Joint BAuA/BfR Workshop

REACH Article 57 (f): Non-Endocrine Disrupting Human Health Hazards Leading to SVHC Identification

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Workshop Report

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1. EXECUTIVE SUMMARY

Following an invitation from the German Federal Institute for Occupational Safety and Health (BAuA) and the Federal Institute for Risk Assessment (BfR), 40 experts from different European Member State Competent Authorities (MSCAs), the European Commission (COM), the European Chemicals Agency (ECHA), industry and non-governmental organisations including the European Trade Union Confederation (ETUC) joined a one-day workshop on REACH Article 57 (f) on March 29, 2012, in Berlin, Germany. The workshop presented and discussed stakeholder views on possible Article 57 (f) requirements for non-endocrine disrupting human health hazards. The aim of this exchange of opinions was to initiate the necessary discussion process at the European level and to constitute a first step towards a harmonised concept for SVHC identification according to the Article 57 (f) route.

During the first part of the programme, the legal framework around Article 57 (f) was explained and preliminary ideas were presented by the German CA on how to fill this provision with life. It was suggested that harmonised criteria should be developed in order to differentiate between human health hazards with the potential to cause an Equivalent Level of Concern (ELoC) to that posed by carcinogenic, mutagenic and/or reprotoxic (CMR) substances of CLP categories 1A and 1B, and those not qualifying for the Article 57 (f) route.

Factors named as important for this differentiation included seriousness of effect, strength of evidence, relevance for humans, and potency. As a consequence, the German CA considers substances causing respiratory sensitisation, but also other severe, delayed and/or persistent health effects, such as those covered by classification for STOT SE/RE 1 (Specific Target Organ Toxicity after Single/Repeated Exposure) as potential SVHC candidates according to Article 57 (f). However, agreeing on and applying harmonised criteria nevertheless would not obviate the need to provide case-by-case justification for each individual SVHC proposal.

In the subsequent discussions it became apparent that there was broad agreement on several issues, in particular among representatives from MSCAs, ECHA, ETUC, and COM. It was, for instance, in general considered helpful to establish a harmonised concept to be used as guidance for SVHC identification according to Article 57 (f). However, the degree of flexibility needed with such a concept and the most appropriate terminology (‘criteria’, ‘indicators’ or ‘principles’) would still require further discussions. Also representatives from industry acknowledged that harmonised criteria might to a certain degree prove helpful and needed. Moreover, there was consensus that RMO analysis should always constitute the first step within the authorisation process.

Representatives from MSCAs, ECHA, and COM also shared the view that the CLH process should be conducted before an SVHC proposal was prepared. This strategy would ensure that the examination of a substance's toxicological properties had been peer-reviewed and approved at the European level. In addition, there was broad agreement that the justification of an SVHC proposal should be evidence-based, applying criteria on a case-by-case basis. In this context, representatives from MSCAs, ECHA, and COM also agreed that risk-based considerations were no requirement on the level of SVHC identification, whereas representatives from industry emphasised that the assessment of exposure and risk should definitely be included.

Regarding specific human health hazards, there was broad agreement across representatives from MSCAs, ECHA, ETUC, and COM that in principle respiratory sensitisers meet Article 57 (f) criteria: They may cause serious and irreversible health effects, raise societal concerns, impair quality of life considerably, and like CMR substances, they are subjected to the CLH process, and the establishment of safe levels of exposure is difficult or impossible. In contrast, there was no general agreement on whether skin sensitisers in general meet Article 57 (f) requirements. Opinions were also divided on some further remaining human health hazards e.g. substances with neurotoxic, highly acutely toxic, or specific target organ toxic properties could in principle qualify as SVHCs. In contrast to the above-mentioned considerations, representatives from industry were of the opinion that Article 57 (f) with respect to non-endocrine disrupting human health hazards exclusively referred to *other* serious effects which were not covered by current CLP hazard classes.

In summary, the workshop proved to be useful for the exchange of views from different stakeholders on possible Article 57 (f) requirements for SVHC identification. Although further discussions will still be needed to determine criteria/indicators/principles, which are generally accepted for a harmonised concept, a concept as such was considered helpful by all participants. Additional work is still needed until a comprehensive and harmonised concept for SVHC identification according to the Article 57 (f) route will become reality.

2. AIM OF THE WORKSHOP

Dangerous substances may be subject to authorisation if they meet the criteria of REACH Article 57 and thus qualify as substances of very high concern (SVHCs). Regarding human health hazards, Article 57 sections (a), (b), and (c) explicitly refer to substances classified as carcinogenic, mutagenic, or toxic to reproduction (CMR) in category 1A or 1B (according to CLP).

Article 57 (f), by contrast, provides only a rather indefinite description. It says that substances may be included in Annex XIV '*for which there is scientific evidence of probable serious effects to human health […] which give rise to an equivalent level of concern to those of other substances listed in points (a) to (e)*'. However, the REACH regulation does not further define which aspects could lead to an equivalent level of concern (ELoC) as compared to CMR effects. Also the associated guidance gives only limited assistance for assessing whether ELoC is met.

Therefore, the German Federal Institutes for Occupational Safety and Health (BAuA) and for Risk Assessment (BfR) invited interested parties to join a one-day workshop on REACH Article 57 (f) in order to initiate the necessary discussion process at the European level. The workshop was meant to present and discuss stakeholder views on possible Article 57 (f) requirements for non-endocrine disrupting human health hazards. This exchange of opinions should constitute a first step towards a harmonised concept for SVHC identification according to the Article 57 (f) route. An overview of the workshop agenda is provided in Appendix 1 to this report.

3. PARTICIPANTS

In total, 40 experts joined the workshop. A rough overview of the different stakeholder groups is shown below. A more detailed list of participants is provided in Appendix 2 to this report.

Stakeholder Group	Number of Participants
European Member State Competent Authorities (MSCAs)	23
Industry	10
European Commission (COM) and European Chemicals Agency (ECHA)	4
Non-governmental Organisations (NGOs) incl. European Trade Union Confederation (ETUC)	3

4. SHORT SUMMARIES OF PRESENTATIONS AND DISCUSSIONS

4.1 WELCOME AND INTRODUCTION

After an introduction by Rüdiger Pipke, head of division 4 of BAuA[1] and facilitator of the workshop, the president of BAuA, Isabel Rothe, and the vice-president of BfR, Reiner Wittkowski, delivered welcoming addresses to the audience, stating the importance of REACH and the SVHC process for their respective institutes.

4.2 PURPOSE AND CURRENT STATUS OF THE AUTHORISATION PROCESS AND OF THE CANDIDATE LIST

Frauke Schröder on behalf of BAuA

This talk provided a brief introduction into the authorisation process under REACH. The goals of this process are to:

- ensure the good functioning of the internal market,
- properly control risks emanating from SVHCs, and
- promote substitution of SVHCs by suitable safer alternatives.

From the REACH regulation as well as the associated guidance it is clear that three conditions must be met for a substance to be identified as SVHC in accordance with Article 57 (f):

- a hazard must be identified,
- this hazard must present an ELoC, and
- these points must be demonstrated on a case-by-case basis.

Therefore the intention behind this workshop is to discuss (for non-endocrine disrupting human health hazards) potential criteria for the determination of an ELoC. In the medium-term, agreement should be sought on common principles to make full use of Article 57 (f). Such principles could define more exactly which substances qualify as SVHCs, thereby ensuring greater transparency and traceability. On the other hand they could also serve to define which substances do not qualify as SVHCs, thereby focusing resources on real problems.

[1] The unabbreviated affiliations of all participants are accessible from the List of Participants (Appendix 2).

However, such common principles are not in contradiction with a case-by-case approach, nor should they be thought of as stipulations, because the final decision on a proposal will always remain with the respective MSCA.

4.3 General Concept for Applying Article 57 (f) to Non-Endocrine Disrupting Human Health Hazards

Wiebke Prutner on behalf of BAuA

In this presentation, an overview was given of the preliminary conceptual ideas for common Article 57 (f) principles as developed by BAuA and BfR. They are based on the notion that an ELoC contains both toxicological and regulatory aspects. Article 57 (f) demands that in order to qualify as SVHC, a substance must display probable serious effects in humans which pose a level of concern equivalent to that posed by CMR Cat. 1 substances. From a toxicological point of view, this has the following consequences:

- the evidence that the hazard is both sufficiently relevant for and likely to occur in humans must be of equivalent strength as for CMR Cat. 1 substances (therefore e.g. Repr. 2 substances would probably not routinely qualify as SVHC),
- the hazardous effects must be of equivalent seriousness to those of CMR Cat. 1 substances. Possible examples include death, major permanent functional changes in organ systems, severe organ damage, or other irreversible effects, whereas reversible and less serious effects leading to classification for skin or eye irritation or Specific Target Organ Toxicity after single exposure Cat. 3 (STOT SE 3) are not considered, and
- substances which elicit such effects only with very low potency will cause less toxicological concern than those with high potency.

In this context it is deemed useful if substances are subjected to the CLH process to obtain harmonised classification and labelling before an SVHC proposal is prepared. Since the CLH process includes peer review by other Stakeholders and ECHA's Risk Assessment Committee (RAC), aspects such as toxicological evidence, relevance for humans, seriousness of effects and potency would be discussed and adopted on a transparent and broad level. It is therefore proposed that in general, SVHC proposals based on human health effects according to Article 57 (f) should only be filed after the CLH process has been completed successfully for the endpoint of concern.

Aside from their seriousness, certain aspects of CMR hazards (e.g. long delay between exposure to a substance and onset of effects, difficulty or impossibility to establish safe

levels) also make them difficult to control from a regulatory perspective. Thus, ELoC might rather not arise for risks which generally are controlled more easily than others. For instance, due to the immediate onset of effects, the risk posed by handling acutely toxic substances of Cat. 1 might be assumed to be generally more easily controllable, as lack of sufficient risk management would become immediately evident.

Conversely, concrete evidence of an insufficiently controlled risk (e.g. reports from the workplace) could trigger specific regulatory concern and prioritisation for annex XIV inclusion. Nevertheless, while this might be an important point for an MSCA when deciding about the selection of potential SVHC candidates (and also for later prioritisation when moving substances from the Candidate List to Annex XIV), it falls outside of the scope of Article 57 (f).

4.4 EQUIVALENT CONCERN FROM A TOXICOLOGICAL VIEW – IDEAS AND EXAMPLES

Agnes Schulte on behalf of BfR

The presentation started with a reminder that according to the REACH legal text, the first step of the authorisation process, i.e. SVHC identification and inclusion into the Candidate List, solely requires demonstration of sufficient concern, while considerations of risk (e.g. by introducing expected exposure levels) are not a requirement. However, this does not preclude that such considerations, which belong to later stages of the process (prioritisation for inclusion into Annex XIV, approval/denial of authorisations) may drive selection of SVHC candidates from the beginning.

Subsequently, some of the aspects of toxicological concern were recapitulated which had been introduced in the previous presentation (seriousness, relevance for humans, strength of evidence, potency). As regards general regulatory concern, the situation in consumer protection bears some particularities when compared to the situation at the workplace. Consumers might be exposed to the same substance (e.g. plasticiser, colorant, fragrance) via multiple products and uses. Data on uses and quantitative exposure are mostly unavailable, at least to the authorities, thus an *a priori* calculation of risk is impossible. Against this background, the instrument of substitution bears high relevance for consumer protection, in particular for high potency substances. On the other hand, regulatory capacities are limited; therefore the focus must be placed on problematic substances, while less problematic ones should not ‘block the pipeline’.

Essential elements of SVHC identification include:

- qualitative consideration of exposure (i.e.: possible or unlikely),
- determination of the hazard profile based on (harmonised) classification,
- focus on serious repeat-dose or delayed effects,
- concentration on highest potency categories, and
- exclusion of effects which lack sufficient relevance in humans or sufficient evidence.

Effects not fitting into this scheme would need specific additional justification (e.g. real-life evidence of serious uncontrolled risk).

Following this introduction, the results of the application of these principles to the different human health hazard classes defined by the CLP regulation were demonstrated. In summary, three different groups of hazards can be distinguished:

- Group 1: generally qualifying as SVHC with high priority, where additional specific reasoning is normally not necessary: STOT SE/RE 1, Resp. Sens.,
- Group 2: qualifying as SVHC if an additional specific justification is provided (e.g. evidence for inadequate risk management or need for substitution): Acute Tox. 1+2, Skin Corr. 1, Eye Dam. 1, Skin Sens., STOT SE/RE 2, Carc. 2 (only threshold carcinogens), Muta. 2 (only threshold mutagens), Lact. (if damage to offspring can be demonstrated), Asp. Tox. 1, and
- Group 3: not qualifying as SVHC (effects of lower seriousness or with lack of sufficient evidence): Skin Irrit. 2, Eye Irrit. 2, STOT SE 3, Carc. 2 (non-threshold carcinogens), Muta. 2 (non-threshold mutagens), Repr. 2.

4.5 Requirements for an Annex XV Dossier Proposing SVHC Identification via the Article 57 (f) Route

Peter Lepper on behalf of ECHA

This presentation gave an outline of ECHA's understanding of the requirements for an Annex XV dossier proposing SVHC identification via the Article 57 (f) route. First of all, before a substance is proposed as SVHC, an RMO analysis should be performed in order to ensure that authorisation is the appropriate route for risk management. Then the proposal itself needs to be properly documented in the form of an Annex XV dossier, in particular with a view as to why the substance's properties are considered to meet the requirements of Article 57 (f). Available information on uses, exposure, and alternative substances or techniques needs to be

included in the dossier in accordance with the provisions set out in Annex XV to the REACH Regulation and will be helpful in later stages of the authorisation process, but is not a requirement for SVHC identification as such.

The function of Article 57 (f) can be understood as a 'safety net', meaning that it was intended to cover all substances with hazardous properties that could possibly be seen as substantiating an ELoC ('equivalent' not necessarily meaning 'similar'), while it would have been hardly possible to establish an agreed, exhaustive list of these aspects during the creation of the REACH legal text.

When preparing an SVHC dossier, the first step is to document the hazardous properties that are believed to constitute the concern. For hazards that can be classified in accordance with the CLP Regulation a classification process should have been carried out before identification of the substance as SVHC is proposed ('no classification via the SVHC dossier'). Then justification for establishing ELoC has to be provided in the Annex XV dossier on a case-by-case basis. This step needs to include the comparison of the impact of the substance's hazardous properties on human health with the concerns associated with CMR substances. Potential factors for comparison include e.g. seriousness, delayed onset, and/or irreversibility of effects, potency, mode of action, degree of impairment of life quality, or uncertainty about dose-response relationships. Finally, all impacts should be evaluated together in a Weight-of-Evidence (WoE) assessment.

4.6 SUMMARY OF DISCUSSIONS

With a view to the specific problems of consumer protection mentioned in the third presentation, Giuseppina Luvara (COM, DG ENTR) asked whether also substances present only in certain parts of articles should be considered. She added that the relevance of substances in articles with a view to consumer protection is a question of several factors e.g. the substances' migration capacities. Agnes Schulte (BfR) replied that most often, detailed information on release, migration, or even the specific uses is not available, therefore only a general assumption of exposure (yes/no) is normally possible.

Sylvain Bintein (COM, DG ENV) made a statement that CLH as a requirement was supported. As to STOT effects, he asked if all organs should be considered when selecting possible effects qualifying for Article 57 (f). Agnes Schulte (BfR) replied that, yes, in principle this should be the case, as no hierarchy of the importance of the individual organs can be established and any damage caused is considered unacceptable. However, irreversibility of effects is a particularly important aspect, also sometimes for non-severe

effects. Moreover, impairment of life abilities or the regenerative capacities of organs could be considered as well.

Giuseppe Malinverno (ECETOC) noted that severity of effect in animals is one thing, but relevance in humans also needs to be discussed. Agnes Schulte (BfR) answered that this will have been considered already at the classification stage.

Edgar Leibold (ECETOC) considered an automatic decision for group 1 questionable. Agnes Schulte (BfR) replied that the proposal and documentation would still be case by case.

In response to the presentation by Peter Lepper (ECHA), Tony Musu (ETUC) noted that at the Candidate List Workshop in 2009 it had been established that this list should be the portal to both authorisation and restriction - did ECHA change its view such that today the list should only be used for authorisation? Peter Lepper (ECHA) replied that there can be different motivations for putting a substance on the Candidate List, however, due to process-related considerations (recommendation of priority substances to be included in Annex XIV, i.e. the list of substances subject to authorisation), a substance should only be proposed for identification as SVHC if authorisation is deemed to be the appropriate route for risk management, but not, if at the stage of the risk management option analysis it already became clear that ultimately restriction would be the superior option.

Agnes Schulte (BfR) pointed out that for non-threshold compounds, e.g. carcinogens, the applicant for an authorisation has to perform a socio-economic analysis (SEA) - should this concept then be extended to respiratory sensitisers? Peter Lepper (ECHA) replied that this applies as well for all SVHCs identified via the Article 57(f) route for which no effect threshold can be determined. In his view, the practical relevance of this question might be rather low, at least in the presence of suitable alternatives, as then the authorisation requirement in effect means a ban.

Eva Stocker (Environment Agency Austria) wondered how much in-depth assessment ECHA would expect for Annex XV dossiers proposing SVHCs according to Article 57 (f). Peter Lepper (ECHA) replied that there is no general answer to this question but that in scientific terms sufficient documentation and sound argumentation in support of the SVHC proposal would need to be provided in the dossier.

4.7 CHEMICAL INDUSTRY'S VIEW ON ARTICLE 57 (F)

Erika Kunz on behalf of VCI

From the chemical industry's point of view, REACH Article 57 (f) constitutes an escape clause that refers only to substances whose effects give rise to an ELoC to that caused by CMR 1A/1B or PBT/vPvB substances due to properties which yet have to be identified. Article 57 (f) is not understood as a general empowerment to include all substances into Annex XIV which are classified according to CLP.

The identification of a substance as SVHC in accordance with Article 57 (f) has to be conducted on a case-by-case basis which also includes a sound risk assessment. Therefore it is *per se* not possible to define general criteria for SVHC identification according to Article 57 (f).

Before such an identification process is started, three main criteria need to be fulfilled:

- there is scientific evidence that the substance causes probable serious effects of an ELoC,
- there is evidence from risk-based considerations that the substance may cause serious effects during use, and
- after thorough consideration, it should have been established that the inclusion of the substance in the Candidate List and eventually in Annex XIV constitutes the most effective risk management option.

4.8 TRADE UNION'S VIEW ON ARTICLE 57 (F)

Tony Musu on behalf of ETUC

As already shown in their Trade Union Priority List for REACH authorisation, ETUC considers neurotoxicants as well as respiratory and skin sensitising substances as potential SVHCs according to REACH Article 57 (f). Within the presentation, this position was substantiated with statistics from the year 2001 on chemical-related occupational diseases in the European Union. Out of all recognised occupational diseases an estimated 0.2 % account for chemical-related neurological disorders, 12.3 % for chemical-related skin diseases and 5-12.5 % for chemical-related respiratory diseases (12.5 % applies if chemical dust is included as causative agent).

ETUC expects considerable benefits for social security, individual life quality, and industrial productivity if neurotoxicants and, particularly, sensitisers are put on the Candidate List or in Annex XIV.

Both sensitisers and neurotoxicants are considered to meet Article 57 (f) criteria as effects are generally irreversible, symptoms are serious (sensitisers: asthma, COPD, dermatitis; neurotoxicants: neuropsychiatric symptoms, permanent nerve damage, senile plaques, neuronal death) and safe thresholds normally cannot be set. Moreover, sensitisation may manifest itself after a relatively short time lag following exposure to a sensitising chemical. Neurotoxic substances may induce effects also in the offspring and cannot be clearly classified for neurotoxicity because a distinct classification is not provided.

4.9 SUMMARY OF DISCUSSIONS

Addressing Erika Kunz's (VCI) presentation, Poul Bo Larsen (MST) asked to which extent exposure considerations should be taken into account for the SVHC identification process. Moreover, Matthias Herzler (BfR) wanted to know how profound risk-based considerations would have to be. Erika Kunz (VCI) answered that the safe use is the key. If the possibility of safe uses is indicated, this will be sufficient for the purposes of risk assessment.

In response to Tony Musu's (ETUC) presentation, industry representatives from ISOPA and CEFIC expressed their doubts about the validity of the statistics presented on chemical-related occupational diseases. Tony Musu (ETUC) replied that there is in reality a huge underreporting of occupational diseases. Giuseppe Malinverno (ECETOC) noted that occupational limit values should normally be sufficient for worker protection, so enforcement of already existing regulatory measures should be the most appropriate measure. Karl-Wilhelm Kroesen (ISOPA) also expressed his view that the problem of sensitisers will be solved at the workplace. Tony Musu (ETUC) pointed out that it is crucial to find synergies between REACH and other occupational safety regulations in order to significantly improve occupational safety.

Sylvain Bintein (COM, DG ENV) asked Erika Kunz (VCI) whether there are any specific hazard classes that industry considers as meeting Article 57 (f) criteria. Erika Kunz (VCI) replied that this is not possible in a generic way, as substances should always be considered case by case. Furthermore, for regulatory purposes, Article 57 (f) is not the only tool provided by REACH.

4.10 VIEW(S) OF THE FRENCH MSCA ON HUMAN HEALTH HAZARDS UNDER ARTICLE 57 (F)

Henri Bastos on behalf of ANSES

Henri Bastos emphasised that the French CA has not yet developed an official position on REACH Article 57 (f). But after first considerations, the French CA questions whether an extension of the scope of Article 57 (f) − e.g. by including other hazards than CMR and endocrine disruption − is relevant at all. It appears probable that Article 57 (f) has been written specifically for endocrine disrupters and to anticipate similar emerging/future concerns. It is also not clear whether such an extension could be challenged from a legal point of view.

However, despite these reservations the French CA acknowledges that substances with respiratory sensitising properties might constitute an exemption because they obviously fulfil the criteria of Article 57 (f) (i. e. serious and often irreversible effects, no threshold, relevant consequences for society) and are – in the same way as CMR substances – principally subject to harmonised classification.

With respect to skin sensitisers the French CA feels that there is still need for discussion about their principal appropriateness for fulfilling Article 57 (f) criteria. Apart from these special cases, the French CA proposes that the term ‘concern’ should be applied rather to categories comprising substances with similar or even the same effects than to single substances having the same hazard classification. In this way a concern will arise if several substances fit the same category, thus increasing the associated health impacts and economic burden for society. Examples for this approach are already endocrine disrupters and might also be neurotoxicants. In any case, authorisation should only be envisaged if this regulatory process is considered the best risk management option.

4.11 DO SENSITISERS MEET EQUIVALENT CONCERN CRITERIA?

Demi Theodori on behalf of RIVM

At the beginning of the presentation, Demi Theodori explained that the primary starting point for the Dutch CA’s considerations was not the intention to interpret Article 57 (f) but the need to most efficiently control the risks arising from sensitising substances. Subsequent to a thorough RMO analysis, it finally turned out that authorisation might be the best option to regulate sensitisers. Therefore the Dutch CA has begun to gather ‘equivalent concern criteria’

that could substantiate the SVHC identification of sensitisers according to Article 57 (f). These criteria refer to the following questions:

- Do sensitisers cause serious health effects?
- Is sensitisation a hazard that can be classified via CLP?
- Do sensitisers cause irreversible health effects?
- Does sensitisation impair a person's quality of life?
- Does sensitisation constitute a societal concern?
- Can a safe level of exposure be established?

In the end, it was concluded that respiratory sensitisers clearly meet all of the above mentioned criteria, whereas skin sensitisers may possibly seem less convincing. However, a common aspect of both types of sensitisers is that exposed subjects may at first lack awareness of their exposure and that this can lead to prolonged or repeated exposure resulting in an increased severity of effects.

Based on these theoretical considerations and using hazard and effect based approaches, the Dutch CA in practice started to select respiratory sensitisers. Currently, the focus is on the groups of diisocyanates and anhydrides. Dependent on further information on manufacture, use, exposure and alternatives, the most relevant substances will then be prioritised and subjected to a thorough RMO analysis.

4.12 VIEW OF THE SWEDISH MSCA ON ARTICLE 57 (F)

Margareta Warholm on behalf of KEMI

Margareta Warholm pointed out that the Swedish CA had just started to deal with the issue of Article 57 (f). Consequently, the presentation did not yet reflect a final Swedish statement. However, the Swedish CA is also of the opinion that respiratory sensitisers do fulfil Article 57 (f) criteria, whereas for skin sensitisers this seems to be less convincing, but nevertheless possible. The underlying considerations largely corresponded to those already presented in the previous presentations.

Moreover, large interindividual differences in sensitivity render respiratory sensitisers particularly difficult from a regulatory point of view. In addition, the Swedish CA takes the view that bioaccumulating and toxic metals (e.g. cadmium) as well as highly toxic compounds (e.g. paraquat) may also constitute SVHCs according to Article 57 (f).

Substances degrading outside the body to CMR category 1 substances can in principle be considered for possible SVHC identification, too. However, in this regard definitions are still required concerning the question of how much of these substances would need to be degraded and how fast.

4.13 SUMMARY OF DISCUSSIONS

There were comments concerning the French reservations that an extension of the scope of Article 57 (f) by including CLP hazard classes other than CMR category 1 might be challenged from a legal point of view. In this regard Vito Buonsante (ClientEarth) remarked that if there is scientific evidence, the legal text of REACH allows for such an expanding adaptation of Article 57 (f). Moreover, Matthias Herzler (BfR) noted that just because further hazard classes are not explicitly mentioned in Article 57 (f), this does not necessarily mean the legislator did not want them to be included at all. Rather one would assume that legislators considered in general the possibility that other hazards than CMR could sometimes pose equivalent concern but – with the intention of keeping the REACH text concise – handed over elaboration of the details to the REACH implementation projects.

With a view to Demi Theodori's (RIVM) presentation claiming that exposure to skin sensitisers could relatively easily be avoided, Agnes Schulte (BfR) commented that this might apply to the occupational area but to a much lesser extent to consumer products.

In response to the presentation from Margareta Warholm (KEMI), Matthias Herzler (BfR) noted that the aspect of bioaccumulation was an interesting additional criterion and that, in his opinion, perhaps the combination of information on bioaccumulation (more often to be found in the environmental than the human health section of risk assessments under REACH) and toxicity could be an interesting line of argumentation when establishing ELoC.

Regarding respiratory sensitisers, Sylvain Bintein (COM, DG ENV) pointed out that there are clear indications in the CLP guidance that respiratory sensitisers are considered equivalent to CMR substances. As to the statement in the presentation from Henri Bastos (ANSES) that Article 57 (f) was probably only referring to future hazard classes not known or sufficiently defined at the time REACH was created, he asked whether classification for STOT does not actually cover all kinds of imaginable effects already. Agnes Schulte (BfR) replied that in her opinion, indeed this is the case.

4.14 PANEL DISCUSSION

The panel which was populated by the speakers (Gisela Stropp taking over from Erika Kunz for VCI) was moderated by Rüdiger Pipke (BAuA). In order to provide a certain degree of structure to this discussion, four major fields of discussion were identified as being perhaps the most controversial. Below, the discussion is reported along these discussion items for better readability. As a consequence, the individual contributions are sometimes not reported in the exact chronological order in which they were made.

1. *What is the role of harmonised criteria/common principles for Article 57 (f) as presented by the German CA? Are they helpful/needed and why? Is current guidance sufficient or does an update appear necessary?*

Margareta Warholm (KEMI) said that when criteria are too strict, this could be seen as being in contradiction to the principle of case-by-case evaluation. On the other hand, such criteria might be helpful to structure the SVHC proposal.

Peter Lepper (ECHA) agreed and added that in his view, generic decision rules are not in line with the REACH legal text. He would prefer the term ‘principles’ or ‘indicators’ over ‘criteria’ in order to retain a certain flexibility, and such principles/indicators could indeed be helpful, also for documentation purposes. As to the need for further guidance, it would not be an exaggeration to say that guidance currently is rudimentary and that there is certainly room for improvement. However this will take some time, in particular because ECHA later this year plans to temporarily stop the development of new guidance in order to avoid confusing registrants during the hot phase of the next REACH registration deadline due by mid-2013.

Agnes Schulte (BfR) agreed that ‘criteria’ might be too hard and perhaps a wording like ‘indicators for substances of highest importance’ could be used. In any case, more guidance than currently available was needed.

Gisela Stropp (VCI) noted that while scientific criteria in principle could be helpful, a combined consideration of science-driven risk management and regulatory concern is necessary.

2. *Have any relevant factors that contribute to establishing an ELoC been missed by the presentations? Is there agreement on the role of seriousness, evidence, potency? Are exposure considerations a prerequisite?*

With a view to exposure, Peter Lepper (ECHA) stated that substances without appreciable exposure should not be considered for authorisation in order to make responsible use of

resources. However this does not imply the need to establish risk already at the SVHC identification stage since this is also not a requirement in subsections (a) to (e) of Article 57. Only concern needs to be demonstrated.

Agnes Schulte (BfR) added that normally, prior to filing a substance for SVHC identification, exposure would already have been considered in the RMO.

Gisela Stropp (VCI) expressed the view that both hazard assessment and risk-based considerations are necessary. With respect to the role of evidence, she agreed with the position of the German CA that Cat. 2 CMR substances in general do not qualify as SVHC, but exceptions based on Mode of Action are possible.

3. *Do the proposed criteria already extend the scope of Article 57 (f) when compared to the original intention of the legislator?*

Henri Bastos (ANSES) repeated his view that if legislators had intended to expand the scope of Article 57 (f) to other known effects, they would have done so by including them into the REACH regulation from the beginning.

Agnes Schulte (BfR) replied that this may not have been possible at the time when REACH was developed (and in the available timeframe), because agreement on this very detailed level had not been achieved. So, in much the same way as for a number of other REACH implementation issues, a detailed solution and corresponding guidance were postponed to a later stage. She added that the proposed 'indicators' in her opinion would not expand the scope of Article 57 (f); rather to the opposite they would limit the scope by excluding certain effects as possible SVHC justification.

Demi Theodori (RIVM) remarked that in her view, the principles constitute an interpretation rather than an extension of Article 57 (f). She also noted that criteria could be helpful tools for the necessary case-by-case consideration because they can help to define at least which substances would not qualify as SVHCs at all.

Gisela Stropp (VCI) commented that in industry's view Article 57 (f) was only a safety net for effects not on the table when REACH was created. So the proposed criteria would indeed already extend the scope of Article 57 (f). She also remarked that as there is currently no procedure to remove substances from the candidate list, it should only be reserved for substances with an established need for regulation beyond other available risk management measures. Matthias Herzler (BfR) replied that during the earlier part of the discussion it had already been said that it was difficult to imagine which relevant effects had 'not been on the table when REACH was created' that would not be covered by the STOT classification. As a

matter of fact, this hazard class comprehensively addresses serious damage to all organs/systems of the human body.

Margareta Warholm (KEMI) noted that it should not be forgotten that one important aim of the Candidate List and the Authorisation process is also substitution.

Peter Lepper (ECHA) commented that Article 57 (f) represents a safety net under which any hazardous property or effect can be addressed that is deemed to give rise to a level of concern equivalent to the hazardous properties addressed in Article 57 (a–e). This would be emphasised by the stipulated case-by-case approach. The most important point is that the submitted data and justifications are of such quality that they can be assessed according to the established scientific principles.

4. *What are the pros and cons of making CLH a prerequisite for SVHC identification? What about urgent cases?*

Peter Lepper (ECHA) confirmed that CLH as a prerequisite corresponds to good regulatory practice. By following this procedure RAC with its specific toxicological competence and experience would be involved in the decision making on the hazard classification instead of the MSC, which has no specific toxicological expertise. For the European Commission, Sylvain Bintein (COM, DG ENV) strongly agreed with the requirement of CLH.

Agnes Schulte (BfR) remarked that currently CLH is limited to CMR substances and respiratory sensitisers, so it has to be ensured that RAC will accept the intention of a later SVHC proposal as sufficient justification for being involved. She suggested that in case unanimous self-classification was available in ECHA's C & L Inventory, this could also be used, so that urgent cases are not unnecessarily slowed down by the time-consuming CLH process.

Ulrich Föst (BAuA) noted that the CLH process includes a thorough peer review, and at least in the first phase of applying Article 57 (f), the focus should be placed on relevant substances with CLH of which plenty are available.

Giuseppe Malinverno (ECETOC) commented that CLH in itself is already a risk management option, so authorisation would only be needed where this RMO is considered to be insufficient. Matthias Herzler (BfR) replied that with regard to substances used in consumer articles, CLH is not a valid RMO, as it only pertains to substances and mixtures.

5. CONCLUSIONS

Rüdiger Pipke (BAuA) summarised the results of the workshop. He noted that even with REACH being in force for some time, everybody is still learning which of the available tools is best suited for a particular regulatory task. He concluded that with regard to Article 57 (f), in his view, good progress had been made by the discussions of the workshop, in particular as the proposed principles/indicators could help in generating transparency and in using resources most efficiently. Thereby the basis for a concise discussion of individual substances is improved. He then thanked all participants for their contributions and wished everybody a safe journey home.

Appendix 1 – Workshop Agenda

Facilitator: R. Pipke (BAuA, Head of Division 4)

Time	Topic	Speaker
09:00 – 10:00	Registration and Coffee	
10:00 – 10:10	Welcome and Introduction	I. Rothe (President BAuA) R. Wittkowski (Vice-President BfR)
10:10 – 10:25	**Purpose and Current Status of the Authorisation Process and of the Candidate List**	F. Schröder (BAuA)
10:25 – 10:35	Discussion	
10:35 – 10:45	**General Concept for Applying Article 57 (f) to Non-ED Human Health Hazards**	W. Prutner (BAuA)
10:45 – 10:55	**'Equivalent Concern' from a Toxicological View – Ideas and Examples**	A. Schulte (BfR)
10:55 – 11:05	Discussion	
11:05 – 11:25	**Requirements for an Annex XV Dossier Proposing SVHC Identification via the Article 57 (f) Route**	P. Lepper (ECHA)
11:25 – 11:35	Discussion	
11:35 – 11:50	**Chemical Industry's View on REACH Article 57 (f)**	E. Kunz (VCI)
11:50 – 12:05	**Trade Union's View on REACH Article 57 (f)**	T. Musu (ETUC)
12:05 – 12:20	Discussion	
12:20 – 13:20	Lunch	
13:20 – 13:35	**View of the French MSCA on Human Health Hazards under Article 57 (f)**	H. Bastos (ANSES, France)
13:35 – 13:50	**Do Sensitisers Meet Equivalent Concern Criteria?**	D. Theodori (RIVM, The Netherlands)
13:50 – 14:05	**View of the Swedish MSCA on Article 57 (f)**	M. Warholm (KEMI, Sweden)
14:05 – 14:25	Discussion	
14:25 – 14:45	Coffee Break	
14:45 – 15:45	**Panel Discussion**	All Speakers
15:45 – 16:00	**Summary and Conclusions from the Workshop**	R. Pipke (BAuA)
16:00	Adjourn of the Workshop	

Appendix 2 – List of Participants

Name	Institution
Alivernini, Silvia	Istituto Superiore di Sanità (ISS), Italy
Aschberger, Karin	European Commission, Directorate-General Joint Research Centre (DG JRC)
Banasiak, Ursula	Federal Institute for Risk Assessment (BfR), Germany
Bastos, Henri	French Agency for Food, Environmental and Occupational Health & Safety (ANSES), France
Bernauer, Ulrike	Federal Institute for Risk Assessment (BfR), Germany
Bintein, Sylvain	European Commission, Directorate-General for the Environment (DG ENV)
Buonsante, Vito A.	ClientEarth
Elbertse, Ingrid	Women in Europe for a Common Future (WECF)
Findenegg, Helene	Federal Institute for Occupational Safety and Health (BAuA), Germany
Föst, Ulrich	Federal Institute for Occupational Safety and Health (BAuA), Germany
Frank, Wolfram	European Diisocyanate & Polyol Producers Association (ISOPA)
Gross, Thomas	Dow Chemical Company
Guhe, Christine	Federal Institute for Occupational Safety and Health (BAuA), Germany
Herbst, Uta	Federal Institute for Risk Assessment (BfR), Germany
Herzler, Matthias	Federal Institute for Risk Assessment (BfR), Germany
Kroesen, Karl-Wilhelm	European Diisocyanate & Polyol Producers Association (ISOPA)
Kunz, Erika	Clariant (on behalf of VCI, Verband der Chemischen Industrie, Germany)
Larsen, Poul Bo	Danish Environmental Protection Agency (MST), Denmark
Leibold, Edgar	BASF (on behalf of ECETOC, the European Centre for Ecotoxicology and Toxicology of Chemicals)
Lepper, Peter	European Chemicals Agency (ECHA)
Luecke-Brunk, Gudrun	Bayer MaterialScience (on behalf of CEFIC, The European Chemical Industry Council)
Luvara, Giuseppina	European Commission, Directorate-General for Enterprise and Industry (DG ENTR)
Malinverno, Giuseppe	SOLVAY (on behalf of ECETOC, the European Centre for Ecotoxicology and Toxicology of Chemicals)
Mervart, Jan	DEZA a.s.
Musu, Tony	European Trade Union Confederation (ETUC)
Peczkowska, Beata	Bureau for Chemical Substances, Poland

Name	Institution
Pipke, Rüdiger	Federal Institute for Occupational Safety and Health (BAuA), Germany
Prutner, Wiebke	Federal Institute for Occupational Safety and Health (BAuA), Germany
Rosenthal, Esther	Federal Institute for Risk Assessment (BfR), Germany
Rouw, Aart	Federal Institute for Occupational Safety and Health (BAuA), Germany
Schröder, Frauke	Federal Institute for Occupational Safety and Health (BAuA), Germany
Schulte, Agnes	Federal Institute for Risk Assessment (BfR), Germany
Schuur, Gerlienke	National Institute for Public Health and the Environment (RIVM), The Netherlands
Soballa, Volker	Evonik Industries (on behalf of ECETOC, the European Centre for Ecotoxicology and Toxicology of Chemicals)
Sommer, Yasmin	Federal Institute for Risk Assessment (BfR), Germany
Stocker, Eva	Environment Agency, Austria
Stropp, Gisela	Bayer HealthCare (on behalf of VCI, Verband der Chemischen Industrie, Germany)
Theodori, Demi	National Institute for Public Health and the Environment (RIVM), The Netherlands
Warholm, Margareta	Swedish Chemicals Agency (KEMI), Sweden
Wiaderna, Dorota	Bureau for Chemical Substances, Poland

Appendix 3 – Presentations

Bundesanstalt für Arbeitsschutz und Arbeitsmedizin

Purpose and current status of the Authorisation Process and of the Candidate List

29.03.2012

1 Dr. Frauke Schröder, BAuA/BfR Workshop Art. 57f

Outline

The Authorisation Process

- Candidate List
  - Purpose
  - Current Status
- Annex XIV
  - Purpose
  - Current Status

Art. 57f and Equivalent Level of Concern

29.03.2012

2 Dr. Frauke Schröder, BAuA/BfR Workshop Art. 57f

The Authorisation Process

Ensure the good functioning of the internal market

Properly control risks from substances of very high concern (SVHC)

Promote substitution of SVHCs by suitable safer alternatives (substances or technologies)

29.03.2012

The Authorisation Process

=> Authorisation process involves several steps:

1. SVHC Identification => Candidate List

2. Inclusion in Annex XIV (involves prioritisation/recommendation by ECHA and final decision by COM)

3. Granting of authorisations

29.03.2012

Purpose of the Candidate List

Primary purpose:

Pool of substances for potential inclusion in Annex XIV

Further reasons:

"Classification" of PBT- and vPvB-substances and substances of equivalent level of concern (e.g. endocrine disrupters)

Generation of further information on substances in articles through notification obligation (Art. 7(2))

Avoidance of substitution of SVHCs with equally or more hazardous substances (grouping approach)

To be discussed further!

29.03.2012

5 Dr. Frauke Schröder, BAuA/BfR Workshop Art. 57f

Candidate List - Current Status

73 substances included in the Candidate List

Thereof: 61 due to CMR properties

5 due to PBT/vPvB properties

6 due to CMR and PBT/vPvB properties

1 due to endocrine disrupting properties

Further 13 Annex XV dossiers (all CMR) currently subject to public consultation (deadline: 12 April)

29.03.2012

6 Dr. Frauke Schröder, BAuA/BfR Workshop Art. 57f

Purpose of Annex XIV

Uses of substances on their own, in a mixture or of the incorporation of these substances into an article are subject to prior authorisation if specific conditions are met (Art. 60 (2 or 4))

Proper control of risks arising from the use of SVHCs

Promotion of substitution of SVHCs by suitable safer alternatives (substances or technologies)

Ensure the good functioning of the internal market

29.03.2012

7 Dr. Frauke Schröder, BAuA/BfR Workshop Art. 57f baua:

Current Status of Annex XIV

14 substances included in Annex XIV

Thereof: 2 PBT/vPvB substances

12 CMR substances

Further 13 substances recommended for Annex XIV inclusion (cobalt and chromium compounds plus trichloroethylene)

29.03.2012

8 Dr. Frauke Schröder, BAuA/BfR Workshop Art. 57f baua:

Art. 57f and equivalent level of concern

Art. 57 f: Substances - such as those having *endocrine disrupting properties* or those having *persistent, bioaccumulative and toxic properties* or *very persistent and very bioaccumulative properties*, which do not fulfil the criteria of points (d) or (e) - for which there is scientific evidence of probable serious effects to human health or the environment which give rise to an **equivalent level of concern** to those of other substances listed in points (a) to (e) and which are identified on a **case-by-case basis** in accordance with the procedure set out in Article 59.

29.03.2012

9 Dr. Frauke Schröder, BAuA/BfR Workshop Art. 57f

Art. 57f and equivalent level of concern

- "safety net" for substances with any kind of properties that give rise to an equivalent level of concern
- endocrine disruptors and PBT/vPvB-like substances explicitly mentioned as examples
- intends to cover as well other (unforseeable) properties
- setting of clear criteria not possible

29.03.2012

10 Dr. Frauke Schröder, BAuA/BfR Workshop Art. 57f

Art. 57f - Implications for SVHC identifications

CMR substances (Art. 57a - c) - criteria in CLP regulation (in practice harmonised classification needed)

PBT/vPvB substances (Art. 57d - e) - use criteria in Annex XIII of REACH

Other hazard properties - Hazard as well as ELoC needs to be proven in case-by-case consideration (even if harmonised C&L exists)

=> see ECHA's presentation on requirements for an Annex XV dossier proposing SVHC identification via the 57f route

29.03.2012

11 Dr. Frauke Schröder, BAuA/BfR Workshop Art. 57f

Art. 57f - considerations

Focus shifting from CMR to other properties

One substance already identified as SVHC according to Art. 57f (4-tert-octylphenol, ED)

What about substances with other properties? Which properties do we consider as eqivalent level of concern?

How to determine "equivalence" of the level of concern?

29.03.2012

12 Dr. Frauke Schröder, BAuA/BfR Workshop Art. 57f

Outlook

This Workshop:

Focus on HH non-endocrine disrupting properties to

- Discuss which properties potentially fall under Art. 57f
- Discuss potential criteria for the determination of an equivalent level of concern

Medium term:

- Agree on common principles to make full use of Article 57f SVHC identification

29.03.2012

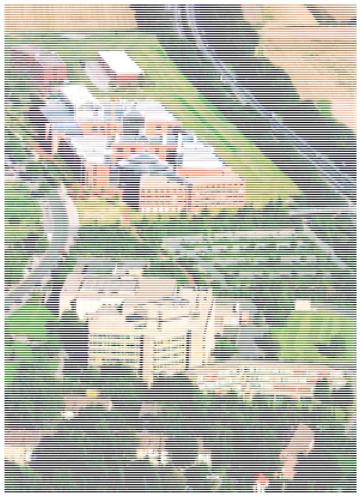
Outlook – Benefit of Common Principles

Harmonised criteria

- define which substances qualify as SVHC:
- => greater transparency and traceability of decisions, consistency across substances
- define which substances do NOT qualify as SVHC:
- => focus available resources on real problems
- are not in contradiction to case-by-case evaluations
- are no stipulations → final decision for proposal will remain with the authorities

29.03.2012

Thank you for your attention



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29.03.2012

Bundesanstalt für Arbeitsschutz und Arbeitsmedizin

General Concept for Applying Article 57(f) to Non-Endocrine Disrupting Human Health Hazards

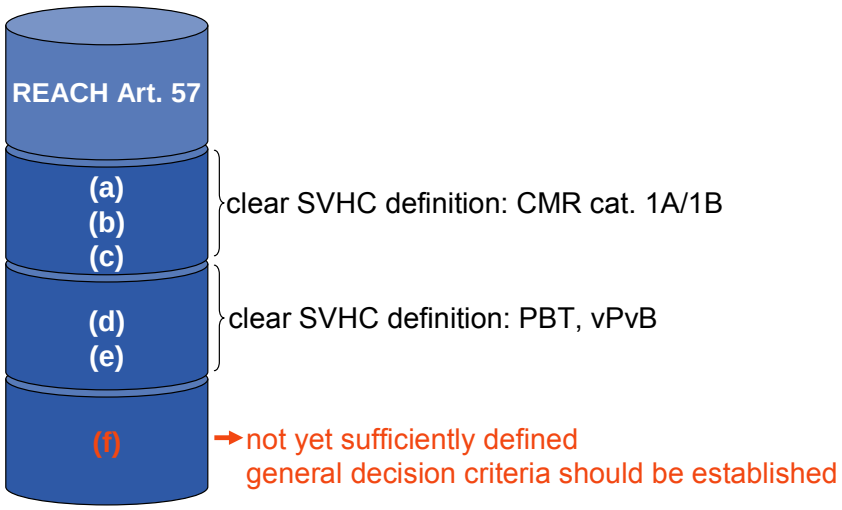
Wiebke Prutner

Joint BAuA/BfR Workshop
29 March 2012, Berlin

REACH Article 57(f):
Non-Endocrine Disrupting Human Health Hazards Leading to SVHC Identification

Introduction

- **Why a general concept?**



Decision criteria should consider whether equivalent level of TOXICOLOGICAL concern is fulfilled

- **Why toxicological concern?**

REACH Art. 57(f):

…substances [may be included in Annex XIV]…for which there is scientific evidence of probable serious **effects to human health**… **which give rise to an equivalent level of concern**…to those of [CMR cat. 1 substances]…

Toxicological Concern - Requirement No. 1

- **Toxicological data of 57(f)-SVHCs should have an equivalent strength of evidence compared to CMR cat. 1**

→ Harmful effects should be **sufficiently relevant to humans**

- Relevance to humans is proved for the majority of health hazard classes and categories on the basis of classification criteria

- However: What about CMR cat. 2?

→ R cat. 2 classification is only based on **some evidence** in humans and experimental animals

→ R cat. 2 might not fulfil this requirement by default

→ …and what about CM cat. 2?

A closer analysis will be given in the following presentation! 

Toxicological Concern - Requirement No. 2

- **Seriousness of effects of 57(f)-SVHCs should be equivalent to that of CMR cat. 1 effects**

  → Type of effects should be **sufficiently serious**

- Examples are

  - death
  - major permanent functional changes in organ systems
  - severe organ damage
  - irreversible effects

- The following health hazard categories might not fulfil this requirement by default:

  - skin irritation
  - eye irritation
  - STOT SE 3

  } These health hazard categories cover only effects which are reversible and not serious.

Toxicological Concern - Requirement No. 3

- **57(f)-SVHCs should have a high toxic potency**

  → Toxic potency should be **sufficiently critical**

  → The higher the toxic potency, the more critical the dose-response relationship

- Example: acute toxicity by inhalation (gases)
  - a broad concentration range is covered (factor >200)

Category 1	Category 2	Category 3	Category 4
≤ 100 ppmV	100 - 500 ppmV	500 - 2500 ppmV	2500 - 20000 ppmV

- Which category should be considered as being equivalent to CMR cat. 1?

A closer analysis will be given in the following presentation! 

Toxicological Concern - Requirement No. 4

- **57(f)-SVHCs should have a harmonised classification (CLH)**

  → This is not so much a toxicological requirement as a **formal requirement**

  → If there is a serious effect of equivalent concern it should be approved by a harmonised classification

  CLH dossier → RAC (technical committee) is involved and provides toxicological expertise by default

  SVHC dossier → RAC is not involved

- **CLP Regulation Art. 36 (3)**
  CLH for other hazard classes or differentiations may be proposed on a case-by-case basis and if justification is provided

Decision criteria should also consider whether a REGULATORY concern is fulfilled

- **Why regulatory concern?**

  → Toxicological concern alone **does not** allow for an **efficient discrimination** between SVHCs
  - that should be regulated through the authorisation process and
  - those where such a regulatory action would not lead to an improvement regarding human health protection

  REACH Article 55:

  …**risks** from SVHCs shall be **properly controlled** and **SVHCs** shall be progressively **replaced**…

- Two "types" of regulatory concern are conceivable
  - a general regulatory concern
  - a specific regulatory concern

"General" regulatory concern

- **Are there specific hazards/hazard categories that can generally be better controlled than others?**

- For example:

hazard/hazard category	characterised by	general controllability
acute toxicity cat. 1	immediate onset of effects	may be assumed to be **less difficult**
STOT RE	delayed onset of effects	may be assumed to be **more difficult**

A closer analysis will be given in the following presentation! 

"Specific" regulatory concern

- **Are data available demonstrating evidence for definite substance-related risks?**

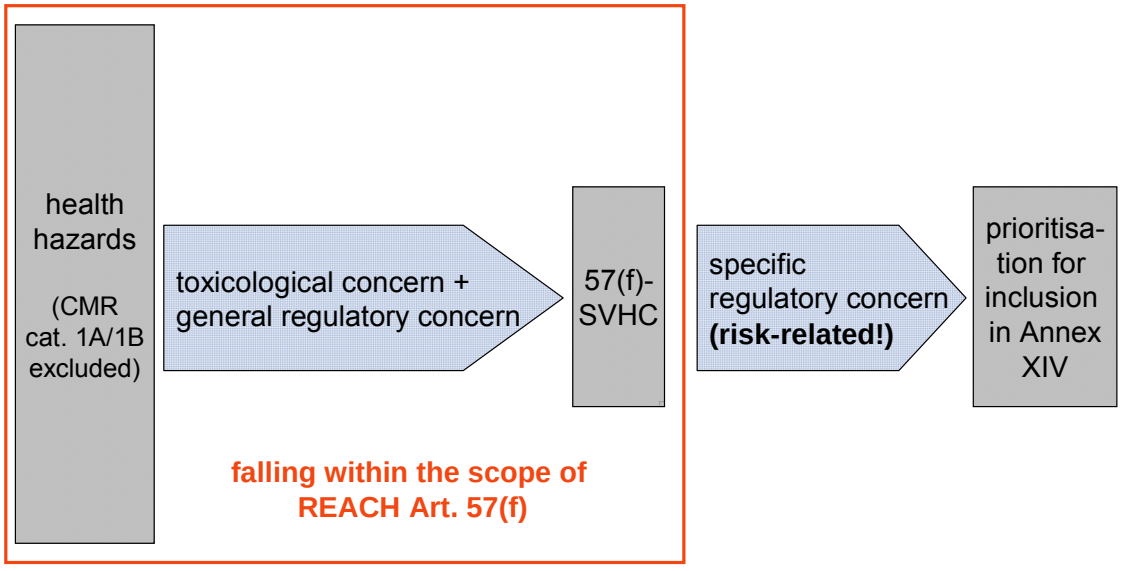
- For example:

substances classified for STOT RE in cat. 1	practical experiences show	consequence
substance A	no reports on health effects	not to be prioritised
substance B	no reports on health effects	not to be prioritised
substance C	no reports on health effects	not to be prioritised
substance D	case studies indicating severe effects due to relevant exposure	to be prioritised for inclusion in Annex XIV
substance E	no reports on health effects	not to be prioritised

Summary I

- **A general concept should comprise decision criteria taking account of toxicological and regulatory concerns**
- **Toxicological requirements are**
  - harmful effects of 57(f)-SVHCs should be **sufficiently relevant to humans**
  - harmful effects of 57(f)-SVHCs should be **sufficiently serious**
  - toxic potency of 57(f)-SVHCs should be **sufficiently critical**
- **57(f)-SVHCs should have a harmonised classification** (formal requirement)
- **Considerations on the general controllability of risks arising from 57(f)-SVHCs may increase or lower the regulatory concern and thus substantiate or weaken their identification as SVHCs**
- **Concrete indications for substance-specific risks increase the regulatory concern and may trigger the prioritisation of 57(f)-SVHCs**

Summary II



FEDERAL INSTITUTE FOR RISK ASSESSMENT

'Equivalent Concern' from a Toxicological View – Ideas and Examples

Agnes Schulte
Matthias Herzler

Steps/Elements of the Authorisation Process

STEP 1: SVHC identification, inclusion into Candidate List

- toxicological domain: justification based on CONCERN, NOT a requirement to prove RISK

STEP 2: Inclusion into Annex XIV

- toxicological and regulatory domain: prioritisation by ECHA
  - ➲ based on capacity, hazard, and exposure

STEP 3: Authorisation

- regulatory domain
- burden of proof on industry
  - ➲ demonstrate proper control of risk, discuss alternatives

There is nothing wrong in considering aspects of step 2 or 3 already at step 1
  - ➲ e.g. known problems with risk control, known alternatives etc.

However: **THIS IS NOT A REQUIREMENT!**

Aspects of Toxicological Concern

Art. 57 (f):

‚PROBABLE [and] SERIOUS effects of EQUIVALENT CONCERN…'

‚SERIOUS':

- seriousness must be equivalent to CMR Cat. 1
  - ➲ definitions from ECHA guidance on preparation of SVHC dossiers:
    - ➔ death, severe organ damage, (consistent signs of) major permanent functional changes in organ systems, irreversibility…

'PROBABLE':

- evidence in animals, relevance in humans must be equivalent to CMR Cat. 1
  - ➲ (harmonised) classification as a pre-requisite
- concern decreases with decreasing potency
  - ➲ consider classification subcategories

Aspects of Regulatory Concern for Consumer Protection

Specific situation for consumer substances/mixtures/articles:

- the same substance e.g. a plasticiser, colorant, fragrance etc. may be contained in numerous products for diverse uses
- data on uses and/or quantitative exposure are mostly unavailable
- a priori calculation of risk is impossible in most cases
- paradigm of substitution, if suitable alternatives are available
  - ➲ particularly relevant for high potency substances

On the other hand there is a need to

- focus regulatory capacities on problematic substances
- filter out less problematic ones, don't 'block the pipeline'

SVHC Identification from the Perspective of Consumer Protection

1. Qualitative consideration of exposure (likely? yes/no)
2. Determine hazard profile based on (harmonised) classification
3. Focus on serious repeat-dose or delayed effects
   - ➲ concentrate on highest potency categories
   - ➲ exclude effects with lack of sufficient evidence or relevance
4. Consider serious acute effects or repeat-dose/delayed effects of lower potency on a case-by-case basis
   - ➲ if specific information is available suggesting problems with risk control (e.g. case reports, epidemiological data)

Decision on relevant effects (points 3. and 4.) is not consumer-specific and is analysed in more detail on the following slides

Repeat Dose/Delayed Effects

Repeat-Dose/Delayed Effects: STOT SE and RE

SERIOUSNESS

- particular (but not exclusive) focus on irreversible effects, significant impairment of life (neuro-/oto-/ocular toxicants, immunotoxicants)
- Cat. 1 and 2 meet criteria, STOT SE Cat. 3 (acute, reversible) does not

POTENCY

- Cat. 1 and 2 have different guidance values, hazard communication
  - ➲ Cat. 1: Signal word 'Danger'
  - ➲ Cat. 2: Signal word 'Warning'

CONCLUSIONS

- STOT Cat. 1 fulfils SVHC criteria by default, high priority
- STOT Cat. 2 may fulfil SVHC criteria on case-by case basis
  - ➲ priority if specific information (e.g. epidemiological data) is available that suggests inadequate risk control or need for substitution

Repeat-Dose/Delayed Effects: Respiratory Sensitisation

SERIOUSNESS

- Delayed, irreversible effect, no threshold
- asthma, allergic rhinitis, from impairment of lifestyle (increasing responsiveness to irritants) to life-threatening condition
- in general, high concern for respiratory sensitisers
  - ➲ harmonised classification required
  - ➲ hazard communication

POTENCY

- little practical experience with new subcategories (2nd ATP CLP)

CONCLUSIONS

- respiratory sensitisers always fulfil SVHC criteria with high priority
- consider revision after introduction of clear criteria for subcategories

Repeat-Dose/Delayed Effects: Skin Sensitisation

SERIOUSNESS

- Delayed, irreversible effect, no threshold
- from impairment of lifestyle to life-threatening condition
- current legislation: lower concern than for resp. sensitisers
- however, very high concern may be caused by high potency, cross-reactivity, potential for allergic reaction via other routes

POTENCY

- little practical experience with new subcategories (2nd ATP CLP)

CONCLUSIONS

- skin sensitisers may cause equivalent concern on case-by case basis
  - ➲ need for discussion of criteria, e.g. priority if specific information suggests high potency or inadequate risk control

Repeat-Dose/Delayed Effects: CMR Cat. 2

SERIOUSNESS

- criteria are fulfilled
  - ➲ unclear for mutagens with evidence in somatic, but not germ cells

EVIDENCE/RELEVANCE

- in general not fulfilled for Cat. 2 CMR substances (otherwise → Cat. 1B)
  - ➲ exceptions: threshold carcinogens/mutagens (spindle poisons)

POTENCY

- for threshold carcinogens: consider STOT guidance values

CONCLUSIONS

- in general, SVHC criteria are not fulfilled for CMR Cat. 2
- possible exceptions case by case: threshold carcinogens, mutagens

Repeat-Dose/Delayed Effects: Lactation

SERIOUSNESS

- criteria are fulfilled

EVIDENCE/RELEVANCE

- if damage to offspring has been demonstrated
- not, if only toxicokinetic studies suggest toxic levels

POTENCY

- not considered for classification

CONCLUSIONS

- fulfilled, if damage to offspring is shown
- not fulfilled, if toxic levels are only assumed

Acute Effects

Acute effects: Acute toxicity

SERIOUSNESS

- criteria fulfilled

Category 1	Category 2	Category 3	Category 4
			
Danger	Danger	Danger	Warning
Fatal if…	Fatal if…	Toxic if…	Harmful if…

POTENCY

- ***DISCUSS***:
  only Cat. 1 and 2 ('Fatal if…') are considered to pose 'very high concern'

REGULATORY CONCERN

- in general: low due to practical need for effective risk management when handling substances of high acute toxicity

CONCLUSIONS

- in general, SVHC criteria are fulfilled for Cat. 1 and 2, but low priority
- case-by-case deviation possible based on information on inadequate risk management or need for substitution

Acute effects: Corrosion, Irritation, Eye Damage

SERIOUSNESS

- criteria fulfilled for Skin Corr. and Eye Dam., not for Skin/Eye Irrit.

POTENCY

- only applicable for Skin Corr.
  - ➲ subcategories 1A, 1B, 1C: no differentiation by pictogram, signal word, or hazard statement → **DISCUSS priority**

REGULATORY CONCERN

- in general: low due to practical need for effective risk management when handling highly corrosive substances

CONCLUSIONS

- in general, SVHC criteria are fulfilled for Cat. 1, but low priority
- Skin Corr. 1 and Eye Dam. 1 case by case based on specific information

Acute effects: Aspiration

SERIOUSNESS

- criteria fulfilled

REGULATORY CONCERN

- in general: low
  - ➲ oral uptake of industrial chemicals likely only in accidental setting or upon misuse

CONCLUSIONS

- in general, SVHC criteria are fulfilled, but rare occurrence
- SVHC identification possible based on specific information on problems with risk control

Summary

Group 1: **Always qualifying as SVHC with high priority**

- repeat-dose or delayed effect and high potency
  - ➲ STOT SE 1, STOT RE 1, Resp. Sens.

Group 2: **Qualifying as SVHC on a case-by-case basis**

- specific information is needed, either toxicological (Carc./Muta Cat. 2, lactation) or regulatory (evidence for inadequate risk management or need for substitution)
  - ➲ Acute Tox. (1+2), Skin Corr. 1, Eye Dam. 1, Skin Sens., STOT SE 2, STOT RE 2, Carc. Cat. 2 (threshold), Muta Cat. 2 (threshold), Lactation (damage to offspring), Aspiration

Group 3: **Never qualifying as SVHC on a case-by-case basis**

- non-serious effects, lack of sufficient evidence
  - ➲ Skin Irrit. 2, Eye Irrit. 2, STOT SE 3, Repr. Cat. 2

FEDERAL INSTITUTE FOR RISK ASSESSMENT

Thank you for your attention

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Requirements for an Annex XV Dossier Proposing SVHC Identification Via the Article 57(f) Route

Peter Lepper
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Joint BAuA/BfR Workshop –REACH Article 57 (f)
Berlin, 29 March 2012

Content

- Before proposing ….
- SVHC identification – dossier requirements
- Article 57 (f) – specific dossier structure
  - Annex XV report tiered structure
  - Level of concern assessment - Potential factors for comparison
  - Further information to be provided in the Annex XV report
- Conclusions

Before ….

proposing a substance be identified as SVHC consider whether:

- it might fulfil any criteria set out in Article 57 a – f
- SVHC identification connected with Candidate listing and eventual subjection to the Authorisation requirement (inclusion in Annex XIV) is the appropriate route for risk management
  (e.g. RM requirements resulting from manufacture, certain exempted uses or imported articles are not in the scope of authorisation)

➢ Other RM instruments (or combinations thereof) may be more suitable and efficient, e.g.:
- Restriction
- Classification and Labelling
- other Community legislation *(occupational health, industrial emissions, etc.)*

☞ Recommended to conduct a Risk Management Option Analysis (RMOA) to facilitate decision on the appropriate RM route/instruments

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SVHC identification – dossier requirements

➢ REACH Article 59 requires SVHC proposals to be documented in a dossier in accordance with the relevant sections of Annex XV

- **Proposal**
  Substance ID
  Indication which properties listed in Art. 57 are considered to be met
- **Justification**
  CMR - reference to harmonised classification
  PBT and vPvB - comparison of available information with Annex XIII criteria
  Equiv. concern – assessment of the hazards and comparison in accordance with Art. 57(f)
- **Information**
  Provide available information on uses and exposure and on alternative substances and techniques
  (☞ *Not relevant for SVHC identification but for potential subsequent risk management steps*)

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Structure Annex XV report - if proposal based on Art. 57(f)

Article 57(f):

Substances [...] for which there is scientific evidence of probable serious effects to human health or the environment which give rise to an equivalent level of concern to those of other substances listed in points (a) to (e) and which are identified on a case-by-case basis […]

☞ Art. 57(f) has a *'safety net'* function.
Hardly possible to establish an exhaustive list of aspects / impacts that might be relevant for concluding that probable effects are of equivalent level of concern

☞ *'equivalent'* does not necessarily mean *'similar'*

➢ Article 57(f) requires case by case:

- Assessment of hazard properties and comparison of impact of the potential serious effects of the substance concerned on health or environment with that of CMRs or PBT/vPvB
- Evidence that the substance is of equivalent level of concern - by concluding on the results of comparison of relevant hazard properties

⇨ Documentation in Annex XV SVHC report

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Structure Annex XV report - if proposal based on Art. 57(f)

Tier I

➢ Document/justify that the substance concerned has the hazard properties claimed to constitute a concern in accordance with Art. 57(f)

➢ For hazards that can be classified a classification process in accordance with the CLP Regulation should be carried out before identification of the substance as SVHC
– no classification via the SVHC dossier! *(MSC Manual of decisions)*

➢ Compare the impact on human health or environment of the hazard properties relevant for the concern with that of
CMRs (Art. 57 (a-c) or of
PBT/vPvB (Art. 57 (d-e)

➢ Potentially consider further factors, such as e.g. 'mode of action', 'quality of life impaired'

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Structure Annex XV report - if proposal based on Art. 57(f)

Level of concern assessment–Examples of potential factors for comparison

- Health effects
  - Seriousness of possible health effects
  - Irreversibility of health effects
- Other factors
  - Quality of life impaired
  - Uncertainties in establishing dose-response relationships - difficulties in / possibility of deriving a 'safe concentration'
  - Delay of health effects
  - Potency
  - Mode of action (e.g. ED)
  - Long range transport potential / spatial aspects

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Structure Annex XV report - if proposal based on Art. 57(f)

Tier II

- Conclude whether the substance is of equivalent level of concern - based on the results of the comparison of the relevant hazard properties (and potentially other factors) of the substance with that of CMRs or PBT/vPvB
- Consider all impacts in WoE assessment

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Further information to be provided in the Annex XV report

- Need to define whether the properties concluded to be of 'equivalent level of concern' refer to human health and / or environmental concerns for purpose of:
  - Potential exemptions under Art. 56 (5) for substances in cosmetic products or in food contact materials if only identified under Art. 57 (f) because of their hazards to human health
  - Clarity on risks to be assessed in authorisation applications under Art 62 (4d)

- Information (Part II of Annex XV report)

  Available information on uses and exposure and on alternative substances and techniques

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Conclusions

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Annex XV report structure in case of SVHC proposal in accordance with Article 57 (f)

- Document hazard properties and potential other relevant factors
- Conduct comparative assessment of substance properties *(i.e. potential serious effects)* versus properties of CMRs and/or PBTs/vPvBs
- Conclude on 'equivalent level of concern' on the basis of the comparative assessment
- Indicate whether the 'equivalent level of concern' refers to human health and / or environmental concerns to enable decisions in relation to Art. 56(5) and Art. 62 (4b)
- Include in Part II of the AXV report information referring to uses and exposure and to alternative substances and techniques *(support to potential further RM steps following CL inclusion)*

☞ *But before consider whether Candidate listing and potentially Authorisation are the appropriate risk management instruments (conduct RMO analysis!)*

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Thank You.

Risk Management Identification Unit - ECHA

Dr. Erika Kunz
Corporate Product Stewardship
Head of Registration and Evaluation of Chemicals
29.03.2012

Chemical Industry's View on Article 57(f)

Clariant
Exactly your chemistry.

Setting the Scene

Clariant
Exactly your chemistry.

Which substances may qualify as SVHC based on the criteria defined in Art 57(f)?

- Substances identified, on a case-by-case basis, from scientific evidence as causing probable serious effects to human health or the environment of an equivalent level of concern as:
  - Substances being Carcinogenic, Mutagenic or toxic to Reproduction (CMR),according to new CLP Regulation classified as 1a or 1b.
  - Persistent, Bioaccumulative and Toxic (PBT) or very Persistent and very Bioaccumulative (vPvB) according to the criteria in Annex XIII of the REACH Regulation

Our view on criteria for Art 57 (f):

Clariant
Exactly your chemistry.

- The procedure to identify substances according to Art 57(f) should strictly follow the REACH Regulation - a broadening of the scope not being covered by the regulation is not acceptable.
- The focus has to be maintained on substances causing serious effects to human health and environment equivalent to Art 57 a-e
- Scientific evidence is a pre-requisite for a case by case approach which is mandatory for the identification procedure taking into account risk based considerations for a specific substance. Based on a case by case approach it is per se not possible to define general criteria for the definition of a substance as being eligible for becoming a SVHC.

 29.03.2012 Slide 3

Our view on criteria for Art 57 (f):

Clariant
Exactly your chemistry.

- Art 57(f) is understood as an escape clause for substances having other serious risks to human health and environment than those defined at the time of drafting the regulation
- Art 57(f) is not understood as a general empowerment to include any substance classified according to the CLP regulation to the SVHC substance list but is understood as the legal instrument to regulate those substance which during use may cause other serious effects
- Identification of SVHC according to Art 57(f) only after thorough evaluation of all available data including assessment of risks

 29.03.2012 Slide 4

Our view on criteria for Art 57 (f):

Clariant
Exactly your chemistry.

- Hazardous substances potentially in the scope of Art 57(f) are already covered by existing regulations:
  - They have to be registered according to their tonnage band, Safe handling has to be demonstrated
  - They may be part of the CoRAP
  - They are classified according to Annex VI (Harmonized classification and labeling for certain hazardous substances)
  - Variety of different national and international regulations (Seveso II etc.)
- We see the need of inclusion of substances to the SVHC process only in cases where other risk management options including existing regulation are not sufficiently effective

 29.03.2012 Slide 5

Consequences of the SVHC status

Clariant
Exactly your chemistry.

- Following the identification as SVHC, a substance shall eventually - subsequent to prioritization - become subject to authorization
- As no procedure to remove a substance from the candidate list exists substances should only be included after thorough evaluation and confirmation of risks with equivalent levels of concern during use as indicated in Art 57(f)
- Art 57(f) decisions are aimed to be based on scientific evidence. Creating this evidence is within the scope of other REACH articles.

 29.03.2012 Slide 6

Key message

Clariant
Exactly your chemistry.

- An SVHC status has considerable economical and practical consequences for concerned companies; thus when applying Art. 57(f) a very sound risk assessment based on scientific evidence taking into account probable serious effects to human health or the environment instead of cross-the-board criteria is mandatory for each substance and the relevant particular endpoint.

- Before applying Art. 57(f), it must be checked in each case whether SVHC listing and subsequent authorization is the most appropriate risk management option. There may be alternative regulatory instruments to achieve more focused outcomes.

 29.03.2012 Slide 7

Trade Union's View on Article 57(f)

Tatiana Santos & Tony Musu

REACH Article 57(f): Non-endocrine disrupting human health hazards leading to SVHC identification

Berlin, 29th March 2012

European Trade Union Confederation (ETUC)

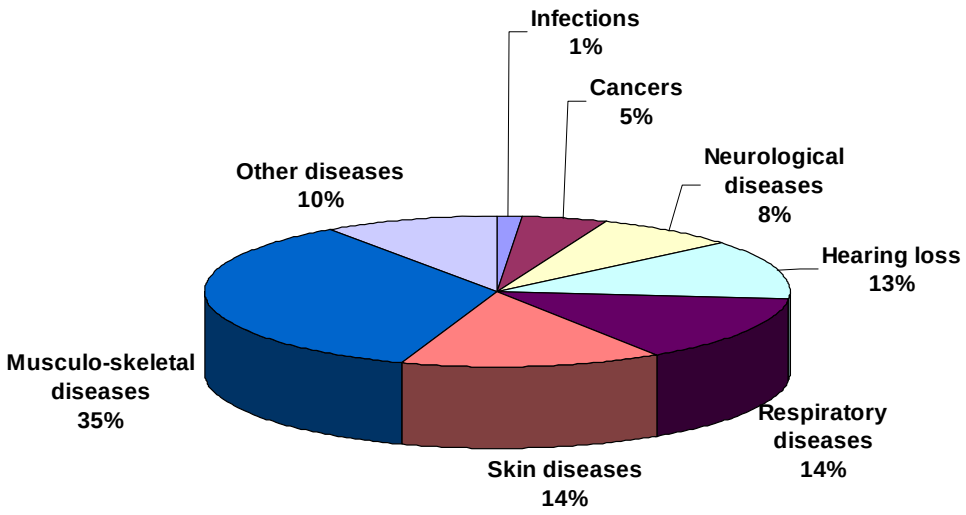
- ETUC is the European social partner representing workers
- The Maastricht Treaty (1992) guarantees this formal status
- Together with the employers, ETUC is involved in consultation in areas such as employment, social affairs, macroeconomic, industrial and regional policy

- 82 National member organisations
- 36 European countries
- 12 European industry federations
- 60 million workers

Overview

- Statistics on recognized occupational diseases in the EU
- Trade Union Impact Study on REACH benefits for workers
- Trade Union Priority List for REACH authorisation
- Sensitizers and neurotoxicants as SVHC under 57f
- Conclusions

Recognized occupational diseases in the EU



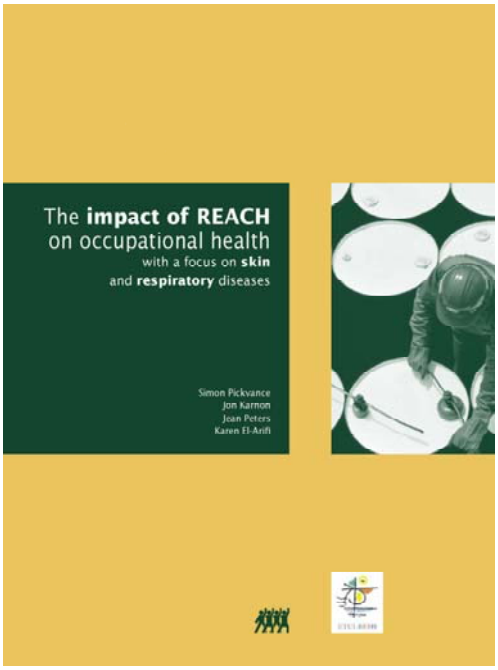
Source: Reaching the workplace, T. Musu, ETUI, 2006

How many occupational diseases are chemicals related ?

Occupational diseases	% amongst all recognised diseases	% linked to chemicals exposure	% chemicals related amongst all recg. diseases
Cancers	5 %	4 – 90* %	0.2 - 4.5* %
Neurological diseases	8 %	2 %	0.2 %
Respiratory diseases	14 %	36 – 89* %	5.0 – 12.5* %
Skin diseases	14 %	88 %	12.3 %
Total			~ 18% to 30* %

(*) Including chemical dust

Impact study on REACH benefits for EU workers' health



- Focus on asthma, chronic obstructive pulmonary diseases & dermatitis for EU workforce (200 million people)
- Respiratory diseases: 50 000 cases/year avoided
- Skin diseases : 40 000 cases/year avoided
- € 3.5 billion benefits over 10 years
- € 90 billion benefits over 30 years

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Impact study on REACH benefits for EU workers' health

Why REACH will help avoiding those occupational diseases ?

- Progress in Harmonized Classification & Labelling
- Better communication on risk management measures in the supply chain (eSDS)
- Authorisation & Restriction procedures to promote substitution of sensitizers

Where do the benefits come from ?

- Savings for social security
- Quality of life gains for workers
- Productivity gains for industry (absenteeism avoided)

http://www.etui.org/Publications2/Reports/The-impact-of-REACH-on-occupational-health-with-a-focus-on-skin-and-respiratory-diseases

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Trade Union Priority List for REACH Authorisation

- Constructive contribution to the choice of SVHC
- 334 high production volume chemicals (version 2.0)
  - *Article 57* (*a* to *e*) + edc + sensitizers + neurotoxicants
  - widely used at the workplace
  - ranked according to their eco-toxicological properties
  - linked to EU recognized occupational diseases
- If they are included in the candidate and authorisation list:
  - workers will get better information on their uses
  - development of safer alternatives will be promoted
  - occupational diseases will be reduced
- The TU list is available on line: www.etuc.org/a/6023

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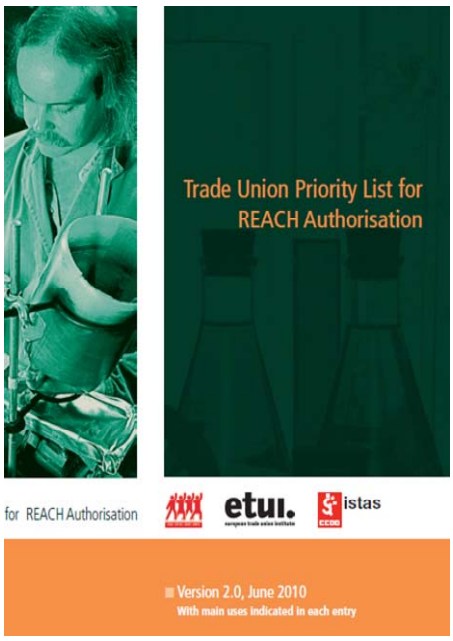
Impact of the TU Priority List ?



- 54 out of 73 substances currently on the Candidate List are also on the TU list
- 11 out of 14 SVHCs included in the Authorisation list are also on the TU list
- 131 substances in common with the Member States List
- Many inquiries from industry

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Sensitizers as SVHC under REACH article 57f

[…] Probable serious effects to human health […] which give rise to an equivalent level of concern to those of other substances listed in points (*a*) to (*e*) […]

- Sensitization to chemicals are recognized as occupational diseases in the EU like cancers
- Irreversibility once a person is sensitized to a chemical agents (short time lag between exposure and symptoms – i.e. few months)
- Symptoms are serious: asthma, COPD, dermatitis
- No available threshold: traces of sensitizers can cause symptoms at the skin or respiratory tract

Strict * 57 f sensitizers from the Trade Union Priority List

Name	CLP skin or respiratory	Occupational health effects
Diisocyanates	S + R	Contact dermatitis, rhinits, conjuctivitis, asthma, allergic alveolitis
Cobalt	S + R	Contact dermatitis, bronco-pulmonary ailments, asthma
Ethylenediamine	S + R	Contact dermatitis, rhinits, conjuctivitis, asthma
Glutaral	S + R	asthma
Trifluralin	S	Hypersensitivity in the skin and respiratory tract
Phthalic anhydides	S + R	asthma
Phenylenediamines	S	Hypersensitivity in the skin and respiratory tract
Aniline	S	Hypersensitivity in the skin and respiratory tract
3,4-dichloroaniline	S	Hypersensitivity in the skin and respiratory tract
Bisphenol A	S	Hypersensitivity in the skin
Alkyl acrylates	S	Contact dermatitis

(*) : sensitizers that are also CMR 1A or 1B removed from this list

Neurotoxicants as SVHC under REACH article 57f

[…] Probable serious effects to human health […] which give rise to an equivalent level of concern to those of other substances listed in points (*a*) to (*e*) […]

- Neurological disorders to chemicals are recognized as occupational diseases in the EU
- Irreversibility of effects (neurodegenerative diseases),
- Symptoms are serious (neuropsychiatric symptoms, permanent nerve damage, senile plaques, neuronal death)
- Specially concerning effects to offspring
- There is no cure
- No available threshold
- Lack of classification
- High impact on occupational health and frequent use in industry

Strict * 57 f neurotoxicants from the Trade Union Priority

Name	Vela et al. classification	Occupational health effects
Acrolein (acrylaldehyde)	Level 4	peripheral nervous system pathology and neuropsychological problems
Manganese	Level 4	neurodegenerative diseases like Parkinson's and Alzheimer's disease. Hyperactivity or learning disabilities in children
Hydrocarbon solvents (e.g. toluene, xylene)	Level 1	neuropsychiatric symptoms and permanent nerve damage. structural birth defects, hyperactivity, attention deficits, reduced IQ, learning and memory deficiencies. offspring to exhibit impulsive behavior and lasting deficits in social adaptability.
PER, and carbon tetrachloride	Level 1	Parkinson's disease
Brominated Flame Retardants		adverse effects on the developing brain
phthalates		Mental and Psychomotor Developmental adverse effects (prenatal exposure)
Mercury	Level 4	Mental retardation, gait and visual disturbances. fetal exposures, have been implicated in language, attention, and memory impairments that appear to be permanent.

(*) : neurotoxicants that are also CMR 1A or 1B removed from this list

Conclusions

- Skin and respiratory sensitizers :
  - meet the REACH article 57f criteria for SVHC identification
  - Substantial benefits for society, workers & industry if they are included in the Candidate list or in Annex XIV
- Neurotoxicants :
  - meet the REACH article 57f criteria for SVHC identification
  - Potential high benefits for society, workers & industry if they are included in the Candidate list or in Annex XIV
- Trade Union Priority List is a good starting point to select 57f SVHC candidates

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Thank you, further info on:

http://www.etuc.org > Our activities > REACH

http://www.etui.org/Topics/Health-Safety/Chemicals-and-REACH

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View(s) of the French MSCA on Human Health Hazards under Article 57(f)

Anses, on behalf of the French Competent Authority

Thoughts, not a fixed view

- Anses = MNI in support of the French CA
- First thoughts related to the issue of 57(f) in relation to CMR properties
- Result of how we have reasoned…

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Context and objectives of the WS

- Art. 57 f: substances that cause '[…] probable **serious effects to human health** […] which give rise to an equivalent level of concern to those of other substances listed in points (a) to (e) […]' i. e. as compared to CMR Cat. 1 substances [Art. 57 (f)]
- no further definition of what could constitute equivalent level of concern to that associated with CMR effects
- Issue as we understand it:
  - Discuss views on **possible Article 57 (f) criteria** for non-ED human health hazards
  - Criteria should allow to identify at least serious effects to humans
- CLP hazard classes ?

anses

3

57(f): how and why ?

- "White Paper" of COM (2001) →New regulatory tool (Authorisation)
- specifically dedicated to regulate "SVHC"
  - CMR 1 or 2
  - POPs
  - EDs were mentioned as new type of substances of concern
- After negotiations with stakeholders and COM/MS works on PBT/vPvB critieria → Art. 57 (legal text 2006)
  - CMR 1 or 2 (1A or 1B)
  - PBT and vPvB (annex XIII criteria)
  - 57(f)

anses

4

57(f) assumption

- It is probable that 57(f) has been written specifically for ED **and** to anticipate similar emergent/future concerns
- Objectively: other « non-CMR » classes (for ex. STOT-RE/R48) were not included as possible SVHC in art. 57 by the legislator
- → not considered (at this time?) as equivalent concern
- Is it relevant to extend indirectly the scope of potential SVHC through Art. 57f ?
- Could it be challenged from a legal point of view?

anses

5

Sensitizers: a concern for the society

- Increasing allergy/asthma cases were already identified as an increasing concern in the white paper
- "*The incidence of some diseases, **e.g. testicular cancer** in young men and **allergies**, has increased significantly over the last decades*." (White paper, p.4)
- *" **Allergy costs** are estimated at € 29 billion/year in Europe. Chemical substances are considered to play a major role in inducing allergies either directly or by increasing susceptibility to natural allergens (e.g. pollen). For example a US study has shown that **asthma cases have risen by 40 % since the 1970s**." (White paper, p.32)*
- *University of Sheffield, Commissioned by ETUC (2005):*
  - *90 000 professional cases could be avoided (skin and resp. sensitizers)*
  - *3.5 billions euros saved (EU-25)*
- *Expert forecast on emerging chemical risks related to occupational safety and health (EU-OSHA, 2008)*

anses

6

An exception: Sensitizers - Equivalent concern?

- Objectively sensitizers are not identified in the legal text as possible SVHC as CMR

BUT

  - Fulfil the criteria of 57(f)
    - seriousness of effects (permanent impairment of lung functions – possible death)
    - often irreversible nature of the effects
    - difficulty in performing concentration-based risk assessments (no threshold)
    - consequences for the society

AND

  - As CMR, **Resp. Sens.** shall be subject to harmonised classification

  → Indirect regulatory acknowledgement of the concern ?

- Skin sens. = more questionable – to be discussed

anses

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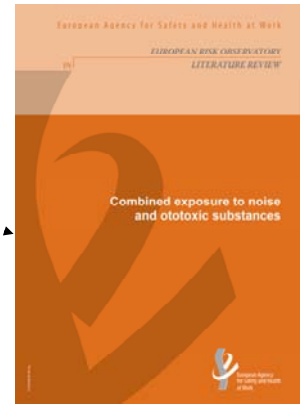
57(f): we know concerns…

Major and chronic diseases (defined as diseases affecting at least 50 per 100 000 people) → together cause 86 % of deaths in the EU (*EU COM, public Health*)

- cardiovascular diseases
- cancer
- neurodegenerative disorders (Alzheimer's…)
- asthma / chronic obstructive pulmonary disease
- metabolic diseases (diabetes…)
- renal diseases
- visual impairment
- hearing disorders
- …



anses

8

Do we have appropriate tools?

- Concern: several substances contributing directly / indirectly to increase « categories » with expected/demonstrated long-term health impacts and economic burden to the society
  - Ex.: Endocrine Disrupters
  - Ex.: Neurotoxicants
- A concern = substance alone ?
- Improve/adapt CLP classes when new concern identified ?
- Need to improve OECD guidelines based on new scientific data
- Even if SVHC: authorisation not always the best management option → need to elaborate best RMO

anses

9

Thank you !

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anses

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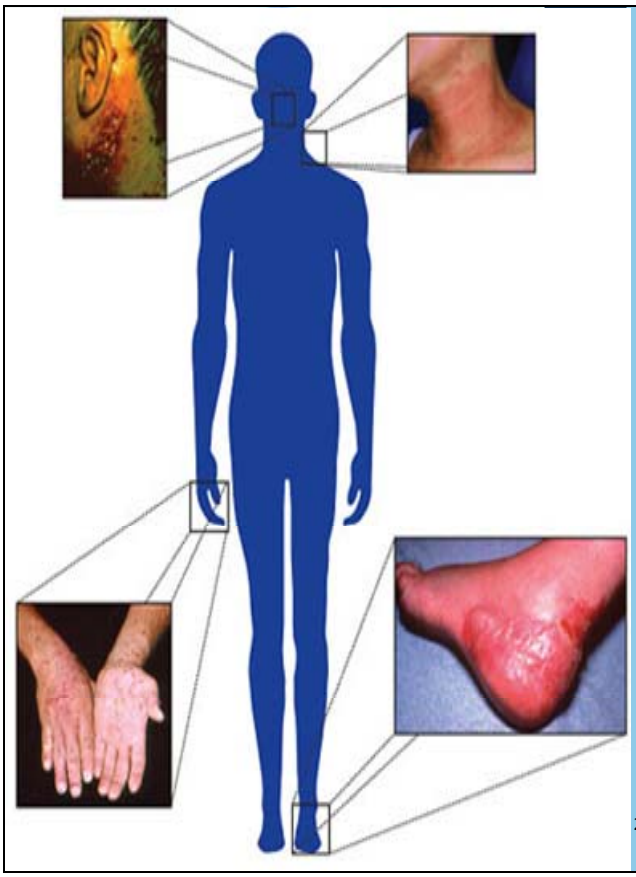

National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

Do sensitizers meet equivalent concern criteria?

Content:

- Equivalent concern for sensitizers
- Respiratory vs skin sensitizers
- Selection and prioritisation

29 March 2012, BAuA Berlin

Do sensitizers meet equivalent concern criteria?

- Serious health effect?
- Is it a hazard that can be classified via CLP?
- Irreversible health effect?
- Quality of life impaired?
- Societal concern?
- Can a safe level of exposure be established?

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Serious health effect?

Respiratory sensitizers

- Yes
- Dyspnea, chronic cough, irreversible airflow limitation due to lung dysfunction (COPD), hospitalization and severe, even life-threatening asthma attacks

Skin sensitizers

- Less serious?
- Skin lesions, permanent scars, malfunction of the immune system
- Still, skin sensitization can not lead to life-threatening situations

True for both respiratory and skin sensitizers: Lack of awareness at first among exposed subjects leads to prolonged or repeated exposure, which can result in more severe effects.

Is it a hazard that can be classified?

Yes, true for both respiratory and skin sensitizers

Irreversible health effect?

Yes, true for both respiratory and skin sensitizers. Although health effects may subside once exposure has ceased, the allergy remains and cannot be cured; possibly leading to health effects upon every next exposure.

'Irreversibility' = permanent adverse change of lung function, permanent malfunction of the immune system, permanent increased risk of manifestation of health effects (asthma, skin sensitization reactions)

Quality of life impaired?

Respiratory sensitizers

- Yes
- Dyspnea, long-term illness, hospitalization, medication

Skin sensitizers

- Less serious?
- Permanent skin scars can have a psychological impact on affected individuals

True for both respiratory and skin sensitizers:

- Workers are not able to perform their original work anymore and have to be assigned other work.
- Affected individuals may find it difficult to avoid consumer products containing allergic agents

Siocietal concern?

True for both respiratory and skin sensitizers:

- In developed countries, allergic diseases affect up to 15-30% of the population
- Prevalence in Europe 20% of the population and is still increasing
- The incidence of occupational asthma in the Netherlands is estimated to be around 500 to 2000 new cases per year
- Estimates of contact eczema in the Dutch population, based on registrations by general practitioners, are around 330,000 subjects

For skin sensitizers: Exposure can relatively easy be avoided

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Can a safe level of exposure be established?

Respiratory sensitizers

- Up till now identified using human data (epidemiology studies) or based on case reports.
- Estimating safe levels at which subjects are not expected to be at risk is therefore very difficult to establish for respiratory sensitizers.

Skin sensitizers

- For some substances possible to derive a No Expected Sensitization Induction Level (NESIL)

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Do sensitizers meet 57(f) criteria?

A clear case for respiratory sensitizers

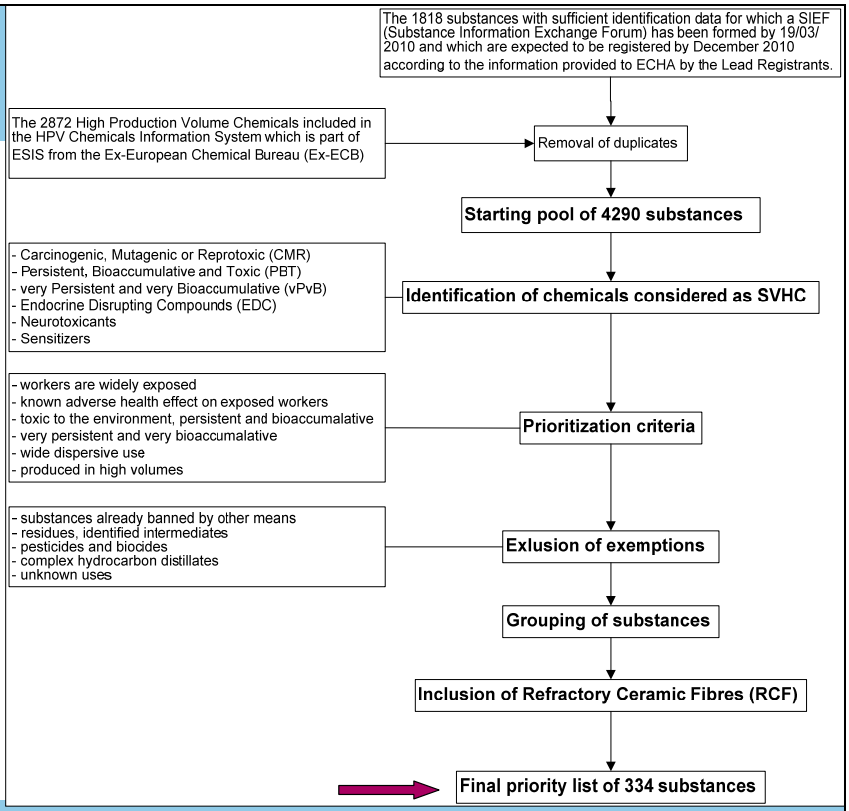
Case for skin sensitizers less obvious

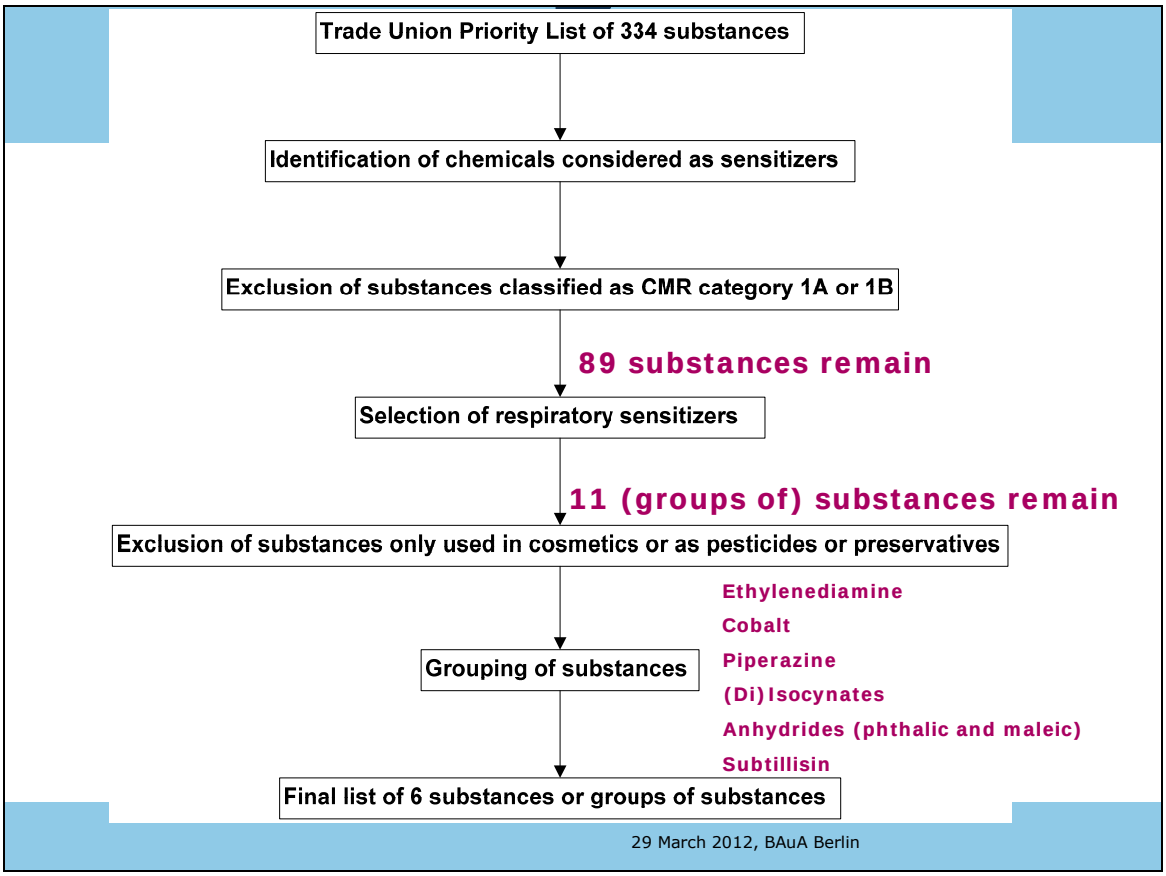
- Exposure can relatively easy be avoided
- Classification is not always based on human evidence
- For some skin sensitizers a "no expected sensitization induction level" (NESIL) can be derived

Selection and prioritisation

- ETUC approach + additional criteria (hazard based approach)
- Information from reported effects for workers and consumers in the Netherlands (effect based approach)

ETUC hazard based approach





Effect based approach

Information from:

- Incidence report on allergic contact dermatitis and asthma
- Registration project Netherlands Centre for Occupational Diseases
- Several RIVM reports with epidemiological data

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Agents

- Rubber chemicals
  → 4,4-dithiodimorpholine, thiuram mix, diphenylguanidine
- Hair (dye) products
  → p-phenylene diamine
- Preservatives (excluded from further analysis)
- Metalworking fluids and oil
  → monoethanolamine, formaldehyde
- Soaps and detergents
  → sensitizing effect by additive like perfume, lonaline, turpentine, preservatives and enzymes
- Acrylates
  → 2-HEMA, TREGDA, DEGDA, BUDA
- Fragrances
  → isoeugenol and many others
- Epoxy substances
  → uncured epoxy resin

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Expert meeting on RIVM

Hazard based approach:

- Diisocyanates (TDI, MDI or HDI)
- Anhydrides (phthalic or maleic)

Because wide spread use and known respiratory properties

Effect based approach:

- Isoeugenol

Because fragrances show sensitization both for worker and consumer, iosoeugenol is chosen based on its strong sensitizing potency.

See: Priority setting and Risk Management Option under REACH for sensitizers, W. ter Burg and W.P. Jongeneel, RIVM letter report 601030001/2011

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NL activities

- Short papers on selected substances have been prepared and discussed with the Dutch Ministries
- Agreed to continue our work on these substances:
  - Further argumentation of hazard
  - Data gathering on manufacture, use, exposure and alternatives
  - Selection of the relevant substances within the groups of diisocyanates and anhydrides
- Decision on most appropriate risk management option, for example:
  - Inclusion in the Candidate list
  - REACH Authorization
  - REACH Restriction (not necessarily a total ban)
  - REACH Substance evaluation
  - Other measures (like measures on the workplace or voluntary action)
  - No action needed

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View of the Swedish MSCA on Article 57(f)

Contact: margareta.warholm@kemi.se

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

Article 57 (f) – legal text

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

Questions to be answered

•Is there scientific evidence of serious (irreversible) effects?

•Is there scientific evidence to conclude that such effects are probable?

•Can these risks not be adequately addressed by "normal" risk assessment?

If YES - SVHC

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Respiratory sensitisers

- Serious and irreversible effects
- Induction phase irreversible
  - Not serious without exposure
  - Can hamper everyday life
  - Change of workplace / profession
- Elicitation phase usually reversible
  - Can be serious
  - Lung damage, anaphylactic shock, death
- Recognised cause of occupational asthma
  - Diisocyanates, cyclic anhydrides

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Respiratory sensitisers

- Difficult to establish ”safe” exposure levels
  - Dose-response relationships unclear
  - Very low exposures can cause effects
  - Large interindividual differences in sensibility
- Fulfil criteria according to Article 57(f)
- CLP: Harmonised classification for CMRs and respiratory sensitisers
- Can be quite costly for society

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Skin sensitisers

- Similar to respiratory sensitisers, but effects (at elicitation) are usually less severe and in most cases reversible
- Easier risk management (avoid skin contact)
- Skin contact can also induce respiratory sensitisation

- Might fulfil criteria according to Article 57(f), but less convincing

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”BT” metals, eg.cadmium

- By definition elements like Cd can not be PBT
- Cadmium is stored in the kidney
  - Half life 10-20 years
  - ”persistent” and ”bioaccumulating”
- Kidney effects are not (or very slowly) reversible
  - possibly due to continued internal exposure
- Osteoporosis/fractures are expensive for society

- SVHC?

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Highly toxic compounds - example Paraquat

- LD_{50}: 10-15 ml of 20 % solution
- Pneumatocytes selectively accumulate Paraquat
- Delayed effect (pulmonary fibrosis)
- No antidote

- SVHC?

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Art. 57(f) in addition to 57(c)

- Authorisation only needed for identified SVHC effects
- The ”cut-off” limits for authorisation of mixtures are different for 57(c) and 57(f)
- General concentration limit for reprotoxic compounds (57(c)) is 0.5% (0.3 % according to CLP)
- General concentration limit for 57(f) is 0.1%
- It is thus of importance that all eligible hazards are identified for the 57(c) compounds
- Example: Reprotoxic compound with an endocrine disrupting mode of action

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Is it possible to apply article 57(f) to identify as SVHC a substance that degrades (outside the body) to CMR category 1A or 1B substances?

- In principle - yes
- Important to define how much needs to be degraded and how fast
- ”Stable” concentration above classification limit?

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In summary

- Respiratory sensitisers – Yes

- Skin sensitisers – Possibly
- Bioaccumulating and toxic metals - Possibly
- Highly toxic compounds – Possibly
- Degrade to CMR compound - Possibly

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Thank you for your attention

Questions?

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