Committee for Risk Assessment (RAC)
Committee for Socio-economic Analysis (SEAC)

Opinion

on an Annex XV dossier proposing restrictions

DIISOCYANATES

ECHA/RAC/RES-O-0000001412-86-174/F
ECHA/SEAC/[reference code to be added after the adoption of the SEAC opinion]

Adopted

5 December 2017

5 December 2017

ECHA/RAC/RES-O-0000001412-86-174/F

30 November 2017

ECHA/SEAC/[reference code to be added after the adoption of the SEAC opinion]

Opinion of the Committee for Risk Assessment

and

Opinion of the Committee for Socio-economic Analysis

on an Annex XV dossier proposing restrictions of the manufacture, placing on the market or use of a substance within the EU

Having regard to Regulation (EC) No 1907/2006 of the European Parliament and of the Council 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (the REACH Regulation), and in particular the definition of a restriction in Article 3(31) and Title VIII thereof, the Committee for Risk Assessment (RAC) has adopted an opinion in accordance with Article 70 of the REACH Regulation and the Committee for Socio-economic Analysis (SEAC) has adopted an opinion in accordance with Article 71 of the REACH Regulation on the proposal for restriction of

Chemical name(s):	**Diisocyanates**
EC No.:	**-**
CAS No.:	**-**

This document presents the opinion adopted by RAC and the Committee's justification for its opinion. The Background Document, as a supportive document to both RAC and SEAC opinions and their justification, gives the details of the Dossier Submitter's proposal, amended for further information obtained during the public consultation and other relevant information resulting from the opinion making process.

PROCESS FOR ADOPTION OF THE OPINIONS

Germany has submitted a proposal for a restriction together with the justification and background information documented in an Annex XV dossier. The Annex XV report conforming to the requirements of Annex XV of the REACH Regulation was made publicly available at http://echa.europa.eu/web/guest/restrictions-under-consideration on **22 March 2017**. Interested parties were invited to submit comments and contributions by **22 September 2017**.

ADOPTION OF THE OPINION

ADOPTION OF THE OPINION OF RAC:

Rapporteur, appointed by RAC: ***Veda Marija VARNAI***

Co-rapporteur, appointed by RAC: ***Sonja KAPELARI***

The opinion of RAC as to whether the suggested restrictions are appropriate in reducing the risk to human health and/or the environment was adopted in accordance with Article 70 of the REACH Regulation on **5 December 2017.**

The opinion takes into account the comments of interested parties provided in accordance with Article 69(6) of the REACH Regulation.

The opinion of RAC was adopted **by a simple majority** of all members having the right to vote. The minority position including its grounds is made available in a separate document which has been published at the same time as the opinion.

ADOPTION OF THE OPINION OF SEAC

Rapporteur, appointed by SEAC: ***Johanna KIISKI***

Co-rapporteur, appointed by SEAC: ***Karmen KRAJNC***

The draft opinion of SEAC

The draft opinion of SEAC on the proposed restriction and on its related socio-economic impact has been agreed in accordance with Article 71(1) of the REACH Regulation on **30 November 2017*.***

The draft opinion takes into account the comments from the interested parties provided in accordance with Article 69(6)(a) of the REACH Regulation.

The draft opinion takes into account the socio-economic analysis, or information which can contribute to one, received from the interested parties provided in accordance with Article 69(6)(b) of the REACH Regulation.

The draft opinion was published at http://echa.europa.eu/web/guest/restrictions-under-consideration on **20 December 2017.** Interested parties were invited to submit comments on the draft opinion by **20 February 2018.**

The opinion of SEAC

The opinion of SEAC on the proposed restriction and on its related socio-economic impact was adopted in accordance with Article 71(1) and (2) of the REACH Regulation on ***[date of adoption of the opinion]***. **[**The deadline for the opinion of SEAC was in accordance with Article 71(3) of the REACH Regulation extended by ***[number of days]*** by the ECHA decision ***[number and date]*****]**[1].

[The opinion takes into account the comments of interested parties provided in accordance with Article[s 69(6) and][5] 71(1) of the REACH Regulation.**] [**No comments were received from interested parties during the public consultation in accordance with Article[s 69(6) and][3] 71(1)**]**[6].

The opinion of SEAC was adopted ***by*** **[*consensus*.][*a simple majority*]** of all members having the right to vote. [The minority position[s], including their grounds, are made available in a separate document which has been published at the same time as the opinion**.]**[6].

[1] Delete the unnecessary part(s)

Contents

OPINION OF RAC AND SEAC

The restriction proposed by the Dossier Submitter is:

Substance Identity (or group identity)	Conditions of the restriction
Diisocyanates	1. Shall not be used as substances on their own, as a constituent in other substances or in mixtures for industrial and professional uses, unless: a) the cumulative concentration of diisocyanates in the substance or mixture is less than 0.1 % by weight, or b) the substance or mixture in the form in which it is supplied to the user, including the combination of such substance or mixture, its packaging and any application aid is placed on the market in accordance with paragraph 2b), or c) the employer or self-employed worker ensures that measures and trainings are taken prior to the use of the substances or mixtures in accordance with the provisions described in Appendix 13[2] (Trainings and Measures). Member States may implement or continue to apply own provisions for the use of these substances and mixtures as long as the minimum requirements of Appendix Trainings and Measures are met. The employer or self-employed worker shall document the compliance to the requirements of Appendix 13 (Trainings and Measures). Proof of successful completion of a training according to Appendix 13 (Trainings and Measures) shall be recognised in all other Member States.

[2] The texts of Appendix 12 (Exemptions) and Appendix 13 (Trainings and Measures) should become part of the final legal text. Elements to be included in the final text are available in Appendix 7 and Appendix 8 to this proposal. A short summary can be found in A.2.2. Additional background information can be found in Appendix 5 to the dossier.

	2. Shall not be placed on the market as substances on their own, as a constituent in other substances or in mixtures for industrial and professional uses, unless: a) the cumulative concentration of diisocyanates in the substance or mixture is less than 0.1 % by weight, or b) the substance or mixture in the form in which it is supplied to the user, including the combination of such substance or mixture, its packaging and any application aid is compliant with Appendix 12 (Exemptions), or c) the supplier ensures that the recipient of the substance or mixture is provided with information according to paragraph 3. 3. For the purpose of 2c) manufacturers and importers of diisocyanates on their own or as a constituent in other substances and importers of mixtures containing diisocyanates shall develop a set of teaching material in accordance with the provisions of Appendix 13 (Trainings and Measures) in an official language of the Member State where the substance or mixture is placed on the market before placing the substance or mixture on the market. They shall ensure that training courses based on the training material are available to the recipients of such substances or mixtures. They shall review and update the training material after a maximum of 8 years, or without delay if new information, which may affect the risk management measures, becomes available and inform the recipients accordingly. Natural or legal persons formulating mixtures containing diisocyanates within the EU shall provide necessary information for the development of the teaching

	material upon request of their substance suppliers. All downstream users may be consulted for the purpose of the development and update of the teaching material.

THE OPINION OF RAC

RAC has formulated its opinion on the proposed restriction based on an evaluation of information related to the identified risk and to the identified options to reduce the risk as documented in the Annex XV report and submitted by interested parties as well as other available information as recorded in the Background Document. RAC considers that the proposed restriction on ***diisocyanates*** is the most appropriate Union wide measure to address the identified risk in terms of the effectiveness, in reducing the risk, practicality and monitorability as demonstrated in the justification supporting this opinion, provided that the conditions are modified, as proposed by RAC.

The conditions of the restriction proposed by RAC are:

Substance Identity (or group identity) Diisocyanates of the chemical structure, O=C=N-R-N=C=O, where R is an aliphatic or aromatic hydrocarbon unit of unspecified length	RAC suggests that the conditions of the restriction should be rewritten to include the training requirements and the relevant measures in the Annex XVII entry in such a way that those affected by the restriction can clearly understand their duties. The text should also re-define the exemptions from specific products (as discussed in the justification). See Annex for example conditions agreed by RAC and SEAC to show how they could be set out. The Commission will draft the final conditions and this is for their consideration.

THE OPINION OF SEAC

See the opinion of SEAC.

JUSTIFICATION FOR THE OPINION OF RAC AND SEAC

IDENTIFIED HAZARD, EXPOSURE/EMISSIONS AND RISK

Justification for the opinion of RAC

Description of and justification for targeting of the information on hazard(s) and exposure/emissions) (scope)

Summary of proposal:

The main goal of this restriction proposal is to prevent new cases of respiratory sensitisation from exposure to diisocyanates among all workers and professionals who may be exposed to diisocyanates in the workplace. The approximate number of new cases of isocyanate-related[3] occupational disease, primarily asthma, is estimated at several thousand each year in the European Union (EU).

The diisocyanates considered in the scope of this restriction proposal (see table 1, section B.1.1 of the Background Document) are generally classified as Resp. Sens. 1 and as Skin Sens. 1 according to CLP. The majority of them have an EU-wide harmonised classification. The three substances methylenediphenyl diisocyanate (MDI), toluene diisocyanate (TDI), and hexamethylene diisocyanate (HDI) together account for more than 95% of the total isocyanate market volume in the EU and thus exposure to these three substances may be the cause of most of the diisocyanate-related asthma cases.

It is acknowledged that the presence of the (double) isocyanate group is responsible for binding to proteins, which is known as the "molecular initiating event" of sensitisation induced by low molecular weight chemicals. Therefore, the Dossier Submitter considered it was justified to address all diisocyanates under the same restriction proposal. Another reason for the group approach is that for most of the cases of respiratory sensitisation (occupational asthma) the specific (di)isocyanate is not documented.

Diisocyanates are used in a wide range of sectors and applications (e.g. foams, sealants, coatings) throughout the EU, with a **total tonnage of about 2.5 million tonnes per year**. At the same time, air monitoring data (supported by biomonitoring data) for the most relevant diisocyanates and the most relevant uses indicate levels of exposure considered to pose a risk for sensitisation. The main exposure routes are via inhalation and the skin.

Since no suitable alternatives for the majority of uses are expected to be available in the near future, the Dossier Submitter proposes measures to reduce workers' exposure to diisocyanates. This will be achieved by limiting the use of diisocyanates in industrial and professional applications to those cases where effective risk management measures and a minimum standardised training package have been implemented (according to Appendix 7 and Appendix 8 of the proposal). Exemptions are defined for cases where either the content of diisocyanates in the substance or mixture placed on the market or used is less than 0.1% w/w or where it is shown that the potential for exposure via the inhalation as well as the

[3] In the restriction proposal the Dossier Submitter uses the term "isocyanate asthma". They point out that in many publications reporting diisocyanate-related hazards the terms "diisocyanates" and "isocyanates" are used rather loosely (the term "isocyanates" usually referring to formulations, i.e. mixtures, containing diisocyanates), and that occupational asthma related to diisocyanate exposure is often referred to as "isocyanate asthma" in the literature. However, both terms refer to occupational disease caused by diisocyanate(s).

dermal route is "very low" (although the content of diisocyanates in the mixture is equal or higher than 0.1% w/w). The Dossier Submitter stresses that the proposed restriction would be applied without prejudice to existing occupational safety and health regulations, i.e. obligations under existing regulations would still apply.

The limit value of 0.1% w/w was chosen by the Dossier Submitter as it represents the lowest Specific Concentration Limit (SCL) stated for diisocyanates (as shown in the Background Document (Table 7, Annex B)). For some diisocyanates SCL of 0.1% or 0.5% has been derived, while for others there is yet no harmonised classification available.

The Dossier Submitter points out that the scope of this restriction does not include products that are marketed exclusively to consumers or used exclusively by consumers, since data on exposure and risks from diisocyanates in such products is very limited and there is no established monitoring system in the consumer sector that could distinguish between diisocyanates-related asthma cases and asthma cases related to other causative agents. In addition, trainings for consumers would be difficult to perform.

RAC conclusion(s):

RAC considers the proposed targeting (scope) justified.

RAC agrees that the focus of the proposal is correctly directed towards diisocyanate-related respiratory hypersensitivity, primarily asthma (as the most prevalent occupational disease related to diisocyanates exposure).

RAC considers that the restriction proposal might also have a preventive effect on irritant-induced asthma and allergic and irritant contact dermatitis due to exposure to diisocyanates. This is because most of the diisocyanates are also skin sensitisers and irritants.

RAC also agrees with the Dossier Submitter that the restriction proposal should address diisocyanates as a group, due to the common mechanism of inducing hypersensitivity reactions.

Key elements underpinning the RAC conclusion:

RAC considers that the Dossier Submitter satisfactorily demonstrates that occupational exposure to diisocyanates is not adequately controlled.

RAC agrees with the Dossier Submitter that diisocyanate-related respiratory diseases are markedly more prevalent than diisocyanate-related skin diseases. However, RAC notes that the measures proposed are targeted not only at preventing respiratory sensitisation but also skin sensitisation and potentially all of the other symptoms related to sensitisation to diisocyanates (e.g. allergic rhinitis, airway hyper-responsiveness).

Regarding the appropriateness of a chemical group approach, RAC agrees with the Dossier Submitter that in addition to the fact that diisocyanates share a common mechanism of inducing hypersensitivity reactions, workers may be exposed to more than one diisocyanate in their workplace and cross-reactivity between different diisocyanates has been demonstrated.

There are indications that sensitisation in humans could also be induced by diisocyanate-free polyisocyanates, which are not covered by the Dossier Submitter´s proposal (Vandenplas et al., 1992a; Aalto-Korte K et al., (2010)). Scientific data on this issue are still very limited.

Another group of isocyanates that are not covered by this restriction proposal, but for which there is a concern that they could induce hypersensitivity in humans, are monoisocyanates,

such as methyl isocyanate, isocyanic acid, tolyl isocyanate, ethyl isocyanate or phenyl isocyanate. According to the information provided by the Dossier Submitter and from the UK HSE report WATCH/2008/4 the primary use of methyl isocyanate is as a chemical intermediate in the production of carbamate pesticides. It is a potent respiratory irritant but although it is shown that it can induce immunological response in humans (IgE, IgG and IgM class, measured in subjects exposed to the industrial gas leak in Bhopal accident (Karol MH et al., (1987)), the primary concern for human health is its high acute toxicity if inhaled. Isocyanic acid is highly unstable and it does not have commercial uses, but occupational exposure may occur when it is generated as a thermal degradation product of other industrial processes. Ethyl isocyanate is used in production of pharmaceuticals and pesticides. Phenyl isocyanate is a trace constituent in commercial diphenyl methane diisocyanate products and is also an intermediate chemical. Animal experiments showed that it can induce contact sensitisation and humoral immune response (Karol and Kramarik, 1996). Tolyl isocyanate is an intermediate chemical in pharmaceutical industry. For this substance it was also shown that it can induce immunologic response (IgE class) in humans (Baur X et al.). According to UK HSE report WATCH/2008/4 and more recent literature data, there is no direct evidence that any of the monoisocyanates can cause respiratory sensitisation in humans.

In Annex A of the Background Document, the Dossier Submitter points out that the use of monoisocyanates is not in the scope of the restriction, since they mainly have entirely different uses (e.g. as intermediates in the production of pharmaceuticals and biocides), and not in polyurethane (PU) chemistry. Data on specific risks of the uses of monoisocyanates were therefore not included in the Background Document. RAC also points out that workplace exposure to chemicals that are released due to thermal degradation (e.g. isocyanic acid) is not in the scope of this restriction.

To summarise, regarding other types of isocyanates, namely polyisocyanates (diisocyanate-free) and monoisocyanates, which are not in the scope of this restriction proposal, RAC considers that although there is no direct evidence for respiratory sensitisation in human population, indirect evidence from humans and animals stated above indicates that the risk of respiratory sensitisation in humans cannot be excluded. Nevertheless, RAC accepts that the scientific data on human health hazards and risks posed by these substances is rather limited, and why the Dossier Submitter decided not to include them in the scope of the restriction.

Consumer use of diisocyanates-containing products is not covered by this restriction proposal either. There is an existing European wide regulation for MDI (entry #56 to Annex XVII to Regulation (EC) No. 1907/2006 (REACH) which focuses on the risk of skin sensitisation to address the recognised risk. Spray applications are advised against for these substances. For the other two diisocyanates used at high tonnages in the European market (which together account for more than 95% of the market volume of diisocyanates), all consumer uses are either strongly advised against (HDI) or consumer uses are not relevant (TDI), according to the Chemical Safety Reports. There is no available information on health risk of application of diisocyanates-containing products by consumers (Lockey et al. 2015; Verschoor and Verschoor 2014; and Web of Science-all databases (literature search performed by the rapporteurs)), and no new information on exposure and health risks related to consumer use of diisocyanates was provided during the Public Consultation. RAC, therefore, agrees with the Dossier Submitter's justification for omitting the diisocyanate-containing consumers' product from the scope of this restriction proposal, but stresses that this issue should be reconsidered when more information on exposure and health risk in consumers becomes available.

Description of the risk(s) addressed by the proposed restriction

Information on hazard(s)

Summary of proposal:

The main hazard triggering this restriction proposal is respiratory sensitisation to diisocyanates which may lead to allergic respiratory symptoms (e.g. diisocyanate-related occupational asthma) in workers already sensitised. If sensitisation is prevented, elicitation of hypersensitivity reactions upon re-exposure will also be prevented thus avoiding new cases of allergic respiratory diseases related to diisocyanate exposure.

In the hazard assessment the Dossier Submitter analysed a large body of both human and animal data. Although both types of studies clearly show the sensitising potential of diisocyanates, the uncertainties and limitations of the studies prevented derivation of a meaningful and reliable DNEL, which could be used for quantitative risk assessment.

RAC conclusion(s):

RAC considers that the description of the identified hazard is adequate and supported by relevant data. RAC agrees with the qualitative assessment of the identified hazard (respiratory sensitisation) and considers it well justified.

Key elements underpinning the RAC conclusion(s):

Although in theory respiratory sensitisation can be regarded as a threshold effect, the available human and animal data at present do not allow determination of such a threshold or accurate DNEL derivation in line with REACH[4]: "*…currently there are no available methods to determine thresholds and DNELs for respiratory sensitisers… Therefore, substances classified as a respiratory sensitiser (Category 1/1A/1B/1C) in CLP should normally result in a qualitative assessment for the hazard level of concern*".

Added to this, there is currently no formally recognised and validated animal test for assessing respiratory sensitisation.

Therefore, RAC confirms that although a large body of non-human experimental data on diisocyanates was evaluated in the proposal, a Point of Departure for risk characterisation could not be derived due to the following reasons: most of the available studies only covered a limited range of effects; the most relevant species to be used is unclear; agreement on critical effect levels is lacking; and there is great uncertainty regarding the extrapolation (especially quantitative) of results from animal studies to the human population. In addition, many studies also showed other deficiencies.

Regarding human data, there are a large number of studies available. However, none of them is considered adequate for deriving a reliable exposure-response relationship curve due to a number of limitations in those studies. The limitations include lack of reliable information on exposure (including difficulties in assessing dermal exposure and peak inhalatory exposures), lack of sensitive predictive markers for diisocyanate sensitisation, low statistical power (e.g. due to small sample size or low disease incidence), inadequate correction for the presence of confounding factors (e.g. for concomitant exposure to other respiratory sensitisers and irritants or for previous exposure to sensitising agents), lack of an unexposed control group or the "healthy worker effect".

[4] ECHA Guidance on Information Requirements and Chemical Safety Assessment (Part E: Risk Characterisation, Version 3.0, May 2016; Annex I, paragraphs 1.1.2 and 6.5)

In addition, respiratory sensitisation to diisocyanates can be induced both via the dermal and the inhalation route, and thus both exposure routes have to be considered. An important role of dermal route in respiratory sensitisation to diisocyanates has been shown in animal studies (e.g. Pauluhn, 2013; North et al. 2016), and is considered to be relevant for humans as well (Bello et al., 2007). However, as for either route a threshold is unknown, and neither the quantitative nor mechanistic interaction between the inhalation and dermal route is sufficiently understood, it is not possible for RAC to set any DNEL that will be meaningful for the risk characterisation.

The mechanism responsible for respiratory sensitisation as well as skin sensitisation to diisocyanates is the one proposed for other low-molecular weight chemicals: the chemical (hapten) binds to a protein and alters the three-dimensional shape of this protein, which triggers the immune system to recognise the protein-hapten complex as foreign to the body. The resulting hypersensitivity reaction in humans can be of immediate (seconds to minutes) or delayed onset (up to several hours).

Diseases mediated through this mechanism are of a broad range (including allergic asthma allergic rhinitis, allergic conjunctivitis, allergic (extrinsic) alveolitis, and allergic contact dermatitis). RAC points out in this context that potential **cross-reactivity** with other structurally related sensitisers and increased sensitivity to non-specific stimuli as a consequence of sensitisation often further negatively impact on the quality of life of sensitised individuals.

Some diisocyanates (e.g. MDI, TDI) have a harmonised classification as Carc. Cat. 2 but the carcinogenic endpoint was not further considered by the Dossier Submitter. However, the restriction proposal aims at preventing exposure and therefore the risk for workers with regards to all hazard classes would be reduced. RAC agrees with this approach.

In the restriction proposal, the Dossier Submitter considers diisocyanate-related occupational asthma as an irreversible disease, which can result in permanent remodelling of the airways due to chronic airway inflammation. The changes of the airways are not only irreversible, they also lead to a poor clinical outcome, including decreased responsiveness to asthma therapy, severe dyspnoea and lung function decline. Early avoidance of further exposure should be a prerequisite for diisocyanate-related occupational asthma management, since deaths have been reported even for workers on asthma medication and using respiratory protection (Jolly et al. 2015). Nevertheless, even in the case of exposure avoidance, respiratory sensitisation to diisocyanates "has to be considered an irreversible condition in many, if not most of the cases", with life-long negative consequences according to the restriction proposal.

However, fading of symptoms is also possible. RAC agrees with the Dossier Submitter that if a diseased worker is removed from the exposure early after onset of diisocyanate-related occupational asthma, respiratory symptoms may in time subside. For example, literature data indicate that four years after removal of workers from exposure to the offending low-molecular weight agent, more than 50% of the patients were no longer under treatment for asthma (Beach et al. 2005). Cessation of asthma symptoms was observed in approximately 1/3 of patients with isocyanates occupational asthma, either after approximately 4.5 years (Pisati et al. 1993) or after more than 10 years of isocyanates avoidance (Padoan et al. 2003, Rüegger et al. 2012). Nevertheless, RAC considers that the available data are too limited to allow a reliable quantitative assessment of average recovery period and proportion of recovered patients, either regarding symptoms, anti-asthmatic drugs' use, or non-specific or specific bronchial hyper-responsiveness. In addition, it seems that occupational asthma

severity differs depending on the causative diisocyanate (TDI > MDI > HDI) (Piirilä et al. 2000). Nevertheless, even in the case the symptoms may disappear, the sensitisation remains, and renewed exposure to the same or another diisocyanate may again trigger the condition.

Therefore, taking into account the above discussion, RAC agrees with the Dossier Submitter´s proposal to consider diisocyanate-related occupational asthma as an irreversible condition for the purpose of SEA.

Information on emissions and exposures

Summary of proposal:

Worker exposure to diisocyanates mainly occurs via the inhalation and dermal routes. Non-occupational exposure can arise if a person enters the working area and/or has dermal contact to uncured materials that still contain free diisocyanates. The potential for inhalation exposure is determined by the intrinsic substance properties (e.g. volatility, which is related to molecular size; volatility is, for example, significantly lower for MDI with molecular weight of 250.20, compared to TDI and HDI with molecular mass of 174.16 and 168.20, respectively; Table 1) and by how the substances are used and handled (e.g. increased risk of exposure during hot processes or in spray applications). Volatility, which is directly related to substance's vapour pressure, is inversely correlated with molecular weight. Therefore, diisocyanates with a low molecular weight (TDI and HDI, for example) easily vaporise already at room temperature. In contrast, MDI, with approximately 1.5 times higher molecular weight compared to TDI and HDI, has negligible volatility at 20 °C (Table 1).

The potential for dermal exposure may also depend on the factors stated above, but it is indicated that this route of exposure is nearly always possible when diisocyanates are handled.

Table 1. Comparison of selected physicochemical properties of MDI, TDI and HDI (data extracted from Tables 1 and 2 in the Background Document and from registration dossiers available at ECHA website)

Abbreviated name (EC name)	**Molecular formula**	**Molecular weight (g/mol)**	**Physical state**	**Vapour pressure** (Pa) (at 20 °C)
4,4'-MDI (4,4'-methylenediphenyl diisocyanate)	$C_{15}H_{10}N_2O_2$	250.20	crystalline solid	0.00049
TDI (4-methyl-m-phenylene diisocyanate; 2-methyl-m-phenylene diisocyanate)	$C_9H_6N_2O_2$	174.16	solid	1.5*
HDI (hexamethylene diisocyanate)	$C_8H_{12}N_2O_2$	168.20	liquid	0.7

* For mixture of 80% 2,4-toluene diisocyanate and 20% 2,6-toluene diisocyanate.

The Dossier Submitter did not provide an exhaustive description of all uses for all types of diisocyanates, due to the wide spread use of diisocyanates across the EU (with a total tonnage of about 2.5 million tonnes per year). Instead they focused on **the most relevant substances** (i.e. MDI, TDI and HDI) and/or **the most relevant uses** with respect to the amount and/or volume of diisocyanates in use and the level of workplace exposure. These uses are in the manufacturing of:

- diisocyanate compounds themselves;
- PU and PU composite materials;
- foam, in spray foam applications;
- coatings, and
- adhesives.

More than 90% of diisocyanates are used in the direct manufacture of PU plastic materials. In the other uses diisocyanates are utilised in preparations where the final reaction is intended to take place later.

RAC notes that the exposure assessment was performed by the Dossier Submitter for the most relevant diisocyanates and uses. The restriction proposal, however, should apply for all workers occupationally exposed to diisocyanates, and for all diisocyanates (i.e. including the uses and diisocyanates for which exposure was not assessed in the Background Document).

The information on occupational exposure levels to diisocyanates presented in the dossier is based on:

- The Chemical Safety Reports (CSRs) of the Registration Dossiers, where the exposure estimates are based on measurement data published by ISOPA[5] (where data were insufficient for a contributing scenario, a worst case approach was applied and the value of another, similar but more conservative PROC, was taken instead), and on modelled data (Advanced REACH Tool (ART) v 1.0) for HDI use in coatings;
- Measured workplace exposure data (gathered from 2000 to 2011) from Germany (MEGA database) evaluated in a study by the Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA 2010, 2012, 2013);
- Air monitoring data from the UK Health and Safety Executive (HSE) (most collected between 1986 and 1993); and
- Selected literature data (mainly selected since 2000 and relevant for the EU; this includes data presented for factories in Finland, Sweden, the UK, Poland, the Netherlands, Belgium, Romania, Spain and the USA).

The Dossier Submitter points out that although for most of the uses the majority of the measured **air concentrations** are quite low (near or below the limit of quantification (LoQ)), relatively high exposure levels can occur in an unpredictable manner in all sectors and uses (peak exposures), including those that appear to be well controlled. Furthermore, it is emphasised that measurement of airborne diisocyanates is technically challenging (e.g. some of the measurement methods might be less sensitive to highly reactive diisocyanate species; challenging sampling of spray foam aerosols which contain fast curing droplets of highly reactive mixtures), and may underestimate the actual exposure levels. In addition, peak

[5] The European Diisocyanate and Polyol Producers Association

exposures to diisocyanates might be not detected by some of the standard measurement methods. Therefore, even if air monitoring data are generally found below the limit of detection (LoD) or below the LoQ, such findings do not necessarily support the assumption that the actual exposure is adequately controlled for all such cases.

According to information presented in the restriction proposal, **dermal exposure** is nearly always possible when diisocyanates are handled, even if airborne concentrations are minimal. However, quantification of dermal exposure to diisocyanates is difficult (e.g. irregular and random occurrence of skin exposure; sampling is challenging due to highly reactive NCO groups that reacts with skin proteins; there is no established standard for measuring skin exposure) and data on dermal exposure to (di)isocyanates are scarce. Therefore, even though some measurement data are available, dermal exposure to diisocyanates is mostly assessed indirectly, by comparison of personal air samples with corresponding biomonitoring data. The Dossier Submitter presents qualitative (the likelihood and frequency of dermal exposure, taking into account the use of personal protective equipment) and quantitative (EASE model) dermal exposure assessment from the CSRs, as well as literature data, where available.

Biological monitoring of diisocyanates is based on the analysis of diisocyanate-adducts with haemoglobin or albumin in the blood or the determination of corresponding diamines in plasma or in urine[6]. The amines are not specific markers for diisocyanates and exposure to the corresponding diamines has to be ruled out since, otherwise, the results can be biased. Since biological monitoring allows the assessment of the total body burden of workers irrespectively of the exposure pathway and exposure source, it is increasingly used for assessment of exposure to diisocyanates.

RAC conclusion(s):

RAC acknowledges that diisocyanates with a low molecular weight (e.g. TDI and HDI) can lead to significant concentrations in the workplace air as they have high vapour pressures and evaporate at room temperature. In addition, RAC confirms that inhalation exposure to diisocyanates is also very likely in processes where fumes and vapours occur (e.g. hot melt adhesives and sealants) or aerosols (e.g. spray painting, blow foaming) are applied. Diisocyanates can also be released by thermal degradation of PU.

In addition, RAC considers that at workplaces using diisocyanates, there is nearly always potential for skin contact (e.g. uncured PU foams, paint or glue splashes), particularly if good industrial hygiene practices and/or the proper use of adequate PPE is lacking. Thus, RAC acknowledges that sensitisation may occur in any sector or use.

Since diisocyanates are so widely used across the EU, with a high number of different exposure scenarios, RAC agrees with the Dossier Submitter's approach to assess exposure only for the most relevant types of diisocyanates and their most prevalent uses (with respect to amount and/or volume and level of workplace exposure).

Taking into account the limitations in the assessment, stated in the Background Document RAC considers that, despite these uncertainties, exposure assessment based on air monitoring data from three databases [ISOPA, MEGA (IFA), HSE] and from relevant literature, together with biomonitoring data, provides reasonable estimates of the overall exposure of workers to diisocyanates in the EU.

[6] In the body, diisocyanate reacts with proteins and other organic molecules before it is excreted. Diisocyanate adducts in urine or plasma are converted in the laboratory (by hydrolysis) to a corresponding diamine derivative (Diisocyanates Panel 2000; Sabbioni and Turesky 2017).

Key elements underpinning the RAC conclusion(s):

Inhalation exposure

As pointed out in the Summary above, the measurement of airborne diisocyanates is technically challenging and is considered to underestimate actual exposure levels. In addition, peak exposures to diisocyanates, both incidental (e.g. spills) or occurring on a more regular and foreseeable basis, are difficult to detect. Incidental peak exposures are unpredictable, whereas more regular peak exposures, such as those occurring during hot processes, are technically challenging to detect (e.g. due to variability in generated heat, when isocyanates release occurs as short peak exposures).

Moreover, several uncertainties regarding data sources for inhalation exposure assessment are pointed out by the Dossier Submitter (see "Uncertainties" in the risk characterisation section). Nevertheless, RAC considers that uncertainties related to databases are alleviated by the use of different types of sources from different countries.

Table 2 and Figure 1 show that **average values** (arithmetic mean, geometric mean or median) of exposure levels of MDI, TDI and HDI indicate relatively low exposure in general (taking into account all data sources presented in the Background Document). For all uses studied, average values (where available) range from 0.7-3.7 µg/m³ for MDI (except for median value of 54.8 µg/m³ in spray foam applications, Roberge et al., 2009), 1.3-31.4 µg/m³ for TDI, and 0.08-7.4 µg/m³ for HDI (except for median value of 716 µg/m³ in use in coatings, Sparer et al., 2004). These ranges apply both to long-term exposure (e.g. 8-hour time-weighted average) and exposure of shorter duration, since literature data in majority of cases do not report long-term exposure values but exposure levels obtained during sampling time of several minutes up to 4 hours (according to task duration).

However, in many cases **upper limits of the ranges** of measured air concentrations (maximal measured values, 90th percentiles), were markedly higher (up to 50 times) than respective average value, both for long-term exposure and exposures of shorter duration. Values for long-term exposure reached 200 µg MDI/m³ in spray foam applications, 142 µg TDI/m³ in foam manufacture, and 208 µg HDI/m³ in use in coatings. Upper range values for exposures of shorter duration reached 2050 µg MDI/m³ in spray foam applications (sampling time 15-20 minutes), 230 µg TDI/m³ in foam manufacture (sampling time 5 to 250 minutes), and 245 000 µg HDI/m³ in use in coatings (short-term value, UK HSE data source).

Both average values and upper range values (both for long-term exposure and exposures of shorter duration) indicate **differences between uses**. Exposure levels were higher in foam manufacture, spray foam applications and for the use in coatings, compared to manufacture of diisocyanates, manufacture of PU and PU composite materials, and for the use in adhesives. It should be noted that for manufacture of diisocyanates only data from CSRs are reported. However, for this use occupational exposure to diisocyanates is expected to be low (as long as the manufacturing processes run under normal operating conditions) since the production processes are carried out in high integrity closed systems due to the dangerous properties of isocyanates themselves and the conversion of diamines with highly toxic phosgene.

To summarise, RAC agrees with the Dossier Submitter's conclusion that although the majority of the measured air concentrations is quite low, a degree of underestimation of actual exposure is expected and relatively high exposure levels can occur in an unpredictable manner in all sectors and uses.

Table 2. Occupational inhalation exposure levels (in µg/m³) for selected uses

	CSRs (90th perc. range)		**IFA** [mean (90th perc range)][§]	**HSE*** (range)	**Literature data*** [range (mean/median)]	**Expected exposure level†**
	Long term	Short term	Long term	Long term		
Manufacture of diisocyanates						**low** (under normal operating conditions)
MDI	5.6–29	-	-	-	-	
TDI	5–32	-	-	-	-	
HDI	3–23.5	-	-	-	-	
Manufacture of PU and PU composite materials						**moderate** (vapour pressure may rise significantly but RMMs are usually applied)
MDI	2–38	3–76	<LoQ‡-18 (mean **2.3**) (N=559)	0.09-32.8 (N=13)	• <0.03-3.3 (mean **0.7**) (N=131) [1] • 0.042-7.8 (med **3.7**) (N=10)¶ [2] • <1-7.2 (N=70) [3] • <0.6-3.3 (N=46)¶ [4]	
TDI	1-32	1-64	4-67.3 (mean **1.3**) (N=293)	-	• 0.08-14.6 (med **1.2-3.9**) (N=14)¶ [2]	
Foam manufacture						often **high**
MDI	6-29	12-58	<LoQ‡-4.2 (mean **1.7**) (N=1013)	0.03-0.17 (N=3)	• **<0.6** (N=26)¶ [4] • **<0.6** (N=20)¶ [5]	
TDI	1-32	1-64	<1.3-72.8 (mean **4.7**) (N=110)	0.06-9.0 (N=14) [Short term: 1.37-45.0 (N=13)]	• <0.2-230 (N=96) [1b] • 0.08-39.9 (med **1.2-31.4**) (N=140)¶ [2] • 0.2-58.8 (med **4.0-9.8**) (N=26)¶ [4] • 0.2 to 58.9 (mean **3.6-26.3**) (N=20)¶ [5] • 5.0-86.5 (med **12.5**) [6]	

				• <7.2-17.4 (N=26)¶ [7] • 4.2-142 (mean **31.1**) (N=21)¶ [8] • <0.71 (49 workers) [9]	
Spray foam applications					
MDI	6-29	11-58	<LoQ‡ (mean **1.9**) (N=33)	0.03-200 (N=8)	• 10-570 (N=61) [10] • 70-2050 (N=13) [11] • 11-591 (med **54.8**) (N=94) [12] • <LoQ-770 [13] • <4.6-410 [14] • 30-90 (experiment) [15]	potentially **high**
Use in coatings					
MDI	6-29	11-58	<LoQ‡-18.8 (mean **2.4**) (N=685)	-	-	potentially **high**
TDI	1-35	1-70	<1.3-6 (mean **1.3**) (N=809)	-	-	
HDI	-	-	<2.3-12 (mean **2.3**) (N=1221)	0.35-208 (N=15) [Short term: 0.82-245000 (N=47)]	• med **133-716** (N=153) [16] • 0.02-57.6 ‖ (med **0.08-7.4**) (N=95) [17] • 0.003-179 (GM **3.2**) (N=88) [18a]	
Use in adhesives					
MDI	5-43	9-87	<LoQ‡-6.5 (mean **2.8**) (N=533)	-	• <0.6-5.2 (N=20)¶ [4]	potentially **high**
TDI	1-35	1-70	<1.3-48.2 (mean **1.9**) (308)	-	-	
HDI	-	-	**<2.3** (N=294)	-	• 0.8-1 (N=20)¶ [4]	

Data from CSRs and IFA reports are presented as the range of 90th percentiles observed for respective dataset (i.e. minimal to maximal 90th percentile found), obtained by personal and static sampling. For IFA reports, data are also presented as average of arithmetic mean/median values provided in the reports. Where available, data from more recent IFA reports (IFA 2012, 2013) are presented in the table since, contrary to IFA 2010, they quantitatively report

LoQ values. In case of MDI use in spray foam applications, average of 95th instead of 90th percentiles is used since all 90th percentiles were below LoQ for which no numerical value was provided in the report.

The use of HDI in the manufacture of PU and PU materials is mostly limited to speciality applications with very limited exposure data available, and was not considered relevant for foam manufacture. TDI and HDI were not relevant for spray foam applications. HDI monomer was not covered in CSRs in use in coatings and adhesives.

PU – polyurethanes; N - number of samples (stated where reported); mean – arithmetic mean; med – median; GM – gemoetric mean;

*Data obtained by personal sampling except in [12], [13] and [15]; †The Dossier Submitter's assessment; ‡LoQ (limit of quantification) was not further specified in IFA 2010 report; §The data are representative for more than six hours exposure time; ǁData are presented for monomeric HDI; ¶Results are expressed for full shift or as 8-hour time-weighted average (TWA).

[1] Kääriä et al., 2001; [1b] Kääriä et al., 2001b (Exposure to 2,4- and 2,6-toluene diisocyanate (TDI) during production of flexible foam: determination of airborne TDI and urinary 2,4- and 2,6-toluenediamine (TDA). Analyst 2001;126:1025-31); [2] Sennbro et al., 2004; [3] Creely et al., 2006; [4] Brezeźnicki and Bonczarowska, 2015; [5] Swierczynska-Machura et al., 2015; [6] Tinnerberg and Mattsson, 2008 (measurements after technical improvements); [7] Austin, 2007; [8] Geens et al., 2012; [9] Gui et al., 2014; [10] Crespo and Galan, 1999; [11] Lesage et al., 2007; [12] Roberge et al., 2009; [13] RPS, 2014; [14] Wood 2013, 2014; [15] Puscasu et al., 2015; [16] Sparer et al., 2004; [17] Pronk et al., 2006; [18a] Fent et al., 2009a

Regarding deficiencies in reporting contextual information related to air monitoring data (especially for data from big databases such as ISOPA, MEGA and HSE database), RAC considers that this uncertainty is alleviated by including wide range of air measurements originating from different information sources and different EU countries covering a range of operational conditions (OCs) and risk management measures (RMMs) applied.

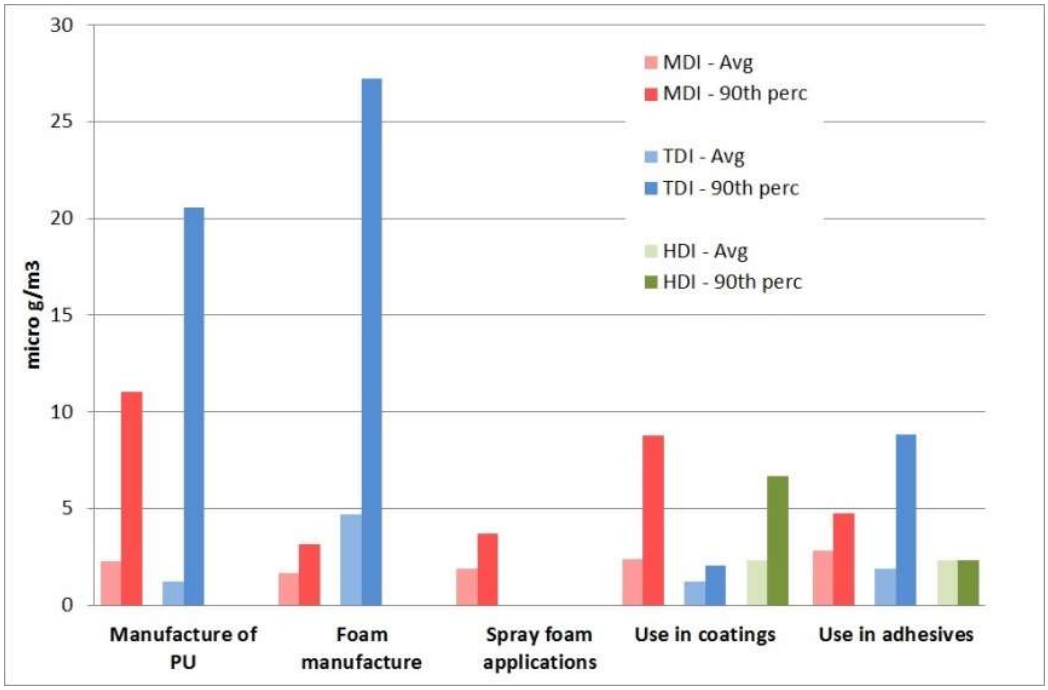

Figure 1. Overall average/median and 90th percentile values of air concentrations of MDI, TDI and HDI for work area groups for selected uses from IFA reports (MEGA database; IFA 2010, 2012, 2013) (calculated by the Rapporteurs)

Dermal exposure

Due to methodological limitations stated in the Summary, measured data on dermal exposure are very scarce and mostly qualitative (e.g. detected diisocyanate on skin; Table 3). Therefore, exposure was estimated by modelling (EASE) and, for selected uses modelled values range between 0.17–0.73 mg/cm² for MDI and between 0.04-0.20 mg/cm² for TDI. RAC agrees with the Dossier Submitter that this assessment is linked to significant uncertainties and that a ranking of the described uses based on dermal exposure data is not practicably meaningful.

Table 3. Assessment of the dermal exposure in the CSRs for selected uses

	Assessment in the CSRs		Literature data†
	Qualitative*	Modelled data‡ (mg/cm²)	
Manufacture of PU			
MDI	medium to high†	0.17 - 0.73	skin staining found [19] 0.00001 - 0.0017 (mg/cm²) [20]
TDI	very low to low	0.04 - 0.20	-
Foam manufacture			
MDI	medium to high†	0.17 - 0.73	-
TDI	negligible; very low to low	0.10 – 0.20	detected on hands [21]
Spray foam applications			
MDI	high†	0.17 - 0.42	-
Use in coatings			
MDI	very low to low (with proper use of PPE)	0.17 - 0.73	-
TDI	negligible; very low to low (with proper use of PPE)	0.04 – 0.20	-
HDI	-	-	0.6 to 40.2 µg HDI (per two gloves) for monomeric HDI [17] whole-body 0.00003-121 ng/mm³ with PPE: GM 0.02 ng/mm³; no PPE: GM 0.21ng/mm³ [18b]
Use in adhesives			
MDI	medium to high†	0.17 - 0.73	-

TDI	negligible; very low to low (with proper use of PPE)	0.04 – 0.20	-

The use of HDI in the manufacture of PU and PU materials is mostly limited to speciality applications with very limited exposure data available, and was not considered relevant for foam manufacture. TDI and HDI were not relevant for spray foam applications. HDI monomer was not covered in CSRs in use in coatings and adhesives.

PU – polyurethanes; GM – geometric mean; *Likelihood and frequency of dermal exposure assessed in four categories: very low, low, medium and high [taking into account the use of personal protective equipment (PPE) like suitable chemical resistant gloves, eye protection and coveralls]; †Assessment in the CSRs corrected to more conservative by the Dossier Submitter, assuming a less than ideal work practice; ‡EASE and/or ECETOC TRA v2 model applied; [17] Pronk et al., 2006; [18b] Fent et al., 2009b; [19] Petsonk et al., 2000; [20] Henriks-Eckerman et al., 2015; [21] Gui et al., 2014

Oral exposure

Oral exposure in workers due to unintentional hand-to-mouth behaviour cannot be ruled out (especially with poor occupational hygiene practice), and very small amounts of inhaled diisocyanates are supposed to be able to reach gastrointestinal tract via lung mucocilliary clearance (ATSDR HDI 1998). However, this route of exposure was not assessed by the Dossier Submitter since inhalation and dermal routes are considered predominant for occupational exposure (ATSDR (2015); WHO CICAD 27 (2000)[7]. In addition, it is unclear whether oral route can pose a risk for respiratory sensitisation in humans. According to ATSDR documents (ATSDR (2015); ATSDR (1998)) and publicly available literature (Web of Science All databases), data are insufficient to assess potential for sensitisation reactions after oral exposure to TDI, MDI and HDI, either in humans or animals. Namely, there is no information available regarding health effects in humans following oral exposure to diisocyanates, and for animal experiments no indications for respiratory sensitisation and/or immunological changes were stated.

Biomonitoring

Table 4. Biomonitoring in exposed workers for selected uses (literature data)

	Urine metabolite (µmol/mol creatinine if not stated otherwise)	**Air concentration** (µg/m³)	**Reference**
Manufacture of PU			
MDI	median 0.04 - 0.12 range 0.015 - 1.38 Controls: 0.012 to 0.022	<0.03-3.3 (64% <0.03)	[1]
	All isocyanates: mean 0.29	<1-7.2 (71% <1)	[3]

[7] Nevertheless, the risk of oral exposure is recognised by the Dossier Submitter in Appendix 13, in training topics for employees in Measures Group 1 ("Participants are aware of exposure routes via inhalation, dermal, oral and the possibility of contamination because of deposition, including basics on industrial hygiene").

	range <LoD - 12.64		
	Working day: 0.1-0.20 Day off: <0.1	-	[20]
	Post shift samples: range <0.10 - 23.60 µg/L Controls: 0.08 µg/L	-	[22]
	<LoD – 14.1	-	[23]
	2 days after exposure median 0.7 µg/L range 0.5 - 8.4 µg/L	0.04 - 9.7	[24]
Foam manufacture			
	Exposed: <0.05 - 39 Controls 0.02 - 0.1	<0.2-230	[1b]
	Direct skin contact with uncured PU: mean post shift: 2.21 No direct contact: mean post shift: 0.11	<7.2 – 17.4 (no difference between groups)	[7]
TDI	Before technical improvements median 43.3 µg/L range 11.8 - 55.7 µg/L	median 62.9 range 46.5-75.4	[6]
	After technical improvements median: 3.0 µg/L range 0.9 - 22.4 µg/L	median 12.5 range 5.0-86.5	
	<LoD - 3.9 (<LoD to 8.85 µg/L)	mean 3.6 – 26.3 range 0.2 – 58.9	[5]
Use in coatings			
	median 19.5 range 1.9-146.2	median 0.08 – 7.4 range 0.02 – 57.6	[17]
HDI	mean 0.003 range <LoD-21.0	0.003 to 179	[25]
	Before SHAD* 90th perc. 1.34 After SHAD 90th perc. range 0.55-0.76	-	[26]

cr = creatinine; *SHAD = "Safety and Health Awareness Day"

There is no biomonitoring data for manufacture of diisocyanates, spray foam applications and use in adhesives.

[1] Kääriä et al., 2001; [1b] Kääriä et al., 2001b; [3] Creely et al., 2006; [5] Swierczynska-Machura et al., 2015;

[6] Tinnerberg and Mattsson, 2008; [17] Pronk et al., 2006; [20] Henriks-Eckerman et al., 2015; [22] Robert et al., 2007; [23] Gries and Leng, 2013; [24] Tinnerberg et al., 2014; [25] Gaines et al., 2010; [26] Jones et al., 2013

Since biomonitoring data show the combined exposure of the inhalation and the dermal routes, biomonitoring is regarded as a useful tool to assess workers' total exposure to diisocyanates. As a long-term parameter, diisocyanate-adducts with haemoglobin can be measured in blood, and respective diamines in urine or plasma, as a short term parameter (please see footnote no 7). For diamine measurement, workers should not be externally exposed to diamines (i.e. occupationally exposed to respective diamine), since that could lead to an overestimation of exposure to diisocyanates.

However, since biological monitoring reflects total exposure to diisocyanates (via inhalation and dermal exposure routes), it cannot differentiate relative contributions of particular sources of exposure (inhalation and/or dermal), even if workplace personal air measurements are available (due to limitations already stated in sub-section "Inhalation exposure").[8]

One further limitation of biological monitoring is that it reflects average daily exposures as peak exposures are not accessible by these methods since (urine) metabolites have a poor correlation to short-term peak exposures.

Bystander exposure

In the restriction proposal, the Dossier Submitter differentiates between workers, professionals and bystanders. While workers and professionals are considered to be potentially exposed to diisocyanates due to the tasks they have to fulfil, in general the potential exposure to bystanders is considered to occur only indirectly (e. g. third working parties, office staff in a factory). In addition, there even might be indirect exposure to residents living near a construction side or to inhabitants/owners of objects where diisocyanates were applied (e.g. insulation of house crawl cellars using MDI based PU spray foams as reported in the Netherlands (Nuon, 2013)).

RAC agrees with the Dossier Submitter that bystanders and other potentially indirectly exposed people may be at risk and should be protected from indirect exposure to diisocyanates.

Characterisation of risk(s)

Summary of proposal:

As described in previous sections, DNEL derivation and quantitative risk characterisation is not possible in the case of diisocyanate exposure. Therefore, the Dossier Submitter decided to base the risk characterisation on the occurrence of diisocyanate-induced occupational asthma cases in exposed workers in the EU.

Although the Dossier Submitter is aware that induction of sensitisation to occupational allergen is the first and crucial step in the development of allergic occupational asthma, in the case of diisocyanates this endpoint is not considered as suitable for the risk characterisation since sensitive predictive markers for diisocyanate sensitisation are missing, and

[8] In addition to air monitoring and biomonitoring, detailed workplace anamnesis (e.g. regarding work tasks, technical and organisational RMMs, PPE, occupational hygiene) and on-site observance of worker's behaviour, could help to identify main source(s) of exposure to diisocyanates.

asymptomatic sensitisation to diisocyanates (sensitisation without asthmatic symptoms) is not feasible to be monitored in occupationally exposed subjects.

For the calculation of the number of occupational asthma cases, the Dossier Submitter uses three different approaches:

1. Occurrence of isocyanate occupational asthma[9] based on an EU-wide request for occupational asthma statistics (survey performed in autumn 2015);
2. Occurrence of diisocyanate occupational asthma observed in occupational epidemiological studies;
3. Assessment of adult-onset asthma in the population and quantifying the fraction that is due to occupational exposure to isocyanates.

The incidence is estimated by relating the absolute number of cases to the number of exposed workers in the EU (estimated by industry, i.e. ISOPA/ALIPA[10]). Based on the assessment (by expert judgement) of the potential for exposure under certain conditions and working characteristics in the various industry sectors (Table 5), and considering 10% prevalence of isocyanate-related occupational asthma, 1.45 million healthy (i.e. free of isocyanate occupational asthma) workers are exposed to a higher level of isocyanates ("high risk" group, Table 5), and are therefore at risk.

The Dossier Submitter assigned the workers occupationally exposed to diisocyanates into two groups, "high risk group" and "low risk group". This assignment is not based on measurements, but on expert judgement (by the expert group consisting of representatives of the Dossier Submitter, the major manufacturers of diisocyanates and relevant industry associations) of the potential for exposure under certain conditions and working characteristics in the various industry sectors.

In the opinion of the Dossier Submitter, the "low risk group" comprises part of the construction industry and automotive repair, since *"the sector 'construction chemicals' (with a low risk for healthy workers) could e.g. be assigned to the (cold) uses of adhesives (also including sealants) as these uses are linked to common construction chemicals"*, and *"a similar assignment is also true for the second sector, automotive repair (excl. motor vehicle refinish), addressing the use of adhesives e.g. for fixing or replacing wind-screens or other gluing tasks"*. The so called "low risk group" includes the workers that use diisocyanate containing products for only a small fraction of their worktime and under conditions where a reduced potential for exposure is highly likely (e.g. special glues, foams for windows and doorframes, i.e. products which do not emit aerosols under ambient use conditions; products with specific application equipment that minimises exposure, such as the combination of a small foam cartridge with a special application nozzle preventing potential for dermal contact and minimising inhalation exposure).

The "high risk group" relates according to the Dossier Submitter to 'other sectors', i.e. to all sectors which cover the uses with the highest exposure levels, such as uses with expected aerosol formation (e.g. spray coatings, spray foam applications, or the use of volatile diisocyanates, mostly TDI, in the manufacture of foam and PU and composite materials) and increased probability of dermal contact.

[9] Please see footnote 4 on page 6.
[10] European Aliphatic Isocyanate Producers Association

Table 5. Overview on exposed workforce in sectors (modified Table 1 in the Background Document)

Sector	Workforce	Healthy workers*	Risk for healthy workers
Construction chemicals	1 800 000	1 620 000	Low
Automotive repair (excluding motor vehicle refinish)	1 800 000	1 620 000	Low
Other sectors (e.g. metal treatment, insulating panels, motor vehicle refinish etc.)	1 608 306	1 447 475	High**
All sectors	5 208 306	4 687 475	

Source: ISOPA, data modified (see chapter G)

*Free of asthma. Corrected for asthma prevalence of 10% in exposed population. See Section B.5.6.5.2 for more details **0.2 – 0.7%/year

The estimated annual absolute number of new isocyanate occupational asthma cases and incidences are shown below (Table 6).

Table 6. Summary table of estimated occurrence of isocyanate occupational asthma in the EU (as number of new cases per year and as annual incidence)

	Approach of occupational asthma assessment		
	Approach 1. OD statistics	Approach 2. Epidemiological studies	Approach 3. Estimation based on adult-onset asthma incidence
New isocyanate occupational asthma cases in the EU/year (N)	470 - 2 350	2 900 – 10 150	6 058 – 7 269
Exposed workers in the EU, "high risk" group (N)		1.45 million	
Annual incidence in the EU (%)	0.03 - 0.16	0.20 – 0.70	0.42 – 0.50

The Dossier Submitter concluded that although over the past several decades the number of occupational asthma cases has declined (including a significant decrease in the number of fatal occupational asthma cases) in parallel to declining exposure levels, the estimated incidences still indicate an unacceptably high risk. In the "high risk group" (see the Dossier Submitter's description of "high" and "low" risk groups on previous page), the annual incidence (excess risk) of asthma due to diisocyanate exposure in workers is estimated to range from 0.03% to 0.70%, meaning that every year 16 to 70 out of 10 000 workers exposed in the high risk group will develop diisocyanate-related occupational asthma.

RAC conclusion(s):

RAC agrees with the Dossier Submitter's approach to base the risk characterisation on incidence of occupational asthma cases. Taking into account the uncertainties in the Dossier Submitter's estimation of occupational asthma incidence in the working EU population, which can both underestimate and overestimate the magnitude of risk, RAC supports the Dossier Submitter's calculation, and their conclusion that the identified risk to the workers is not adequately controlled and needs to be addressed.

Key elements underpinning the RAC conclusion(s):

RAC points out that in this restriction proposal risk characterisation is not based on exposure assessment.

Justification for diisocyanate-related occupational asthma incidence as a basis for risk characterisation

Although epidemiological data, which provide exposure-response assessment (e.g. Tarlo et al., 1997; Ott, 2002; Ott et al., 2003; Pronk et al., 2009), show that the risk of respiratory sensitisation and occupational asthma increases with an increase in inhalation exposure to diisocyanates ("*…even at low concentrations, the higher the exposure the greater the risk",* Meredith et al., 2000), and there are some indications that 8-hour time-weighted average exposure levels <5 ppb (i.e. <36 µg TDI/m^3, <52 µg MDI/m^3, <35 µg HDI/m^3) might be protective against induction of respiratory sensitisation[11], certain studies showed that occupational asthma cases occurred at average exposure below 5 ppb as well (Tarlo et al., 1997; Gui et al., 2014). The reasons could include inadequate protection by 5 ppb limit, peak exposures, underestimated inhalation exposure, or dermal exposure (importance of which has been described in the section "Information on hazards"), or a combination of these factors. Therefore, RAC supports the Dossier Submitter's conclusion that a threshold for respiratory sensitisation and diisocyanate-related occupational asthma occurrence cannot be currently established.

Also, as already mentioned in previous section, quantity and quality of dermal data do not allow exposure-effect assessment, and biomonitoring data do not pose a reliable basis for prediction of work-related health disorders (Kaaria et al., 2001).

Justification for proposed approaches to assess the incidence of diisocyanate-related occupational asthma

As stated in the summary, the Dossier Submitter applied three approaches to assess the occurrence of (di)isocyanate occupational asthma[12] in the isocyanate exposed workers in the EU.

Approach 1 was based on the 15-year occupational disease (OD) statistics (2000-2014, for the majority of countries) from 16 countries[13] (representing 74% of the EU working population

[11] According to American Conference of Governmental Industrial Hygienists, Dotson et al., 2015, and ECETOC expert group, Cochrane et al., 2015

[12] RAC uses the term „isocyanate occupational asthma" when the causative isocyanate species (i.e. isocyanate dimer, oligomer or polymer) was not stated, and the term „diisocyanate occupational asthma" otherwise.

[13] Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Germany, Slovakia, Spain, Finland, France, Hungary, Ireland, Poland, Sweden and the UK

according to EUROSTAT) which provided data on isocyanate-related occupational disease[14] cases or stated that there were none. The annual number of cases was extrapolated to the working population of the EU. This extrapolation resulted in an average annual number of 270 cases, out of which respiratory disease cases were estimated to 235. Applying correction factors of 2 or 10 to account for well-known under-reporting of occupational diseases, a range of occupational diseases due to isocyanates in the EU was estimated to be 540 – 2700 cases per year, including about **470 – 2350** respiratory diseases per year.

Approach 2 was based on data from four epidemiological studies, three longitudinal (Ott et al., 2000; Bugler et al., 1991; Jones et al., 1992) (Table 7) and one case-control study (Tarlo et al., 1997) (Table 8), selected as being the nearest to the present day exposure situation. In three longitudinal studies respiratory effects of TDI were investigated, and in the case-control study annual incidences of occupational asthma due to diisocyanates (TDI, MDI, HDI) were analysed, based on compensation claims for occupational asthma. As shown in the tables below, an incidence in the range from 0.2 - 0.7% per year could be assumed, which, when applied to the 1.45 million exposed workers in the EU results in an estimation of **2900 – 10150** new diisocyanate asthma cases in the EU per year in the high risk group.

The number of exposed workers in the EU was estimated by expert judgement (by industry, i.e. ISOPA/ALIPA), taking into account the potential for inhalation and dermal exposure under certain conditions and working characteristics in the various industry sectors. It was estimated that out of approximately 5.2 million workers who have contact with isocyanates or isocyanate based products, 1.6 million workers are exposed to a higher level of isocyanates ("high risk" group in the following text). After subtracting (estimated) 10% of workers who already became diseased, 1.45 million workers are assumed to be exposed to a higher level of isocyanates and to be at risk.

Table 7. Annual incidence of TDI-induced occupational asthma (taken from Ott 2002) (copied from the Background Document)

Study	Time period (facility)	Annual incidence of TDI-induced occupational asthma [%] (case identification)	TDI concentration [ppb], assessed by personal sampling
(Ott et al., 2000)	1980 - 1996 (TDI production unit)	0.7 (Assessment by physician)	0.3 - 2.7 (TWA; range by job) (0.5 - 0.9 times/shift in moderate to high-exposure jobs, STC was > 20)
(Bugler et al., 1991)	1981 – 1986 (PU foam production facility)	0.8 (Self-reporting)	0.9 - 2.6 (TWA; range by job) 22% of 8-hour samples with short-term conc. > 20 and 10% > 40
(Jones et al., 1992)	1982 – 1986 (PU foam production facility)	0.7 (Assessment by physician)	1.4 - 4.5 (TWA; range by job) (3% time in production and 0.1 % of time in finishing jobs, STC was > 20)

STC: short-term concentration (9 - 12 minutes); TWA: time-weighted average

[14] For most of the recorded cases in national registries the causative isocyanate was not documented (overall, a specific agent is not given for 87% of all cases). Nevertheless, for those cases for which information on the specific isocyanate was documented, MDI, TDI and HDI were reported in 97% of the cases, with 65% of the cases attributed to MDI, 18% to TDI and 14% to HDI.

Table 8. Diisocyanate occupational asthma incidence provided by a Canadian case-control study (Tarlo et al., 1997) (copied from the Background Document)

	Incidence	
	% in 4 years, 1984-1988 (as provided in the study)	**% per year**
Overall (223 companies)	0.9	0.2
High exposure companies with claims (ever ≥ 5 ppb)	2.7	0.7
Low exposure companies with claims (always < 5 ppb)	2.2	0.6

Approach 3 is based on estimation of 0.099% overall incidence of adult-onset asthma (from an international prospective population-based study[15] by Kogevinas et al., 2007) and 10% to 25% attributable fraction for adult-onset asthma due to occupational exposures, or 250 – 300 cases per million people per year (Kogevinas et al., 2007; Toren and Blanc, 2009). Taking into calculation EU working population of 242.3 million people (according to EUROSTAT), 10% of occupational asthma that could be assigned to isocyanates exposure (according to data sources presented in Annex B, Table 66), and 1.45 million workers in high exposure group, the Dossier Submitter estimated a range of **6058 – 7269** new isocyanate asthma cases in the EU per year in the high risk group.

RAC stresses that all three estimates of diisocyanate-related occupational asthma incidence in the Background Document do not apply only to occupational asthma defined in a narrow sense (i.e. as a disease due to causes and conditions attributable to a particular working environment and not to stimuli encountered outside the workplace), but applies to a wider definition of work-related asthma, encompassing work-aggravated asthma as well. In the Background Document, the Dossier Submitter points out that in the EU context "a case of occupational disease is defined as a case recognised by the national authorities responsible for recognition of occupational diseases", and uses the term „occupational disease" in "a broader sense to encompass the diseases reported to the different recording and compensation systems of the Member States". According to EODS Report (European Occupational Diseases Statistics (EODS) Phase 1 Methodology, European Commission 2000), a majority of EU countries stated that the cases with a previously diagnosed non-occupational disease (e.g. asthma) which is later exacerbated by occupational factors are recognised as an occupational disease in their national system, and in none of these countries was possible to differentiate these cases (i.e. work-aggravated disease) from occupational disease in a narrow sense.

[15] The European Community Respiratory Health Survey (ECRHS-II), 6837 participants from 13 countries were included.

Conclusion

The Dossier Submitter estimated the annual incidence of diisocyanate-related occupational asthma in the EU in the range of 470 to 10150 cases by three approaches, employing different types of data sources, reflecting significant uncertainties of the estimate, especially regarding magnitude of under-reporting of occupational diseases in EU Member States.

Nevertheless, comparing the first approach with other two approaches (see Table 9 below), RAC considers that even the factor of 10 applied to correct underreporting in Approach 1 seems not to be unrealistically high, and narrower range of 2350 to 7269 cases could be robust enough for impact assessment, despite the uncertainties identified in the risk characterisation. These uncertainties are presented in the following section.

Table 9. Annual number of new (di)isocyanate occupational asthma cases in the EU, estimated using three different methodologies

	New OA cases	Data based on	Comment
Approach 1	470 – 2350	Occupational disease statistics mainly from 2000 to 2014 from 16 EU Member States	A correction factor of 2 and 10 for underreporting was applied
Approach 2	2900 – 10150	Four epidemiological studies, three longitudinal and one cross sectional	Selected as being the nearest to the present day exposure situation
Approach 3	6058 – 7269	An overall estimate of 0.099% adult-onset asthma incidence in the EU, with 10% to 25% attributable to occupational exposures, 10% of which could be assigned to isocyanates exposure	Data from various sources, see text above

Uncertainties in the risk characterisation

Exposure

Inhalation exposure

- Measurement of airborne diisocyanates is technically challenging and may **underestimate** actual exposure levels.
- Peak exposures to diisocyanates are difficult to detect, also leading to **underestimation** of exposure.

Data sources for inhalation exposure assessment

- Exposure values in the CSRs reflect situations with good occupational hygiene standards, and are not expected to cover some maybe more realistic workplace practices with questionable effectiveness of RMMs, probably **underestimating** real exposure levels;

- The measurement data in the MEGA database do not reflect the total concentration of a specific diisocyanate, but differentiate between the respective isomers; since it seems plausible to assume that isomers' concentration values are linked (e.g. according to the ratio of TDI isomers in mixtures used), the presented data probably **underestimate** total exposure;
- The specific UK HSE dataset referred to represents a selection of the sites according to HSE interest in specific substance or process, and not a random selection of workplaces and circumstances. Therefore, it cannot be regarded as being truly representative of occupational exposure in the UK. Both **underestimation** and **overestimation** of exposure levels is possible.

Dermal exposure

- As for most chemicals in the workplace, measured data on dermal exposure to diisocyanates are very scarce and mostly qualitative - both **underestimation** and **overestimation** of exposure levels is possible.
- The use of modelled data, in RAC's opinion, does not reduce the above stated uncertainties. In general, it is considered that the EASE model (applied in relevant CSRs) tends to **overestimate** exposure (ECETOC Technical Report No 119). On the other hand, the models were run in the frame of CSR's exposure assessment which is expected to reflect situations with good occupational hygiene standards, potentially leading to an **underestimation** of real exposure. This is illustrated by the Dossier Submitter's re-assessment of the qualitative dermal exposure assessment presented, in which more stringent categories than those stated in the CSRs were assigned to the same PROCs.

Oral exposure

- Although oral exposure to diisocyanates in workers is possible (hand-to-mouth activities, ingestion of inhaled particles), this exposure route was not assessed by the Dossier Submitter since inhalation and dermal routes are considered predominant for occupational exposure (please see section "Information on emissions and exposures - Key elements underpinning the RAC conclusion(s)"). Potentially, this can lead to an **underestimation** of exposure levels. Nevertheless, the potential role of oral exposure in diisocyanate-induced respiratory sensitisation is unclear.

Biomonitoring

- The amines are not specific markers for diisocyanates and if exposure to the corresponding diamines has not been ruled out, **overestimation** of exposure is possible.
- Biomonitoring cannot detect peak exposures, which can result in an **underestimation** of risk in the case of allergic disease induced by diisocyanates.

RAC points out, however, that although the above stated uncertainties can significantly affect the exposure assessment, they do not have an impact on the risk characterisation which is based on the occurrence of diisocyanate-related occupational asthma cases.

Risk characterisation

The number of exposed workers in the EU ("high risk" vs. "low risk" group)

As explained by the Dossier Submitter, a differentiation between "high risk" group (1.45 million isocyanate occupational asthma-free workers) and "low risk" group (3.6 million isocyanate occupational asthma-free workers) is based on expert judgement (by the expert group consisting of representatives of the Dossier Submitter, the major manufacturers of diisocyanates and relevant industry associations), and not on the basis of measurements. RAC acknowledges the value of expert judgement, especially in the case when empirical data are scarce. Nevertheless, this introduces an uncertainty in the estimation, both regarding magnitude and direction. Both **underestimation** and **overestimation** of the number of exposed workers is possible.

The number of diisocyanate-related occupational asthma cases

Uncertainties related to Approach 1:

- National Occupational Disease (OD) registries are heavily influenced by the national reporting systems, as well as health care and workers' compensation systems, which can introduce variable magnitude of uncertainty in estimation of isocyanate-related occupational asthma incidence among different EU countries. Both **underestimation** and **overestimation** is possible.
- There is an uncertainty related to incorrect coding of causal agent in the registries, especially in countries where the reporting system is not connected to a compensation system, so no verification of the actual exposures will take place. Both **underestimation** and **overestimation** is possible.
- Underreporting of occupational diseases, including asthma, is a well-known phenomenon, and includes various reasons, such as lack of knowledge among medical personnel, bureaucracy of the system, pressure from employers causing a lack of independence of occupational physicians, the worker's fear of job loss or degradation, characteristics of compensation system, or inadequate coverage of specific sectors (e.g. self-employed workers). However the magnitude of underreporting is uncertain, since quantitative data on this issue are very limited and are not specifically focused to occupational asthma (European Commission 2013a). Relevant data for only six EU countries were presented in European Commission (2013a) document (for Hungary, Latvia, Norway, Slovenia, Sweden and UK), showing a range between 40% (UK) to almost 100% (Norway and Slovenia). Also, out of 28 EU countries, 16 countries (57%) provided information on diisocyanate-related asthma incidence. While it could be hypothesised that asthma incidences for the countries that did not provide data are similar to the ones that did, uncertainty remains, especially due to high variation in incidences between countries (one order of magnitude). To compensate for this uncertainty, the Dossier Submitter used in the calculation a factor of 2 and 10. Both **underestimation** and **overestimation** is possible.

Uncertainty related to Approach 2:

- Due to healthy worker effect in epidemiological studies it is plausible that the true incidence may be higher, leading to **underestimation** of risk.

- On the other hand, epidemiological studies on which Approach 2 is based were conducted 26 to 17 years ago, so the exposure levels could be higher than expected today. This uncertainty can lead to **overestimation** of risk.

Uncertainties related to Approach 3:

- The fraction of diisocyanate-related occupational asthma among total number of cases of occupational asthma may vary between the countries, and is influenced by the frequency of exposure to other causative agents. Both **underestimation** and **overestimation** is possible.

Other uncertainties:

- Not quantifying the cases of occupational allergic contact dermatitis related to diisocyanates leads to **underestimation** of risks.
- Not quantifying the cases of allergic respiratory and skin diseases related to residential diisocyanate exposure leads to **underestimation** of risks.
- Asymptomatic sensitisation to diisocyanates (immunological evidence of sensitisation without asthmatic symptoms) is well known (US National Research Council, 2004; Park et al., 1992), but its prevalence and the risk related to its progress to overt clinical feature of asthma is not known. In addition, screening of workers for asymptomatic sensitisation is not feasible since sensitive predictive markers for diisocyanate sensitisation are still missing. An **underestimation** of risks could be expected.
- In all three approaches to estimate diisocyanate-related occupational asthma incidence in the EU, the Dossier Submitter calculated that all cases emerge in the "high risk" group since "the more or less reliable quantification of risk is solely available for the use sectors at relatively high risk" due to lack of data of the incidence rate for the "low risk" group. The Dossier Submitter later provided the number of confirmed cases of occupational obstructive respiratory disease and alveolitis cases due to isocyanates in Germany during 2002-2012 (BK1315)[16] reported by the various occupational accident insurance bodies "Berufsgenossenschaften". It may be assumed that around 80% of these cases occur in the "high risk" group, i.e. in the following occupational insurance areas: raw materials, chemical industry (manufacturing of products), wood and metal, energy, textile, electro and media. However, since the insurance sectors cannot be simply identified with the "low risk" or "high risk" groups, and since the data are available only for sectors and not for specific tasks performed by diseased workers, this estimate is highly uncertain (i.e. some of the cases recorded in "low risk" sectors could occur in workers performing "high risk" tasks, and (although less likely) *vice versa*). This uncertainty could lead both to an **underestimation** and **overestimation** of diisocyanate-related occupational asthma incidence in "high risk" and "low risk" groups of workers, but it is not expected to affect the estimated total number of cases in the EU.

Uncertainty related to a causative asthmagen

1. The Dossier Submitter's reporting of occupational asthma does not differentiate between occupational asthma caused by diisocyanates or by other isocyanate species

[16] BK1315 comprises respiratory diseases due to isocyanates such as asthma, chronic obstructive pulmonary disease and alveolitis.

(e.g. diisocyanates-free polyisocyanates). Since a specific bronchial challenge test to diisocyanate(s) is rarely performed even in clinical settings (although it is regarded as the gold standard for the diagnosis of occupational asthma, it is time consuming, expensive, and requires special facility and expertise), exposure to isocyanate species other than diisocyanates cannot be excluded. Even exposure to other asthmagens (both allergens and irritants) cannot be ruled out. In addition, in many cases patients are not subjected to a challenge test, to save the patients from severe stress in case the test provokes strong allergy reactions. This uncertainty, which applies both to occupational asthma cases documented by national occupational diseases registries and to epidemiological studies, could lead to an **overestimation** of diisocyanate-related occupational asthma cases. Regarding different isocyanate species (i.e. dimers, oligomers, polymers), RAC acknowledges, however, that it is considered that increasing molecular weight lowers the sensitising potential of isocyanate. Therefore, diisocyanates are expected to have the highest potential for respiratory sensitisation when compared to higher isocyanate species (oligomers and polymers). As previously described in the RAC's justification for the scope, monoisocyanates are not expected to contribute to this uncertainty, since there is no direct evidence that any of them can cause respiratory sensitisation.

RAC considers that the majority of uncertainties related to the risk characterisation have been adequately recognised and taken into account by the Dossier Submitter, and that they indicate either an underestimation or overestimation of the risks, or their direction cannot be defined.

Evidence if the risk management measures and operational conditions implemented and recommended by the manufactures and/or importers are not sufficient to control the risk

Summary of proposal:

The Dossier Submitter assumes that the exposure assessments contained within the CSRs, including information on operational conditions (OCs) and risk management measures (RMMs), are probably most applicable to workplaces with good working practices and a high level of occupational hygiene, noting that it is the registrants' obligation[17] to describe in the exposure scenarios how the manufacturer (or importer) controls and recommends downstream users to control exposures of workers.

The Dossier Submitter further points out that the respective RMMs taken into account often include the use of personal protective equipment (PPE). Since the effectiveness of PPE depends very much on its correct use by the worker, the reliability on PPE is prone to variation or even failure in terms of effectiveness by factors such as deliberate or negligent incorrect (or non-)use. In addition, and quite significantly, the Dossier Submitter notes that due to the very limited published data on the appropriateness/effectiveness of the implemented OCs and RMMs in the diisocyanates industry, a clear picture of real workplace situations could not be provided.

[17] Regulation (EC) No 1907/2006; Annex I, 0.7

RAC conclusion(s):

Evidence of the effectiveness of implemented RMMs and OCs at workplaces throughout the EU in reducing the risk related to exposure to diisocyanates is rather limited. Nevertheless, available data show that, despite the observed decline in diisocyanate-related occupational asthma incidence over the past decades due to improvements in RMMs and OCs in the sectors where diisocyanates are used, according to open literature and other open sources (see below) deviations from safe working practices are still present resulting in a significant number of occupational asthma cases recorded.

On the basis of the information mentioned above, especially the number of still occurring occupational asthma cases, RAC draws the conclusion that technical improvements to reduce exposure, as well as improvements to the general occupational hygiene practices, might be necessary in a number of companies throughout the EU dealing with diisocyanates.

RAC further notes that particularly micro and small enterprises (SMEs) are known to have difficulties in complying with occupational health and safety (OSH) regulations owing to fewer resources (e.g. financial, but also lower awareness and directly available expertise). This shortcoming is reflected in the EU Occupational Safety and Health (OSH) Strategic Framework 2014-2020[18] (*"SMEs have more difficulties in complying the regulatory requirements in this area. In most cases, the scope and effectiveness of OSH management remains a particular challenge for micro and small enterprises. Smaller establishments still tend to show lower levels of compliance with national and EU rules, and report fewer OSH management measures as compared with large establishments.")* For such companies there is still a need on consultation to changes to organisation and working conditions and to information on safety and health protection (incl. information on adequate RMMs).

RAC concurs with the Dossier Submitter that in situations in which PPE (e.g. gloves, respiratory protection equipment (RPE)) has to be worn, the correct use of appropriate PPE is crucial. This is because any failure of PPE leads to exposure and thus very likely to uptake of the substance which would often not even be recognised by the concerned worker/person (e.g. leakage of RPE due to inappropriate fit, incorrect taking off of gloves and reuse, etc).

RAC further notes that even if exposure minimisation is achieved by technical measures, there might still be the need for PPE for some tasks (e.g. cleaning of equipment). Therefore, RAC notes that as long as PPE is needed, it is imperative that it is appropriate and used correctly. Furthermore, every worker/person in charge of operations/activities using diisocyanates should be able to identify appropriate PPE for the tasks to be performed.

In conclusion, RAC agrees with the Dossier Submitter that to be effective, the correct RMMs which are appropriate for each use need to be in place in industrial and professional situations where diisocyanates are handled. Without such RMMs and OCs as identified in the registration dossiers, including the use of PPE, adequate protection may not be achieved in real workplace situations, leading to a higher exposure of workers to diisocyanates than expected. In addition, RAC points out that at workplaces where dermal and/or inhalation exposure cannot be avoided by technical and organisational measures, effective exposure protection is only guaranteed if correctly chosen PPE is used accordingly. Adequate implementation and control of RMMs, including the use of PPE, are required to achieve an effective protection of workers

[18] COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS on an EU Strategic Framework on Health and Safety at Work 2014-2020, Brussels, 6.6.2014 COM(2014) 332 final

from diisocyanates exposure.

Key elements underpinning the RAC conclusion(s):

As described in the previous section, for most of the uses the majority of the measured air concentration data provided in the CSRs are quite low (near or below the LOQ). However, RAC agrees with the Dossier Submitter that these values probably reflect situations with good occupational hygiene standards, underestimating real exposure levels, and that the information on OCs and RMMs in the CSRs might not be representative for all real workplace situations. In addition to the information in the CSRs, the effectiveness of RMMs and OCs in reducing exposure to diisocyanates is illustrated in the Background Document by a limited number of studies available in the open literature. These studies showed exposure reduction after introducing technical measures (Tinnerberg and Mattsson, 2008) and effectiveness of workers´ safety-at-work training proven by decreased uptake of HDI (Jones et al., 2013) linked with occupational asthma incidence reduction (Stocks et al., 2015).

When exposure to diisocyanates in 13 Swedish industry plants was assessed (Tinnerberg et al., 2000), particularly high exposure levels of total TDI (median value of 62.9 µg/m^3) were measured in one forming plant. After replacement of a semi-enclosed foaming tunnel by an enclosed one and a more airtight system with increased ventilation as well as a reduction of amine in the mixture to slow down the reaction), measurements performed in 2005 showed a decrease in exposure levels of around 80% (median value of 12.5 µg/m^3) (Tinnerberg and Mattsson, 2008). These studies clearly indicate that exposure reduction can be quite extensive if technical measures and adjustment of the mixture used are applied at a level near to the state of the art. Unfortunately, these studies do not attempt to make any connection between exposure and occupational asthma incidence.

Jones et al., 2013 compared biomonitoring data on adducts of HDI from spray painters in the motor vehicle repair industry in the UK before and after they participated in 'Safety and Health Awareness Days' (SHADs) which started in 2004 to increase the spray painters understanding of the hazard and the way of controlling exposure. They monitored the trends in the incidence of work related asthma and urinary HDA (hexamethylendiamin) levels, which both declined significantly from 2006 to 2013. Between 2013 and 2014 an increase in urinary HDA was observed, which the authors interpreted as a reduction of the impact of the SHADs and recommended to consider refresher trainings.

An important point in the context of dermal exposure is the fact that not only direct exposure to (di)isocyanates occurs (due to ineffective containment, inappropriate PPE and/or false use of PPE) but also indirect exposure from deposition of aerosols from the air onto workers´ skin, from splashing (e.g. during pouring or mixing activities), from contact with contaminated surfaces (Liu et al., 2007) or handling of contaminated items, e.g. tools or used PPE (Liu et al., 2007). If good working practices are lacking, there is even (di)isocyanate contamination outside the working/process areas where such substances are used, e.g. hand rails, doors, stairways (Leng et al., ASU Arbeitsmed Sozialmed Umweltmed 2013; 48: 392-396).

Regarding the gaps in knowledge of safe working practice, the Dossier Submitter presents examples published in the open literature (e.g. Clayton and Baxter, 2015; Gui et al., 2014; Robert et al., 2007), as well as information available in non-scientific open sources, such as company advertisements, in which lack of knowledge on safe working practice is obvious[19].

According to the EU Occupational Safety and Health (OSH) Strategic Framework 2014-2020, there is a need to improve the implementation of existing health and safety rules, *"in particular by enhancing the capacity of micro and small enterprises to put in place effective and efficient risk prevention strategies",* as the first out of three identified major health and safety at work challenges. Also, the European Survey of Enterprises on New and Emerging Risks[20] which aims to assist workplaces to deal more effectively with health and safety and to promote the health and well-being of employees, reported that *"the lack of human, economic, and technological resources and the inadequate OSH standards and guidelines, mainly targeted at large firms, can explain the generally low commitment of SMEs towards OSH management".*

Evidence if the existing regulatory risk management instruments are not sufficient

Summary of proposal:

The Dossier Submitter states that exposure at workplaces is controlled when all RMMs are applied correctly. As the correct use of RMMs includes the correct use of appropriate PPE, this might only be valid for workplaces with a good working practice and a high level of occupational hygiene.

Due to the high number of new cases of occupational asthma every year caused by diisocyanates, the Dossier Submitter is of the opinion that the risk of respiratory sensitisation resulting in occupational asthma has not yet been adequately controlled by means of EU-wide existing regulations (e.g. the OSH "Framework Directive"[21] and the Chemical Agents Directive[22]).

At the moment, there are no EU-harmonised Occupational Exposure Limit values (OEL) for diisocyanates, either binding (BOELV) or indicative (IOELV). Only national OELs exist (Table 14, Annex to the Background Document), ranging from 5 to 20 ppb and 0.001 to 1 mg/m^3 (for 8-hour exposure). As stated in the Background Document, "the available background information to the different OELs in the different Member States does not always allow to judge if this value was derived from toxicological studies, epidemiological considerations, or represents a concentration that was deemed to be a reasonable technical achievable value". The implementation of OELs leads to the reduction of exposure but does not prevent new cases on occupational asthma as it is evident from literature data (e.g. Gui et al., 2014) that occupational asthma does not only occur at workplaces where the OELs are exceeded. At the current stage of knowledge, it is not even clear to what extent the existing national OELs are

[19] https://www.youtube.com/watch?v=CSND2PM2ze4 (PPE is not appropriate, e.g. arms and face are unprotected, googles do not seem to be adequate, the correct fit of PPE is questionable as the worker often touches it); https://youtu.be/BoaC97-_qE8 (two of the workers are showing unprotected skin); https://youtu.be/heWdrX_ypWk (instructors do not wear adequate PPE, e.g. gloves).

[20] ESENER; European Agency for Safety and Health at Work, 2012

[21] OSH "Framework Directive" (Directive 89/391/EEC)

[22] Chemical Agents Directive, CAD (Directive 98/24/EC)

protecting employees against the risk of sensitisation as the threshold for the sensitising effect is not known.

According to some investigators, unrecognised situations of increased exposure as well as unrecognised peak exposures of short duration (e.g. due to lapses of attention in handling) contribute to new cases of occupational asthma. This includes situations of significant dermal exposures which often go unnoticed.

As stated in previous text, for consumers, there is already an existing European wide regulation for MDI (entry #56 to Annex XVII to Regulation (EC) No. 1907/2006 (REACH) which focuses on the risk of skin sensitisation to address the recognised risk.

RAC conclusion(s):

RAC agrees with the Dossier Submitter´s conclusion that the current functioning of the existing regulatory risk management instruments are not sufficient to control the risk related to occupational exposure to diisocyanates. Particularly, micro and SMEs are known to show lower levels of compliance with the OSH requirements due to fewer resources (see section above).

RAC notes that there is no existing health protection legislation for self-employed persons. Therefore the restriction would improve the awareness of risks for this type of manpower.

People in charge with diisocyanates might not be very familiar with the fact that not only inhalation exposure but also dermal contact plays an important role for the sensitising effect.

RAC points out that appropriate training is therefore a basic necessity. Every worker handling diisocyanates should have a sufficient knowledge of the hazards of these substances and an awareness of the risks related with their use as well as sufficient knowledge of good working practices and appropriate RMMs (including the correct use of appropriate PPE). RAC notes that particularly training measures are needed to raise the awareness for the importance of health protection by means of appropriate RMMs and safe handling practices.

RAC agrees with the Dossier Submitter that the implementation of an indicative or binding OEL would not be a sufficient measure to reduce the number of occupational asthma cases to a level as low as possible as currently no threshold is known for the sensitising potential of diisocyanates.

Key elements underpinning the RAC conclusion(s):

As described in the previous section ("Characterisation of risk(s)"), cases on occupational asthma occurred at average exposure of TDI below a TWA (8 hours) of 5 ppb (Tarlo et al., 1997; Gui et al., 2014). Most of the present OEL values for TDI in the EU (Table 14 in the background document) are at a level of 5 ppb; in some Member States they are even higher (up to 20 ppb). However, as there is currently no available threshold for respiratory sensitisation, lowering OELs might indeed be a welcomed step in the right direction but it might not be possible to define an adequate protection limit.

In addition, the fact that peak inhalation exposure of short duration and dermal exposure both contribute to the onset of occupational asthma caused by diisocyanates, makes the determination of an adequate level of protection even more complex.

RAC points out that for substances for which the recommended OEL is not protective enough such as diisocyanates, there is a particular necessity for sufficient and adequate training for workers on the hazards and risks and on the way in which exposure control should be

managed, including the correct use of PPE (if needed). Although OSH legislation includes a requirement of regular trainings on hazardous substances, some companies, especially SME (small and medium enterprises), often do not have an adequate structure to provide sufficient training for their workers. Furthermore, they are more difficult to reach in terms of safety communication and therefore less likely to be aware of the risk which the use of chemicals can imply.

Particularly when rather detailed knowledge of the hazards and risks of dangerous substances is needed for sufficient and adequate information and training of workers, mainly SMEs but also bigger companies might have difficulties to bring the relevant information forward as they might not be aware of the crucial issues (e.g. important role of dermal exposure for respiratory sensitisation) for minimisation of risks to the extent needed for appropriate workers´ protection.

JUSTIFICATION IF ACTION IS REQUIRED ON AN UNION WIDE BASIS

Justification for the opinion of RAC and SEAC

Summary of proposal:

Diisocyanates are used in many applications[23]: e. g. for the manufacture of polyurethanes (PUs), rigid and flexible PU foams, rigid and flexible integral skin foams, assembly foams (e. g. insulation panels), elastomers, adhesives and glues, protective and decorative coatings (paints, lacquers, varnishes), sealants, elastomers and binders, throughout the EU, although the relative importance (and therefore the number of people potentially at risk) may differ from country to country. While the production of rigid foams in many cases is closely linked to the location of existing automotive suppliers, the production of flexible foams appears to expand particularly in some Eastern European countries. Car repair shops using aliphatic diisocyanates (mainly HDI) and the building and construction sector (using MDI), however, exist in all countries and regions.

Several years ago, suppliers of diisocyanates have already started to improve the awareness of situations with potentially increased risks to these substances by implementing product stewardship programmes (e.g. ISOPA: "Walk the talk"; ALIPA[24] "We care that you care"). However, these programmes primarily reach only the first layer of downstream users, mainly large industrial customers. All the further downstream users and the end users might not be enough informed about the risks of handling diisocyanates as the number of cases of occupational asthma is still considerably high (see section "Characterisation of risk(s)").

In order to

- improve the effectiveness of such programmes,
- implement a level of awareness and competence needed to handle diisocyanates in a way that reduces risks as far as possible throughout the supply chain, and
- make it a clear element in the marketing,

EU-wide action is required.

[23] The predominant use of diisocyanates (>90%) is in the direct manufacture of polyurethane plastic materials (PUs), where diisocyanates are reacted with polyols and/or other nucleophiles like polyamines.
[24] European Aliphatic Isocyanate Producers Association

So the main arguments for an action on an Union wide basis are that diisocyanates are being used EU-wide, occupational exposure to diisocyanates is wide spread across the EU, and diisocyanate-related occupational diseases are registered in many Member States.

RAC conclusion(s):

Based on the key principles of ensuring a consistent level of protection across the Union, RAC supports the view that any necessary action to address risks associated with the use of diisocyanates should be implemented in all Member States.

As there is no Member State in the EU, for which an occupational exposure to diisocyanates can definitely be excluded, RAC does not see a possibility to suggest an exception for any Member State from this restriction proposal.

Key elements underpinning the RAC conclusion(s):

The wide spread attention for diisocyanates is shown in several publications. In Denmark, MDI and TDI are part of the "List of undesirable Substances 2009". In the Netherlands, MDI also is listed in a report (RIVM Letter Report 601030001/2012) which claims further regulations for this substance. In UK, the website of HSE informs quite detailed about the hazards of isocyanates and how to control the risks handling these substances. In Sweden, the Swedish Trade Union Confederation worked out a common union action programme for the area of isocyanates and similar plastics more than 15 years ago, which resulted in an information brochure named "Isocyanates at work". In this brochure it is clearly pointed out that not only free isocyanate monomers are problematic, but also finished products containing polyurethanes, formaldehyde, phenol or urea when they are heated.

In addition, some Member States did not only publish information related to the risks of diisocyanates, they even have implemented additional national regulations to assist OSH regulation. E.g., Germany has published the TRGS 430 "Isocyanate – Gefährdungsbeurteilung und Schutzmaßnahmen" which provides quite detailed requirements regarding the use of isocyanates including RMMs but also information and training of workers. In Denmark, a recognition issued by the Danish Working Environment Authority is required for persons who wish to work permanently with isocyanates (and epoxy)[25]. There is also a training programme[26] in the national OSH legislation for isocyanates, which the employer must provide to the workers prior to starting the work. In Sweden, the national regulations in place for more than 20 years require training and medical examinations among other requirements for workers exposed to diisocyanates and their supervisors.

An action on an Union wide basis like this restriction proposal would synchronise the efforts already taken in some Member States and would implement the same protection level for all workers and self-employed workers throughout the EU. To sum up, this restriction proposal would harmonise the regulations related to industrial and professional uses of diisocyanates in all Member States.

[25] https://danishbusinessauthority.dk/work-epoxy-and-isocyanates

[26] http://engelsk.arbejdstilsynet.dk/en/regulations/executive-orders/292-arb-med-stoffer-og-materialer/bilag-3

JUSTIFICATION WHETHER THE SUGGESTED RESTRICTION IS THE MOST APPROPRIATE EU WIDE MEASURE

Justification for the opinion of RAC and SEAC

Scope including derogations

Justification for the opinion of RAC

Summary of proposal:

Potential regulatory measures

The observation of diisocyanate-related occupational asthma is the main driver behind this restriction proposal. Respiratory sensitisation to diisocyanates is a pre-requisite for developing diisocyanate-related occupational asthma, and it is not possible to set a reliable exposure limit preventing sensitisation and subsequent development of manifest asthma. Therefore, reducing the number of workers with respiratory sensitisation to diisocyanates is the main step that must be taken to avoid new cases of diisocyanate-related asthma.

The fact that exposure to diisocyanates may lead to occupational ill-health has been known for a long time. Therefore many EU-countries have introduced occupational exposure limits for the use of such compounds knowing that this would not completely solve the problem of sensitisation. In some Member States, additional measures and actions have been implemented to prevent adverse effects from handling diisocyanates. This has been done in the framework of national OSH regulations or as support actions of national occupational health authorities as already pointed out in the previous section. Unfortunately, these actions have never been synchronised within the EU.

In order to achieve in future improved similar conditions for the safety use of diisocyanates throughout the EU, a restriction under REACH aiming to establish stricter mandatory handling habits through training and instruction would be the most effective option according to the current restriction proposal. The Dossier Submitter notes that REACH as a regulation for placing on the market of substances is well suited to ensure a comprehensive quality management programme with regard to effective training measures and improvement of RMMs based on the knowledge and experience of the actors at the top of the supply chain. In addition, the Dossier Submitter considers that the restriction proposal will also create an incentive to develop and use products with "very low" potential of exposure.

In the Annex XV report, the Dossier Submitter proposes to restrict the placing on the market and the industrial and / or professional use of diisocyanates as substances on their own, or as a constituent in other substances or mixtures (including also prepolymers, oligomers and polymers of diisocyanates which can contain free (residual) diisocyanates), unless a combination of technical and organisational measures as well as a minimum standardised training package have been implemented. Information on how to get access to this package is communicated throughout the supply chain. Exemptions are identified by the Dossier Submitter as described below.

According to the Dossier Submitter´s proposal, the proposed restriction would apply without prejudice to existing occupational safety and health regulations, i.e. obligations from such regulations shall still be followed.

The Dossier Submitter stresses that the authorisation process would not be an option due to the huge number of uses and the relatively complex supply chain.

Derogations / exemptions

The following exemptions from the restriction have been proposed:

1) A substance or mixture placed on the marked or used containing free diisocyanates in a cumulative concentration < 0.1% w/w does not fall within the scope of the restriction proposal.

2) Derogations are also defined for "products" containing diisocyanates in a concentration ≥ 0.1% w/w for which a very low potential for exposure has been shown, both by the inhalation and the dermal route. This is the case if the 8-hour time-weighted average (TWA 8 hours) on the airborne cumulative concentration of all diisocyanates is demonstrated to be below 0.001 ppm[27] and the indication for dermal exposure is demonstrated to be very low by a "Dermal Assessment Tool", which predicts the potential for dermal exposure based on the description and characteristics of the task. Further details of the Dossier Submitter's proposal can be found in Appendix 5 and 7 of the Background Document.

According to the Dossier Submitter, a "product" is meant to describe a substance or mixture in the ready-to-use form (mainly used in the construction industry and in the, automotive sector) which includes the diisocyanate as such or in a mixture, possibly with other auxiliary substances, packaging (e.g. cartridge) and application devices (e.g. a longer or specially shaped application nozzle, special mixing devices).

The Dossier Submitter stresses that even showing very low potential for exposure does not make these products safe. Residual risk remains and the usual precautions identified in the SDSs and the on-site risk assessment should still be taken, including training and instruction according to OSH. Moreover all products containing diisocyanates above the classification limits defined in the CLP Regulation still have to comply with the corresponding classification and labelling requirements.

The Dossier Submitter also points out that since the inhalation and dermal evaluation methods proposed for the process of defining exempted products are not suited to determine peak exposures, uses where such peak exposures are more likely to occur are completely excluded from the evaluation for a potential exemption. In addition, all uses with high-energy-spraying (with the potential for aerosol formation) and uses at elevated temperatures (≥ 45 °C), will not qualify for an exemption. In these cases it is considered that in practice it is not possible to sufficiently reduce the potential for exposure. Also, other factors that could lead to peak exposures (related to, for example, mechanical disturbance such as container's opening or strong stirring, or some maintenance procedures), should be reduced.

[27] MDI (CAS no: 101-68-8): 10 µg/m³; TDI (CAS no: 91-08-7; 584-84-9): 8 µg/m³; HDI (CAS no: 822-06-0): 7.5 µg/m³

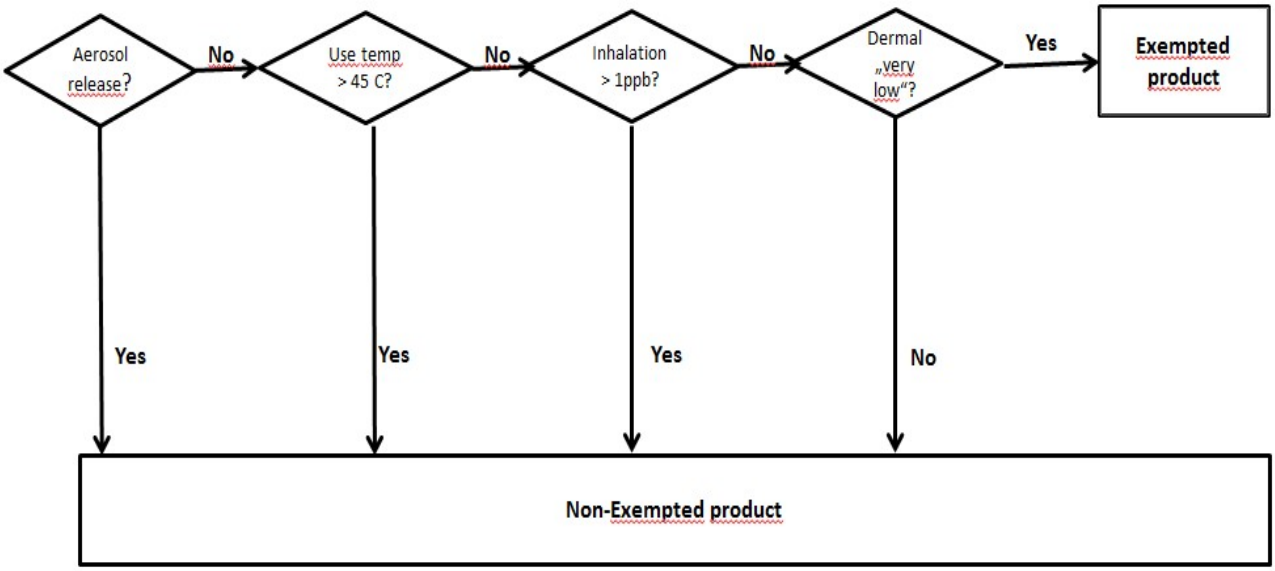

Figure 2. Graphic scheme on exemptions

The Dossier Submitter states that validated measurement methods for determination of inhalation exposure (DFG Air Monitoring Methods, HSE method, IFA methods, NIOSH methods; Table 5-1 in Appendix 5) exist, and points out that the measurements have to be conducted under realistic use conditions and should cover all tasks in the context of the application. A description of the conditions under which the measurements have been performed has to be included in the documentation describing the tests.

For a product to qualify for an exemption, the potential for exposure over all pathways has to be so low that personal protection equipment or technical ventilation are unnecessary from the risk control point of view (although they may still be recommended as an extra layer of protection or for personal hygiene purposes).

The evaluation of a substance or mixture as candidates for possible exemption has to be conducted by the manufacturer, importer or formulator placing the substance in its final form on the market.

Last but not least, the Dossier Submitter points out that there are many situations where workers will use such diisocyanate(s) containing products only during a small fraction of their working time. They further emphasise that these products might be more favourable with respect to their occupational risk profile than other alternatives (e.g. solvent-based products with higher emissions).

RAC conclusion(s):

Potential regulatory measures

RAC agrees with the Dossier Submitter that due to the huge number of uses and the relatively complex supply chains, the authorisation process may become time-consuming and impractical.

RAC acknowledges that a restriction offers a straightforward approach to address all diisocyanates, including prepolymers, oligomers and polymers of diisocyanates still containing ≥ 0.1% w/w of free diisocyanates, in one regulatory action.

RAC concurs with the Dossier Submitter that the knowledge and experience of the actors at the top of the supply will be helpful with regard to the elaboration of adequate up-to-date training material and content.

RAC supports the Dossier Submitter´s view that a restriction could not only ensure that a comprehensive and effective training programme is implemented but could also result in improvements with regards to the implementation of RMMs, particularly the correct use of adequate PPE.

Acknowledging that in some Member States additional measures and actions have already been implemented to prevent adverse effects from handling diisocyanates and also considering that some industry sectors have taken actions with a view to the same target, RAC points out that the suggested restriction is the most appropriate EU wide measure to prevent new cases of respiratory sensitisation from exposure to diisocyanates by implementing harmonised training for the workforce.

Nevertheless, RAC recommends that to ensure the quality and the credibility of the training programs, Members States in which the training is to be implemented should be responsible for the approval of the training material and the development of the training system.

Derogations / exemptions

RAC agrees with the proposal to set a cut-off limit at 0.1% w/w of cumulative diisocyanate content in a substance or mixture as this corresponds to the lowest limit for classification as Resp. Sens. 1 for diisocyanates (see bullet point 1. above).

RAC supports a derogation for ready-to-use products containing diisocyanates ≥ 0.1% for which a very low potential for exposure has been shown (see bullet point 2) above), both by inhalation and dermal route, where:

1. Aerosols are not generated, and
2. Warming or heating the substance or mixture above 45 °C is not required, and
3. The sum of the concentrations for all diisocyanates measured during air monitoring shall be < 1 ppb as a time-weighted average of 8 hours, and
4. Very low dermal exposure[28] is demonstrated by a recognised and adequate dermal assessment tool.

For the assessment of the dermal exposure, RAC proposes that an adequate dermal assessment tool should be used (e.g. ECETOC TRA, Riskofderm, etc.), without limiting the assessment to the use of the dermal assessment tool proposed by the Dossier Submitter. RAC recognises the merit of the Dossier Submitter's dermal assessment tool as a qualitative way of demonstrating the potential for dermal exposure of a specific ready-to-use diisocyanates containing product. Nevertheless, to increase the implementability of the tool, support for users is recommended by RAC to be made available by the Dossier Submitter.

While modelling the dermal exposure of the ready-to-use product (either with the dermal assessment tool proposed by the Dossier Submitter or any other acceptable modelling tool) all the input parameters related to the process (duration and frequency of task, quantity of the product used, size of the room where the task is carried out, distance to skin during

[28] The criteria for the identification of "very low dermal exposure" are elaborated in detail in the Background Document.

application, body parts at risk of being exposed) and to the product (energy score[29] and curing time) that may vary depending on the specific conditions in place at the site of use, should be selected taking into account the realistic worst case scenario for a given application, including cleaning and maintenance tasks.

It may be considered, in the future, that the exemption dossier is evaluated by an independent body with adequate expertise in the field. This requirement would potentially mean one or more bodies are accredited and have the responsibility to check and verify the dossier. This would have a cost implication but the number of exemption dossiers at least at first would be limited.

Key elements underpinning the RAC conclusion(s):

Potential regulatory measures

Regarding the authorisation process, it is also to be noted that if the applications for authorisation show that risks have not been minimised to an acceptable level, RAC would recommend conditions (e.g. improvement of technical RMMs and OCs, measurements, adequate PPE, training, etc.) to reduce the risks. As the restriction proposal also foresees improvements in RMMs with particular emphasis on behavioural changes in handling diisocyanates, the restriction seems to be the most appropriate measure to achieve the declared goal, namely, the reduction of the number of workers with respiratory sensitisation to diisocyanates although the restriction does not promote substitution per se. However, RAC stresses that the legal requirements for substitution do exist despite of the restriction proposal.

In addition, the restriction process is much more comprehensive as it may comprise all diisocyanates in one regulatory action whereas for the authorisation process more regulatory actions would be needed (e.g. classification under CLP of the not yet classified substances, entry in the SVHC list, entry in Annex XIV, etc.). Furthermore, as it has already been shown that there is a need to improve the training of workers (including self-employed workers) dealing with diisocyanates, this need can be directly addressed by a restriction.

Another reason why the authorisation process would not be an appropriate measure is that large scale substitution is unlikely as diisocyanates and PU polymers show unique properties, and a major shift towards the use of diisocyanate-free products is not foreseen anytime soon.

In addition the current restriction proposal based on the identification of training requirements for the handling of diisocyanates under the REACH Regulation is considered to be preferable by RAC to an OSH regulatory action. It is understood that actors at the top of the supply chain (producers/importers/formulators) can define more effectively best practices and approaches for the safe handling of the substance they produce. Therefore, since under the present restriction proposal the training material (content) would be elaborated by those with greater experience and knowledge, the risk of implementation of inadequate training decreases. Also the restriction sets out the training in some detail specific for the handling of diisocyanates, unlike the present OSH legislation requirements. Another advantage of a restriction under REACH versus a regulatory action within the OSH legislation is that the restriction allows the introduction of common requirements on an EU wide basis, which cannot be effectively implemented under OSH. As the Dossier Submitter points out, establishing a communication structure that allows performing such a task is a complicated matter for the companies

[29] Energy score: qualitative estimate of degree of input of mechanical energy during the task.

(manufacturers/importers/formulators) of various sizes in all EU Member States.

Taken all these considerations into account, RAC agrees with the Dossier Submitter that this restriction proposal is not a replacement for OSH requirements, but it builds on them and is expected to enhance employer's capacity to achieve a higher level of risk control, primarily through improved safety-at-work training. This is especially true for smaller companies, since the proposed structure of this restriction proposal is expected to cover the gaps in the implementation of the present OSH requirements, particularly in SMEs, providing diisocyanate-specific training programmes all the way down the supply chain.

Additionally, RAC considers that the Members States in which the training is to take place should be responsible for the approval of the training material and the development of the training system required to ensure that the training programmes implemented are effective in promoting the safe handling of diisocyanates in the workplace.

Derogation/exemptions

The Dossier Submitter considers, after discussion with experts from various industry sectors, that there are situations (mainly in the construction but also in the automobile sector) where "the potential risk of handling diisocyanates in the form of ready-to-use products, even if they contain diisocyanates in a concentration ≥ 0.1% w/w may be considered to be so low that the present OSH requirements would be sufficient to ensure the safe use of the substances and the prevention of the initiation of sensitisation."

In these cases, the Dossier Submitter is of opinion that:

- introduction of additional duties may be considered to be no longer proportional, especially when such products are used only during a small fraction of the worktime (e.g. less than once a week);

- use of exempted products with "very low risk" of exposure to diisocyanates might be more favourable with respect to their occupational risk profile than other alternatives (which might contain solvents with a higher risk profile);

- use of exempted products will also create an incentive to develop and use products with "very low" potential of exposure.

On the other hand, obligatory training for all diisocyanate uses and products could be expected to decrease industry's motivation to implement the proposed restriction and to lower the incentives to develop and use products with "very low" potential of exposure.

RAC is aware that allowing an option for exempted products containing diisocyanates in a concentration ≥ 0.1% w/w would imply a residual risk, which could not be quantified at the present moment due to lack of data of exposure and health effects in workers exposed to such eligible products. However, RAC also considers that allowing for an exemption for products with "very low" potential for exposure may lead to long-term benefits for workers' health (e.g. developing and use of products with "very low" potential of exposure, including products with decreased diisocyanate concentration; more efficient implementation of the proposed restriction).

In order to alleviate the identified uncertainties and decrease the residual risk, RAC proposes that all input parameters for the dermal assessment tool that could vary under real-life conditions (e.g. varying work settings, number of workers and their rotation, climate factors,

etc.) should be selected considering a "realistic worst case" scenario.

Justification for the opinion of SEAC

Summary of proposal:

See the opinion of SEAC.

SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the SEAC conclusion(s):

See the opinion of SEAC.

Effectiveness in reducing the identified risks

Justification for the opinion of RAC

Summary of proposal:

The effectiveness of the restriction proposal in reducing the identified risks is expressed by the potential to avoid a certain fraction of asthma cases in future relative to the baseline. It is assumed that mandatory standardised training may lead to a 50-70% reduction in the yearly number of cases of newly reported occupational asthma due to handling diisocyanates.

The estimation for the reduction of incidence rate after implementation of the proposed restriction is based on a previous study on the effectiveness of a training programme on health and safety in the motor vehicle repair industry (Stocks et al., 2015, Piney et al., 2015). According to this study, after an initial increase the incidence rate of occupational asthma in vehicle spray painters was reduced by between 50% and 70%. Although the Dossier Submitter recognises that there are distinct differences between the measures described in this study and the current restriction proposal, the "best guess" on the effectiveness of the proposed training measures according to the Dossier Submitter is a range between 50% (presented as "Low Bound Anticipation") and 70% effectiveness (presented as "High Bound Anticipation"). In the calculation of benefits, SEAC uses the 50% effectiveness as basis, however, reporting also the results for the 30% and 70% effectiveness.

RAC conclusion(s):

RAC considers that the obligation to train the users of diisocyanates, repeated after a certain interval, will improve the fundamentals of handling diisocyanates throughout the EU.

Consequently, the risk of respiratory and dermal sensitisation among trained users will decrease. Therefore RAC acknowledges that not only the number of newly cases on occupational asthma but also the number on diisocyanate-related dermal diseases will be reduced.

RAC agrees with the Dossier Submitter that the reported number of diisocyanate-related occupational diseases may increase in the first years of the implementation of the restriction due to the higher awareness for cases of respiratory sensitisation.

RAC recognises rather significant uncertainties related to the risk reduction capacity of 50-70% estimated in this restriction proposal. On the one hand, there are distinct differences between the HSE study and the restriction proposal (discussed further in "Key elements underpinning the RAC conclusion(s)"). Furthermore, it is not clear to what extent the HSE study may be applicable to other sectors in which diisocyanates are used. So, RAC assumes that the magnitude of risk reduction might be much lower. As some important aspects for estimating the risk reduction will be elaborated after the implementation of the restriction, RAC cannot properly assess the risk reduction capacity at the moment, or quantify the uncertainty of the estimate. However, RAC notes that UK example, as well as several other studies related to non-diisocyanate respiratory and skin sensitisers and irritants, show that risk reduction in the range proposed for this restriction proposal is not impossible to achieve, and points out that any risk reduction would be of benefit as human health would be ensured to a greater extent as until now.

It is to be noted that RAC did not reach a conclusion on the effectiveness of the RMMs proposed (listed in Appendix Y of the Annex to the opinion) since neither the information provided in the restriction dossier nor in the public consultation allowed for a detailed assessment of the proposal in this regard. The risk reduction capacity of the restriction has therefore been assessed based exclusively on the estimated effectiveness of the training requirements described in the conditions of the opinion. Nevertheless RAC considers that ensuring that adequate RMMs for the handling of diisocyanates are in place will further enhance the effectiveness of the restriction.

Key elements underpinning the RAC conclusion(s):

There is very limited data on preventive programmes in diisocyanate industry, namely, only the above mentioned study from the motor vehicle repair industry. For other sectors handling diisocyanates data are not available. Another study described in the restriction proposal which showed similar effectiveness of a preventive programme in reducing occupational asthma and skin diseases was performed in a rather different population of workers and working conditions (prevention of latex allergy in healthcare workers in the non-public healthcare sector; Latza et al., 2005). Due to the very small and partially not specific dataset on the reduction capacity on occupational asthma, RAC agrees with the Dossier Submitter that an exact quantitative prediction of the expected reduction rate of occupational asthma is not possible based on these studies.

The estimation of a reduction capacity by training measures of 50 to 70% in the yearly number of cases of newly reported occupational diseases was derived by the Dossier Submitter mainly based on a HSE study on the use of diisocyanates in the motor vehicle repair sector (Stocks et al., 2015, Piney et al., 2015). The reason for the Dossier Submitter´s decision to base their estimates on the HSE study is that this study specifically addresses one of the sectors covered in the restriction proposal; nevertheless the Dossier Submitter recognises the existing differences between the approach in the HSE project (e.g. follow-up visit of labour inspectors in the body-shops) and the current restriction proposal (e. g. staged approach depending on the expected level of potential risk; training with subsequent examination; repetition cycle of 4 years). Additionally, the Dossier Submitter has not explicitly identify in which way the HSE study could serve as the basis for a reliable estimation of the risk reduction capacity of the

proposed restriction for all the other sectors concerned by the restriction proposal.

Comments by the Swedish Work Environment Authority during the Public Consultation do support the assumption that further training requirements for handling diisocyanates might be successful in reducing the number of occupational diseases. However, detailed information on effectiveness was not provided.

RAC is aware of the high uncertainty related to estimation of the risk reduction capacity, but is also aware that due to the lack of data on training effectiveness in sectors other than MVR (motor vehicle refinish) and countries other than UK, a more precise estimate is hard to achieve before implementation of the restriction. Nevertheless, although data for other health risks and industries show wide range of effectiveness (from less than 10% to more than 80%, according to the Background Document), several studies related to non-diisocyanate respiratory and skin sensitisers and irritants, showing 45% to > 60% reduction of skin and respiratory symptoms (e.g. Held et al. 2001, Loffler et al. 2006, Latza et al. 2005, Semple et al. 2007Bregnhøj et al. 2012), indicate that efficiency in the range proposed for this restriction proposal is not impossible to achieve. In conclusion, remaining uncertainties regarding training effectiveness are high, but are not likely to be quantified or reduced before the implementation of the proposed restriction.

Human health and environmental hazards of alternatives for diisocyanates

The Dossier Submitter considers that there are no adequate available alternatives at the present moment that would cover all uses of diisocyanates, and that a major shift towards the use of isocyanate free products is not foreseen anytime soon. In the restriction proposal it is stated that isocyanate based products had been introduced as substitutes for products with more hazardous characteristics, such as formaldehyde resins or traditional solvent based products with a history of recurring severe accidents because of flammability of the solvent and/or post-application emissions.

Research project "Market research of available alternative products (with content of isocyanates less than 0.1% (w/w)) as possible substitutes for diisocyanate-containing products in the skilled crafts sector", with an emphasis on the building industry, was performed by the Dossier Submitter's external consultant, chromgruen Planungs- und Beratungs- GmbH & Co. KG. The project showed that in certain areas alternatives are available and in some cases are in commercial use, such as sealants (e.g. bitumen), water based coatings for wooden substrates, and silyl modified hybrid resin as parquet adhesives. Nevertheless, drawbacks of these alternatives compared with diisocyanate-containing polyurethane products were stressed out, as well as the fact that diisocyanate-containing polyurethane products in most cases are used due to specific technical requirements and for uses with especially high technical demands (e.g. with regard to the mechanical and/or chemical surface robustness). For such uses the only identified suitable alternatives are epoxy-based products, which, compared to diisocyanates, do not represent safer alternatives. Regarding lower-risk alternatives, the research report states limited availability of MDI based products with low diisocyanate content (< 0.1%), since only few manufacturers deliver the necessary monomer-diminished MDI. Another group of lower-risk alternative products, based on silane-terminated polymers, is stated as not technically feasible in all application fields.

Another document mentioned in the restriction proposal, „Alternatives to MDI in consumer products - with focus on coatings, adhesives and sealants" (Danish EPA, Møller Christensen

et al. 2015), focused on consumer uses of MDI, but most of the products discussed may also be used in the professional sector. The report summarises the assessment of health and environmental properties for three types of alternatives (also pointed out by the Dossier Submitter in the restriction proposal): prepolymer MDIs with reduced amount of residual free diisocyanate monomer, monomers for hybrid non-isocyanate-based polyurethane (HNIPU), and monomers for 'other hybrid silane' (modified silanes).

Information on human health and environmental hazards of the main alternatives identified and described in the restriction proposal, Market research project by chromgruen Planungs- und Beratungs- GmbH & Co. KG and Danish EPA report, are summarised below:

- **Epoxy resins** - although there are applications where use epoxies is feasible, this alternative cannot be considered as a general low risk alternative for diisocyanates (polyurethanes). A major drawback is the fact that dermal contact with the uncured product may induce skin sensitisation, which, according to information cited in the restriction proposal (Ziegler and Kersting, 2012), appears to be more frequent than the respiratory sensitisation related to the use of diisocyanates.
- **Prepolymer MDIs with reduced amount of residual free diisocyanate monomer** according to Danish EPA report „seem to inherently possess the same toxicity as 'pure'/'free' MDI and the available information on use and exposure potential does not indicate any significantly reduced risks from using these alternatives". Namely, although the number of free isocyanate groups is reduced, these molecules still contain free isocyanate groups for further polymerization and crosslinking. According to ISOPA, they should be considered as toxic as free isocyanates, although some suppliers claim reduced need for labelling. It is stated in the restriction proposal that these alternative substances still need to be labelled with EUH 204 – "Contains isocyanates. May produce an allergic reaction".
- **Monomers for hybrid non-isocyanate-based polyurethane (HNIPU)** are assessed to potentially lead to significant reduction in hazards and risk, but it is pointed out in Danish EPA report that the assessment is based on limited knowledge about the composition of the HNIPU monomers, which is based only on the suppliers' Safety Data Sheets (i.e. on the statement that they contain "no dangerous substances"). However, there is limited knowledge about possibly toxic co-formulants needed for formulating adhesives, coatings and sealants. The Dossier Submitter points out that "the basic building blocks for this chemistry have not been registered under REACH", meaning that their toxicology profile is largely unknown. Some commercially available products are in fact two component epoxy/amine systems, similar to the normal epoxy/amine systems, bearing the same health hazards and risk as other epoxy products (skin sensitisation) and primary amines substances (strongly corrosive or skin or respiratory sensitisers).
- **Modified silanes (monomers for hybrid polymers based on silane chemistry).** Although this alternative is not technically feasible in all application fields (according to Market research project by chromgruen Planungs- und Beratungs- GmbH & Co. KG), it is stated as a technology that is well established for sealants in the building industry, with widely available products. In the restriction proposal it is stated that "sealant foams based on this technology seem to present one of the few cases where an alternative comes at least close to comparable PU products". However, according to Danish EPA, although they seem to possess lower severe inherent toxicity

(carcinogenicity and sensitisation property), they could introduce other hazards/risks, including higher potential for irritation/effects on eye and skin (classified for eye damage and skin corrosion), and hazards related to phthalates which might be used as plasticizers in these products. Also, amount, rate and resulting exposure to methanol from these products remain unclear, which is especially important for the uses in confined spaces. Namely, reaction of the silane with moisture or with a prepolymer with hydroxyl groups may liberate methanol. For example, in one Safety Data Sheet (GENIOSIL® WP 1, Wacker Chemie AG) it is stressed out that if these sealants are applied indoors sufficient ventilation is essential, because of the curing mechanism during which methanol is released. It is also stated that if good ventilation is provided, methanol air concentration lies well below German workplace exposure limit of 270 mg/m^3 (indicative occupational exposure limit value for methanol is 260 mg/m^3 for 8 hour TWA, according to Directive 2006/15/EC).

RAC points out that information on human health and environmental hazards of alternatives are very limited, except for epoxy resins, for which hazard properties are well studied (e.g. Report prepared by TWI Ltd for the UK Health and Safety Executive 2003). Especially for modified silanes, which present the most promising alternative, already in use (although limited to selected uses), health risks are still not well defined according to available literature.

Nevertheless, RAC agrees in general with the Dossier Submitter's assessment of alternatives, including the Dossier Submitter's conclusion that a major shift towards the use of isocyanate free products is not foreseen in near future.

Socio-economic impact

Justification for the opinion of SEAC

Costs

Summary of proposal:

See the opinion of SEAC.

SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the SEAC conclusion(s):

See the opinion of SEAC.

Benefits

Summary of proposal:

See the opinion of SEAC.

SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the SEAC conclusion(s):

See the opinion of SEAC.

Other impacts

Summary of proposal:

See the opinion of SEAC.

SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the SEAC conclusion(s):

See the opinion of SEAC.

Overall proportionality

Summary of proposal:

See the opinion of SEAC.

RAC and SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the RAC and SEAC conclusion(s):

See the opinion of SEAC.

Uncertainties in the proportionality section

See the opinion of SEAC.

Practicality, incl. enforceability

Justification for the opinion of RAC and SEAC

Summary of proposal:

The Dossier Submitter concludes on the practicality of the proposed restriction on the basis of its implementability and enforceability. However, they point out that not all of the aspects have yet been developed to the detail needed for a full implementation of the restriction as the development of some aspects (e.g. dissemination of the training content, elaboration of detailed training material) takes a lot of resources and depends therefore on the prerequisite that the restriction will be implemented.

Implementability

The Dossier Submitter concludes on the implementability on the basis of the following issues:

a) Responsibility for developing the necessary training material (content)

The practical implementation of the restriction proposal will be facilitated by the fact that the trade associations ISOPA and ALIPA have already established a system for customers at the top of the supply chain ("Walk the talk"[30] and "Safeguard – We care that you care!"[31]). Both associations organised the so called "PU exchange panel" where preliminary discussions on practical aspects of the implementation took place. Stakeholders of all users of diisocyanates were invited to participate. The final responsibility for the development of the training process and content will be transferred to a "training working group", a not-for-profit body representing industry and the other Stakeholders. The status of this body has not yet been determined.

b) Quality assurance of material (content) that is developed

The "training working group" will be responsible not only for the elaboration of qualitative training content but also for its further improvement. It should be open for all contributing parties to the training material. Further development of training content is being discussed in cooperation with an external consultant. An exchange with the institutes/instructors providing the actual training material (e.g. slides with a particular lay-out and sequence) and also trainings is considered by the Dossier Submitter.

Training material will take into account existing national regulations.

Industrial representatives have indicated their willingness to translate the training material in different EU languages.

In order to reach a level playing field in the EU, a mutual recognition system should be in place to recognise trainings and the qualification of trainers across the EU. The Dossier Submitter recommends establishing an advisory board where competent independent outsiders have the possibility to provide input.

c) Organising the trainings in practice (or training licenced trainers)

[30] See http://isopa.org/walkthetalk/index.htm
[31] See http://www.alipa.org/index.php?page=alipa-safeguard---we-care-that-you-care

The developed training material (content) will be made available to downstream users as well as to existing (public and/or private) training institutes/education centers/ competence academies (e.g. Shield group, TÜV, DEKRA) to use it. It is still under discussion how this should work in detail, but it is considered that the training institutes or the downstream user(s) should transform the training content into proper education material, train qualified instructors, which in turn would train the workforce. Several options of trainings are considered (e.g. courses on-site or off-site; integration of trainings into the product presentation, E-learning, train the trainer principle) but have not yet been decided.

In general, different training formats are expected (e.g. classroom training, video instructions, supervised work-assignments). However, details have not yet been elaborated.

d) The case of self-employed workers (one-man companies)

The Dossier Submitter considers that self-employed workers will be made aware of their training duties in the communication actions provided at a national level or when purchasing products in the scope of the restriction.

e) Roll-out planning

A time period of approximately 3 to 5 years will be needed for the implementation of the training system in all Member States for all use sectors.

For the communication of the requirements related to this restriction proposal several activities are foreseen which are listed in the Background document (e.g. referencing the existing restriction in an SDS; make it an obligation to meet restriction requirements with a provision in supply contracts). Some of these activities need to be set according to the REACH Regulation.

Evaluation of trainings

According to the Dossier Submitter, the trainer (any certification of the "commissioned expert" who performs the trainings is not specified) or the training centre (if the training is established in a training centre) is responsible for training evaluation and certifying training success whereas the "training working group" is responsible for the training process and the training content.

The testing of the attendees of the training (post-course testing) will be an integral part of the training course. Successful completing will be confirmed by a written document.

Enforcement

The restriction proposal intends primarily to enhance the safe working behaviour of workers (including self-employed workers) who are exposed to diisocyanates by attending trainings in an interval of four years. The second objective is to improve the technical and organisational RMMs in place, according to the requirements listed in Appendix 8 Trainings and Measures. In Appendix 8, the Dossier Submitter describes a three tier system (measure group 1, 2 and 3) which is based on the frequency and duration of potential skin contact and on the likelihood of inhalation exposure due to vapour and/or vapour formation. The technical and organisational measures and the type and duration of the trainings are based on these measure groups.

The training status of companies as well as the implementation of the necessary RMMs can be checked by enforcement as both have to be documented.

RAC and SEAC conclusion(s):

RAC considers that to ensure the practicability of the restriction, the requirements of the restriction proposal need to be mandatory and standardised and effectively communicated throughout the supply chain.

RAC considers it is essential that all downstream users (including those who are not members of industry associations) are aware of the existence of the (new) regulations related to diisocyanates as soon as they have been implemented.

RAC agrees with the Dossier Submitter that building measures upon an established system and sharing common measures and trainings will be very important for the practicality of the proposed restriction.

RAC agrees with the Dossier Submitter that initiatives from the top of the supply chain have to be transmitted to the (end) downstream user(s), in such a way that the same basic standards and competencies are reached for all persons handling diisocyanates (workers and self-employed workers) for uses not to be considered exempted.

According to RAC, it is imperative that formulators of mixtures containing diisocyanates within the EU as well as other downstream users should be consulted for the purpose of the development and update of the training material as it is necessary to know how the substances are used along the supply chain.

RAC stresses that the access to relevant trainings in various languages in all Member States is essential and that the manufacturers/importers should be responsible not only for the elaboration and the quality of the training material but also for its translation.

RAC agrees with the Dossier Submitter that the training material should refer to National Regulations.

RAC notes that as the manufacturers/importers (through the "training working group") are responsible for the training content but the responsibility on the training format lies with the trainers, the different responsibilities might be challenging with regards to the level of quality control of the final training material.

RAC acknowledges that the achievement of such behavioural changes needs special trainings as behaviour in the workplace is generally not easily changed.

RAC acknowledges that the analytical methods regarding the content of (free) diisocyanates in a substance/mixture are adequately specified in the restriction proposal.

Although the Dossier Submitter did not consider the manageability of the proposal, RAC, would like to point out that for the manageability of this restriction it would be crucial that every aspect of the implementation has been worked out in detail with a clear structure and with unambiguous responsibilities. In addition, all of the requirements have to be very well communicated top down (in the supply chain) as otherwise the level of administrative burden for the users but also for the Member States to find out the relevant information might be unbearably high.

RAC considers that the proposed restriction will improve the implementation of existing health and safety rules, in particular by enhancing the capacity of micro and small enterprises to put in place effective and efficient risk prevention strategies.

RAC concludes overall that as all aspects on the implementability and the enforceability have not been fully elaborated the practicality of the proposed restriction has not been completely justified, although in principle the restriction carries a number of merits. This is in line with the Forum advice.

Key elements underpinning the RAC and SEAC conclusion(s):

Although ISOPA and ALIPA represent the major producers of diisocyanates and cover about 80% of the market (based on information from ISOPA/ALIPA), it will be a challenge to communicate the requirements by the restriction throughout the supply chain because a huge number of companies are affected. According to ISOPA, in Western Europe about 200 companies are directly involved in the production of PU (ISOPA 2002), about 4 600 companies are direct customers of these companies, and more than 18 300 companies are producing PU-based final articles. The aliphatic diisocyanate raw material is supplied to about 1 500 formulators, and further used by about 87 000 companies to produce PU-based articles (ALIPA 2006).

In addition, the remaining 20% of the diisocyanate producers should also follow the communication requirements down the supply chain as otherwise one important prerequisite to reach all users of diisocyanates and inform them about the requirements of the restriction will not be fulfilled.

RAC acknowledges that diisocyanates are used on the one hand in many large, medium and small scale industry, on the other hand they are used by professionals (including very small companies) and self-employed workers what makes the situation rather complex. Therefore RAC is of the opinion that it has to be very clear from the beginning of the legal validity of the measure taken (e.g. restriction) who is responsible for:

a. the elaboration, translation and dissemination of the training material,

b. the implementation of the training in each of the Member States;

c. the review and update of the training material.

It is obvious that a clear structure for the implementation of the restriction have to be worked out and that someone has to take responsibility for the training process and content of training as well as for the distribution of the translated training material as otherwise the information and the requirements will get lost somewhere in the supply chain as the whole issue is quite complex. In addition, ideas/claims for improvement of trainings have also be managed in order to implement them in a structured way.

A good enough communication is a crucial issue. With regards to the training process it is particularly of importance that a structured way of communication between the "training working group" and the users of the training material will/can be elaborated as otherwise the success of the training and consequently the risk reduction will be highly questionable.

In REACH, downstream users have the right to make their own uses known to their suppliers by providing them with process details as well as information on the RMMs implemented to minimise the risk. This communication up the supply chain is essential (e.g. for the elaboration of the exposure scenarios) as uses that are not included in any registration dossier after the legal deadline will not be permitted. However, in the present restriction proposal the communication up the supply chain is also necessary to provide the "training working group" with details which should be known to prepare adequate training content (as specific as possible for the uses but also for the companies). The transferability of training to actual

jobsite demands among many other aspects affects the success of the training (Cohen and Colligan, 1998).

The appropriate implementation of the training, and of the implemented RMMs (including proper use of PPE), is the most important prerequisite to reduce exposure to hazardous substances used (e.g. diisocyanates). However, prerequisite for the appropriate use of RMMs is the sufficient knowledge to do so. This is why there is a strong demand for adequate training material particularly with regards to this restriction proposal. According to a statement by the United States Department of Labour *"Employers may find it challenging to institute and maintain effective hazard communication training, either because of a lack of understanding of what kind of training is required, or because of a lack of knowledge on how to conduct effective training"*, there might be a need of at least offering adequate training material to employers. So the efforts to work out the training content by a "training working group" seems to be sensible.

Regarding training measures in general, it is stated in the Background Document that a conceptual model of OSH training might comprise a stepwise process of acquisition of new knowledge on hazards and safe behaviour, modification of attitudes/beliefs, and behavioural change. It is considered that a successful training measure reduces unsafe behaviour and accident risks or exposure to hazardous substances resulting in a lower accident rate or lower rate of occupational diseases. The Dossier Submitter describes different formats of training and their effects. Although these trainings are not comparable to the needs of the training in this restriction proposal, the information provided gives an incomplete overview on the aspects that should be considered in the elaboration of the training content and training formats.

RAC considers that one of the reasons why training obligations in OSH might not have been efficient enough in the past to prevent cases of occupational asthma is that the quality of the trainings was difficult to enforce, as quality requirements had not been implemented in the legislation. Therefore RAC considers the quality requirements set out in the proposal of crucial benefit to this restriction, since they will not only result in a higher quality trainings among others, they may facilitate the enforcement of the trainings and therefore lead to a higher effectiveness.

However, RAC acknowledges that REACH enforcement officers might require some specific training for the enforcement of the restriction, at least at the beginning of the restriction implementation. Besides, in some Member States REACH inspectors might be of a much smaller number than OSH inspectors (e. g. in Austria).

Monitorability

Justification for the opinion of RAC and SEAC

Summary of proposal:

According to the Dossier Submitter the following aspects (broken down in three different time frames, called by the Dossier Submitter "aspects") have to be considered regarding the monitoring of the effectiveness for the restriction proposal.

a) Short term aspects: National enforcement authorities can check if companies have fulfilled their training duties as defined in Appendix 8.

b) Medium term aspects: Member States can organise audits to check if companies have implemented the RMMs as listed in Appendix 8. This could be done in a coordinated union-wide action via SLIC (Senior Labour Inspectors Committee).

c) Long term aspects: The monitoring of the reduction of the number of new cases on occupational asthma which is assumed to be performed by surveys by the Dossier Submitter at regular intervals (e.g. every three years). However, a first conclusion will be drawn on a time scale of eight to ten years.

In addition, the Dossier Submitter calls upon industry to generate longitudinal epidemiological data that allow the evaluation of risks at current workplaces as well as the risk reduction due to this restriction.

RAC and SEAC conclusion(s):

RAC agrees that the restriction should be monitored in three different steps (i.e. aspects) as proposed by the Dossier Submitter.

RAC concurs with the Dossier Submitter that monitoring in the first instance can be performed by tracking the degree of implementation of training throughout the different Member States. In addition, RAC acknowledges that any successful participation of workers in training sessions could be monitored by certificates. RAC assumes that a standardised template would facilitate the acceptation throughout the EU.

RAC points out that the monitoring of the implementation of the RMMs listed in Appendix 8 (medium term aspect) might be much more difficult. RAC considers that a SLIC campaign might be an adequate option for the checking the medium term aspects of the restriction proposal.

RAC agrees with the Dossier Submitter that monitoring the reduction of the number of new cases on occupational asthma (the main goal of this restriction proposal), should be performed on a long run.

RAC notes that the number of reported occupational asthma cases might increase in the first years due to the raised awareness of this issue.

RAC concurs with the Dossier Submitter that large changes with regards to training materials should only be undertaken after the completion of two cycles of trainings. Otherwise the monitored effectiveness could be too much influenced by the revisions of the training material, so that the data would underlie a bias.

RAC appreciates the generation of epidemiological data evaluating a trend in diisocyanate-related occupational asthma incidence.

Key elements underpinning the RAC and SEAC conclusion(s):

Short term aspects:

As the number of occupational asthma cases can only indicate on a longer run a certain trend, monitoring a short term aspect (implementation of trainings) might be sensible.

Medium term aspects:

As the restriction proposal also includes the improvement of some RMMs according to Appendix 8 and as the implementation of these measures is considered to have a positive effect on the risk reduction capacity (as the exposure level would be reduced), these aspects should be monitored as proposed by the Dossier Submitter.

Although a certification attesting the implementation of the requested RMMs could be of help to monitor this aspect, there does not seem to be an adequate certification programme. A certification according to OSHAS 18001 (future: ISO 45001:2018) standard might not be specific enough. In addition, RAC agrees with the Dossier Submitter that transferring government enforcement responsibilities to outside organisations should be avoided.

Long term aspects:

The monitoring of the reduction of new cases of occupational asthma is the most important issue as the number of new cases on occupational asthma was the starting point of the restriction proposal. Monitoring is considered to be performed on the long term (10 to 15 years) on the basis of a regular survey by the Dossier Submitter.

Epidemiological data could be of valuable support to set further actions (e.g. the implementation of exemptions for trainings for some specific uses/tasks).

UNCERTAINTIES IN THE EVALUATION OF RAC AND SEAC

RAC

The main uncertainties in the evaluation of RAC are summarised below.

Summary of proposal:

Uncertainties regarding risk characterisation

The majority of uncertainties related to risk characterisation are recognised and elaborated by the Dossier Submitter (please see section "Uncertainties in the risk characterisation", p. 27-29), and they could lead both to underestimation and overestimation of the risks

Uncertainties regarding evidence whether the implemented risk management measures and operational conditions are not sufficient to control the risk

The Dossier Submitter notes that the published data on the appropriateness/effectiveness of the implemented OCs and RMMs in the diisocyanates industry are very limited, and a clear picture of real workplace situations could not be provided.

Uncertainties regarding risk reduction capacity

There is a severe paucity of data on safety training effectiveness in workers exposed to diisocyanates, and the Dossier Submitter points out that an exact quantitative prediction of the expected reduction rate of cases of occupational asthma is scientifically not possible. The Dossier Submitter bases his assessment on a single study on the safety training effectiveness

in the diisocyanate industry - the motor vehicle repair industry in the UK, although recognises that there are distinct differences between the measures described in this study and the current restriction proposal. Data on training effectiveness for other industry sectors and occupational hazards are also provided in support of the proposed assessment.

RAC conclusion(s):

RAC notes that there are significant uncertainties regarding the risk reduction capacity, the residual risk which remains if exemptions are allowed for products containing diisocyanates in a concentration ≥0.1% w/w for which a very low potential for exposure has been shown, and the implementation and enforcement of the proposed restriction.

RAC nevertheless considers that the implementation and enforcement issues could be solved during the transition period, and that any measure to improve the actual knowledge of workers regarding the safe handling of diisocyanates will have some effects. These effects might not be only related to the use of diisocyanates as such but might also improve the use of dangerous substances in general because the training might raise the awareness of workers´ and self-employed persons regarding the appropriate use of RMMs and the adherence to good hygiene practices and how they might be of benefit for their health. Therefore, taking into account the mentioned limitations, **RAC considers the proposed restriction a justified measure** provided that the "training working group" identified in the restriction proposal is able to provide appropriate training content (specifically addressing all different uses, particularly in micro and small enterprises) and distribute it in a structured way in all the different languages of the Member States down the supply chain.

Key elements underpinning the RAC conclusion(s):

Uncertainties regarding risk characterisation

The uncertainties related to diisocyanate-related occupational asthma incidence, including those raised during Public Consultation, are discussed in the section "Uncertainties in the risk characterisation" (p. 27-29). It was concluded that there are significant uncertainties on the estimation of the annual incidence of diisocyanate-related occupational asthma in the EU, especially regarding the magnitude of under-reporting of occupational diseases in EU Member States, and that both underestimation and overestimation is possible.

Uncertainties regarding evidence whether the implemented risk management measures and operational conditions are not sufficient to control the risk

RAC agrees with the Dossier Submitter that evidence on the effectiveness of implemented RMMs and OCs in reducing the risk related to exposure to diisocyanates is rather limited at workplaces throughout the EU, but that nevertheless, according to open literature and other open sources, deviations from safe working practices are still present, and significant number of occupational asthma cases is still recorded across the EU. RAC notes that particularly micro and small enterprises (SMEs) are known to have difficulties in complying with occupational health and safety (OSH) regulations due to lower expertise and financial resources.

Uncertainties regarding exemptions for products containing diisocyanates in a concentration ≥0.1% for which a very low potential for exposure has been shown

The Dossier Submitter considers that there are situations (mainly in the construction sector) where the potential risk of handling diisocyanates in the form of ready-to-use products, even if they contain diisocyanates in a concentration ≥ 0.1% w/w, may be considered to be so low that present OSH requirements would be sufficient for safe use and the prevention of

respiratory sensitisation. Nevertheless, they point out that these products are not "absolutely safe", and residual risk remains.

This residual risk cannot be quantified at the present moment due to lack of data on exposure and health effects in workers exposed to products that would be eligible for exemptions according to the restriction proposal. In order to alleviate these uncertainties and decrease the residual risk, RAC proposes a number of modifications to the Dossier Submitter's proposal regarding the exemption process.

However, RAC considers that although this pragmatic approach could lead to long-term benefits for the workers' health (e.g. development and use of products with "very low" potential of exposure, including products with decreased diisocyanate concentration; more efficient implementation of the proposed restriction, etc.), uncertainties remain:

- It is still not clear which different types of uses might be considered in future for exemptions.
- For dermal exposure assessment, a Dermal Assessment Tool is proposed ("dermal banding tool") which has been developed by the Dossier Submitter and an industry expert group on the basis of multiple sources, including Marquart et al. (2003), Stoffenmanager version 6, TRGS 401, and ECETOC TRA. Although it is stated in the Background Document (Appendix 5) that a preliminary evaluation of this tool was done by the German BG-BAU and the German Adhesives Association, and is reported to be rather conservative, the results of the validation were not provided (e.g. there is no information on sensitivity analysis for important input parameters).
- Although dermal contact might be minimised for those products that may be exempted there is a high uncertainty regarding whether a regular OSH training would be enough to point out the important role of a dermal contact in respiratory sensitisation.
- Particularly in the construction area, awareness of the need of skin protection and therefore the correct use of PPE (e.g. adequate gloves and working clothes) might not be as high as in other industry sectors (e.g. motor vehicle refinish). In addition, access of workers to adequate washing facilities might sometimes be rather difficult for this sector.

Uncertainties regarding risk reduction capacity

RAC is aware of the high uncertainty related to the estimation of risk reduction capacity, but is also aware that due to the lack of data on training effectiveness in sectors other than MVR (motor vehicle refinish) and countries other than UK, more precise estimate is hard to achieve before implementation of the restriction. Nevertheless, although data for other health risks and industries show a wide range of effectiveness (less than 10% to more than 80%), several studies related to non-diisocyanate respiratory and skin sensitisers and irritants indicate that efficiency in the range proposed for this restriction proposal is not impossible to achieve. These uncertainties are to a certain extent alleviated by the fact that the Dossier Submitter stated in the Appendix 8 "Trainings and Measures" an obligatory content of training according to Measures groups, and took into account factors known to positively influence behavioural changes in training attendees.

In conclusion, remaining uncertainties regarding training effectiveness are high, but are not likely to be quantified or reduced before implementing the proposed restriction.

Uncertainties regarding alternatives

Information on human health and environmental hazards of alternatives are very limited, except for epoxy resins, for which hazard properties are well studied. Especially for modified silanes, which present the most promising alternative, already in use (although limited to selected uses), health risks are still not well defined according to available literature.

Uncertainties regarding implementability and enforceability

- Communication of the requirements posed by the restriction proposal, both up and down the supply chain, is a crucial issue in this restriction, and could be challenging due to a huge number of affected companies, especially micro and small enterprises and self-employed workers. While for the communication of the requirements related to this restriction proposal several activities are foreseen and are stated in the Background document (A.3.1.6.5. Aspects of practicability, Organising the trainings in practice (or training licenced trainers)), it is still not clear enough how the process should work on the whole. Nevertheless RAC points out that according to Article 32, REACH, there is a duty to communicate information down the supply chain.
- The requirements with regards to this restriction proposal should be included in the safety data sheet and/or in the instructions of use. However how exactly this should be done has not been elaborated yet.
- The status of a "training working group", a not-for-profit body representing industry and the other Stakeholders which will have the final responsibility for the development of the training process and content, has not yet been determined.
- While the development and evaluation of the training content is foreseen to be centralised (as a responsibility of a "training working group"), transforming the training content into proper education material and training of qualified instructors is proposed to be performed by the training institutes or downstream user(s). This separated responsibility for the training content and the material will, on one hand allow to take into account national legislation and national (including cultural) specificities, as well as the characteristics of the actual application, but on the other hand is expected to decrease the level of quality control of the final training material, as well as of harmonisation of trainings across the EU. RAC considers that these uncertainties could be alleviated by developing content in a modular form, which then requires only minimal adaptation from the training institutes or downstream user(s). RAC also recommends that the Member States have a role in the development of the training material and ensure that the specificities at the national level are taken into account.
- The certification of the "commissioned expert" who performs the trainings for managers and qualified trainers is not yet specified.
- It is unclear which type of different training formats (e. g. classroom training, video instructions, supervised work-assignments) will be available as details have not yet been developed.
- Regarding mutual recognition for training completeness, it is unclear how this process should look like. E.g., should the certificate always be at least bi-lingual – in official language of the Member State and in English language? To solve issues like this, the Dossier Submitter recommends establishing an advisory board where competent independent outsiders have the possibility to provide input, but details regarding this board (e.g. who will constitute it, and at which EU level) are not yet defined. It could

also be considered that Member States would participate in the advisory board to facilitate the development of the training material.

Enforceability

- RAC acknowledges that REACH enforcement officers might face significant challenge related to enforcement of this restriction proposal. Particularly the inspection of the appropriateness of the implemented RMMs might be difficult for them as they do not have a special expertise in this field. While in some Member States labour inspection services might also have authority to enforce Annex XVII of REACH, in most Member States the inspection services with authority for REACH inspections are not at all linked to labour inspection and therefore do not have the expertise for such inspections.
- Enforcement of exemptions related to the ready-to-use products before placing them on the market might not be possible as local enforcement authorities might not be able to check the assessment of products eligible for an exemption. However, in case the evaluation of an exemption would be done by an independent body with adequate expertise in the field, enforcement by local enforcement bodies would be possible because they would only have to check the evaluation certificate provided by the independent body.

To summarise, RAC considers that as the Dossier Submitter has not yet elaborated all issues related to a full implementation of the restriction proposal (e.g. dissemination of the training content), several uncertainties remain. Nevertheless, RAC acknowledges that the participation of the Member States in the development of the training material and the implementation of the training system would decrease the present uncertainties.

SEAC

Summary of proposal:

See the opinion of SEAC.

SEAC conclusion(s):

See the opinion of SEAC.

Key elements underpinning the SEAC conclusion(s):

See the opinion of SEAC.

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ANNEX

Conditions of the restriction

[Diisocyanates with the chemical structure, O=C=N-R-N=C=O, where R is an aliphatic or aromatic hydrocarbon unit of unspecified length]

1. Shall not be used as substances on their own, as a constituent in other substances or in mixtures for industrial and professional use(s) after dd.mm.yyyy (date of entry into force plus 1 (or 2) year(s)), unless:

    a) the cumulative concentration of diisocyanates in the substance or mixture is less than 0.1% by weight, or

    b) measures are implemented according to paragraph 9 and

    c) adequate training is successfully completed according to paragraph 8 by the worker or self-employed worker handling substances according to paragraph 1.

2. Shall not be placed on the market as substances on their own, as a constituent in other substances or in mixtures for industrial and professional uses after dd.mm.yyyy (date of entry into force plus 1 (or 2) year(s)), unless the:

    a) cumulative concentration of diisocyanates in the substance or mixture is less than 0.1% by weight, or

    b) the supplier ensures that the recipient of the substance(s) or mixture(s) is provided with information on the requirements of paragraph 1 b and c.

3. Paragraphs 1 and 2 shall not apply to those use(s) where the supplier (manufacturer, importer or formulator) ensures that the specific use of a ready-to-use product[32] containing ≥ 0.1% diisocyanates in the substance or mixture leads to very low risk of exposure for the dermal and inhalation route. The relevant section of the Safety Data Sheet shall be updated accordingly.

In this context very low risk of exposure means that:

i. aerosols are not generated, and

ii. warming or heating the substance or mixture above 45 °C is not required, and

iii. the sum of the concentrations for all diisocyanates measured during air monitoring shall be < 1 ppb as a time-weighted average of 8 hours, and

[32] A ready-to-use product includes the diisocyanate(s) as a substance or mixture in the ready-to-use form, with other auxiliary substances, packaging and application devices.

iv. very low dermal exposure is demonstrated by a recognised dermal assessment tool.

4. Manufacturers and importers of diisocyanates which are not exempted according to paragraph 2a or paragraph 3 shall co-operate to:

   a) develop a minimum set of training material in accordance with paragraph 8, supported by information provided by downstream user;

   b) ensure that adequate training material is available to the recipients of the substance(s) or mixture(s) in an official language of the Members State(s) where the substance(s) or mixture(s) is placed on the market;

   c) review and update the training material after a maximum of 8 years, or without delay if new information, which may affect the risk management measures, becomes available and inform the recipients accordingly..

5. Users[33] of diisocyanates which are not exempted according to paragraph 1a or paragraph 3 and their employer shall keep documentary evidence to demonstrate successful completion of a training according to paragraph 8.

6. Proof of successful completion of any training according to paragraph 8 taken in one Member State shall be recognised in all other Member States.

7. The training according to paragraph 8 should be provided by trainers who have undergone specific training covering at least the aspects set out in part 1 of Appendix X.

8. The content of the training according to paragraph 1c should cover:

   a) at least the aspects set out in part 2 of Appendix X;

   b) at least the additional aspects set out in part 3 of appendix X for the following uses: Handling open mixtures at ambient temp. (incl. foam tunnels); spraying in a ventilated booth; application by roller; application by brush; application by dipping and pouring; mechanical post treatment (e.g. cutting) of not fully cured articles which are not warm anymore; cleaning and waste; and any other uses with similar risk of exposure for the dermal and inhalation route.

   c) At least the additional aspects set out in part 4 of appendix X for the following uses: Handling incompletely cured articles (e.g. freshly cured, still

[33] For the purposes of this entry users means workers and self-employed workers undertaking tasks and/or subtasks with diisocyanates on their own, as a constituent in other substances or in mixtures for industrial and professional use(s) or supervising these tasks and/or subtasks.

warm); foundry applications; maintenance and repair that needs access to equipment; open handling of warm or hot formulations (> 45 °C); spraying in open air, with limited or only natural ventilation (includes large industry working halls) and spraying with high energy (e.g. foams, elastomers); and any other uses with similar risk of exposure for the dermal and inhalation route.

Users performing various tasks shall complete the training for the highest requirements for his working tasks according to paragraph 8.

The training should be carried out at least every 4 years.

9. For any use of diisocyanates which is not exempted according to paragraph 1a or paragraph 3, the user shall ensure that exposure is minimised[34]. Minimisation in this context means at least that the conditions should include:

   a) the additional measures set out in part 2 of Appendix Y for the following uses: Handling open mixtures at ambient temp. (incl. foam tunnels); spraying in a ventilated booth; application by roller; application by brush; application by dipping and pouring; mechanical post treatment (e.g. cutting) of not fully cured articles which are not warm anymore; cleaning and waste; any other uses with similar risk of exposure for the dermal and inhalation route.

   b) the additional measures set out in part 3 of Appendix Y for the following uses: Handling incompletely cured articles (e.g. freshly cured, still warm); foundry applications; maintenance and repair that needs access to equipment; open handling of warm or hot formulations (> 45 °C); spraying in open air, with limited or only natural ventilation (includes large industry working halls) and spraying with high energy (e.g. foams, elastomers); and any other uses with similar risk of exposure for the dermal and inhalation route.

10. This restriction should apply without prejudice to other Community legislation on workers protection.

[34] In this restriction minimised means compliance with at least the conditions set out in part 1 of Appendix Y.

Appendix X

Part 1: Trainers' training

a) Basic information on restriction, training requirements and implementation.

b) Measuring devices and their limitations

c) Deposition and distribution

d) Protection of bystanders

e) PPE needed and its limitations

f) Storage requirements

g) Behaviour-based safety management

h) Emergency plans

i) Management of Change

j) Certification requirements for attendees.

Part 2: Basic training of workers (employed and self employed)

a) Chemistry

b) How can you be exposed

c) Signs of sensitisation

d) Odour of hazard

e) Importance volatility /…something missing??

f) Viscosity/ Temperature / Mol. Wt

g) Personal Hygiene

h) PPE needed and its limitations

i) Clothing

j) Risk of dermal contact

k) Risk of exposure to not fully cured polyurethane

l) Skin protection scheme

m) Ventilation

n) Cleaning , leakages, maintenance

o) Discarding empty packaging

p) Protection of bystanders

q) Identification of critical handling stages

r) Specific national code systems (if applicable)

s) Behaviour-based safety

t) Certification requirements for attendees.

Part 3: Intermediate training of workers (employed and self employed) (classroom training)

a) PPE needed and its limitations

b) Behaviour-based aspects

c) Maintenance

d) Management of change

e) Evaluation of safety instructions

f) Risk in relation to application process used

g) Certification requirements of attendees.

Part 4: Advanced training of workers (employed and self employed) (classroom training)

a) Feedback

b) Additional certification

c) Spraying in open air

d) Open handling of hot or warm formulations (>45°C)

e) Certification requirements for attendees.

In the context of part 3 and part 4, classroom training could mean on the job training or training in a work related environment. The classroom training should have a minimum duration of four hours.

Appendix Y

Part 1: General conditions of use to ensure minimisation of exposure

- RMMs as defined in the supporting documents (e.g. in exposure scenarios in eSDS for substances, or measures prescribed in SDSs for mixtures) are in place.
- Application equipment is regularly maintained at least once per year.
- Equipment critical for safety protection (e.g. temperature indicators, overheating safety switches, ventilation systems) is working according to specification and has been checked according to predefined schedules. This shall be proven by relevant documentation.
- If heated application systems are used, these are equipped with an overheating switch-off protection that will bring the equipment temperature to a safe level.
- If exhaust equipment is used (either fixed or mobile) this is constructed in such a way that fresh air replaces exhaust air and that nobody is exposed to exhaust air.
- Facilities, machines and tanks shall be constructed and arranged in such a way that also when an equipment part fails, uncontrolled release of isocyanate at the workplace is prevented.
- Where required (e.g. in (e)SDS) exhaust equipment is available.
- Emergency kits (cleaning small spills, splashes) are available.
- Cleaning solutions, cured waste and residual diisocyanate shall only be stored in dedicated areas, in separate containers outside the normal working area.
- Organisational measures are implemented to ensure engineering controls are used and maintained.
- Companies have documented proof that their workers have been trained according to the requirements of this restriction.
- Workers are offered to undergo a medical consultation when taking up work and offered follow-up consultations after that yearly. The offer for such a consultation and the decision of the worker shall be documented.
- Companies have documented the risk for neighbouring workplaces and bystanders both during normal use and during emergencies.
- Companies have tools or implement systems that prevent non-workers from entering the work area when in use and during specified time of restricted access, unless accompanied by a person trained according to the specifications of this Appendix. Access shall only be permitted with PPE specified for the ongoing work stage.

- Companies have a check and maintenance schedule for their ventilation equipment.
- Written instructions are available for the performed tasks.
- Personal protective measures.
- Protective equipment has been defined and has been made available dependent on product properties and use.
- Sufficient skin cleaning and conditioning materials are made available.

Part 2: Additional technical measures

- Qualitative detection tools (e.g. wiping tissues) for detection of deposited isocyanate are available.
- Companies provide evidence that technical equipment is sufficient for risk management.
- Organisational measures.
- Effectiveness of protection measures should be regularly checked and documented.
- If open systems are used, reasons for not using closed systems have been documented. This includes steps such as maintenance and repair.

Part 3: Additional organisational measures

- Quantities available during use and quantities stored are limited to the amount necessary to allow a smooth workflow.
- The emergency planning is appropriate for release of large amounts of isocyanate. Appropriate protection equipment for first aiders and/or technical personnel is available.
- Documented work procedures exist for the task carried out. These list specific precautions needed (e.g. installation of LEV, the sealing of rooms to prevent uncontrolled emissions).
- Define and communicate a minimum time to re-entry of the working area to avoid exposure of other workers, and a minimum time to re-occupation of rooms by persons from the general population, according to information in SDS.
- Tools, including written instructions, are made available to those concerned in order to communicate and control blocking of workspaces for bystander access.
- Companies have introduced a behavioural based management system for performance improvement. For professionals a Behaviour Based Performance Program (BBP) is part of training.

- Biomonitoring options are offered.