure when it is compared with a relevant chronic health endpoint?
- How to deal with background exposure (from food or air) or exposure resulting from other products?
- How to deal with genotoxic carcinogens? Which point of departure needs to be taken? A point of departure based on a 10^{-6} risk per lifetime?

In a pragmatic approach, three different recommendations are given in this working document:

1. Develop a definition of 'serious risk' with relevance to chemical risks.
2. Make a guidance document for chemical risk assessment within RAPEX. This should take into account the issues of comparison of incidental exposure against chronic health effects, background exposure and the point of departure for carcinogenic endpoints.
3. Add a column to the RAPEX notifications with 'reason for RAPEX notification'.

1 Introduction

The Dutch Food and Product Safety Authority (NVWA) has encountered a problem in the past few years with the definition and the implementation of the concept of 'serious risk' as used within the EU Rapid Alert system (RAPEX). More specifically, for chemical risks no clear definition of 'serious risk' exists, with the consequence that 'serious risk' is interpreted differently by EU Member States using RAPEX.
For the NVWA it is common practice to notify via RAPEX when a concentration of a substance shows a two times exceedance of an existing concentration limit. These legal concentration limits mostly are general regulatory requirements and rules and are in most cases not directly risk assessment- based. In some of the cases where legal concentration limits were exceeded, the subsequent performance of a risk assessment did not lead to the conclusion that the substance in the product posed a (serious) health risk. In the RAPEX context (for instance the Consumer Safety Network in which RAPEX notifications are discussed), this gave rise to discussions.

The new RAPEX guidelines (2010) indicate that before deciding on 'serious risk', a risk assessment should be performed. The risk assessment method as provided in Appendix 5 to the new RAPEX-guidelines, deals with a wide range of risks. These include, in addition to chemical risks, mechanical risks, electrical risks, fire hazard, and radiation risk. The guidelines provided on chemical risks is of a very general nature and does not specify criteria for 'serious risk' due to chemical exposures resulting from consumer product use. As is noted also in the same Appendix, non-compliance with standards or concentration limit values does not automatically mean that the product presents a 'serious risk'. Thus, an additional risk assessment with clear definition of criteria is needed.

The subject of the present working document is the exploration of the issue of how to deal with the definition of 'serious risk' for chemical exposure due to consumer product use within the RAPEX framework. In 2013, we will also look into the need for more guidance within the framework of the GPSD resulting in more consistent consumer exposure estimations, together with NVWA.

For a useful perspective on this problem, the present working document starts with some background information on RAPEX (Chapter 2). Subsequently the information on risk assessment (for chemical risks) as given in the guidelines is summarized (Chapter 3). Additional information on limit values and requirements is given in Chapter 4. In Chapter 5, the 'serious risk' problem is described in more detail.
To illustrate the different issues in assessing serious risk in relation with RAPEX examples of interpretations of RAPEX notifications are given (Chapter 6).
In Chapter 7, an attempt is made to summarize and conclude on the problem of 'serious risk'. Furthermore, suggestions are presented to deal with the problem in the future.

2 Background RAPEX

2.1 RAPEX, the rapid alert system for non-food dangerous products

RAPEX is the European rapid alert system that facilitates the rapid exchange of information on consumer product safety between Member States and the European Commission (EC). This information is focussed on measures taken to prevent or restrict the marketing or use of consumer products posing a 'serious risk' to the health and safety of consumers. Food, pharmaceuticals and medical devices are excluded from the RAPEX system, since they are covered by other frameworks.

The main objective of the RAPEX system is to ensure that only safe products enter the European Single Market. RAPEX helps to stop dangerous products from reaching the buying public in 30 European countries. The success of RAPEX not only relies on close collaboration between national market surveillance authorities and the Commission but also on rigorous enforcement of appropriate legislation, a commitment of safety to all economic operators in the supply chain and close cooperation between the EU and its international trading partners (including China as a major player).

RAPEX has been established under Article 12 of the General Product Safety Directive (GPSD). With the entry into force of Article 22 of Regulation (EC) No. 765/2008 in January 2010, the scope of RAPEX has been extended to risks other than those affecting health and safety of consumers (workplace, environment and security) i.e. to products intended for professional use as well.
According to article 12 of the GPSD, relevant measures have to be notified by the Member States "immediately". These are preventive or restrictive measures on products presenting a 'serious risk' to the health and safety of consumers. These measures can either be taken by national authorities, e.g. by stopping or banning of sales, or carried out voluntarily by economic operators, e.g. withdrawal from the market, recalls from consumers (RAPEX Annual Report, 2011).
In principle, all measures to ensure safety of the product are taken under Article 11 of the GPSD. These are measures taken by national authorities with regard to products posing "risks classified as less than serious". Notification of measures under Article 11 is waived if notification is already required under Article 12 (RAPEX notification – requires serious, immediate danger/effects beyond own territory) or any specific Community legislation" (DG SANCO, 2003).

2.2 Working of the RAPEX alert system

In short, the RAPEX alert system operates as follows:
- When a product (e.g. a toy, a childcare article or a household appliance) is judged as posing a 'serious risk', the national competent authority takes appropriate action to eliminate the risk. It can withdraw the product from the market; recall it from consumers or issue warnings. The National Contact Point then informs the European Commission (Directorate-General for Health and Consumer, DG SANCO) via RAPEX about the product, the risks it poses and the measures taken by the authority to prevent risks and accidents.
- The European Commission via RAPEX disseminates the information that it received to the National Contact Points of all other EU countries. It publishes

weekly overviews of products reported to represent a 'serious risk' and the measures taken to eliminate the risks on the internet.
- The National Contact Points in each EU country ensure that the authorities responsible check whether a newly notified product is present on the market. If so, the authorities take measures to eliminate the risk, either by requiring that the product be withdrawn from the market, by recalling it from consumers or by issuing warnings.

The weekly overviews are presented on the internet: http://ec.europa.eu/consumers/dyna/rapex/rapex_archives_en.cfm. Information on the product is provided as well as the possible danger and the measures taken by the reporting country. Examples of RAPEX notifications that were published in week 9 to 17 of 2012 are described in Appendix 1.

2.3 Activities of the Netherlands

The RAPEX National Contact Point for The Netherlands is the Dutch Food and Consumer Product Safety Authority (NVWA).
The NVWA is represented in the Consumer Safety Network (CSN). This network, formed in 2008 from the Consumer Safety Working Party (CSWP) and the Product Safety Network (PSN), aims to "stimulate reflection and discuss topics related to consumer product and service safety and knowledge base for policy work"
(http://ec.europa.eu/consumers/safety/committees/index_en.print.htm#csn). It is a consultative experts group chaired by the European Commission and composed of national experts from the 27 Member States and EFTA/EEA countries. In recent years, the main areas of discussion have been the safety of consumer products (such as lighters, joint actions on market surveillance), and of consumer services, including fire safety in hotels and relevant data collection. The CSN meets three times a year on average, usually in conjunction with the General Product Safety Committee meetings. This GPSD Committee assists the European Commission in several tasks related to the implementation of the GPSD. In particular, when the Commission takes decisions requiring the Member States to urgently introduce temporary measures restricting the placing on the market of products or requiring the withdrawal of products posing serious risks, it is assisted by the GPSD Committee
(http://ec.europa.eu/consumers/safety/committees/index_en.htm).

2.4 RAPEX notifications

The current RAPEX system was introduced in 2004. The total number of notifications validated by the Commission rose steadily in the past years, increasing more than fourfold between 2004 (468) and 2010 (2244). In 2011, the total number of notifications decreased (by 20%) when compared to the previous year, for the first time since the start of the operation of the system. The number of notifications of products presenting a 'serious risk' was 21% lower than in 2010.

2.4.1 Notifications in 2011

In total 1803 notifications on consumer products posing risks to health and safety were distributed through the Commission in 2011 (RAPEX Annual report, 2011). The majority of notifications (1556) was distributed under Article 12 of the GSPD and Article 22 of Regulation (EC) No 765/2008 (presenting a 'serious risk'). Fifty-eight notifications were distributed to Member States under Article

11 of the GPSD and Article 23 of Regulation (EC) No 765/2008. These may also concern voluntary measures by economic operators. In 2011, 189 notifications were distributed to Member States for information purposes only as they did not qualify for distribution under either of above-mentioned legal bases (RAPEX Annual report, 2011). The product category "Clothing, textiles and fashion items" was the most notified (27%), followed by toys (21%).
In 2011, 27 Member States plus Iceland and Norway sent notifications through the RAPEX system. The following five countries accounted for 47% of all notifications concerning a 'serious risk': Spain (189 notifications, 12%), Bulgaria (162, 10%), Hungary (155, 10%), Germany (130, 8%), United Kingdom, 105, 7%).

2.4.2 Factors that contribute to the number of notifications

The growth in number of notifications over the years resulted from increased attention given to product safety by authorities and companies, a greater number of market surveillance actions and the effect of training and seminars (RAPEX Annual report, 2011).
Various factors contributed to the reduction in the number of notifications in 2011. First, a number of targeted joint enforcement actions by Member States were finalized in 2010. Furthermore, the resource constraints due to budgetary restrictions presumably have affected Member States' activity levels. Further more experience with the RAPEX risk assessment guidelines will have allowed Member States to identify the correct level of risk posed by specific products at an earlier stage and to give priority in their notifications to those products most likely posing a 'serious risk'. Accordingly, while a decreased number of notifications were received, they were of higher quality and reliability (RAPEX Annual report, 2011).

It should be stressed that RAPEX statistics do not reflect all market surveillance activities in the Member States. Some measures taken against dangerous products do not result in notifications. One of the reasons is that some of the products are not available outside the specific Member State concerned. The participation rate of countries in RAPEX is the result of various factors, such as the different ways the national surveillance networks are organised, the different size of the countries and the different production and market structures that exist across the EU (RAPEX Annual report, 2011).

2.4.3 Notifications in the Netherlands

In the past 4 years, the Netherlands has reported between 33 and 73 dangerous products per year (33 products in 2008, 73 in 2009, 38 in 2010 and 40 in 2011). This is about 3% of the total number of notifications by all Member States. The Dutch notifications were based on data generated in NVWA research projects or because of a notification by industry. Notifications are only made when a serious failing has been identified for the product and the product is available on the market in other EU countries. For chemical risks, it is common practice for NVWA to notify when a concentration of a substance shows a two times exceedance of a concentration limit.
Apart from its own notifications, dangerous products are removed from the market in the Netherlands following notifications by other Member States. In 2009 for example, 230 dangerous products have been removed (average of 4 times a week).

2.4.4 Notifications by type of risk

A notification can be linked to 14 different risk categories. As to frequency of notifications in individual risk categories, chemical risks are second in rank. These are the figures for 2011 (RAPEX Annual report, 2011):
- Injuries (481 notifications, 26%)
- Chemical (347 notifications, 19%)
- Strangulation (275 notifications, 15%)
- Choking (224 notifications, 12%)
- Electric shock (216 notifications, 12%)

The percentages are based on the total amount of notifications by the various Member States. In the Netherlands, the percentage of chemical risks was 62,5% (25 out of 40 notifications) and much higher than the 19% in Europe.

Together, the above five risk categories account for 84% of all notified risks. Some RAPEX notifications relate to products concerning more than one risk. For instance, a toy can pose a choking risk because of small parts and a chemical risk due to excessive levels of a chemical substance. Therefore, the total number of notified risks can be higher than the total number of notifications.

3 RAPEX guidelines

In EU Commission Decision 2010/15/EU, new guidelines were adopted for the management of the RAPEX-system[1]. These new guidelines explain for which categories of consumer products RAPEX is intended and which categories of consumer products are excluded from RAPEX. Within the relevant consumer product categories, only the products constituting a 'serious risk' are to be notified via the RAPEX system. According to the guidelines, an appropriate risk assessment is needed to determine if a product indeed poses a 'serious risk' (which is the highest risk level covered by these guidelines) (see text box 1).

2.3. Serious risk

2.3.1. Serious risk
Before an authority of a Member State decides to submit a RAPEX notification, it always performs the appropriate risk assessment in order to assess whether a product to be notified poses a serious risk to the health and safety of consumers and thus whether one of the RAPEX notification criteria is met.
As RAPEX is not intended for the exchange of information on products posing non-serious risks, notifications on measures taken with regard to such products cannot be sent through RAPEX under Article 12 of the GPSD.

2.3.2. Risk assessment method
Appendix 5 to the Guidelines sets out the risk assessment method to be used by Member State authorities to assess the level of risks posed by consumer products to the health and safety of consumers and to decide whether a RAPEX notification is necessary.

2.3.3. Assessing authority
The risk assessment is always performed by an authority of a Member State that either carried out the investigation and took appropriate measures or monitored voluntary action taken with regard to a dangerous product by a producer or a distributor.
Before a RAPEX notification is sent to the Commission, the risk assessment performed by an authority of a Member State (to be included in the notification) is always verified by the RAPEX Contact Point. Any unclear issues are resolved by the Contact Point with the authority responsible before a notification is transmitted through RAPEX.

Text box 1: A selection of the text extracted from guideline 2010/15/EU.

A dedicated working group of Member State experts has developed the risk assessment method intended for this purpose. Appendix 5 to the RAPEX-guidelines, titled 'Risk Assessment Guidelines for Consumer Products' provides the description of this risk assessment method. The method seeks to define specific criteria for identifying 'serious risks' for different consumer products;

[1] Full title: Commission Decision of 16 December 2009 laying down guidelines for the management of the Community Rapid Information System 'RAPEX' established under Article 12 and of the notification procedure established under Article 11 of Directive 2001/95/EC (the General Product Safety Directive) *(notified under document C(2009) 9843)*

* the product is a consumer product,
* the product is subject to measures that prevent, restrict or impose specific conditions on its possible marketing or use ('preventive and restrictive measures'), —
* the product poses a 'serious risk' to the health and safety of consumers, —
* the 'serious risk' has a cross-border effect.

All national authorities should use this risk assessment method to assess the safety of consumer products (see text box 2).

APPENDIX 5
……
Risk assessment – an overview
2.1. Risk – Combination of hazard and probability
Risk is generally understood as something that threatens the health or even the lives of people, or something that may cause considerable material damage. Nevertheless, people take risks while being aware of the possible damage, because the damage does not always happen. For example:

— Climbing a ladder always includes the possibility of falling off and injuring oneself. 'Falling off' is therefore 'built into the ladder'; it is an intrinsic part of using a ladder and cannot be excluded. 'Falling off' is thus called the intrinsic hazard of a ladder.
This hazard, however, does not always materialise, since many people climb ladders without falling off and injuring themselves. This suggests that there is a certain likelihood (or probability), but no certainty, of the intrinsic hazard materialising. Whereas the hazard always exists, the probability of it materialising can be minimised, for example by the person climbing the ladder being careful.
— Using a household cleaner with sodium hydroxide to free blocked sewage water pipes always entails the possibility of very severe damage to the skin, if the product comes into contact with skin, or even of permanent blindness if drops of the product get into the eye. This is because sodium hydroxide is very corrosive, meaning that the cleaner is intrinsically hazardous. Nevertheless, when the cleaner is handled properly, the hazard does not materialise. Proper handling may include wearing plastic gloves and protective glasses. Skin and eyes are then protected, and the probability of damage is much reduced.

Risk is thus the combination of the severity of possible damage to the consumer and the probability that this damage should occur. The combination of severity of possible damage and probability of the damage leads to four categories of risks; serious, high, medium and low. This is further specified in the table below.

Text box 2: description of risk assessment method in Appendix 5 to the RAPEX guidelines

The risk assessment method as provided in Appendix 5 to the new RAPEX-guidelines deals with a wide range of risks, including mechanical risks, electrical risks, fire hazard, and radiation risk.
In paragraph 2.3 the guidelines provide some brief explanation including a reference to REACH guidance and to specific guidance for cosmetics by SCCP. However, no detailed guidance on the risk assessment method to be used within the RAPEX framework is given. Thus the guidelines provided on chemical risks remains very general in nature only and does not specify criteria for 'serious risk' due to chemical exposures resulting from consumer product use. A clear

definition of 'serious risk' is not given in the RAPEX guideline document. The document points out that in market surveillance, consumer products are often tested against limit values or requirements laid down in legislation and in product safety standards. Such standards or requirements provide a reference value for demonstrating the safety of the product in question. Non-compliance with such standards or requirements, however, does not automatically mean that the product presents a 'serious risk'. Therefore, additional risk assessment is needed. However, for chemical exposures due to consumer product use the categorisation of risks in serious, high, medium, and low risk as developed for the other types of risks (see table below), cannot readily be applied. This has led to the situation that in the Netherlands, the NVWA is not using this table for identification of a chemical risk.

Probability of damage during the foreseeable lifetime of the product		Severity of injury			
		1	2	3	4
high	> 50%	H	S	S	S
	> 1/ 10	M	S	S	S
	> 1/ 100	M	S	S	S
	> 1/ 1 000	L	H	S	S
	> 1/ 10 000	L	M	H	S
	> 1/ 100 000	L	L	M	H
	> 1/ 1 000 000	L	L	L	M
low	< 1/ 1 000 000	L	L	L	L

Table 1. Categorisation of risks as described in the RAPEX guidelines

S = serious risk
H = high risk
M = medium risk
L = low risk

The subject of the present report is the exploration of the issue of the definition and use of 'serious risk' for chemical exposure due to consumer product use. For useful perspective on this problem, further information of the limit values and requirements referred to above, is needed. This will be explored in Chapter 4, where in short a background on different limits is given.

4 Existing limit values for substances in consumer products

Different regulations are in place for chemicals used in several categories of consumer products. In addition, there are general regulations applicable to chemicals in consumer products not regulated in any specific category.

4.1 General regulations

The European Classification Labelling and Packaging (CLP) (EC No 1272/2008) regulation specifies classification criteria and labeling elements for chemical substances and mixtures. For chemicals classified as Carcinogenic class 1 & 2, Mutagenic class 1 & 2, and Reprotoxic class 1 & 2, CLP prescribes general concentration limits of 0.1% (carcinogenic 1 & 2, mutagenic 1 & 2) or 0.3% (reprotoxic class 1 & 2). For some individual chemicals, compound-specific lower concentration limits have been allocated. In Annex VI of the CLP regulation, a list of chemicals is provided including their classification within CLP and their concentration limits.

Within the chemical regulation REACH (Registration, Evaluation, Authorisation and Restriction of Chemical substances; EC 1907/2006), the concentration limits as specified in CLP have become subject to 'Restriction'. Annex XVII to the REACH regulation provides the specifications of these restrictions. The restrictions are applicable to chemical substances and mixtures but not to articles[2]. In addition, REACH Annex XVII also lists restrictions for individual chemicals adopted from the former EU-Directive 76/769/EEC ('Verbodsrichtlijn'). REACH Annex XVII for example includes the restriction for six phthalates in toys and as previously laid down in EU Directive 2005/84/EC. As the processes in REACH move forward, more individual restrictions will probably be included in Annex XVII. The current Annex XVII already restricts more than 1000 substances.

Another process within the REACH-regulation potentially leading to consumer product regulations is the 'Authorisation' process. Substances identified as 'Substances of Very High Concern' (SVHC), thus placed on Annex XIV based on their toxicological properties, are subject to 'Authorisation'. This means that registrants have to apply for individual uses of these substances. This will lead to a list of authorised specific uses with other uses being prohibited.

More general, is the General Product Safety Directive (GPSD). The GPSD aims at ensuring that only safe consumer products are sold in the EU. The objective and scope of the GPSD (2001/95/EC; applicable as from 15 January 2004) are both to protect consumer health and safety and to ensure the proper functioning of the internal market. It is intended to ensure a high level of product safety throughout the EU for consumer products that are not covered by specific sector legislation (e.g. toys, chemicals, cosmetics, machinery). The Directive also complements the provisions of sector legislation which do not cover certain

[2] This is the reason why REACH provides elaborate guidance on how to decide what is an article under REACH. Note that substances released from articles are nevertheless covered by REACH (see http://echa.europa.eu/documents/10162/13632/articles_en.pdf)

matters, for instance in relation to producers' obligations and the authorities' powers and tasks.
The Directive provides a generic definition of a safe product. 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, and the state of the art and the expectations of consumers.

4.2 Specific regulations

4.2.1 Cosmetics

The EU Cosmetics regulation (EC) no. 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products replaces earlier Directives. Given the wide variety of different categories of cosmetic products as to their purpose of human use, an important question is the definition of a cosmetic product. The Regulation states that the assessment of whether a product is a cosmetic product has to be made based on a case-by-case assessment, taking into account all characteristics of the product. The Regulation then provides a list of individual product groups considered to qualify as cosmetic products. This includes various skin care products, bath products, make-ups, deodorants, hair products, shaving products, teeth care products, lipsticks, sunbathing products.

As laid down in the Regulation, the use of chemicals classified as CMR category 1A, 1B and 2 is, in principle, prohibited in cosmetics. However, in exceptional cases such use may be allowable, provided its safety has been adequately demonstrated via an SCCS evaluation. The Regulation promotes the use of alternative *in vitro* test systems as a replacement for animal studies. The Regulation deals with known human skin allergens, indicating that either their presence in cosmetic products should be stated on the product (so that sensitized consumers can avoid them) or, for substances that cause allergy to a significant part of the population, further restrictive measures such as a ban or a restriction of concentration should be considered. The Cosmetics regulation includes four Annexes in which individual substances are regulated. Annex II provides a list of prohibited substances (n=1328). Annex III provides a list of restricted substances (specifies allowed use concentrations in cosmetics), Annex IV lists colorants allowed in cosmetic products (n=153) and Annex V lists preservatives and their allowed use concentrations (n=57).

4.2.2 Toys

The EU 'Directive 2009/48/EC of the European Parliament and of the Council of 18 June 2009 on the safety of toys' replaces the older Directive from 1988. Article 18 of the 2009 Directive rules that manufacturers carry out an analysis of the chemical, physical, mechanical, electrical, flammability, hygiene and radioactivity hazards that the toy may present, as well as an assessment of the potential exposure to such hazards. Part III of Annex II to the 2009 Directive specifies the chemical properties that toys must comply with. Substances that are classified as CMR of category 1A, 1B or 2 shall not be used in toys unless 1) they are contained within inaccessible parts of the toy or 2) the relevant Scientific Committee has established conditions under which they may be used safely in toys.
A number of allergenic fragrances (n=55) should not be present in toys (for unavoidable traces of these fragrances under GMP the tolerance is 100 mg/kg).

For a further group of 11 allergic fragrances the presence should be stated on the toy product packaging if the concentration is above 100 mg/kg.
For elements (n=19), the Directive establishes migration limits in mg/kg for (1) dry, brittle, powder-like or pliable toy material, (2) liquid or sticky toy material and (3) scraped-off toy material. The Directive states that these limit values shall not apply to toys or components of toys which, due to their accessibility, function, volume or mass, clearly exclude any hazard due to sucking, licking, swallowing or prolonged contact with skin when used as intended or in a foreseeable way, bearing in mind the behaviour of children.

It is important to note that the parts of the Directive relating to chemical content as outlined above, will come into force only on 20 July 2013. During the transitional period, part III of Annex II of 1988 Directive will continue to apply.

4.2.3 Detergents EU Regulation

Regulation (EU) No 259/2012 of The European Parliament and of the Council of 14 March 2012 Amending Regulation (Ec) No 648/2004 as regards the use of phosphates and other phosphorus compounds in consumer laundry detergents and consumer automatic dishwasher detergents.

4.2.4 Biocides

The biocide 'Regulation (EU) No 528/2012 Of The European Parliament And Of The Council of 22 May 2012 Concerning The Making Available On The Market And Use Of Biocidal Products' replaces the earlier 1998 Directive 98/8/EC. The biocidal product types as defined in this regulation include a wide range of products available for purchase by consumers. This includes human skin products such as disinfectant soaps and disinfectant washing liquids, antimicrobials for private use indoors such as those used in swimming-pools, chemical toilets, disinfectant and algaecidal products for surface treatments, drinking-water disinfectants for private use, wood preservatives or treated wood products, pest control products against mice and rats or insects, insect repellents, molluscicides, anti-fouling products for pleasure boats. A special case are the 'treated articles', i.e. consumer products such as textiles, tissues, masks, paints and other products with biocides incorporated into them providing disinfecting properties during their use.
As envisaged by the EU biocide regulation, only products with proper authorisation should enter the market.

5 Description of the 'serious risk' issue within RAPEX with respect to chemical exposure

The definition of 'serious risk' is open to differences in interpretation, especially in the case of determination of risk on chemical exposure due the use of consumer products. The decision on the seriousness of the risk can be different in the Netherlands when compared to other Member States.
As was noted within the Consumer Safety Network (CSN), the risk assessment method as described in the RAPEX guidelines is not sufficient for chemical risks (see also Chapter 3). The discussion with regard to 'serious risk' for chemicals in consumer products within RAPEX is ongoing, aimed at harmonization at EU-level. See, for example, the report of the CSN meeting of 29 January 2010 (http://ec.europa.eu/consumers/safety/committees/docs/sum29012010_csn_en.pdf) and of the GPSD Committee of 28 January 2010 (http://ec.europa.eu/consumers/safety/committees/docs/sum28012010_gpsd_en.pdf).

The RAPEX notification should include various supporting documents, such as a risk assessment, a list of distributors and a testing report. The final assessment of a product is based on the information in these documents, sometimes a manufacturer is visited. Member States have their own competence to come into action, only the risk assessment is harmonised at the EU level and made available to the other Member States. This is the case for the reaction to RAPEX notifications, but also for the notifying process itself (VWA, 2007).

5.1 Three different scenarios of RAPEX notifications

In Table 1 (Appendix 1), examples of RAPEX notifications associated with a chemical hazard are presented (this is a selection of chemical notifications from week 9 to week 17, 2012). Products in this list are notified because of the presence of a potentially hazardous chemical with a potential consumer exposure. Various chemicals are notified in consumer products in multiple Member States.

As these examples show, most recent notifications are from consumer products in which a regulatory concentration limit has been exceeded. Chemicals that are notified frequently are phthalates (DEHP, DBP, DIBP and DINP) in toys, because of the ban of these chemicals in toys. Also metals like nickel and chromium-VI are reported frequently, mostly in jewelry and belts. For nickel there is a maximum permitted level of 0.5 ug/cm^2/week, that has been exceeded. For chromium in leather, there is a ban in Germany (http://www.cbi.eu/marketinfo/cbi/docs/germany_legislation_chromium_vi_in_leather_and_textile_products_additional_requirement). Furthermore, a REACH restriction proposal for chromium (Sweden) is under discussion at the moment. RAPEX notifications for chromium are reported as "chromium (VI) is classified as sensitising and may trigger allergic reactions".

Some notifications are based on acute health problems, complaints or incidents. These notifications are very rare, with only two cases being reported in this list. These are notifications of carbon monoxide from a gas refrigerator and allergic complaints for example for chromium or dimethylfumarate (DMFu).

In addition to these two categories (exceedance of product concentration limit and possible acute complaints) there is another scenario of notifications possible, i.e. the situation in which a substance in a consumer product possibly poses a 'serious risk', without a legal concentration limit being available.

In summary, three different scenarios for RAPEX notifications based on a chemical risk can be distinguished:

1. A concentration limit/limit value is exceeded (with a factor of 2 to x-fold). *For example DEHP in dolls or toluene in glue*.
2. A substance in a product resulted in actual complaints or incidents *For example DMFu in couches or GHB formed from magic beads*.
3. A substance in a product is a possible 'serious risk', but there is no actual legal concentration limit available. *For example chromium VI in leather products or azo-dyes and cadmium in tattoo inks.*

According to the guidelines a notification in RAPEX should be accompanied by a risk assessment. What this means for the different scenarios is described below.

For scenario 1, in many cases, no additional risk assessment will be performed. However, a concentration limit is in many cases not directly health-based, since in many cases the limit value is not derived via a chemical specific risk assessment for the scenario in question.

Limit values set for risk management purposes.
An important and well known example of such a limit is the general 0.1% limit for CMR substances (see also Chapter 4). These limits are set for risk management reasons (a consumer should not be exposed to CMR substances). An exceedance of such limit will not necessarily mean that there is a risk. Similarly it should be noted that the CMR endpoints carcinogenicity, mutagenicity and in some cases reproductive toxicity are usually assessed for a lifetime exposure. Thus the dose-response assessment and the risk characterization will also be aimed at deriving chronic health based limit values. A short-term exposure to higher levels will therefore usually not result in a risk above accepted (long term) reference levels.

Relevance of the exposure scenario in question when using a limit value
When performing a risk assessment, the first step is the exposure assessment. For RAPEX notifications, an assumption concerning the duration of exposure will have to be made, i.e. for which period it is assumed that the chemical contamination has been in place. The most plausible choice for this duration will vary from case to case. In the context of serious risk, acute or short-term exposure duration will be the most appropriate choice in most cases. Furthermore, it may be warranted to look at additional background exposure to the chemical (from other sources than the consumer product notified to RAPEX, such as food).
The subsequent hazard assessment needs to be based on the relevant key endpoint, using the related NOAEL or BMDL. For many substances, the concentration limit (e.g. of 0.1%) cannot be used for that, as it is not derived on health effects.

For scenario 2, actual health effects are observed. A risk assessment needs to be performed, however, a clear case can be made.

For scenario 3, no legal limit is available. However, the substance is measured for a reason, resulting from existing national legislation or other information. A risk assessment can be performed, for which the specific issues mentioned for scenario 1 also apply.

6 Examples of different interpretations of 'serious risk'

As illustration of the different scenario's possible, examples are worked out in the following paragraphs.
More detailed information regarding the calculations used for the risk assessment can be found in Appendix 2.

6.1 Chloroform in solution glue

Introduction
In RAPEX notification 0551/10 from 2010 (notified by the Netherlands) chloroform in superglue at a concentration of 7.1% had been notified. As chloroform is classified as a carcinogen, group 2B (possibly carcinogenic to humans), the limit of 0.1% has been exceeded (REACH Annex XVII) which makes this an example of a scenario 1 situation.

Subsequently other EU member states indicated that their risk assessment did not show a 'serious risk' at 7.1% chloroform in superglue.
Therefore, NVWA requested RIVM to perform a risk assessment aimed at determining the concentration at which chloroform (and also benzene and toluene) in glue represent a 'serious risk' as intended within RAPEX. The outcome of this assessment by RIVM was reported by Janssen and Bremmer (2010).

Is there a 'serious risk'?
For chloroform, for acute exposure, the calculated exposure estimate (0.57 mg/m^3) is not much lower compared to the acute acceptable air concentration of 0.7 mg/m^3. However, since the assumptions in the exposure scenario are rather worst-case, it can be concluded that there is no (serious) risk for the acute exposure to chloroform in the case of using solution glue.
For the chronic situation (exposure 0.002 mg/kg bw/day compared to an acceptable chronic systemic body dose of 0.05 mg/kg bw/day), there is no (serious) risk in case of using solution glue once a month per year.
See for further information, Janssen and Bremmer (2010). They describe also a limit value for chloroform in solution glue, resulting in a concentration limit of 8% based on acute neurological effects.

6.2 NDELA in cosmetics

Introduction
Nitrosodiethanolamine (NDELA) is a common contaminant in many cosmetic products. In the past, restrictions have been put in place on the use of secondary dialkanolamines and the presence of nitrosating agents in cosmetics in order to prevent formation of NDELA in cosmetics. Cosmetic products containing nitrosamines including NDELA have been banned under the Cosmetics Directive and its Annex III refers to the limit of 50 µg/kg for nitrosamines.

NDELA in cosmetics is often notified within RAPEX as is described in the following table and in more detail in Appendix 3.

Table 2. Examples of notifications of NDELA in cosmetics

Year-week	Notifying Country	Product	NDELA levels in product (µg/kg, ppb)
2006-26	The Netherlands	Cosmetic eyeliner	142, 206, 84
2006-5	The Netherlands	Shampoo	286, 301
2006-3	Germany	Mascara	204
2006-1	Germany	Eyeliner	1002
2005-48	Germany	Mascara	142, 133, 111
2005-2	Germany	Shampoo	489

Is there a 'serious risk'?
The Systemic Exposure Dosage (SED) calculation of NDELA in shampoo as example resulted in 0.000249 ng/kg bw/day (see Appendix 2). This is compared with the Virtually Safe Dose (VSD; the daily dose on lifelong exposure that is associated with an additional cancer risk of 1 in 1,000,000) of 13.2 ng/kg bw/day, as proposed by SCCS. Based on this calculation it can be concluded that the (single) use of this shampoo containing NDELA does not present a 'serious risk'.

Using the SCCS approach it can be demonstrated that for several products that have been notified in the past, none of these products presented a 'serious risk' based on the concentration NDELA in the product.

It must be noted here, that the SCCS (2012) decided to us a pragmatic cut-off point for 'serious risk' for NDELA, equivalent to a cancer risk of 1:100000. SCCS adds that the choice of this cut-off level in principle is a risk management decision.
In addition, it needs to be noted that RAPEX relates to safety of products. In the SCCS calculation, aggregate exposure (NDELA exposure from other cosmetic products or other sources) is not taken into account.

For more information: Based on default daily cosmetics use levels, retention factors etcetera, SCCS calculated the levels in NDELA in cosmetic products at which the SED equalled this BMDL10/10000 (SCCS 2012). Janssen et al. (2004) made additional calculations for short-term (accidental) exposure: this means extrapolating the lifetime VSD to a preselected short-term period and calculating the SED at which this short-term VSD is reached (this leads to considerably higher 'serious risk' levels of NDELA).

6.3 DEHP in toys

Introduction
Bis(2-ethylhexyl)phthalate (DEHP) or other phthalates in toys are often notified within RAPEX notifications. One of the examples as described in Appendix 1 is depicted below (table 3).

Table 3. Example of DEHP notification

0629/12	DEHP	Doll (SP)	6.53% by weight	Prohibited in toys

As DEHP is classified as a group 2B carcinogen, this concentration exceeds the limit for DEHP of 0.1% (REACH Annex XVII).

Is there a 'serious risk'?
The DNEL (internal) as established in the REACH restriction dossier (2012) is 0.035 mg/kg bw/day for DEHP. Comparing the internal exposure estimate for the mouthing scenario of 0.019 mg/kg bw/day (child of 8 kg) or the total internal exposure estimate after dermal contact of 0.015 µg/kg bw/day (child of 15 kg) with the internal DNEL, a conclusion of no 'serious risk' can be drawn. Especially when taking into account that the exposure calculation is very worst case because of the 3 hours mouthing and dermal contact time (see above) and only mouthing/playing this specific doll.
Also when the background of food and indoor air is included, still a conclusion of no concern can be drawn (for references see the advice on phthalates in scoubidou (RIVM, 2004) and the advice on phthalate replacers (RIVM, 2009)). However, one could argue that since these substances are prohibited in toys these products need to be on the RAPEX list but with a comment in an additional column that the risk is not a serious risk.

7 Discussion and recommendations

7.1 Discussion

As explained in the previous chapters, 'serious risk' for chemicals in consumer products within RAPEX has not yet been clearly defined. This is probably caused by the different risks noted within RAPEX, including mechanical and electrical risks. The term 'serious' as a qualifier to risk is difficult to interpret within the accepted framework of risk assessment for chemicals.

As described in Chapter 5, RAPEX notifications based on chemical risks occur according to three different scenarios:

1. A concentration limit/limit value is exceeded (with a factor of 2 to x-fold).
2. A substance in a product results in actual complaints or incidents.
3. A substance in a product poses (or may pose) a concern but there is no limit value available.

In the first situation, risk assessment may show that there actually is no serious risk or even no risk at all in terms of risk assessment. Concentration limits in consumer products frequently are not health-based limits, but are set for risk management reasons, for example in the case of 0.1% for CMRs in preparations for consumers. It is a matter of definition whether this exceedance is considered a 'serious risk'.

According to the RAPEX guidelines, in any case of notification, a risk assessment should be performed. However, guidance on how to perform this risk assessment is not given in the guidelines, only reference is made to the SCCS notes of guidance and the REACH guidance.
In the previous chapters of this document, various points of concern regarding this risk assessment are given, such as:

- How to assess the, in most cases incidental (acute or short-term), exposure when it is compared with a relevant chronic health endpoint?
- How to deal with background exposure (from food or air) or exposure resulting from other products?
- How to deal with genotoxic carcinogens? Which point of departure needs to be taken? A point of departure based on a 10^{-6} risk per lifetime? (see for more information Appendix 4).

7.2 Recommendations

7.2.1 Definition of 'serious risk'

The categorization of risk into 'serious', 'moderate', 'low' might be practical for mechanical of physico-chemical risks, but for health risks resulting from chemicals in consumer products this approach is difficult to apply. At present a usable definition of 'serious risk' for chemical exposures via consumer product is not available. The necessary generally applicable gradation and classification of health effects (serious versus non-serious) in the context of consumer products represents an enormous challenge given the wide variety of such products on the market, each with its own exposure characteristics (oral, dermal, inhalation), use frequencies and use populations.
If a clear usable definition can be established, including criteria, it should be included in the RAPEX guidelines. At present a certain level of pragmatism in

applying the RAPEX-guidelines for chemical risks seems inevitable. It is important to have an approach that is flexible and easy to apply. Very often exceedance of generic product concentration limit will be the trigger for RAPEX notification. It needs to be stressed that this does not immediately imply a health risk.

Clearly, the recommendation would be to *change the use of 'serious risk' in the case of chemical risks*. However, as the term is a legal term in the Directive, a pragmatic approach is necessary.
Another approach could be to establish clear criteria to decide when the presence/concentration of a substance in a product is associated with a serious risk (in that case it could be possible to include the exceedance of a limit).

7.2.2 Risk assessment

According to the RAPEX guidelines a risk assessment should be performed. In this context, the guidelines refer to the REACH guidance and the SCCPs Notes of Guidance.
As mentioned above, in the framework of RAPEX, risk assessment needs to be performed for different scenarios. Some important issues in this context are:

- incidental (acute) exposure compared in relation to a chronic endpoint
- concentration limits which are legally based, and are not health-effect based (therefore, a health-based limit needs to be established in the case of performing a risk assessment)
- when notification is based on incidents (such as for sensitizers, or acute effects), an acute effect limit should be established
- when no limit at all is available, a limit should be established (here for starters DNELs/DMELs resulting from REACH could help)
- is there a need to take into account background exposure or exposure from other sources (products)?
- what is the point of departure for genotoxic carcinogens, without a threshold? Is that based on an additional risk of 10^{-5} per lifetime as proposed by the SCCS (2012) for NDELA?

There is a need for specific guidance for risk assessments performed within the framework of RAPEX.
The recommendation here is that guidance for performing such risk assessments should be written in which the issues mentioned above are specifically addressed. However, it should be realized that such a guidance only deals with product safety. Since consumers are exposed to substances via more that one product and also via other sources, product safety is not equivalent to consumer safety.
Actual risk assessment for the presence of a hazardous chemical in a consumer product requires definition of an appropriate exposure scenario and evaluation of the health effects produced by the chemical in question.

7.2.3 Practical proposal

In addition to the recommendations above, a more pragmatic approach is proposed that can be introduced for a RAPEX notification of a chemical risk.
Even though the exceeding of a concentration limit (for example for CMR substances) is not always leading to a health risk, the exceeding is not desirable from the perspective of risk management and/or enforcement, since there are good reasons for the regulation of these substances. Therefore, a practical solution, that can be implemented quickly, is to add a column to the RAPEX

notification with "reason for RAPEX notification". Possible remarks could be (see Table 4 for the examples):

- "exceeding of limit according to Directive XX".
- "incident(s) / complaints reported". This could be relevant in the case of sensitizers or for substances causing acute effects.
- "RA based reason for concern" . This should then be accompanied by a well-performed risk assessment.

Table 4. For example, an additional column at the end.

Ref.	**Chemical**	**Consumer product/ MS**	**Measured concentration**	**Permitted level/ limit**	**Reason for RAPEX notification**
0589/12	DEHP	Doll (GE)	3.6-16.7% by weight	Prohibited in toys	Exceeding of limit (factor xx)
0588/12	Chromium VI	Wristwatch strap (GE)	6.1 mg/kg	?	complaint/health effects (severe skin irritation)
0569/12	4-Amino azobenzene	Work gloves (GE)	138 mg/kg (release)	?	RA based reason for concern

Recommendations summarized

1. Define 'serious risk' with relevance to chemical risks. This could be performed by setting criteria.
2. Make a guidance document for risk assessment within RAPEX. This should take into account the issues of comparison of incidental exposure against chronic health effects, background exposure and the point of departure for carcinogenic endpoints.
3. Add a column to the RAPEX notifications with 'reason for RAPEX notification'.

References

Baars AJ, Theelen RMC, Janssen PJCM, Hesse JM, Van Apeldoorn ME, Meijerink MCM, Verdam L, Zeilmaker MJ (2001). Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report 711701025.

Bremmer HJ, Prud'homme de Lodder LCH, van Engelen JGM (2006). General Fact Sheet. Limiting conditions and reliability, ventilation, room size, body surface area. Updated version for ConsExpo 4. RIVM report 320104002/2006. .

Bremmer HJ, Blom WM, van Hoeven-Arentzen PH, Prud'homme de Lodder LCH, van Raaij MTM, Straetmans EHFM, van Veen MP, van Engelen JGM (2006b). Pest Control Products Fact Sheet. To assess the risks for the consumer. Updated version for ConsExpo 4. RIVM report 320005002/2006. August 2006.

Cosmetics Directive (76/768/EEC) available at http://ec.europa.eu/enterprise/cosmetics/index_en.htm (June 2012)

Guidance document on the relationship between the General Product Safety Directive and Certain Sector Directives with provisions on product safety. DG SANCO, 2003

Janssen PJCM and Bremmer HJ (2009). Risk assessment non-phthalate plasticizers in toys. http://www.nvwa.nl/actueel/bestanden/bestand/2000552

Janssen PJCM and Bremmer HJ (2010). Health-based migration limits for benzene, toluene and chloroform in solution glue. SIR Advisory report. http://www.nvwa.nl/actueel/bestanden/bestand/2200603

Keeping Europeans safe, 2011 Annual report on the operation of the Rapid Alert System for non-food dangerous products RAPEX.

Lijinsky W and Kovatch RM (1985). Induction of liver tumors in rats by nitrosodiethanolamine at low doses. Carcinogenesis 6:1679-1681.

Peto R, Gray R, Brantom P and Grasso P (1991a). Effects on 4080 rats of chronic ingestion of *N*nitrosodiethylamine or *N*nitrosodimethylamine: a detailed dose–response study. Cancer Res. 51: 6415– 6451.

Peto R, Gray R, Brantom P and Grasso P (1991b). Dose and time relationships for tumor induction in the liver and esophagus of 4080 inbred rats by chronic ingestion of *N*-nitrosodiethylamine or *N*nitrosodimethylamine. Cancer Res. 51: 6452–6469.

REACH guidance (2010). Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health. http://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf

RIVM (2004). Advies inzake de blootstelling van Nederlandse kinderen aan ftalaten via scoubidou-touwtjes. http://www.nvwa.nl/actueel/bestanden/bestand/10887

SCCP (2006). The SCCP's Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation, 6th revision.

SCCS (2012). SCCS Opinion on NDELA in Cosmetic Products and Nitrosamines in Balloons.
http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_100.pdf

US-EPA (1993). N-nitrosodimethylamine, carcinogenicity assessment. IRIS (Integrated Risk Information System), 2003; US Environmental Protection Agency, Washington DC, USA. http://www.epa.gov/IRIS/subst/0252.htm

Voedsel en Waren Autoriteit (VWA), Factsheet RAPEX systeem, 2007
http://www.vwa.nl/onderwerpen/werkwijze-food/dossier/melden-en-traceren/nieuwsoverzicht/nieuwsbericht/2002940/veel-onveilig-speelgoed-opgespoord-via-rapex

Appendix 1

Table 1: Selection of RAPEX notifications (week 9 to week 17, 2012)

Ref.	Chemical	Consumer product/ MS	Measured concentration	Permitted level/ limit
0722/12	Hydrogen peroxide	Teeth whitening pen (FR)	0.6-1.0%	
0721/12	Hydrogen peroxide	Teeth whitening pen (FR)	4.6%	
0680/12	DMF	Children's slippers (EST)	3.4 mg/kg	Prohibited in consumer products
0679/12	DBP DEHP	Rubber toys (SP)	5.54-5.60% 0.22-0.30%	Prohibited in toys
0677/12	DEHP	Doll (SP)	19.52-23.13% by weight	Prohibited in toys
0672/12	Benzene	Ladies Boots (GE)	8-27 mg/kg	
0656/12	DEHP	Bath toys (SP)	0.07-8.59% by weight	Prohibited in toys
0651/12	Bisphenol A	Babies bottle (SP)	?	
0641/12	DEHP	Doll (head)(CR)	6.55% by weight	Prohibited in toys
0639/12	Cadmium	Jewellery (ring)(FI)	16%	0.01%
0638/12	Hydrogen peroxide	Teeth whitening product (FI)	6%	?
0637/12	Carbamide peroxide	Teeth whitening product (FI)	35%	?
0629/12	DEHP	Doll (SP)	6.53% by weight	Prohibited in toys
0620/12	Chromium VI	Ladies leather jacket (GE)	76 mg/kg, 56 mg/kg	?
0619/12	Chloroform Dichloormethane Dichloorethane	Cyanoacrylate glue (IT)	20% 0.08% 0.03%	?
0617/12	4-Amino azobenzene	Children's sports Shoes (GE)	210 mg/kg 765 mg/kg (release)	30 mg/kg
0615/12	DEHP	Doll (GE)	3.7-25% by weight	Prohibited in toys
0611/12	DEHP	Doll (GE)	6.6-24% by weight	Prohibited in toys
0610/12	DEHP	Doll (GE)	4.4-25% by weight	Prohibited in toys
0608/12	Clobetasol propionate	Beauty cream (Por)	?	Prohibited in cosmetics
0607/12	4-Amino azobenzene	Ladies suède gloves (FI)	424.2 mg/kg (release)	30 mg/kg
0595/12	DEHP	Toy carnival mask "Spiderman" (GR)	49.6% by weight	Prohibited in toys
0593/12	Carbon monoxide	Portable gas heater (NL)		
0590/12	DEHP	Doll (GE)	2.9-19.4% by weight	Prohibited in toys
0589/12	DEHP	Doll (GE)	3.6-16.7% by weight	Prohibited in toys
0588/12	Chromium VI	Wristwatch strap (GE)	6.1 mg/kg	?
0569/12	4-Amino azobenzene	Work gloves (GE)	138 mg/kg (release)	?

0553/12	Nickel	Jewellery earrings (IT)	13.44 µg/ cm^2/week	0.5 µg/ cm^2/week
0552/12	Chromium VI	Soft toy with key ring (FR)	? (higher than permitted)	?
0547/12	DEHP	Flashing toy duck (UK)	0.21% by weight	Prohibited in toys
0546/12	Nickel	Sunglasses (CY)	2.1 µg/ cm^2/week (frame) 0.56 µg/ cm^2/week (left temple)	0.5 µg/ cm^2/week
0545/12	Nickel	Men's leather belt (CY)	28 µg/ cm^2/week	0.5 µg/ cm^2/week
0544/12	Nickel	Pencil (CY)	2.6 µg/ cm^2/week (punt) 1.3 µg/ cm^2/week (clip)	0.5 µg/ cm^2/week
0543/12	Nickel	Ladies belt (CY)	0.83 µg/ cm^2/week	0.5 µg/ cm^2/week
0524/12-0515/12	"Smoke"	Incense (several) (Por)	?	?
0514/12*	Benzidine	Men's jeans (PO)	84.5 mg/kg	?
0502/12	Chloroform	Super glue (LI)	16.7 % by weight	?
0495/12	DEHP	Doll (LI)	38 % by weight	Prohibited in toys
0489/12	DEHP	Doll (LI)	34 % by weight	Prohibited in toys
0479/12	DEHP	Doll (LI)	30 % by weight	Prohibited in toys
0478/12	DEHP	Doll (LI)	33 % by weight (head) 0.12 % by weight (body)	Prohibited in toys
0476/12	DEHP	Plastic animal set (GE)	4.6 % by weight (cow) 5.9 % by weight (straps)	Prohibited in toys
0474/12	DMF	Girl's slippers (sachet)	0.2 mg/kg	Prohibited
0465/12	DEHP	Doll (SP)	25 % by weight (head)	Prohibited in toys
0464/12	Chromium VI	LEather gloves with lining (GE)	16.2 mg/kg (extractable chr) 7.3 mg/kg	?
0463/12	Nickel Arsenic	Tattoo ink	30.1 mg/kg 7.5 mg/kg	0.5 µg/ cm^2/week 2.0 mg/kg ResAP
0461/12	DEHP	Doll (SP)	0.2 % by weight (head)	Prohibited in toys
0449/12	DBP	Nail polish	0.42%	?
0442/12	DEHP	Doll (GE)	20.5% by weight	Prohibited in toys
0441/12	DEHP DBP	Children's shoes (BU)	0.32% by weight 0.24% by weight	?
0438/12	Chromium VI Dispersion Orange 37	Leather gloves	16.5-35.2 mg/kg 385.8 mg/kg	?
0437/12	Chromium VI	Working gloves	40-67 mg/kg	?
0433/12-0429/12	Nicotine	Liquid for electronic cigarette (FR)	0.6% - 1.8%	?

0407/12	DEHP	Doll (SP)	> 0.2 % by weight (head)	Prohibited in toys
0403/12-0400/12	Methyl metacrylate (MMA)	Nail modeling product (GE)	80- 86%	80-90% in nail modelling cosmetics is harmful to health (BfR)
0398/12	DEHP	Nail polish (CR)	0.23%	?
0397/12	DEHP DINP	Swim ring (HU)	1.8-29% 44%	Prohibited in toys
0395/12	DEHP	Nail polish (CR)	0.09%	?
0384/12	Chromium VI	Leather gloves (protective)	11.65-17.1 mg/kg	?
0383/12	DEHP	Doll (GE)	32.92 % by weight	Prohibited in toys
0381/12*	Carbon monoxide	Gas refrigerator (DE)	"excessive amounts"	?
0378/12	DEHP	Toy car (GE)	19.6 % by weight	Prohibited in toys
0376/12	DEHP DIBP	Plastic toy tea set (GE)	3.5 % by weight 14.5 by weight	Prohibited in toys
0374/12	DBP	Doll (SP)	10.13 % by weight (head)	Prohibited in toys
0352/12	Chromium VI	Leather gloves (GE)	17.5/ 29.3/ 35.9 mg/kg	?
0339/12	DEHP	Doll (SP)	0.2 % by weight (head)	Prohibited in toys
0338/12	Chromium VI	Women's shoes (GE)	17.3 mg/kg	
0337/12	Formaldehyde	Hair treatment product (FR)	3.5%	0.2%

** for these notifications, one or more incidents have been reported*

Appendix 2

More detailed information on the examples of different interpretations of 'serious risk' from Chapter 5

As illustration of the different scenario's possible, examples are worked out in the following paragraphs.

1. Chloroform in solution glue

Introduction
In RAPEX notification 0551/10 from 2010 (notified by the Netherlands) chloroform in superglue at a concentration of 7.1% had been notified. As chloroform is classified as a carcinogen, group 2B (possibly carcinogenic to humans, the limit of 0.1% has been exceeded (REACH Annex XVII) which makes this an example of a scenario 1 situation.

Subsequently other EU member states indicated that their risk assessment did not show a 'serious risk' at 7.1% chloroform in superglue.
Therefore, NVWA requested RIVM to perform a risk assessment aimed at determining the concentration at which chloroform (and also benzene and toluene) in glue represent a 'serious risk' as intended within RAPEX. The outcome of this assessment by RIVM was reported by Janssen and Bremmer (2010).

Risk assessment

* Exposure assessment:
Description of the scenario for consumer use of solution glue:
Estimated amount of solution per event: 0.5 ml
Estimated specific gravity: 0.8 à 0.9 g/cm^3 .
Amount of solution per event: 0.5 x 0.85 = 0.43 g.
Room in which tire is fixed is a shed of 4 m^2, 10 m^3, with room ventilation rate of 1.5 hr^{-1} (Bremmer et al. 2006).
The amount of 430 mg solution is applied to a surface of 12.5 cm^2 by spreading, using the top of one finger (1 cm^2). After spreading the remaining solution is removed from the finger. The rubber pad is then applied to the treated surface after three minutes. The person subsequently remains in the shed for an additional 4 hours (worst case).

Inhalation exposure
For estimating inhalation exposure, the total amount applied is assumed to evaporate from the 12.5 cm^2 application site. Within ConsExpo, inhalation exposure increases linearly with concentration in glue.

Dermal exposure
Contact surface: 1 cm^2
Exposure period: 1 minute
Amount of solution on finger: ¼ of the total amount, i.e. 100 mg (worst case).

Dermal absorption during 1 minute: 10% for chloroform. This is based on relatively high dermal absorption rates known for these chemicals in combination with high expected evaporation rates.

ConsExpo was run using the above scenario. Separate calculations were made for single event exposure as estimated by ConsExpo (for inhalation 0.57 mg/m^3) and for average exposure over 1 year based on 1 event per month (chronic dose), resulting in 0.00198 mg/kg bw/day.

* Hazard characterisation of chloroform
For chloroform a EU Risk Assessment Report (RAR; 2008) is available. For acute inhalation of chloroform, the RAR proposes a Lowest Observed Adverse Effect Level (LOAEL) of 249 mg/m^3 derived from human data (1 hour study) with the effect at or even below this level described as "discomfort". A further critical endpoint for chloroform is local irritation and cellular damage in upper airways. For this effect the RAR presents an acute LOAEL of 50 mg/m^3 in rats, with a minimal Margin of Safety (MOS) of 75. This leads to an acute acceptable air concentration of 0.7 mg/m^3.
As to repeated dose toxicity, the RAR gives a semichronic No Observed Adverse Effect Level (NOAEL) of 25 mg/m^3 to be used for combined exposures (inhalation, dermal, oral). This concentration can be converted to a systemic dose of 8.2 mg/kg bw/day. The minimal MOS for this NOAEL is 175. This leads to a chronic acceptable systemic dose of 0.05 mg/kg bw.

Is there a 'serious risk'?
For chloroform, for acute exposure, the calculated exposure estimate (0.57 mg/m^3) is not much lower compared to the acute acceptable air concentration of 0.7 mg/m^3. However, since the assumptions in the exposure scenario are rather worst-case, it can be concluded that there is no (serious) risk for the acute exposure to chloroform in the case of using solution glue.
For the chronic situation (exposure 0.002 mg/kg bw/day compared to an acceptable chronic systemic body dose of 0.05 mg/kg bw/day), there is no (serious) risk in case of using solution glue once a month per year.
See for further information; Janssen and Bremmer (2010). They describe also a limit value for chloroform in solution glue, resulting in a concentration limit of 8% based on acute neurological effects.

2. NDELA in cosmetics

Introduction
Nitrosodiethanolamine (NDELA) is a common contaminant in many cosmetic products. In the past, restrictions have been put in place on the use of secondary dialkanolamines and the presence of nitrosating agents in cosmetics in order to prevent formation of NDELA in cosmetics. Cosmetic products containing nitrosamines including NDELA have been banned under the Cosmetics Directive and its Annex III refers to the limit of 50 µg/kg for nitrosamines.

NDELA in cosmetics is often notified within RAPEX as is described in the following table and in more detail in Appendix 3.

Table 2. Examples of notifications of NDELA in cosmetics

Year-week	Notifying Country	Product	NDELA levels in product (µg/kg, ppb)
2006-26	The Netherlands	Cosmetic eyeliner	142, 206, 84
2006-5	The Netherlands	Shampoo	286, 301
2006-3	Germany	Mascara	204
2006-1	Germany	Eyeliner	1002
2005-48	Germany	Mascara	142, 133, 111
2005-2	Germany	Shampoo	489

Risk Assessment:

* Exposure assessment
According to the SCCP Notes of Guidance, it is necessary to calculate the Systemic Exposure Dosage (SED), the amount expected to enter the blood stream (and therefore be systemically available) per kg body weight and per day. It is expressed in mg/kg body weight/day. For this definition, a mean human body weight of 60 kg is commonly accepted.
The SCCP also points out that "since the majority of cosmetic products are applied topically, systemic availability will strongly depend on the dermal absorption of the compound."

There is some discussion on the dermal penetration rate, or absorption percentage, of NDELA. An absorption factor of 23% for stay-on products was proposed by RIVM (Janssen et al., 2004); the initial absorption flux in the first hour has been reported to be 1.5%. This one hour value is also used for rinse-off products (although the real contact time is obviously much shorter). For dermal uptake SCCS used an absorption percentage of 65% (SCCS, 2012).

As an example, an exposure estimation is performed for shampoo with 286 µg NDELA/kg.
The daily external exposure (DEE) to a cosmetic product, taking into account the use frequency and retention factor, is 0.08 g/day for shampoo (8 g per day and 0.01 as retention factor). For this shampoo, the external exposure to NDELA is then: 286 ng/g * 0.08 g/day /1000 = 0.023 ng/day. The SED is calculated using the DEE * [penetration rate] / BW. In this example using the absorption percentage of 65% and the body weight of an adult, the SED would be 0.023 * 0.65 / 60 = 0.249 pg/kg bw/day.

* Hazard characterisation of NDELA
Risk assessors have used different values of the Virtually Safe Dose (VSD): the daily dose on lifelong exposure that is associated with an additional cancer risk of 1 in 1,000,000 (see appendix III for discussion about this assumption).

After many discussions and different approaches to derive a VSD, in the SCCS opinion of 2012, a VSD was decided upon which equalled the BMDL10/10000 (SCCS 2012). This resulted in a VSD on lifetime of 0.0132 µg/kg bw/day.

Is there a 'serious risk'?
Based on the above mentioned calculation it can be concluded that the (single) use of this shampoo containing NDELA does not present a 'serious risk'. The Systemic Exposure Dosage (SED) calculation of shampoo as example resulted in 0.000249 ng/kg bw/day. This is compared with the Virtually Safe Dose (VSD; the daily dose on lifelong exposure that is associated with an additional cancer risk of 1 in 1,000,000) of 13.2 ng/kg bw/day, as proposed by SCCS.

Using the SCCS approach it can be demonstrated that for several products that have been notified in the past, none of these products presented a 'serious risk' based on the concentration NDELA in the product.

It must be noted here, that the SCCS decided to define 'serious risk' as the level of NDELA that is equivalent to a cancer risk of 1:10-5. Whether this is an appropriate cut-off level is a risk management decision.
In addition, it needs to be noted that RAPEX relates to safety of products. In the SCCS calculation, aggregate exposure (NDELA exposure from more sources such as food and other cosmetic products) is not taken into account.

For more information: Based on default daily cosmetics use levels, retention factors etc., SCCS calculated the levels in NDELA in cosmetic products at which the SED equalled this BMDL10/10000 (SCCS 2012). Janssen et al. (2004) made additional calculations for incidental exposure: this means extrapolating the lifetime VSD to a preselected short-term period and calculating the SED at which this shortterm VSD is reached (this leads to considerably higher 'serious risk' levels of NDELA).

3. DEHP in toys

Introduction
Bis(2-ethylhexyl)phthalate (DEHP) or other phthalates in toys are often notified within RAPEX notifications. One of the examples as described in Appendix 1 is depicted below (table 3)

Table 3. Example of DEHP notification

0629/12	DEHP	Doll (SP)	6.53% by weight	Prohibited in toys

As DEHP is classified as a group 2B carcinogen, this concentration exceeds the limit for DEHP of 0.1% (REACH Annex XVII).

Risk Assessment
* Exposure assessment
Oral exposure
To describe the oral exposure of a child mouthing a toy, the starting point is a child with a body weight of 8 kg (age: about 10 months), who mouths a toy 3 hours per day. Children of this age show the most frequent mouthing-behaviour and have a low body weight. The exposure due to mouthing by children of this age will be the highest, expressed in mg/ kg bw.

This particular scenario, proposed by the CSTEE (1998, 1998a), is frequently used in the EU, for example in the EU-RAR for DEHP (2008) and should be viewed as a worst-case default for mouthing by a young child.

Dermal contact

To describe dermal contact, the scenario is a child with a body weight of 15 kg (age: about 3 years), who has skin contact with the toy during 3 hours a day. It is assumed that the skin contact area with the toy is 100 cm^2. This scenario for dermal exposure is also used in the EU-RAR of DEHP (2008). We assume that, due to hand-to-mouth contact, 10 % of the total amount on the skin will be taken up orally, as described in Bremmer et al. (2006b).

Inhalation exposure

Because of the small size of the toys and the low vapour pressure of the three plasticizers, inhalation exposure due to individual toys is considered negligible compared to the oral and dermal exposures.

Non-toy sources of exposure

For all phthalates, there is some exposure resulting from indoor air and food. For DEHP, this can be assumed 22.4 and 19.4 µg/kg bw/day (internal) as concluded in the RAR on DEHP.

Calculation of the exposure

The exposure is calculated for a child (8 kg) who mouths a toy and for a child (15 kg) who has dermal contact with the toy.

In this RAPEX notification, only a percentage of DEHP is given. There is no correlation between the content and the migration rate. A migration rate of 50 µg/10 cm^2/hr (based on data reported in the EU-RAR) is chosen for the exposure calculation.

Exposure is calculated as the internal dose, taking into account dermal and oral absorption. For DEHP, also based on assumptions in the RAR, dermal penetration is set at 5%, oral absorption at 100% for children (and 70% for adults).

Exposure due to mouthing

A child of 8 kg mouths a surface of 10 cm2 of the toy during 3 hours per day.

External (and internal) oral exposure:

50 µg/10 cm^2 x hr: 50 x 3 [hr/day]/ 8 [kg bw] = 18.8 µg /kg bw /day

Exposure due to dermal contact

A child of 15 kg has dermal contact with a surface of 100 cm^2 of the toy during 3 hours a day. 5% of the total amount on the skin is taken in orally, due to hand to mouth contact.

Total amount on the skin

50 µg/hr x 10 $cm^{2:}$ 50 x 3 [hr/day] x 100/10 [cm^2/cm^2] / 15 [kg bw]= 100 µg/kg bw/day

Internal dermal exposure: 0.05 x 100 = 5 µg/kg bw/day

Internal oral exposure: 0.1 x 100 = 10 µg/kg bw/day

Total internal exposure after dermal contact: 15 µg/kg bw/day

Is there a 'serious risk'?

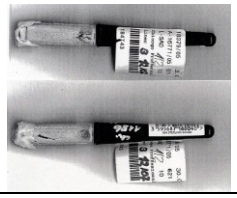
The DNEL (internal) as established in the REACH restriction dossier (2012) is 0.035 mg/kg bw/day for DEHP. Comparing the total internal exposure estimate of 0.019 mg/kg bw/day for mouthing and 0.015 µg/kg bw/day for dermal contact with the internal DNEL, a conclusion of no 'serious risk' can be drawn. Especially when taking into account that the exposure calculations are very

worst case because of the 3 hours mouthing and dermal contact time (see above) and only mouthing/playing this specific doll.
Also when the background of food and indoor air is included, still a conclusion of no concern can be drawn (for references see the advice on phthalates in scoubidou (RIVM, 2004) and the advice on phthalate replacers (RIVM, 2009)). However, based on the fact that these substances are prohibited in toys these products, it could be argued that they should be on the RAPEX list.

Appendix 3

Table 2: Details on products notified with NDELA

Year-week	No.Ref	Notifying country	Product	Danger	Measures adopted by notifying country	Products were found and measures were also taken in
2006-26	8 0391/06	The Netherlands	Cosmetic Eyeliner Rimmel Professional Liquid eyeliner. Type/ number of model: Sterling silver 004. Three different batches with batchcodes: 3126, 3224 and 4020. Country of origin: UK 	Chemical risk. Tested eyeliners contained Tested eyeliners contained N-nitrosodiethanolamine (NDELA) at levels of 142, 206 and 84 µg/kg respectively. According to the Cosmetics Regulation nitrosamines are permitted in cosmetic matrixes only as technically unavoidable residue at levels that do not pose a risk to health. The substance is placed on the list of banned substances (Annex I, rank number 410) on basis of its carcinogenic properties.	Voluntary withdrawal from the market by the distributor. Placing on the market prohibited by the authorities	
2006-5	8 0047/06	The Netherlands	Shampoo "Deba" Type/model: 1. Deba Green Apple 2 in 1 Green Tea Shampoo & Conditioner; 2. Deba Eggs 2 in1 D-Pantenol, sham-poo & Conditioner. Country of origin: Bulgaria. 	Chemical risk. Performed tests showed that the shampoos contained N-nitrosodiethanolamine (NDELA) at levels of 286 and 301 µg/kg. According to the Cosmetics Directive nitrosamines are permitted in cosmetic matrixes only as technically unavoidable residue at levels that do not pose a risk to health.	Voluntary withdrawal from distribution and placing on the market prohibited by the authorities.	
2006 - 3	1 0019/06	Germany	Volume mascara. Type/model: Lot 3074, article No 88350 Country of origin: Netherlands.	Chemical risk. Product contains high level (204 µg/kg) of N-Nitrosodiethanolamin (NDELA) above the maximum limit allowed by the Cosmetic Directive.	Voluntary withdrawal of the product from the market by distributor	

						
2006-1	13 0728/05	Germany	Eyeliner "Chicogo" Professional Liquid Sterling Silver Charge 1186 Country of origin: United Kingdom 	Chemical risk. Product contains high levels (1002 ppb) of contaminating carcinogenic nitrosamines (NDELA) above the 50 ppb maximum limit allowed by the Cosmetics Directive.	Withdrawn by the manufacturer.	
2005 - 48	1 0609/05	Germany	Extension mascara blue "IKOS" Customs (3304 20 00). batch No L01073 Country of origin: Italy. 	Chemical risk. Performed tests showed that extension mascara blue contained N-nitrosodiethanolamine (NDELA) at the levels of 142, 133 and 111 µg/kg (products are available on the market that contain no detectable levels of N-nitrosodiethanolamine (<10 µg/kg). According to the Cosmetics Regulation nitrosamines are permitted in cosmetic matrixes only as technically unavoidable residue at levels that do not pose a risk to health.	Voluntary withdrawal from distribution by the German importer.	
2005 - 2	7 0381/04	Germany	Shampoo "Zydot - Ultra Clean" (N° 701 on the packaging, N° 1299 on the product), with deep cleanser and cure product. Country of origin: Unknown. 	Chemical risk. Excessive content (489 ug/kg) of N-Nitrosodiethanolamine (NDELA) in the shampoo.	Voluntary recall and withdrawal from the market.	

Appendix 4

Discussion of 10^{-6} per lifetime

In a discussion in January 2010 within the Consumer Safety Network (CSN), a cut-off point for 'serious risk' of 10^{-6} per lifetime was selected as the most appropriate. Accordingly this cancer risk level was used for benzene as a genotoxic carcinogen. It should be noted that the cancer risk level of 10^{-6} per lifetime is often denoted as the virtually safe dose (VSD).

In its opinion SCCS (2012) addresses the question of the appropriate cut-off point for serious risk for genotoxic carcinogens. SSCS prefers the approach for genotoxic carcinogens as laid down by EFSA (2005). EFSA (2005) proposed a Margin Of Exposure (MOE) approach based on the $BMDL_{10}$, the lower benchmark dose for a 10% increase in tumour incidence. Choosing a MOE of 10000 in this context would represent a practical approach for distinguishing 'serious risk' from 'less serious risk', SCCS concludes. SCCS proposes a similar approach (the T_{25}-method) as an alternative to the EFSA approach. In terms of cancer risk these two approaches (BMDL-MOE and T_{25}) are identical.
See the SCCS opinion on NDELA in cosmetics (2012).

As to the use of an extra factor for protecting children SCCS (2012) recommends applying such a factor only in case exposure is exclusively during childhood years. For age groups 0-2 and 3 -16 factors of 10 and 3 respectively are recommended. For lifetime exposure using the extra factors for the childhood years would lead to minor differences in outcome only and therefore SCCS considers their application for lifetime exposure unnecessary.

The REACH guidance (2010; R8) offers two possibilities in deriving a Derived Minimal Exposure Level (DMEL) for non-threshold mutagens and carcinogens. Per definition, a dose without a theoretical cancer risk cannot be derived. Therefore the establishment of a reference risk level for the DMEL clearly is of societal concern and needs policy guidance. Although there is no EU legislation setting the 'tolerable' risk level for carcinogens in society, cancer risk levels have been set and used in different contexts (see APPENDIX R. 8-14 for various values previously applied within and outside the EU).

Two quantitative risk assessment formats can be followed to derive a DMEL for a non-threshold carcinogen: the 'Linearised' approach, essentially results in DMEL values representing exposure levels where the likelihood that effects (as asses by the lifetime cancer risk) are avoided is appropriately high and considered to be of very low concern. The other format, called 'Large Assessment Factor' approach (used by EFSA), is formally similar to the overall assessment factor approach applied for threshold effects in deriving DNELs, and results in DMEL values representing exposure levels where the likelihood that effects (cancer) are avoided is appropriately high and of low concern from a public health point of view.

National Institute for Public Health and the Environment
P.O. Box 1 | 3720 BA Bilthoven
www.rivm.com