COMMENTS AND RESPONSE TO COMMENTS ON OEL: PROPOSAL AND JUSTIFICATION

Comments provided during consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the consultation have been provided in full to the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the public consultation and are also published together with the opinion (after adoption) on ECHA's website.

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Last data extracted on 17.12.2019

Substance name: diisocyanates
EC number: -
CAS number: -

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
12.12.2019	Sweden	The Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (NEG)	International NGO	1

Comment received

See attached document for comments

ECHA note – An attachment was submitted with the comment above. Refer to public attachment NEG comments ECHA Diisocyanates 2019.pdf

ECHA/RAC response

General comments

- In support of the Commission's request to deliver an opinion within a certain timeline, ECHA prepared a scientific report, on which parties were invited to submit comments. These comments are taken into account during the opinion development and the further aligment of the report into an Annex of the opinion. In this RAC process a second consultation on its opinion is not included. However, RAC regular- and occasional stakeholders are invited to comment during the RAC opinion development stage.

Comments concerning Existing OELs

The tables on existing OELs have been modified as suggested by the comments (Norwegian OELs added, corrections to Swedish OELs implemented and notations added)

Comments concerning animal and human data and mechanistic considerations:

- Discussion on mechanistic considerations and potency issues has been included in the Annex.
- The strengths and weaknesses of both animal and human data have been further elaborated. The reasons why neither of these data allow identifying a threshold are

outlined in the RAC opinion and further described in its Annex. As regards the issue of peak exposures, it is to be noted that now also a 15 minute STEL value is proposed
- Along with the animal data, human data related discussion has been included when justifying the NCO group approach.
- The Daniels study as well as the individual studies included therein were further assessed. For reasons outlined in the Annex neither the Daniels study nor individual studies therein were considered suitable for deriving an exposure-response relationship.
- Editorial changes have been made based on your suggestions.

Date	Country	Organisation	Type of Organisation	Comment number
16.12.2019	Belgium	Europur and Euromoulders	Industry or Trade Association	2

Comment received

Please see attached detailed response to the ECHA Scientific Report on Diisocyanates by Europur and Euromoulders. In addition, Prof Dr Thomas Schupp prepared a submission based on his own work on the subject, which is also attached.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Europur PC Input and Complementary Submission Prof Dr Schupp.zip

ECHA/RAC response

Information about the current practice of using direct reading equipment at the workplaces and the limit of quantification of this type of equipment has been added to the document.

A recommendation concerning medical surveillance is now made and using the Pisati et al study as a justifying agument.

Text on the complementary nature of the OEL proposal and Restriction proposal has been added underlining the need to prevent also peak and dermal exposure and the importance of training. Also a STEL value based on human data is now proposed.

The Daniels study as well as the individual studies included therein were further assessed. For reasons outlined in the Annex neither the Daniels study nor individual studies therein were considered suitable for deriving an exposure-response relationship.

Date	Country	Organisation	Type of Organisation	Comment number
16.12.2019	Belgium	European Furniture Industries Confederation	Industry or Trade Association	3

Comment received

In the furniture industry, PUR hotmelt adhesives based on diphenylmethane diisocyanate (MDI) are mainly used in wood and wood-based coatings, the use of adhesives and in the manufacture of upholstered furniture.

In Germany, there is an OEL value of 0.05 mg/ m³ according to TRGS 430 or TRGS 900, which has always been reliably undercut in corresponding investigations of various areas

of application and various workplaces. Therefore this value can be implemented in practice on the one hand and on the other hand it also stands for the state of the art in technology, occupational medicine and industrial hygiene.

Analogous to the experiences in the field of wood dust, attention should be paid not only to the pure limit value consideration but also to a uniform measuring method and evaluation.

However, prior to setting an OEL at EU level, there is a need to put in place a harmonised method for sampling and analysis for this family of substances.

ECHA/RAC response

- The existing OEL values, including the German OEL value, are taken into consideration in the Annex.
- More information on the state of art and the challenges in exposure moniting (air and dermal) is now added

Date	Country	Organisation	Type of Organisation	Comment number
16.12.2019	Germany	Blickle Räder+Rollen GmbH u. Co.KG	Company Manufacturer	4

Comment received

Dear Ladies and Gentlemen,
After reading 'The ECHA Scientific report for evaluation of limit values for diisocyanates at the workplace', we would like to give the following comments:
1) ECHA has not proposed a specific OEL value, but recommends only 3 epidemiological studies to the RAC to derive a value in the further process. Extensive further studies have not been considered. In our view, this procedure is not appropriate as controlled circumstances over the whole observation period – that are necessary to draw firm conclusions – only exist in animal studies.
Epidemiological studies carried out on human beings have the disadvantage that certain situations as being subject to peak exposures or skin contact may not be captured in the study.
2) ECHA concludes from the epidemiological studies that one cannot derive a biological limit value, but must take a risk-based approach.
In our opinion, both studies on animals and human beings allow the deduction of a limit value.
3) ECHA does not make any differentiation between different isocyanates.
From our perspective, different diisocyanates have a different potential to trigger sensitizations. Having said that, we don’t consider a common OEL-value for all diisocyanates scientifically justified.
In principle, the discussion about lowering the OEL has to be done be very careful and has to include all scientific facts, since lowering the OEL would existentially weaken the competitiveness of polyurethane production in Europe. Some applications or business could come to a stop.
In our opinion, this duty of care, to recommend the broadest possible database for this existential question of the entire PU production in Europe, was not taken into account in the present report
We therefore demand:
a) to take into account all relevant studies and experiences regarding this topic.
b) Only lower the OEL if new scientific evidence and hard facts make this absolutely necessary

Kind regards
Rolf Hölle

ECHA/RAC response

1) The studies identified by RAC ECHA are selected on the basis of the quality of the studies
2) The studies identified do not allow identification of a threshold below which there is no residual risk.
3) The available evidence does not allow a quantitative assessment of differences in potency to cause health effects for the different di-isocyanate molecules.

In general, the strengths and weaknesses of both animal and human data have been further elaborated. The reasons why neither of these data allow identifying a threshold are outlined in the RAC opinion and further described in its Annex. It is to be noted that now also a 15 minute STEL value is proposed. The socio-economic aspects of setting OEL values do not fall under the mandate of RAC opinion, they will be considered under the consequent steps of decision-making according to Directive 98/24/EC.

Date	Country	Organisation	Type of Organisation	Comment number
16.12.2019	Germany		MemberState	5

Comment received

In its scientific report ECHA uses the description and the evaluation of the epidemiological studies on diisocyanates from the Annex XV restriction report prepared by Germany in 2016 (BAuA, 2016), adding new information and recent studies. ECHA largely follows the argumentation of the restriction report concerning the derivation of exposure limits for diisocyanates. This concerns the hypothesis that the NCO group of the isocyanates plays the relevant role for the toxicological effect. In case an eligible study for dose-response assessment would be found, use of this data for the whole group of diisocyanates could be considered. It also concerns the consideration that an exposure limit value should prevent the induction of sensitisation in the first place, which is currently not possible due to missing reliable markers. For elicitation, it is also not possible to derive a safe threshold. The German restriction report concluded in 2016, that the uncertainties in the derivation of a DNEL or DMEL from the animal or human studies were too high to provide a reliable value. The report stressed that for respiratory sensitizers also the REACH guidance recommends a qualitative approach to risk characterisation. Concerning the human studies a major point raised in the restriction report was the fact that dermal exposure as well as inhalation peak exposure likely contribute to the induction of sensitisation, but cannot be appropriately quantitatively assessed to date.

Therefore, every association between diisocyanate air concentration and asthma incidence observed in an epidemiological study contains the uncertainty that the incidence was not solely caused by the measured air concentration, but may have been caused to a certain part by peak inhalation exposure or dermal exposure. This also means, that meeting an inhalation exposure limit value may not be sufficient to protect from sensitisation, but that peak exposures and dermal exposure have to be reduced, too. This was one explanation Germany proposed with respect to the issue that at EU workplaces despite existing OEL still occupational asthma cases occur (besides the possibilities that the inhalation OEL may be too high and that actual exposure may be higher than measured).

ECHA recommends to RAC to further develop the approach for deriving an exposure-response relationship (ERR), based on a weight of evidence assessment of three identified

key documents/reports presenting exposure responses for respiratory sensitisation. The derivation of risk-based values, as known for carcinogens in member states like Germany and in the EU (DMEL), is not yet established for respiratory sensitizers on a European level. However, a risk-based approach is in place in the Netherlands. Two of the ERR to be considered by RAC are from the recent paper of the Dutch Expert Committee on Occupational Safety (DECOS) (DECOS, 2018) and are based on single studies on HDI and TDI, respectively (Collins et al., 2017; Pronk et al., 2009; Pronk et al., 2007). The third ERR is provided by a paper by Daniels et al., which summarises several studies on TDI (Daniels, 2018). The German CA considers the risk-based approach using epidemiological data as the most appropriate approach for diisocyanates. However, the following further aspects (besides the uncertainties named above) should be considered:
• First of all, when describing an ERR, the relevant outcome has to be defined. The endpoint of interest here is respiratory sensitisation, which finally leads to the clinical picture of allergic asthma in humans. Asthma diagnosis differs between the studies and may have an impact on the observed prevalence/incidence.
• The difference between the DECOS values and the value by Daniels et al. (2018) has to be analysed. It is likely that the higher risk found by DECOS as compared to Daniels et al. is due to the different approaches using different depth of investigation.
• A DNEL or DMEL or other exposure limit value has to be defined concerning its protection goal. An acceptable excess risk target level is not yet established for sensitizers in the EU. To be precise, the value to be derived would have to be an estimate of the human dose in a predefined time-frame of exposure/exposure scenario (e.g. 8 h/d, 40 working years, for workers) associated with protecting a defined percentage (e.g. 95 or 99 %) of the population (for most scenarios: healthy workers/professionals of both sexes, but potentially including children or elderly persons for some scenarios with bystander involvement) from a predefined added sensitisation risk (e.g. of 1 % or more) when exposed to diisocyanates in the workplace. The DNEL should meet these protection goals with predefined confidence (e.g. 95 or 99 %).

As diisocyanates also possess irritating properties and because peak exposures may contribute to the risk of sensitisation, it is necessary to also derive a Short Term Exposure Limit (STEL). ECHA proposes that the STEL should not be more than 5 times higher than the OEL, deriving this factor from the ratio of OEL and STEL provided by other bodies. The German CA recommends, that a justification should not only be based on using a ratio proposed by others, but a justification based on all available data should be provided.

BAuA (2016): ANNEX XV RESTRICTION REPORT, PROPOSAL FOR A RESTRICTION, SUBSTANCE NAME(S): DIISOCYANATES, date: 06 October 2016

Collins J.J., Anteau S., Conner P.R., Cassidy L.D., Doney B., Wang M.L., Kurth L., Carson M., Molenaar D., Redlich C.A., and Storey E. (2017): Incidence of Occupational Asthma and Exposure to Toluene Diisocyanate in the United States Toluene Diisocyanate Production Industry. J Occup Environ Med 59 Suppl 12, S22-S27. DOI: 10.1097/JOM.0000000000000890

Daniels R.D. (2018): Occupational asthma risk from exposures to toluene diisocyanate: A review and risk assessment. Am J Ind Med 61 (4), 282-292. DOI: 10.1002/ajim.22815

DECOS (2018): Di- and triisocyanates. Health-based recommendation on occupational exposure limits. Report to the State Secretary of Social Affairs and Employment. No. 2018/20. The Hague, Health Council of the Netherlands.

Pronk A., Preller L., Doekes G., Wouters I.M., Rooijackers J., Lammers J.W., and Heederik D. (2009): Different respiratory phenotypes are associated with isocyanate exposure in

spray painters. Eur Respir.J 33 (3), 494-501. DOI: 09031936.00091408 [pii];10.1183/09031936.00091408 [doi]

Pronk A., Preller L., Raulf-Heimsoth M., Jonkers I.C., Lammers J.W., Wouters I.M., Doekes G., Wisnewski A.V., and Heederik D. (2007): Respiratory symptoms, sensitization, and exposure response relationships in spray painters exposed to isocyanates. Am J Respir Crit Care Med 176 (11), 1090-1097. DOI: 10.1164/rccm.200702-215OC

ECHA/RAC response

- The outcome definitions are given for the Pronk et al and Collins et al studies both the Annex and the opinion itself. It should be noted that sensitization would be the ideal endpoint for consideration. However, as argued in the Annex, different mechanisms likely play a role and explain the occurrence of respiratory allergies. No single test exists that captures sensitization through different mechanisms.
- The Daniels study as well as the individual studies included therein were further assessed. For reasons outlined in the Annex neither the Daniels study nor individual studies therein were considered suitable for deriving an exposure-response relationship. The Daniels study evaluated exposure response relations across different studies. This approach was not considered adequate for instance because different individual studies evaluated different endpoints and had different study designs, among other reasons. The studies used did not present internal exposure-response relations which could be used in an alternative evaluation.
- The opinion extensively discusses uncertainties resulting from dermal exposure and peak exposures. It is concluded that since available data do not allow to quantitatively differentiate the contributions of air and dermal exposure, RAC considers that any limit value intended to protect workers from diisocyanate-related asthma should be based on data that inherently take into account both routes of exposure.
- As pointed out in the comment, there is no EU level agreement on acceptable residual risk for sensitisation. The opinion does not propose identifying a threshold 8-hour TWA OEL. Instead, an exposure-response relationship is established describing the excess risk as a function of average exposure level. This relationship is recommended to be used according to the procedures set by the Chemicals Agent Directive 98/24.
- A 15 minute STEL value is now proposed together with a justification

Date	Country	Organisation	Type of Organisation	Comment number
22.11.2019	Belgium	ISOPA Aisbl; ALIPA Aisbl	Industry or Trade Association	6

Comment received

Please see the documents attached as zip file.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment ISOPA_ALIPA_Documents.zip

ECHA/RAC response

Comments on uses and analytical methods

- ISOPA/ALIPA information on the use of diisocyanates has been addressed in the Annex.

- ISOPA/ALIPA comment concerning analytical methods for diisocyanates (number 4) have been addressed in Annex I. However, the costs of the methods are not taken into account in this document.

Comments concerning animal and human data and mechanistic considerations:

- More details on animal data on respiratory sensitisation and irritation, and interpretation of such data have been included in the Annex.
- Risk factors related to the development of occupational asthma are discussed in the Annex.
- The strengths and weaknesses of both animal and human data has further been elaborated. The reasons why neither of these data allow identifying a threshold are outlined in the RAC opinion and further described in its Annex. As regards the issue of peak exposures, it is to be noted that now also a 15 minute STEL value is proposed
- Along with the animal data, also human data related discussion has been included when justifying the NCO group approach.
- The Daniels study as well as the individual studies included therein were further assessed. For reasons outlined in the Annex neither the Daniels study nor individual studies therein were considered suitable for deriving an exposure-response relationship.
- The methodological issues raised for Collins et al study and the related uncertainties are now further described e.g. as regards peak exposure assessment, risk as function of time since start of exposure, consideration of altenaive models, restrictive pattern observed by Wang et al. Also the methodological aspects of the Pronk et al studies are further described.
- The rationale towards the Ott studies and reviews from early 2000s and the related methodological uncertainties is elaborated more.
- The Lynch et al (2018) paper is now described.
- Text on the complementary nature of the OEL proposal and Restriction proposal has been added underlining the need to prevent also peak and dermal exposure and the importance of training. Also a STEL value based on human data is now proposed. A recommendation concerning medical surveillance is also made.
- The challenges inherent to identifying a threshold from human data alone or in a weight of evidence approach together with animal data are further described.

Date	Country	Organisation	Type of Organisation	Comment number
15.12.2019	Austria	Austrian Workers' Compensation Board	National Authority	7

Comment received

See attached file for further Explanation on: Diamines in urine do not provide evidence of dermal absorption of diisocyant; Respiratory sensitization is likely and often induced by skin contact; avoidance of skin contact must be a top priority; NCO group Approach is inappropriate; reasons to refuse biological limit or guidance value; "Skin notation" is inadequate.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment ECHA_Isocyanate-OEL_comments.pdf

ECHA/RAC response

- The justification on not to propose a Biological Limit Value is added in the Annex. However,in the Annex a Biological Guidance Value is now proposed at the limit of quantification for relevant diisocyanate metabolites (diamines) in urine. More justification is added in the Annex in section on 'Mode of action considerations'
- More justification on the proposed notations is added in the Annex..

Date	Country	Organisation	Type of Organisation	Comment number
15.12.2019	Germany	Deutsche Gesetzliche Unfallversicherung	National Authority	8

Comment received

In Deutschland wurden für monomere Diisocyanate bereits eine Reihe von Arbeitsplatzgrenzwerten in der TRGS 900 festgelegt. So für Hexamethylen-1,6-diisocyanat 0,035 mg/m3, 2,2'-Methylendiphenyldiisocyanat 0,05 mg/m3, 4,4'-Methylendiphenyldiisocyanat 0,05 mg/m3, Methylisocyanat 0,024 mg/m3, 4-Methyl-m-phenylendiisocyanat 0,035 mg/m3, 2-Methyl-m-phenylendiisocyanat 0,035 mg/m3, 1,5-Naphthylendiisocyanat 0,05 mg/m3, Phenylisocyanat 0,05 mg/m3. Die Ableitung dieser Grenzwerte beruht auf den Reizwirkungen dieser Stoffe, nicht auf deren sensibilisierenden Wirkungen.

Wir teilen die Meinung der ECHA, dass die Ableitung einer unteren Expositions-grenze, zur Verhinderung der Sensibilisierung und damit der Entstehung von Asthma, mit den aktuell zur Verfügung stehenden wissenschaftlichen Daten, nicht möglich ist. Dies gilt vor allem für Beschäftigte, die bereits sensibilisiert sind und/oder schon ein Asthma entwickelt haben. Die ECHA schlägt deshalb abweichend von den in Deutschland festgelegten Arbeitsplatzgrenzwerten keine Grenzwerte vor. Diese Position nehmen wir zur Kenntnis.

Neben den Arbeitsplatzgrenzwerten für monomere Diisocyanate wurde in Deutsch-land ein Expositionsleitwert (ELW) von 0,018 mg/m³ eingeführt, mit dem die Summe aller reaktionsfähigen NCO-Gruppen (TRIG - Totalkonzentration Reaktiver Isocyanat-Gruppen) von Monomeren und Polymeren in der Luft am Arbeitsplatz beurteilt werden kann. Eine Überschreitung des ELW deutet auf eine gesundheitsschädliche Exposition durch Diisocyanate am Arbeitsplatz hin, weil die toxische Wirkung von den freien NCO-Gruppen der Diisocyanate ausgeht. Bei Einhaltung des ELW sind auch die Arbeitsplatzgrenzwerte für die monomeren Diisocyanate eingehalten (TRGS 430).

Der in Deutschland in der TRGS 430 gewählte Ansatz zur Bestimmung der Exposition von Diisocyanaten in der Luft am Arbeitsplatz über die Konzentration der NCO-Gruppen, wurde von verschiedenen Ländern in der EU aufgegriffen. Die ECHA beschreibt verschiedene Studien, die versuchen über Dosis-Wirkungs-Beziehungen den Zusammenhang zwischen der Konzentration der NCO-Gruppen und dem Risiko der Auslösung von Asthma bzw. der Sensibilisierung der Atemwege zu beschreiben. Dabei wurden Fälle mit Expositionen gegenüber Toluol-2,6-diisocyanat (2,6-TDI), Toluol-2,4-diisocyanat (2,4-TDI) und Hexamethylen-1,6-diisocyanat (1,6-HDI) untersucht. Es ergaben sich drei verschiedene Ansätze, die aufgrund der unterschiedlichen Methodik nicht miteinander vergleichbar sind. Die ECHA kam zu der Empfehlung, alle drei Ansätze weiter zu verfolgen. Diese Empfehlung unterstützen wir seitens der DGUV.

Überschreitungen der heute geltenden Grenzwerte für Diisocyanate kommen nach unserer Kenntnis bei den uns bekannten Anwendungen nur in Ausnahmefällen vor. Ein Grund dafür ist, dass die Dampfdrücke vieler Diisocyanate sehr niedrig sind und bereits wirksame Schutzmaßnahmen umgesetzt wurden. Nur Hexamethylen-1,6-diisocyanat weist mit 0,7 Pa bei 20 °C einen relativ hohen Dampfdruck auf. Höhere Expositionen treten insbesondere bei Spritzverfahren und Heißanwendungen auf. Typische Anwendungen sind z. B. Verfahren für Oberflächenbeschichtungen, Lackierungen oder Heißverklebungen.

Für die Begrenzung der Kurzzeitexposition wurde in Deutschland wegen der akuten Reizwirkungen ein Überschreitungsfaktor von 1 festgelegt, d. h. der Arbeitsplatz-grenzwert darf zu keinem Zeitpunkt überschritten werden.
Die ECHA schlägt hingegen einen maximal fünffach höheren Kurzzeitwert vor, um die Entwicklung von Asthma zu begrenzen. Der vorgeschlagene Kurzzeitwert ist damit höher als der in Deutschland festgelegte Überschreitungsfaktor von 1. Aufgrund der oben aufgeführten Argumentation ist es fraglich, ob es überhaupt sinnvoll ist einen Kurzzeitwert für monomere Diisocyanate zum Schutz vor Sensibilisierungen abzuleiten. Diese Fragestellung sollte deshalb Gegenstand weiterer Untersuchungen sein.

Biologische Grenzwerte (BGW nach TRGS 903 und BLW nach DFG) werden in Deutschland zur Bewertung der Ergebnisse aus dem Biomonitoring herangezogen und beziehen sich bei der Bewertung ebenfalls nur auf die monomeren Diisocyanate und nicht auf den TRIG. Es ist daher schwierig, einen Zusammenhang zwischen dem Biomonitoring und der Exposition der Diisocyanate in der Luft am Arbeitsplatz herzustellen, wenn letztere über die Summe aller NCO-Gruppen bestimmt wird. Zur Beurteilung der Exposition gegenüber Diisocyanaten ist die Kenntnis zum Wirkungsmechanismus und zum Metabolismus entscheidend. Die Bewertung der Diisocyanate erfolgt aus der Bestimmung der Metabolite (z. B. Amine im Urin und/oder Hämoglobin-Addukte im Blut der Beschäftigten) vor und nach der Schicht.

Für Hexamethylen-1,6-diisocyanat wurde in Deutschland ein BGW für das korrespondierende Hexamethylendiamin von 15 □g/g Kreatinin im Urin festgelegt (TRGS 903).

Weiterhin hat in Deutschland die MAK-Kommission der Deutschen Forschungs-gemeinschaft (DFG) für 4,4' -Methylendiphenyldiisocyanat einen Biologischen Leitwert (BLW) für das korrespondierende 4,4' -Diaminodiphenylmethan von 10 □g/L im Urin abgeleitet. Der BLW beschreibt die Quantität eines Arbeitsstoffes bzw. Arbeitsstoff-metaboliten oder die dadurch ausgelöste Abweichung eines biologischen Indikators von seiner Norm beim Menschen, die als Anhalt für die zu treffenden Schutzmaß-nahmen heranzuziehen ist, für die keine anderen biologischen Grenzwerte beschrieben werden können. Es wird eine Arbeitsstoffbelastung von maximal 8 Stunden täglich und 40 Stunden wöchentlich über die Lebensarbeitszeit zugrunde gelegt. Auch bei Einhaltung des BLW ist das Risiko einer Beeinträchtigung der Gesundheit nicht auszuschließen. Dabei ist zu beachten, dass die Angaben der MAK-Kommission der DFG wissenschaftliche Empfehlungen und kein geltendes Recht sind.
Weitere biologische Grenzwerte sind uns nicht bekannt.
Die im Urin gefundenen aromatischen Amine können aber auch aus anderen Quellen am Arbeitsplatz oder aus der Umwelt aufgenommen werden. Es ist auch möglich, dass im Biomonitoring keine Metabolite gefunden werden, am Arbeitsplatz aber trotzdem Expositionen durch Diisocyanate in Form von Aerosolen vorliegen. Daher muss die Bewertung von Ergebnissen aus dem Biomonitoring immer im Zusammen¬hang mit der Exposition in der Luft am Arbeitsplatz gesehen werden.
Eine Hintergrundbelastung der Allgemeinbevölkerung durch Diisocyanate zu beschreiben ist nicht möglich, weil in den meisten Fällen keine Metabolite nachgewiesen werden können.
Die ECHA hat aufgrund der oben beschriebenen Zusammenhänge keine Biologischen Grenzwerte abgeleitet. Diese Entscheidung nehmen wir zur Kenntnis.

Diisocyanate wirken nicht nur sensibilisierend auf die Atemwege, sondern auch auf die Haut. Beim Einatmen können eine Allergie, asthmaartige Symptome oder Atembeschwerden verursacht werden. Bei Hautkontakt können allergische Hautreaktionen

auftreten. Kanzerogene Effekte sind jedoch auf die Wirkung der aromatischen Amine, die durch Hydrolyse der aufgenommenen Diisocyanate entstehen, zurückzuführen.
Wir teilen die Meinung der ECHA, dass ein Hautkontakt zur Auslösung von Asthma beitragen und das Risiko zur Entwicklung von Atemwegsbeschwerden erhöht sein kann. Hier weisen wir auf eine von unserem Institut für Prävention und Arbeits-medizin (IPA) initiierte Studie zum Arbeits- und Gesundheitsschutz bei Tätigkeiten mit diisocyanathaltigen Materialien hin.

Eine weitere Absenkung der Grenzwerte würde unserer Ansicht nach nicht zu einer Verbesserung des Arbeitsschutzes führen. Vielmehr muss das Ziel sein, bereits vorhandene technische Schutzmaßnahmen auf ihre Wirksamkeit zu überprüfen und die Unterweisung der Beschäftigten durch besondere Schulungsmaßnahmen zu ergänzen. In den Unterweisungen sollen die Gefährdungen und die umzusetzenden Schutzmaßnahmen bei Tätigkeiten mit Diisocyanaten besonders hervorgehoben werden. Weitere Details sind dem Entwurf zur Beschränkungsregelung nach REACH zu entnehmen.
Mit dem Beschränkungsvorschlag wird eine einheitliche Regelung zur Verringerung der Exposition unter Fortführung der Tätigkeiten mit Diisocyanaten an Arbeitsplätzen geschaffen. Aus unserer Sicht ist es sinnvoll, eine Beschränkungsregelung der Zulassung vorzuziehen, weil es in der Regel keine Alternativen gibt und eine sehr große Anzahl an Betrieben mit vielseitigen Anwendungen innerhalb der EU betroffen sind. Dazu gehören auch viele kleine und mittelständige Unternehmen. Diese Betriebe verfügen nicht über ausreichende Ressourcen, um aufwändige Zulassungsanträge zu stellen.

ECHA/RAC response

- The information on the German OELs is added in the Annex.
- More justification is added in the Annex on the proposed STEL and the challenges in exposure and biological monitoring methods are further described.

Date	Country	Organisation	Type of Organisation	Comment number
13.12.2019	Belgium	ISOPA Aisbl; ALIPA Aisbl	Industry or Trade Association	9

Comment received

We refer to the documents provided as zip archive.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2nd Contribution by ISOPA and ALIPA_Public Consultation on OEL for Diisocyanates.zip

ECHA/RAC response

As the 1st submission of ISOPA/ALIPA comments (comment Nr 6) and the 2nd comment submission (this one) contained partially the same or similar attachments, all ISOPA/ALIPA comments are addressed under the section of comment Nr 6.

PUBLIC ATTACHMENTS
1. Europur PC Input and Complementary Submission Prof Dr Schupp.zip [Please refer to comment No. 2]
2. ECHA_Isocyanate-OEL_comments.pdf [Please refer to comment No. 7]
3. 2nd Contribution by ISOPA and ALIPA_Public Consultation on OEL for Diisocyanates.zip [Please refer to comment No. 9]
4. NEG comments ECHA Diisocyanates 2019.pdf [Please refer to comment No. 1]
5. ISOPA_ALIPA_Documents.zip [Please refer to comment No. 6]