ECHA
EUROPEAN CHEMICALS AGENCY

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DECISION ON SUBSTANCE EVALUATION PURSUANT TO ARTICLE 46(1) OF REGULATION (EC) NO 1907/2006

For N-1-naphthylaniline, CAS No 90-30-2 (EC No 201-983-0), registration number: [redacted]

Addressee: [redacted], registrant of N-1-naphthylaniline (Registrant(s))

This decision is addressed to all Registrants of the above substance with active registrations on the date on which the draft for the decision was first sent, with the exception of the cases listed in the following paragraph.

Registrant(s) meeting the following criteria are *not* addressees of this decision:
i) Registrant(s) who registered the above substance exclusively as an on-site isolated intermediate under strictly controlled conditions and ii) Registrant(s) who have ceased manufacture/import of the above substance in accordance with Article 50(3)of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation) before the decision is adopted by ECHA.

Based on an evaluation by Federal Institute for Occupational Safety and Health (BAuA) as the Competent Authority of Germany (evaluating MSCA), the European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 52 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

This decision does not take into account any updates of the registration of the Registrant after 31 October 2013, the date upon which the draft decision was circulated to the other Competent Authorities of the Member States and ECHA pursuant to Article 52(1) of the REACH Regulation.

This decision does not imply that the information provided by the Registrant in the registration is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on the dossier of the Registrant at a later stage, nor does it prevent a new substance evaluation process once the present substance evaluation has been completed.

I. Procedure

Pursuant to Article 45(4) of the REACH Regulation the Competent Authority of Germany has initiated substance evaluation for N-1-naphthylaniline, CAS No 90-30-2 (EC No 201-983-0) based on a registration dossier submitted by the addressee and prepared the present decision in accordance with Article 46(1) of the REACH Regulation.

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to Environment/Suspected PBT; Exposure/Wide dispersive use N-1-

naphthylaniline was included in the Community rolling action plan (CoRAP) for substance evaluation pursuant to Article 44(2) of the REACH Regulation to be evaluated in 2012. The CoRAP was published on the ECHA website on 29 February 2012. The Competent Authority of Germany was appointed to carry out the evaluation. In the course of the evaluation, the evaluating MSCA noted additional concerns regarding the human health effects of the substance.

The evaluating MSCA considered that further information was required to clarify the above mentioned concerns. Therefore, it prepared a draft decision pursuant to Article 46(1) of the REACH Regulation to request further information. It submitted the draft decision to ECHA on 28 February 2013.

On 20 March 2013 ECHA sent the draft decision to the Registrant and invited him pursuant to Article 50(1) of the REACH Regulation to provide comments within 30 days of the receipt of the draft decision.

By 19 April 2013 ECHA received comments from the Registrant of which it informed the evaluating MSCA without delay.

The evaluating MSCA considered the comments received from the Registrant. On the basis of this information, section II was amended. The Statement of Reasons (Section III) was changed accordingly.

In accordance with Article 52(1) of the REACH Regulation, on 31 October 2013 the evaluating MSCA notified the Competent Authorities of the other Member States and ECHA of its draft decision and invited them pursuant to Articles 52(2) and 51(2) of the REACH Regulation to submit proposals to amend the draft decision within 30 days of the receipt of the notification.

Subsequently, Competent Authorities of the Member States and ECHA submitted proposals for amendment to the draft decision.

On 5 December 2013 ECHA notified the Registrant(s) of the proposals for amendment to the draft decision and invited them pursuant to Articles 52(2) and 51(5) of the REACH Regulation to provide comments on those proposals for amendment within 30 days of the receipt of the notification.

The evaluating MSCA reviewed the proposals for amendment received and amended the draft decision. The conditional requests for reproductive toxicity and carcinogenicity were removed.

The evaluating MSCA reviewed the comments of the Registrant on the proposals for amendment.

On 16 December 2013 ECHA referred the draft decision to the Member State Committee.

By 7 January 2014, in accordance to Article 51(5), the Registrant provided comments on the proposed amendments. In addition, the Registrant provided comments on the draft decision. The Member State Committee took the comments on the proposal(s) for amendment of the Registrant into account. The Member State Committee did not take into account the Registrant's comments on the draft decision as they were not related to the proposal(s) for amendment made and are therefore considered outside the scope of Article 51(5).

After discussion in its meeting on 3-7 February 2014, a unanimous agreement of the Member State Committee on the draft decision as modified at the meeting was reached on 5 February 2014. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

A. Tests on the registered substance

Pursuant to Article 46(1) of the REACH Regulation the Registrant shall submit the following information using the indicated test methods and the registered substance subject to the present decision:

1) Neurotoxicity study in rat, oral route, 90 d (method B.43 of Regulation (EC) No 440/2008 or OECD 424), and in accordance with paragraph 16 of OECD 424, the study protocol shall be combined with method B.26 of Regulation (EC) No 440/2008 or OECD 408; the following points must be addressed:

   - Characterisation of neurotoxicity (possible effects on central nervous system, suitable assays for effects on peripheral nervous system), that allow identification and discrimination of neurotoxicological, dysfunctional and/or narcotic effects,

   - Measurement of haematological parameters to characterise possible anaemia, methemoglobinaemia and Heinz bodies. The spleen, liver, and bone marrow are putative target organs for secondary effects of haemolytic anemia, and should be examined histologically for such effects.

2) Pre-natal developmental toxicity study in rats or rabbits, oral route (test method: EU B.31/OECD TG 414).

B. Information on a tranformation product of the registered substance to be reflected in the CSR

Pursuant to Article 46(1) of the REACH Regulation the Registrant shall also submit the following information on the degradation products of the registered substance in a revised version of the chemical safety report:

3) Prove that the corresponding N-nitrosamine to N-1-naphthylaniline is not formed during use of N-1-naphthylaniline above a concentration of 0.001 % (w/w) in mixtures or 0.075 µg/m^3 in the air.

C. Information on the registered substance to be reflected in the CSR

Pursuant to Article 46(1) of the REACH Regulation the Registrant shall submit the following information in a revised version of the chemical safety report:

4) Conduct a higher tier exposure assessment for dermal and inhalation exposure in accordance with the procedure laid down in the 'REACH Guidance on information requirements and chemical safety assessment', Chapter R.14 and a risk assessment in accordance with the procedure laid down in Part E for all exposure scenarios.

5) Provide a higher tier exposure assessment for dermal exposure in accordance with the procedure laid down in the 'REACH Guidance on information requirements and chemical safety assessment', Chapter R.14 and a risk assessment in accordance with the procedure laid down in Part E for the use of N-1-naphthylaniline in metal working

fluids involving moving objects (e.g. rotating machinery parts) during which wearing gloves comprises a risk of entanglement.

6) Provide the process temperatures and measure the corresponding vapour pressure for the following exposure scenarios at high temperature: Use in open high temperature processes. The resulting vapour pressure shall be used for exposure estimation and risk assessment.

7) Conduct an assessment of peak exposure and a risk assessment addressing potential acute effects resulting from this peak exposure in accordance with the procedure laid down in 'REACH Guidance on information requirements and chemical safety assessment', Chapters R.8 and R.14 and Part E for all exposure scenarios.

8) Provide information on the specification of personal protective equipment and the duration of use for all scenarios where the use of personal protective equipment is advised:

   In particular:
   a) the type of material, thickness and breakthrough times of the gloves and the duration of use for all exposure scenarios where the use of gloves is advised,
   b) specifying for air-purifying respirators, the proper purifying element (cartridge or canister), the adequate particulate filters and the adequate masks, or self-contained breathing apparatus for the scenarios where the use of respiratory protection is advised.

9) Information on consumer uses, consumer exposure scenarios and risk characterisation for consumers

Pursuant to Article 46(2) of the REACH Regulation, the Registrant shall submit to ECHA by **21 August 2016** an update of the registration dossier containing the information required by this decision

At any time, the Registrant shall take into account that there may be an obligation to make every effort to agree on sharing of information and costs with other Registrants.

III. Statement of reasons

Based on the evaluation of all relevant information submitted on N-1-naphthylaniline and other relevant and available information ECHA concludes that further information is required in order to enable the evaluating MSCA to complete the evaluation of whether the substance constitutes a risk to human health or the environment.

During the consultation phase the Registrant submitted an updated list of identified uses. Nevertheless, the draft decision still addresses the identified uses given in the available registration dossier on 31 October 2013. The Registrant does not need to fulfil the requirements in the present decision for uses which are no longer identified in the updated dossier.

A. Tests on the registered substance

Pursuant to Article 46(1) of the REACH Regulation, the Registrant is required to carry out the following studies using the registered substance subject to this decision:

1) Neurotoxicity study in rat, oral route, 90 d (method B.43 of Regulation (EC) No 440/2008 or OECD 424), and in accordance with paragraph 16 of OECD 424, the study protocol shall be combined with method B.26 of Regulation (EC) No 440/2008 or OECD 408

The evaluation raised a concern for neurotoxicity. The subacute study indicated neurotoxicity in the functional observation battery. On d 25 gait abnormalities were observed in female animals in a dose dependent manner. In the two higher dose groups slight gait abnormalities were also observed in few male animals on d 25. The neurological effects were not observed after 2 weeks of recovery subsequent to the administration of the test substance. In a second study a dose-related increase in gait abnormalities was observed in female and male animals in the functional oberservational battery towards the end of treatment and from day 1 onwards at high doses (> 250 mg/kg bw).

Furthermore, no subchronic toxicity study with N-1-naphthylaniline is available.

The Registrant provided as a read-across adaptation a GLP compliant 90-d-study (OECD 408) with a different substance, diphenylamine (CAS No. 122-39-4) for hazard assessment and justifies this approach with the toxicity profile of both substances. He states that despite the more pronounced acute toxicity of N-1-naphthylaniline compared to diphenylamine (LD50 of 1625 mg/kg bw vs. >15,000 mg/kg bw) the analogue approach should mainly be based on the systemic, e. g. non-lethal effects.

This approach is considered as not applicable for the following reasons: This approach is contradicted by the available toxicity data for both substances. Apart from the differences in acute oral toxicity, N-1-naphthylaniline is a strong skin sensitizer and not irritant to skin or eyes. Diphenylamine has a harmonized classification as skin irritant but is not sensitising to skin and no eye irritant. The Registrant noted that for both substances the blood system is a target organ. For diphenylamine a NOAEL of 11.5 mg/kg bw per day was derived in the provided 90-d-study in rats based on effects on decreases red blood cell parameters, compensatory haematopoesis in the spleen and bone marrow, haemosiderosis in the spleen. In a 90-d study in mice a NOAEL of 1.7 mg/kg bw per day was derived based on altered red blood cell parameters, splenic erythropoiesis, splenic congestion and haemosiderosis at 94 mg/kg bw/day (LOAEL). Due to the unusual high factor between the doses (> 55), the NOAEL is likely to be higher.

Whereas similar effects were seen regarding red blood cell effects, haematopoesis or hemosiderosis were not (yet) observed or reported after treatment of rats with N-1-naphthylaniline for 28 d. A NOAEL of 5 mg/kg bw per day based on reduced red blood cell counts, haemoglobin and haematocrit was derived in this study possibly indicating a higher potency of N-1-naphthylaniline to cause haematotoxic effects compared to diphenylamine. In the same study a dose-related increase in gait abnormalities are observed in female and male animals in the functional oberservational battery towards the end of treatment and from day 1 onwards at high doses (>250 mg/kg bw). These effects raise a concern for neurotoxicity of N-1-naphthylaniline as described already at 1a). Similar effects were not reported or not investigated for diphenylamine.

Overall, based on the 28-d study with N-1-naphthylaniline and the data on repeated dose toxicity for diphenylamine the possible chronic toxicity of N-1-naphthylaniline is not predictable regarding the effects or potency compared to the source substance.

The information provided does not meet the requirements of Annex XI 1.5 of the REACH Regulation. In particular, the Registrant failed to demonstrate that apart from the structural

similarity, the physicochemical and toxicological properties of source and target compound are sufficiently similar to justify the proposed read-across approach.

The haematological effects observed in the subacute study raise an additional concern. As described earlier reduced red blood cell counts, haemoglobin and haematocrit were observed in the subacute study with N-1-naphthylaniline. Methemoglobin formation was not examined in the subacute toxicity study. However, the data of the intraperitoneal application of N-1-naphthylaniline indicate the methaemoglobin formation in the mouse (Nomura, A. (1977). Studies of sulfhemoglobin formation by various drugs (3). Nippon Yakurigaku Zasshi. 73(7): 793-802).

To clarify the concern on neurotoxicity, a neurotoxicity study in rat, oral route (method B.43 of Regulation (EC) No 440/2008 or OECD 424) shall be performed.

To clarify the concern on haematotoxicity the above mentioned study shall be combined, in accordance with paragraph 16 of OECD 424, with method B.26 of Regulation (EC) No 440/2008 or OECD 408. Measurements of haematological parameters are necessary to characterise possible anaemia, methemoglobinaemia and Heinz bodies. The spleen, liver, and bone marrow are putative target organs for secondary effects of haemolytic anemia, and should be examined histologically for such effects.

2) Pre-natal developmental toxicity study in rats or rabbits, oral route (test method: EU B.31/OECD TG 414)

There is no information on reproductive toxicity (neither fertility nor developmental toxicity) available for N-1-naphthylaniline. A prenatal developmental toxicity study is a standard requirement according to Annex IX, 8.7.2. The Registrant offers information on the substance diphenyl amine in order to fill the data gap for N-1-naphthylaniline. As stated in part III.1d the read-across approach is not appropriate in this case. Since the substance raised concern on neurotoxicity and haematotoxicity as described in part III.1a and 1e, the lack of any data on reproductive toxicity raises an additional concern. To clarify the concern on reproductive toxicity the Registrant shall perform a pre-natal developmental toxicity study in rats or rabbits, oral route (test method: EU B.31/OECD TG 414).

Once the information requested by this decision is available in the registration dossiers, the evaluating MSCA will be in a position to reassess the situation and, on the basis of that assessment, they will decide on the need to request further information in order to examine any (remaining) concern for reproductive effects and/or carcinogenicity.

In the following section the comments of the Registrant on the initial draft decision are discussed:

1. The Registrant provided comments regarding the rejection of the read-across approach. In his comment he stated that the differences between the source and target substance regarding local toxic effects, predominantly irritation and skin sensitisation, should be excluded from the read-across and provided arguments regarding toxicokinetics, repeated dose toxicity and neurotoxicity to support the appropriateness of read-across with the source substance.

   The arguments of the Registrant particularly those addressing repeated dose toxicity were considered. However, it is concluded that it is justified to adhere to the initial evaluation and reject the read across. The read-across to diphenylamine is rejected

based on the indication of neurotoxicity and hematotoxicity which can not sufficiently be compared to or explained by the 'toxicity profile' of diphenylamine in order to predict the toxicity of N-1-naphthylaniline after prolonged exposure.

Due to the possible neurotoxic effects only a LOAEL can be derived from the 28-d toxicity study. In females of all treatment groups receiving N-1-naphthylaniline a dose-related (0/5, 2/5, 2/5, 3/5 animals) increase in gait abnormalities (incoordination, stilted) on d 25 was observed in the functional observational battery and to a lesser extend also in males (0/5, 0/5, 1/5, 1/5 animals). Considering the fact that gait abnormalities also occurred in the 7-d dose range finding study prior to the main 28-d study these observations raised concern of neurotoxicity though the gait abnormalities were not observed on days 4 or 11 in the main study. There is no neurotoxicity assessment available for diphenylamine. Therefore the uncertainties in the read-across approach remain and clarification is needed regarding neurotoxic properties of N-1-naphthylaniline.

Furthermore, a NOAEL of 5 mg/kg bw/d for N-1-naphthylaniline in the 28-d study as compared to 11.5 mg/kg bw/d of diphenylamine for haematological effects may point to N-1-naphthylaniline being more potent regarding the blood cell system as target for toxicity. Thus, it is important to characterise possible anaemia, methemoglobinaemia and Heinz bodies in the requested study.

2. In his comment the Registrant acknowledged the deficits in the original dossier and demonstrated a general willingness to improve it by submitting a proposal to update the registration dossier.

   An update of the registration dossier was not provided during the evaluation phase or after commenting the draft decision. The proposal indicates that the Registrant might have additional information that was not available to the evaluating MSCA during the substance evaluation. Based on the available information that could be used and which shows some differences in toxicity between the source and the target substance the read across is further considered as not appropriate and the draft decision was not changed.

3. In his comment the Registrant demonstrated the willingness to clarify the concerns raised during substance evaluation and his readiness to perform the required studies by proposing an alternative testing strategy including consideration of read-across option after finalising the study requested in section A, 1) or, if that is not possible to go on as requested.

   Regarding the 90-d neurotoxicity study the original draft decision was amended: the duration of the study is now stated in the request. The guideline does not define the duration unequivocally. As the 90-d study would be a standard requirement for the tonnage band, in which N-1-naphthylaniline is registered, and the Registrant recognised the study duration himself, the study duration is now clearly stated in the decision.

   As the outcome of the 90-d study can not be predicted it is not justified to agree to the proposed "potential read-across approach". Currently there is concern for the endpoint pre-natal developmental toxicity due to the inappropriatness of read-across from diphenylamine and the according data gap for N-1-naphthylaniline. The decision was not changed regarding studies for pre-natal developmental and reproductive toxicity requested in the original draft decision.

4. In his comment the Registrant rejected the proposal for a carcinogenic study present in the initial draft decision.

   It was concluded that there was no need to change the original draft decision as the request was optional and was only to be considered in the case that the results from the required studies do not allow a waiving of this study. Additionally, a clear statement in the CSR regarding whether there is consumer use of the substance is required. On the basis of proposals for amendment on the draft decision, the conditional requests for reproductive toxicity study and carcinogenicity study were removed from the decision. In a comment on the proposed amendments to the Draft Decision dated 5 December 2013, the Registrant considered a deadline of 27 months insufficient to perform and submit the tests required under point 1 and 2. Thus, they requested that the deadline should be changed to 36 months. However during its 34th meeting the Member State Committee concluded that the Registrant failed to sufficiently substantiate this claim and therefore decided that a deadline of 27 months was sufficient.

B. Information on a transformation product of the registered substance to be reflected in the CSR

Pursuant to Article 46(1) of the REACH Regulation the Registrant shall also submit the following information on the transformation products of the registered substance subject to the present decision in a revised version of the chemical safety report:

3) Prove that the corresponding N-nitrosamine to N-1-naphthylaniline is not formed during use of N-1-naphthylaniline above a concentration of 0.001 % (w/w) in mixtures or 0.075 µg/m³ in the air.

According to Article 44 (1) hazardous transformation products are within the scope of the Substance Evaluation. N-1-naphthylaniline is a secondary amine which means that in principle it can be converted to its corresponding N-nitrosamine. According to the Scientific Committee on Consumer Safety: 'Disubstituted nitrogens attached to aromatic rings may generate nitroso compounds as well' and 'the likelihood of a new nitroso compound of as yet unknown biological activity to be genotoxic/mutagenic/carcinogenic is very high' (Scientific Committee on Consumer Safety, Opinion on Nitrosamines and Secondary Amines in Cosmetic Products, 2012).

Principally non-threshold carcinogenic N-nitrosamines are known to be formed under real work place conditions by reaction with nitrogen oxides.[1] Nitrogen oxides are ubiquitous in the environment and their occurrence at the workplace in particular is frequently unavoidable (exhaust fumes from internal combustion engines, etc.).

The reaction of secondary amines and nitrosating agents depends on a variety of different factors (e.g. the concentration and properties of the precursors, process parameters and

[1] Spiegelhalder, B., Preussmann, R. and Hartung, M.: Biological monitoring in the metal working industry. IARC Sci. Publ., 57:943-946, 1984; Wolf, D.: N-Nitrosamine am Arbeitsplatz. Staub - Reinhaltung der Luft, 49(Nr. 6):183-186, 1989; Jarvholm, B., Zingmark, P.A. and Osterdahl, B.G.: N-nitrosodiethanolamine in commercial cutting fluids without nitrites. Ann. Occup Hyg., 35(6):659-663, 1991; Monarca, S., Scassellati, S.G., Spiegelhalder, B., Pasquini, R. and Fatigoni, C.: Monitoring nitrite, N-nitrosodiethanolamine, and mutagenicity in cutting fluids used in the metal industry. Environ. Health Perspect., 101(2):126-128, 1993; Fadlallah, S., Cooper, S.F., Perrault, G., Truchon, G. and Lesage, J.: N-Nitroso Compounds in the Ambient Air of Metal Factories Using Metal-Working Fluids. Bulletin of Environmental Contamination and Toxicology, 57(6):867-874, 1996; Breuer, D., van Gelder, R.: Nitrosamine in Arbeitsbereichen - ein gelöstes Problem? Gefahrstoffe - Reinhaltung der Luft, 61(Nr. 1/2):49-55, 2001; BGIA: B.I.F.A. N-Nitrosamine 9103. 4. Lfg(VIII), 2003; Breuer, D.: N-Nitrosamine in Korrosionsschutzfolien oder Korrosionsschutzpapieren. IFA-Arbeitsmappe, Kennziffer 8175(IV Lfg.30), 2003; Ducos, P. and Gaudin, R.: N-nitrosodiethanolamine urinary excretion in workers exposed to aqueous metalworking fluids. Int. Arch. Occup Environ. Health, 76(8):591-597, 2003.

external influences). Therefore it is not possible to predict the amount of the corresponding N-nitrosamine formed[2] with the existing modelling tools.

The possibility of nitrosamine formation is not mentioned in the registration dossier and not assessed in the risk assessment. Literature search does not reveal information which could exclude the risk. It has to be assumed that the corresponding N-nitrosamine to N-1-naphthylaniline is formed. On the basis of the current information from the registration dossiers a final conclusion on the risk can not be drawn.

Therefore the Registrant is requested to prove that the corresponding N-nitrosamine to N-1-naphthylaniline is not formed during use of N-1-naphthylaniline above a concentration of 0.001 % (w/w) in mixtures or 0.075 µg/m^3 in the air.

Based on the Registrant's comment that the substance is manufactured outside the EU the request focuses on uses only.

Explanatory note:

N-Nitrosamines are a group of highly potent carcinogens. As no limit values for the corresponding N-nitrosamine to N-1-naphthylaniline exist, information from other N-nitrosamines was used as basis. Only few N-nitrosamines are listed in the Annex VI of the CLP Regulation ((EC) No. 1272/2008). One listed N-nitrosamine is N-nitrosodimethylamine (CAS No. 62-75-9, EC No 200-549-8). As it is assumed to be one of the more potent N-nitrosamines, it has a specific concentration limit of 0.001 %. A scientific derivation of an exposure risk relationship was conducted on behalf of the German Committee on Hazardous Substances (AGS). A risk of 4:10 000 to develop cancer after a worklife exposure to N-nitrosodimethylamine corresponds to an exposure of 0.075 µg/m^3. The derivation was not performed in accordance with the REACH Guidance Documents. According to the guidance a value of 1:100000 should be derived which would correspond to an exposure of 0.0019 µg/m^3. The specific concentration limit of N-nitrosodimethylamine and the exposure concentration corresponding to a risk of 4:10000 were chosen as threshold limits. A risk could be considered of low concern if N-1-naphthylaniline does not form the corresponding N-nitrosamine in concentrations above of 0.001 % (w/w) in mixtures or 0.075 µg/m^3 in the air. Alternatively, the determination of the carcinogenic potency of the N-nitrosamine of N-1-naphthylaniline in a carcinogenicity study according to EU B.32/OECD TG 451 would be possible. As this approach is both time and money consuming the relation to the N-nitrosodimethylamine has been used.

The Registrant commented that he plans to use a worst case approach to cover the different applications of the downstream users.

C. Information on the registered substance to be reflected in the CSR

Pursuant to Article 46(1) of the REACH Regulation the Registrant shall submit the following information in a revised version of the chemical safety report. During the consultation phase the registant stated that he will update the CSR and the risk assessment, taking the proposals of the draft decision into account, for the uses that were reported back from the second survey to identify which uses are conducted by the downstream users. He added that this will happen when all the data is on hand. The efforts of the Registrant are acknowledged. However, timeline and requirements of the draft decision are binding.

[2] Wolf, D., N-Nitrosamine am Arbeitsplatz. Staub - Reinhaltung der Luft, 49 (Nr. 6):183-186, 1989.

4) Conduct a higher tier exposure assessment for dermal and inhalation exposure in accordance with the procedure laid down in the 'REACH Guidance on information requirements and chemical safety assessment', Chapter R.14 and a risk assessment in accordance with the procedure laid down in Part E for all exposure scenarios.

The Registrant has estimated workplace exposure to N-1-naphthylaniline using the Tier 1 model ECETOC TRA V2.0 using non-standard factors for glove efficiency and dermal protection without giving an acceptable justification. In the registration dossiers for exposure estimation an efficiency of 99 % for protective gloves is assumed for all exposure scenarios. Such values are usually not considered realistic and are not justified within the documentation of the used model (e.g. in ECETOC TRA V3 the highest value for professional settings is 90% with basic employee training, 95% for industrial settings and special employee training). Within a Tier 1 approach the assumption of 99 % dermal protection is not considered appropriate to estimate dermal exposure.
In addition, the values for dermal and inhalation exposure estimations were not reproducible for the following exposure scenarios:

- General professional use of lubricants and greases in vehicles or machinery (ES 3): PROC 2, 8a, 8b, 20
- (Professional) Use in open system (ES 5): PROC 2, 8a, 10 13
- (Professional) Use in high energy open processes (ES 9): PROC 8a, 17.

Therefore, it has to be assumed that non-justified parameters were used without disclaiming or justifying its use. The risk assessment on the basis of standard parameters and the newly derived DNELs shows particularly high RCR values (up to [redacted]) for the listed uses.

In addition the read-across approach (and therefore the respective DNEL derivation) using data from the 90-day study of diphenyl amine is not acceptable. Long-term systemic DNELs for workers as derived by Registrant are not valid. Short-term, systemic DNELs are missing in the dossier.

As a consequence, a recalculation of the Registrants' exposure estimates using the standard factors of ECETOC TRA version 3 for glove efficiency was performed. Besides, preliminary DNELs were derived on the basis of the available 28-d study according to 'REACH Guidance on information requirements and chemical safety assessment'. The combined risk characterisation ratios (RCRs) exceed the value of 1 in all exposure scenarios.

The use of protection factors higher than the standard parameters is only valid, when an acceptable justification is given. This justification is missing for the protection factors used in the registration dossiers. These factors can only be determined via experimental justification regarding permeation through the glove fabric, penetration of the gloves and human factors.

The used Tier I approach might lead to a higher exposure estimate than the actual workplace exposure concentration. However, on the basis of the current information from the registration dossier, a final conclusion on the risk can not be drawn.

The use of the LEV modifier in ECETOC TRA worker v2 is advised against in ECHA guidance, as it may also lead to underestimation of dermal exposure. This additional uncertainty further justifies the need for the higher tier assessment.

Therefore, the Registrant is requested to conduct a higher tier exposure assessment for dermal and inhalation exposure in accordance with the procedure laid down in the 'REACH Guidance on information requirements and chemical safety assessment', Chapter R.14 and a risk assessment in accordance with the procedure laid down in Part E for all exposure scenarios.

In a higher tier approach for dermal exposure assessment, higher protection factors for gloves could be used to arrive at more realistic exposure estimates. Nonetheless, these factors can only be used, when an experimental justification is given taking into account potential variables encountered in the workplace (industrial/professional) that can influence glove efficiency (in particular: permeation through the glove fabric; penetration of the glove (drips, flaws, worn gloves); and human factors (taking gloves off, contaminating the hands, then putting the gloves back on). Feasible methods are described by Klingner et al. and Henriks-Eckerman et al[3].

To enable evaluation of the assessment all used models and parameters should be clearly stated. When using non-standard parameters a justification must be given, otherwise the use of the parameter can not be assumed to be justified.

The requested information will allow a full evaluation whether the occupational risks associated with dermal and inhalation exposure at all workplaces are controlled.

If for any use it is not possible to control the risk, the use should be listed as 'use advised against'.

5) Provide a higher tier exposure assessment for dermal exposure in accordance with the procedure laid down in the 'REACH Guidance on information requirements and chemical safety assessment', Chapter R.14 and a risk assessment in accordance with the procedure laid down in Part E for the use of N-1-naphthylaniline in metal working fluids involving moving objects (e.g. rotating machinery parts) during which wearing gloves comprises a risk of entanglement.

'Use (of N-1-naphthylaniline) in high energy open processes' is an identified use for the registered substance. Metal working fluids are used at plants with rotating machinery parts. In these workplaces there exists a particular risk for gloves being caught up by a moving object thereby creating a danger for the user (see also Directve 89/686/EEC). When moving objects are involved in the working process wearing gloves comprise a risk due to entanglement which leads to serious injuries.[4] It is well known that these working conditions are common, even though the registration dossiers do not cover this use.

To assess the risks for this scenario 'use (of N-1-naphthylaniline) in high energy open processes involving rotating machinery parts' the glove efficiency would have to be set to zero because wearing gloves is not possible. The recalculation of ES 8 '(Industrial) Use in high energy open processes' and ES 9 '(Professional) Use in high energy open processes' using standard factors and assumptions where possible. In addition recalculated preliminary DNELs were used as the DNELs used by the Registrant were assumed to be not justified.

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[3] (Klingner T.D. and Boeninger, M.F. A Critique of Assumptions about selecting Chemical-Resistant Gloves: A Case for Workplace Evaluation of Glove Efficacy. Applied Occupational and Environmental Hygiene 360-367, 2002; Henriks-Eckerman M.L., Suuronen K., Jolanki R., Riala R., Tuomi, T., Determination of Occupational Exposure to Alkanolamines in Metal-Working Fluids, Ann. Occup. Hyg., Vol. 51, No. 2, pp. 153-160, 2007)

[4] Hauptverband der gewerblichen Berufsgenossenschaften (HVBG). Tätigkeiten mit Kühlschmierstoffen vom Januar 2006. Berufsgenossenschaftliche Regeln für Sicherheit und Gesundheit bei der Arbeit, BG-Regel 143 (2006).

The risk characterisation ratios (RCRs) for these scenarios are already well above 1 when wearing gloves is assumed. Therefore, the scenario in which moving objects are involved leads to even higher risks.

The used Tier I model might lead to a higher exposure estimates than the actual workplace exposure. On the basis of the current information from the registration dossier a final conclusion on the risk can not be drawn.

The use of the LEV modifier in ECETOC TRA worker v2 is advised against in ECHA guidance, as it may also lead to underestimation of dermal exposure. This additional uncertainty further justifies the need for the higher tier assessment.

Therefore, the Registrant is requested to provide a higher tier exposure assessment for dermal exposure in accordance with the procedure laid down in the 'REACH Guidance on information requirements and chemical safety assessment', Chapter R.14 and a risk assessment in accordance with the procedure laid down in Part E for the use of N-1-naphthylaniline in metal working fluids involving moving objects (e.g. rotating machinery parts) during which wearing gloves comprises a risk of entanglement.

To enable evaluation of the assessment, all used parameters should be clearly stated. When using non-standard parameters a justification must be given, otherwise the use of the parameter can not be assumed to be justified.

The requested information will allow a full evaluation whether the occupational risks associated with dermal exposure from use of N-1-naphthylaniline in metal working fluids involving moving objects are controlled.

If for any use it is not possible to control the risk, the use should be listed as 'use advised against'.

6) Provide the process temperatures and measure the corresponding vapour pressure for the following exposure scenarios at high temperature: Use in open high temperature processes. The resulting vapour pressure shall be used for exposure estimation and risk assessment.

For inhalation exposure estimation the used ECETOC TRA model uses vapour pressure as input parameter. The vapour pressure depends on the process temperature. Temperature is not taken into account and specified for the exposure estimation of the following exposure scenario even though the title indicates high process temperature:

- Use in open high temperature processes (ES 6)

It has to be assumed, that all estimations in the CSR are based on the vapour pressure of N-1-naphthylaniline at ambient temperatures. That may lead to an underestimation of the inhalation exposure level. The correct vapour pressure can only be assessed, if the process temperature is given. On the basis of the current information from the registration dossier a final conclusion on the risk can not be drawn.

Therefore, the Registrant is requested to provide the process temperatures and measure the corresponding vapour pressure for the following exposure scenarios at high temperature: Use in open high temperature processes. The resulting vapour pressure shall be used for exposure estimation and risk assessment.

To enable evaluation of the assessment all used parameters shall be clearly stated. When using non-standard parameters a justification must be given, otherwise the use of the parameter can not be assumed to be justified.

The requested information will allow a full evaluation of whether the occupational risks associated with higher exposure from high temperature processes during use of N-1-naphthylaniline are controlled.

7) Conduct an assessment of peak exposure and a risk assessment addressing potential acute effects resulting from this peak exposure in accordance with the procedure laid down in 'REACH Guidance on information requirements and chemical safety assessment', Chapters R.8 and R.14 and Part E for all exposure scenarios

N-1-naphthylaniline is classified for acute effects (Acute Tox. 4). Therefore, if a peak exposure (a short or acute exposure level clearly higher than the full shift average) is to be expected, it needs to be compared to a relevant DNEL to account for these acute effects. The assessment of peak exposure was not performed by the Registrant, however in all exposure scenarios in the chemical safety report a peak exposure has to be expected or can not be outright excluded.

The REACH Guidance on information requirements and chemical safety assessment, Chapter R.14 states: 'Data should cover personal exposures over the working shift and/or describe short-term and/or peak exposures where acute hazards exist and/or where major tasks are undertaken which could give rise to significant exposure.'

On the basis of the currently available data only a conservative estimation of inhalation peak exposure (e.g. following the procedure described in REACH Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.14 by applying a multiplication factor to the Tier 1 full shift exposure estimates) can be performed. A comparison to the only available relevant DNEL (the recalculated inhalation, systemic, long-term DNEL) leads to RCR values above 1 for all exposure scenarios covering a full shift. This approach is not considered appropriate for a reliable assessment of risks resulting from peak exposure to N-1-naphthylaniline due to the following:

- no acute DNEL is available
- the tier 1 exposure estimation for full shift exposures that is used as a starting point is not considered sufficient to demonstrate safe use (see also statement of reasons 6.)
- the relevance of peak exposure for every single contributing scenario (e.g. uses in a closed system) is unclear
- in comparison to real workplace exposures a significant overestimation is possible

Therefore, the Registrant is requested to conduct an assessment of peak exposure and a risk assessment addressing potential acute effects resulting from this peak exposure in accordance with the procedure laid down in 'REACH Guidance on information requirements and chemical safety assessment', Chapters R.8 and R.14 and Part E for all exposure scenarios.

To enable evaluation of the assessment all used parameters should be clearly stated. When using non-standard parameters a justification must be given, otherwise the use of the parameter can not be assumed to be justified.

The requested information will allow a full evaluation whether the occupational risks associated with peak exposure levels clearly higher than the full shift average are controlled.

8) **Provide sufficient and consistent information on the specification of personal protective equipment and the duration of use for all scenarios where the use of personal protective equipment is advised:**

   a) **the type of material, thickness and breakthrough times of the gloves and the duration of use for all exposure scenarios where the use of gloves is advised**

   b) **specifying for air-purifying respirators, the proper purifying element (cartridge or canister), the adequate particulate filters and the adequate masks, or self-contained breathing apparatus for the scenarios where the use of respiratory protection is advised**

To cope with risks from hazardous substances appropriate risk management measures have to be derived in the risk assessment, recommended and applied during use. The order of risk management measures is laid down in the Directive 98/24/EC. Personal protective equipment is the last resort, in cases were the other measures are not applicable or could not sufficiently reduce the risks.

The Directive 89/656/EEC (on the minimum health and safety requirements for the use by workers of personal protective equipment at the workplace) states that the personal protective equipment used must be appropriate for the risk involved, without itself leading to any increased risk. This Directive has to be considered for the derivation of exposure scenarios as REACH shall apply without prejudice to the community workplace legislation.

The specification of the recommended personal protective equipment is necessary to assure that the equipment does have a protective effect. Without further specification the protection by gloves and respiratory protection equipment can not be judged. Therefore, the efficiency of gloves and respiratory protection equipment has to be set to zero. The recalculation of exposure scenarios including standard protection factors for gloves and respiratory protection resulted in RCRs well above one (see statements of reasons 6.). The exposure would be even higher if no protection factor for gloves and respiratory protection would be assumed.

All exposure scenarios specified by the Registrant comprise contributing scenarios with a duration of the task of up to 8 h. This may imply an 8 h use of personal protective equipment such as gloves and respiratory protection whenever such PPE is recommended. As indicated in Directive 89/656/EEC, wearing of PPE should not comprise a burden to the worker. It is well recognised that exceeding a certain duration of use comprises such a burden and can express a risk for workers by itself. For example the German Technical Rule for Hazardous Substances 401 "Risks resulting from skin contact - identification, assessment, measures" limits the duration of use to a maximum of 4 hours.

Therefore, the specified maximum duration of use of gloves and respiratory protection shall be taken into account in the exposure scenarios. The maximum duration either has to be calculated from the breakthrough time for gloves or the filter capacity of the respiratory protection equipment mentioned or to be specified in accordance with Directive 89/656/EEC.

To conclude that protection factors can be used for the exposure assessment the specification of the personal protective equipment is necessary. On the basis of the current information no final conclusion can be drawn on the level of estimated exposure and consequently not on the risk, as it is not clear whether the use of a protection factor for gloves and respiratory protection is justified.

Therefore, the Registrant is required to provide sufficient and consistent information on the specification of personal protective equipment and the duration of use for all scenarios where the use of personal protective equipment is advised. In particular:

a) the type of material, thickness and breakthrough times of the gloves and the duration of use for all exposure scenarios where the use of gloves is advised

b) specifying for air-purifying respirators, the proper purifying element (cartridge or canister), the adequate particulate filters and the adequate masks, or self-contained breathing apparatus for the scenarios where the use of respiratory protection is advised

The requested information will allow a full evaluation whether the occupational risks are controlled by the use of adequate personal protective equipment.

9) Information on consumer uses, consumer exposure scenarios and risk characterisation for consumers

The CSR states N-1-naphthylaniline as a possible ingredient of the consumer product category PC 24, which includes lubricant, greases and release products. "In general" (CSR 2012) the concentration of N-1-naphthylaniline in these preparations is below 1%. However, no consumer use was identified.

The origin of N-1-naphthylaniline – as mentioned on the ECHA dissemination website – is Rhenofit PAN and Additin RC 7130. Their application areas are described in the corresponding Technical Data Sheets and include consumer applications.

Some national product registers have listed N-1-naphthylaniline as an ingredient in consumer products – mainly in lubricant, greases and release products and rubber articles. Therefore, ECHA concludes that consumer uses have to be identified and provided in the registration dossier.

Pursuant Article 10(a, iii) of the REACH Regulation "information on the manufacture and use(s) of the substance as specified in section 3 of Annex VI" has to be submitted in the technical dossier.

The Registrant provided comments regarding the use of N-1-naphthylaniline in consumer products and stated that after a further survey neither missing consumer uses nor missing information in the eSDS about consumer uses were addressed by the downstream users. The Registrant proposes to remove request C, 11) from the decision.

The draft decision was not revised since the registration dossier was not updated during the evaluation process and only clear statements in the CSR regarding the consumer use as well as in the Technical Data Sheet of e.g. Rhenofit PAN and Additin RC 7130 would clarify the concern.

IV. Adequate identification of the composition of the tested material

The substance identity information submitted in the registration dossiers has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In relation to the required tests, the sample of substance used for the new studies shall have a composition that is within the specifications of the substance composition that are given by all concerned Registrants. It is the responsibility of all the concerned Registrants to agree on the tested materials to be subjected to the tests subject to this decision and to document the necessary information on composition of the test material. The substance identity information of the registered substance and of the sample tested must enable the evaluating MSCA and ECHA to confirm the relevance of the testing for the substance subject to substance evaluation. Finally, the studies must be shared by the concerned Registrants.

V. General requirements regarding Good Laboratory Practice

ECHA always reminds Registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

VI. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Articles 52(2) and 51(8) of the REACH Regulation. Such an appeal shall be lodged within three months of receiving notification of this decision.
Further information on the appeal procedure can be found on the ECHA's internet page at http://echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

[redacted]

Jukka Malm
Deputy Executive Director

Confidential Annex: This annex is confidential and not included in the public version of this decision.