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

For 1,4-Benzenediamine, N,N'-mixed phenyl and tolyl derivatives (BENPAT), CAS No 68953-84-4 (EC No 273-227-8)

Addressees: Registrant(s)[1] of 1,4-Benzenediamine, N,N'-mixed phenyl and tolyl derivatives (BENPAT) (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 for comments, with the exception of the cases listed in the following paragraph. A list of all the relevant registration numbers subject to this decision is provided as an annex to this decision.

Registrants holding active registrations on the day the draft decision was sent for comments are not addressees of this decision if they are: i) Registrant(s) who had on that day 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 the 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 is based on the registration dossiers on 28 August 2014, i.e. the day on which the draft decision was notified to the Registrant(s) pursuant to Article 50(1) of the REACH Regulation.

This decision does not imply that the information provided by the Registrant(s) in the registrations is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on the dossiers of the Registrant(s) 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 1,4-Benzenediamine, N,N'-mixed phenyl and tolyl derivatives (BENPAT), CAS No 68953-84-4 (EC No 273-227-8) based on registrations submitted by the Registrant(s) and other relevant and available information 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/vPvB and Exposure/Wide

[1] The term Registrant(s) is used throughout the decision, irrespective of the number of registrants addressed by the decision.

dispersive use; Consumer use; Aggregated Tonnage, 1,4-Benzenediamine, N,N'-mixed phenyl and tolyl derivatives was included in an update of the Community rolling action plan (CoRAP) for substance evaluation to be evaluated in 2013. This update of the CoRAP was published on the ECHA website on 1 July 2013. 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 Human Health/Gene mutations in mammalian cells, repeat dose toxicity, carcinogenicity and reproductive toxicity.

The evaluating MSCA considered that further information was required to clarify the abovementioned 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 20 June 2014.

On 28 August 2014 ECHA sent the draft decision to the Registrant(s) and invited them pursuant to Article 50(1) of the REACH Regulation to provide comments within 30 days of the receipt of the draft decision.

Registrant commenting phase

By 6 October 2014 ECHA received comments from the Registrant(s) of which it informed the evaluating MSCA without delay.

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

Commenting by other MSCAs and ECHA

In accordance with Article 52(1) of the REACH Regulation, on 5 March 2015 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 10 April 2015 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.

Referral to Member State Committee

On 20 April 2015 ECHA referred the draft decision to the Member State Committee. On 8 May 2015, in accordance to Article 52(2) and Article 51(5), the Registrant(s) provided comments on the proposals for amendment. In addition, the Registrant(s) provided comments on the draft decision. The Member State Committee took the comments on the proposals for amendment of the Registrant(s) into account. The

Member State Committee did not take into account the Registrant(s)' comments on the draft decision that were not related to the proposals for amendment made and are therefore considered outside the scope of Article 52(2) and Article 51(5).

After discussion in the Member State Committee meeting on 8 to 11 June, a unanimous agreement of the Member State Committee on the draft decision as modified at the meeting was reached on 10 June 2015. ECHA took the decision pursuant to Article 52(2) and Article 51(6) of the REACH Regulation.

II. Information required

Pursuant to Article 46(1) of the REACH Regulation the Registrant(s) shall submit the following information using the indicated test methods (in accordance with Article 13 (3) and (4) of the REACH Regulation) and the registered substance subject to the present decision:

1. Transgenic rodent somatic and germ cell gene mutation assays in rats or mice, oral route, test method OECD 488.
Mutation frequencies shall be assessed in liver, urinary bladder and glandular stomach. Germ cells from testes shall be sampled and stored for analysis if positive results are obtained in any of the somatic cells
or
In vivo Mammalian Alkaline Comet Assay in rats, oral route, test method OECD 489. DNA damage shall be assessed in liver, urinary bladder and glandular stomach.

2. Full study report including annexes of the following study: [redacted].

3. Simulation testing on ultimate degradation in surface water (test method: Aerobic mineralisation in surface water - simulation biodegradation test, EU C.25/ OECD 309) as specified in section III. 4 using constituent R-898[1] as representative for BENPAT.

4. In case the test under 3. does not allow to conclude that BENPAT is persistent (P) or very persistent (vP) according to Annex XIII, 1.1.1. / 1.2.1. of the REACH Regulation additional sediment simulation testing (test method: Aerobic and anaerobic transformation in aquatic sediment system, EU C.24/ OECD 308 as specified in section III. 3) using constituent R-898[2] as representative for BENPAT.

Pursuant to Article 46(2) of the REACH Regulation, the Registrant(s) shall submit to ECHA by **08 April 2018** from the date of this decision an update of the registrations containing the information required by this decision[3], including robust study summaries and, where relevant, an update of the Chemical Safety Report.

[2] N,N-bis-tolyl-1,4-Benzenediamine
[3] The deadline set by the decision already takes into account the time that registrants may require to agree on who is to perform any required tests and the time that ECHA would require to designate a registrant to carry out the tests in the absence of the aforementioned agreement by the registrants (Article 53(1) of the REACH Regulation).

III. Statement of reasons

Human Health

1. Transgenic rodent somatic and germ cell gene mutation assays in mice or rats oral route, test method OECD 488.
Mutation frequencies shall be assessed in liver, urinary bladder and glandular stomach. Germ cells from testes shall be sampled and stored for analysis if positive results are obtained in any of the somatic cells
or
In vivo Mammalian Alkaline Comet Assay in rats, oral route, test method OECD 489. DNA damage shall be assessed in liver, urinary bladder and glandular stomach

According to the results of the genotoxicity tests it can be concluded that BENPAT is unlikely to cause structural chromosome aberrations of the DNA *in vivo*. Though equivocal findings were obtained in a chromosome aberration test in vitro, these effects were not confirmed in a micronucleus test *in vivo* after i. p. application. BENPAT caused gene mutations in bacteria. An *in vitro* UDS test was negative which is in line with the fact that no DNA adducts were detected. An *in vitro* cell transformation assay was also negative.

Based on the positive result in the bacterial gene mutation assay, there remains a concern for gene mutation in somatic cells in vivo. In addition there is also a concern for carcinogenicity raised by the 52 week dietary study. Furthermore, the registered substance has wide dispersive uses and potential for consumer exposure. Consequently, depending on the outcome concerning the mutagenicity concern, a clarification on the concern of carcinogenicity may be required.

The most suitable test methods to address this mutagenicity concern according to ECHA Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7a: Endpoint specific guidance Version 4.0, July 2015, Section R.7.7, are either the Transgenic rodent somatic and germ cell mutation assay or the In vivo Mammalian Alkaline Comet Assay.To ECHA's knowledge, there is no alternative that would not use vertebrate animals.

Therefore, pursuant to Article 46(1) of the REACH Regulation, the Registrant(s) are required to carry out a Transgenic rodent somatic and germ cell mutation assay (TGR) or an In vivo Mammalian Alkaline Comet Assay as specified in Section II using the registered substance subject to this decision. The TGR shall be conducted in line with the provisions of the according OECD test guideline. Accordingly, the preferred species is the mouse as transgenic mouse gene mutation detection models are more widely used than transgenic rat models. Germ cells from testes shall be sampled, but only be evaluated for mutation frequency if positive test results are obtained for any of the somatic cells. Alternatively an in vivo comet assay may be performed for which an OECD guideline is now available, published in September 2014. The test shall be performed in rats to investigate a possible link to the proliferative effects seen in repeat dose studies with the substance in rats

The test shall take into account the concern from the proliferating effect of BENPAT on the urinary bladder and the liver as observed in the dietary 52 week study. Therefore, mutation frequencies or DNA damage shall be assessed in the liver, the urinary bladder and, as site of first contact after oral application, in the glandular stomach.

Furthermore it is pointed out that in the case of a positive test result in the requested genotoxicity test, further investigation of germ cell mutagenicity has to be carried out.

In response to ECHA's draft decision the Registrant(s) provided comments that based on the available information on carcinogenicity and genotoxicity there is no further in vivo test required. It is pointed out that genotoxicity testing is not only relevant to conclude on carcinogenicity but also on germ cell mutagenicity. The concern was raised on the basis of a positive result in a bacterial gene mutation test. In both experiments of the test, mutation frequencies were increased in the presence of S9 in a dose dependent manner in two of the tested strains. It is agreed that these positive responses occurred mainly at doses which showed toxicity in the main test and had shown precipitation in the pre-test according to the registration dossier. However, ECHA does not agree to the statement that the increase in strain TA1538 at 16.7 µg/plate (non-toxic dose) is "of no importance". Rather, it is the lowest positive dose which is followed by two higher doses with positive responses in a dose related manner. Following the guidance on information requirements a specific bacterial metabolism has to be taken into account in case of a positive result in the bacterial gene mutation test. Due to the fact that positive responses only occurred in the presence of the metabolising system but not without S9, the positive results neither appear to be caused by bacterial metabolism nor to be due to precipitations. Rather, they appear to be caused by a metabolite of BENPAT. This was also concluded in the Registrant(s)´ chemical safety assessment.

In view of the concerns regarding carcinogenicity and reproductive toxicity, the request of an appropriate follow-up test is considered justified. According to the guidance on information requirements, both tests are appropriate follow-up tests in vivo. The TGR assay detects gene mutations, the comet assay detects DNA damage that would lead to gene mutations. Therefore, the evaluating MSCA has not changed the draft decision regarding this request following the comments of the Registrant(s).

From the MSCAs three proposals for amendments were received, two of which concerned editorials regarding the correct designation of a test method and were accepted. One MSCA proposed an extension of the request on genotoxicity testing on potential follow-up investigations in a stepwise manner including possible testing for carcinogenicity. This proposal was considered in terms of a general remark regarding the consequences for carcinogenicity depending on the genotoxicity outcome in the section below.

In their comments Registrant(s) reacted to the proposals for amendment (PfA) concerning potential follow-up investigations for genotoxicity. Although specifying the steps of testing in advance is generally agreed, the necessity of follow-up testing in relation to the available data on genotoxicity and carcinogenicity is questioned. They stated that a comet assay in rats "might further exclude a concern of a reactive metabolite".

Note for consideration by the Registrant(s)

If a Comet Assay is performed the Registrant(s) may consider examining gonadal cells, as it would optimise the use of animals. ECHA notes that a positive result in whole gonads is not necessarily reflective of germ cell damage since gonads contain a mixture of somatic and germ cells. However, such positive result would indicate that the substance and/or its metabolite(s) have reached the gonads and caused genotoxic effects. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

There is no robust study on carcinogenicity to conclude on the carcinogenic potential of

BENPAT. The available data on genotoxicity give some indication on a genotoxic potential which needs further clarification. Once the information requested by this decision is available in the registration dossiers, the evaluating MSCA will be in a position to assess the need for further information in order to examine any (remaining) concern for carcinogenicity.

Furthermore it is pointed out that in the case of a positive test result in the requested genotoxicity test harmonised classification for mutagenicity according to Articles 36 and 37 of Regulation (EC) 1272/2008 (CLP) will normally be required.

Pursuant to Article 46(1) of the REACH Regulation, the Registrant(s) are requested to submit the following study using the registered substance subject to this decision:

Transgenic rodent somatic and germ cell gene mutation assays in rats or mice oral route, test method OECD 488 or In vivo Mammalian Alkaline Comet Assay in rats, oral route, test method 489.

In response to ECHA's draft decision, the Registrant(s) provided comments that BENPAT shows no evidence of carcinogenic activity, hence the related statements included in the Draft Decision are unsupported.

ECHA does not concur with this statement. Two studies demonstrating the absence of a carcinogenic / initiating / promoting effect of the substance under the respective test conditions used study durations up to 52 weeks (which is much shorter than the usual study duration of 2 years for carcinogenicity studies) and investigated a limited amount of tissues. Thus, there is no robust study on carcinogenicity to conclude on the carcinogenic potential of BENPAT. The available data on genotoxicity on the other hand give some indication on a genotoxic potential which needs further clarification in a step-wise procedure. Depending on the outcome and possible classification for mutagenicity, further considerations on carcinogenicity including further testing may have to be made according to the Regulation. Therefore, a final conclusion on classification of BENPAT as carcinogenic cannot be drawn based on the information currently available.

2. Full study report including annexes of the following study: [redacted]

During substance evaluation, a concern on reproductive toxicity was identified. In a Two-Generation Reproductive Toxicity Study prominent findings were effects on the body weight gain of the dams (with no information on corrected body weight), increased post implantation loss, increased gestational length, decreased pup viability and the occurrence of polycystic kidneys and further effects on the kidneys. As only an incomplete study report (without annexes with detailed listing of findings) was available to the evaluating MSCA, a thorough analysis of the necropsy findings could not be performed.

Based on the non availability of the annexes of the Two-Generation Reproductive Toxicity Study, a thorough analysis of the maternal toxicity and the necropsy findings could not be performed. This is of special importance as it has to be analysed whether the observed effects are a consequence of maternal toxicity or not. Therefore, no firm conclusion could be drawn on the impact of the maternal toxicity on the parturition effects and fetal mortalities, and whether kidney effects resulted from a direct nephrotoxic effect or whether they should be interpreted as a teratogenic effect.

Therefore, a full study report including annexes of the following study is required:

[redacted]

In response to the draft decision, the Registrant(s) provided comments that any questions related to reprotoxicity are already addressed by data included in the substance registration dossier.

For the Two-Generation reproductive toxicity study only an incomplete study report (i.e. a study report without annexes) was available for the evaluating MSCA. After thorough analysis of the study report without annexes, ECHA came to the conclusion that it is not possible to conclude whether observed effects such as increased pup mortalities or fetal toxicities including polycystic kidneys would be attributable to maternal toxicity or not. This information could be retrieved from the study annexes. Therefore it is necessary to provide the requested annexes.

One MSCA agreed to the request but asked in the proposal for amendments why the Registrant(s) did not submit the full study report earlier. In their comments to the proposals for amendment the Registrant(s) clarified why the full study report was not provided earlier. The necessity to deeper analyse details of the studies which could be only obtained from the annexes emerged at a relatively late stage of the evaluation. Therefore the request of the annexes is the most appropriate way to address this issue in order to give the Registrant(s) sufficient time to provide the information.

Environment: Further information on persistence

BENPAT is suspected to be of very high concern due to its PBT (persistent, bioaccumulative, toxic) properties. Evidence shows that BENPAT is bioaccumulative and fulfils the T criterion. As the B and the T criteria are fulfilled the P criterion has to be assessed.

Screening tests on ready biodegradability show only marginal degradation of BENPAT and enhanced screening tests on degradation show that BENPAT does not reach the pass level. Thus the screening tests provided by the Registrant(s) do not allow to conclude that the substance is not persistent but indicate persistence of BENPAT according to Section 3.1.1. of Annex XIII and according to the provisions of the ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11: PBT/vPvB assessment, Version 2.0 November 2014 (chapter R.11.4.1.1). In the enhanced screening tests BENPAT did not reach the pass level. Metabolites were found but not identified. Nevertheless, an enhanced CO_2 evolution test, which was one of the enhanced screening tests mentioned, could indicate incorporation, i.e. degradation and use for growth, of BENPAT into biomass. However some doubts remain whether real incorporation or simple adsorption was measured because the procedure for evidence of incorporation into biomass is not a standard procedure. The supposed incorporation is a further indication of why an in-depth persistence assessment of BENPAT is necessary to elucidate whether the substance is persistent or not.

All provided screening tests show that BENPAT is potentially persistent as defined in Annex XIII. According to Section 1.1.1. of Annex XIII to REACH Regulation, a substance is considered to fulfil the persistency criterion (P) if the degradation half-lives are above certain trigger values in surface water, sediment or soil and the assessment of the persistency in the environment shall be based on available half-life data collected under

the adequate conditions. However, simulation tests on degradation in order to definitely conclude about P are not available. This information is thus needed to verify the concern whether the suspected PBT concern may be realised or not. Therefore, further information on persistence generated by simulation tests on degradation is required in order to enable the eMSCA to assess persistence.

According to Technical Guidance R.7.9 the compartment of concern is to be considered if new data is to be generated. BENPAT has a high adsorption tendency and therefore soil as well as sediment are considered to be the compartments of concern. BENPAT is used as anti-oxidant in rubber products such as tyres. It will reach soil, sediment and water in tire abrasion via runoff and deposition (OECD 2004[4]). Partioning processes will result in exposure of the water phase. Consequently, besides soil and sediment water is a compartment of concern for BENPAT even though the share of released BENPAT to water is small compared to the other compartments (soil and sediment). However, as will be addressed in the following, testing in soil and/or sediment alone will not allow to draw a robust conclusion.

BENPAT will adsorb to solid and suspended matter and will form high percentages of Non Extractable Residues (NER). Interpretation of NER is not straightforward and still a topic of scientific and regulatory debate because the composition of NER remains unclear. There is no way to differentiate NER further and thus the share of parent or metabolites in NER remains unclear, too. ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11: PBT/vPvB assessment, Version 2.0 November 2014 states that NER should be interpreted as removal but makes clear that removal alone is insufficient for P assessment (R.11.4.1.1).

For relieving BENPAT from P suspicion it will need convincing evidence that dissipation is not only caused by mere adsorption processes but that data also show degradation. To this end a test according to OECD 309 mineralisation in surface water in its pelagic version shall be done as in this test NER formation will be low.

As in all simulation tests several parameters will have to be considered together in interpretation of data, i.e. DT_{50}, metabolites and kinetics observed. Evidence and identification of metabolites will be crucial, since only metabolites will prove that degradation processes occur. It is important that a degradation path is modelled so that metabolites found and identified may be compared with the expected metabolites. This is a common procedure for pesticides.

Whereas initially parallel simulation testing in accordance with OECD 308 and OECD 309 was proposed, following several proposals for amendment and the considerations at the meeting of the Member State Committee, a sequential testing is requested in the present decision as the first simulation study following OECD 309 may allow already to conclude on the P/vP criterion in accordance with Annex XIII, 1.1.1. / 1.2.1. of the REACH Regulation.

3. Simulation testing on ultimate degradation in surface water (test method: Aerobic mineralisation in surface water - simulation biodegradation test, EU C.25/ OECD 309

The test system simulates mineralisation in surface water. It either uses surface water only (pelagic test), or surface water with addition of suspended solids or sediment as inoculum (suspended sediment test). It is the aim to test the substance in a test system with a small surface area for adsorption. Thus the pelagic version of the OECD 309 shall

[4] OECD 2004. Emission Scenario Document on Additives in Rubber Industry ENV/JM/MONO(2004)11

be done.

Based on the above and considering the fact that partitioning processes will take place, water is a compartment of concern. A high percentage of Non Extractable Residues (NER) is expected for R-898 as this constituent strongly adsorbs. However, composition of NER remains unknown. Hence, NER will only give information on removal. This is insufficient because in PBT assessment there is a need for degradation data in accordance to Annex XIII. Thus the test system should be such that NER are kept to a minimum. This is given in the pelagic version, i.e. without addition of sediment, of the OECD 309.

It is important that metabolites are identified to show that degradation in the test system was observed. To this end the following conditions shall be fulfilled:

- Metabolites representing crucial steps in transformation pathways (key metabolites) shall be identified by use of QSAR. Standard solutions shall ensure that detection and quantification of these key metabolites is possible.
  The test guideline OECD 309 stipulates a usual test duration of 60 days but it may be extended to a maximum of 90 days. It may be prolonged to several months if the provisions of Annex 3 of the guideline are followed. Annex 3 describes the semi-continuous procedure which shall prevent deterioration of the system by keeping inoculum viable. However, this procedure includes replacement of water with freshly sampled water and could result in loss of a part of the substance. Hence, it shall be started at the latest possible time and the number of repetitions shall be restricted to a minimum. In addition, it will be necessary to closely check the test concentration. All procedures which could impede interpretation or transfer of observations on substance behaviour in environment should be avoided as far as possible.
- Sufficient measurements shall be done to enhance kinetic modelling. The guideline OECD 309 stipulates that a minimum of 5 sampling points are required during the degradation phase. This refers to the test duration of 60 days or 90 days if a semi-continuous procedure is used. A tight pattern of measurements at 1, 6, 12 and 24 hours and at day 7, 14, 28 and 56 and at the end of the test shall be done. If the test is longer than 60 days measure in regular intervals no longer than a month. This is in agreement with the OECD 309 guideline which states that more measurements can easily be done although it does not give a fixed time schedule.
- The test substance shall be radiolabelled due to the low water solubility for an appropriate verification of the degradation. The Registrant(s) shall provide justification for the location of the radiolabel on the molecule.
- The test shall be done as pelagic test without addition of sediment.
  Test evaluation shall be comprehensive and orientate itself at the proceedings usual for pesticides.
- The main constituent R-898 shall be tested instead of BENPAT. R-898 is the most methylated and least water soluble constituent of BENPAT and represents the worst case.

For the registered substance detection and identification of metabolites shall be provided. This is also based on indications in available data.

REACH Guidance (cf. Table R.16-9) defines the average environmental temperature for the EU as 12°C and this is the reference temperature for the assessment of persistency in PBT/vPvB assessment. However, an elevated temperature enhances vitality of the inoculum, the probability of metabolite formation and the possibility of metabolite identification as compared to a lower temperature. In order to achieve this the

Registrant(s) are requested to perform the test at 20°C (293K) but to correct back to 12°C (285K) using the Arrhenius equation.

Pursuant to Article 46(1) of the REACH Regulation, the Registrant(s) are requested to submit the following study using R-898 as representative for the registered substance subject to this decision:

Simulation testing on ultimate degradation in surface water (test method: Aerobic mineralisation in surface water - simulation biodegradation test, EU C.25/ OECD 309).

4. Sediment simulation testing (test method: Aerobic and anaerobic transformation in aquatic sediment system, EU C.24/ OECD 308 as specified in section III 3) using constituent R-898[5] as representative for BENPAT

This request is dependent on the outcome of the simulation test in water (OECD 309) under above 3. In case the OECD 309 test does not allow to conclude that the P/vP criterion for water according to Annex XIII, 1.1.1. / 1.2.1. of the REACH Regulation is met, the sediment simulation test (OECD 308) is required.

As indicated, sediment is also a compartment of concern: BENPAT is highly adsorptive and therefore it will adsorb rapidly and to a high degree to sediment. A high degree of non-extractable residues (NER) is expected to be generated in the OECD 308 and separation of degradation from dissipation processes will probably be difficult. To enhance interpretability of data following conditions shall be fulfilled:

- Metabolites representing crucial steps in transformation pathways (key metabolites) shall be identified by the use of QSAR. Standard analytical solutions shall ensure that detection and quantification of these key metabolites is possible.
- Test duration is preferred to be prolonged to 120 days to facilitate comparison of data with the trigger values. Experience[6] shows that an extension to 120 days or even longer is possible without reducing significance of data even though the test guideline states that test duration normally should not exceed 100 days.
- 11 measurements shall be done to enhance kinetic modelling. The guideline OECD 308 stipulates that the number of sampling times should be at least six including zero time for a test duration of 100 days. This is insufficient for a difficult substance like BENPAT which is expected to adsorb rapidly. Test regime shall be such that it is possible to follow the adsorption process. This is a necessary provision for a successful kinetic modelling in data evaluation because it may be necessary to re-calculate the test concentration and to adequately conform the point in time at which to start calculation of DT_{50}. For this end three samples shall be taken on the first day, after 1 hour, 6 and 12 hours; another sample shall be taken after 24 hours. As it is possible that BENPAT does not act as expected and to facilitate observation of it the next sampling times shall follow at day 7, 14 and day 28. The following sampling times shall be nearly evenly distributed in a 4 weeks interval. Hence, 11 measurements shall be done.
- The test substance shall be radiolabelled due to the low water solubility for an appropriate verification of the degradation. The Registrant(s) shall provide justification for the location of the radiolabel on the molecule.
- Test evaluation shall be comprehensive and orientate itself at the proceedings usual for pesticides. The following aspects are of special interest for test evaluation: Rate and course of kinetics of parent and metabolites in the water

[5] N,N-bis-tolyl-1,4-Benzenediamine
[6] R&D projects 20667460/03 and *22801*, UBA 2012 and 2013

phase shall be compared with the respective results of the OECD 309 and considered in interpretation. Special consideration shall be given to:
1. the kinetics in the water phase of both test systems and the differences found.
2. the kinetics in the water phase compared to the course of NER formation in the sediment phase of the OECD 308,
3. the time at which metabolites emerge and their succession in the respective test system and
4. a comparison of the time at which metabolites emerge and their succession in both test systems.
All of these aspects are needed for the interpretation of the processes observed.

- The main constituent R-898 shall be tested instead of BENPAT. R-898 is the most methylated and least water soluble constituent of BENPAT and represents the worst case.

To assess persistence of BENPAT it is necessary to differentiate between mere elimination and degradation processes (cf. REACH Guidance R 11.4.1.1). To this end detection and identification of metabolites are fundamental requirements. An elevated temperature enhances vitality of the inoculum, the probability of metabolite formation and the possibility of metabolite identification as compared to a lower temperature. However, REACH Guidance (cf. Table R.16-9) defines the average environmental temperature for the EU as 12°C. Thus, the Registrant(s) are requested to perform the test at 20°C (293K) but to correct back to 12°C (285K) using the Arrhenius equation.

Pursuant to Article 46(1) of the REACH Regulation, the Registrant(s) are requested to submit the following study using R-898 as representative for the registered substance subject to this decision:
Sediment simulation testing (test method: Aerobic and anaerobic transformation in aquatic sediment system, EU C.24/ OECD 308)

The Registrant(s) comments on the requests for the simulation tests:

Consistency of the PBT assessment
The Registrant(s) question the test concept for BENPAT as it differs from the structural similar substances N,N'-bis(1,4-dimethylpentyl)-phenylenediamine (CAS No 3081-14-9) and N-1,4-dimethylpentyl)-N'-phenylbenzene-1,4-diamine (CAS No 3081-01-4). The Registrant(s) commented that the requests on persistency testing should be the same for the three substances because of their structural similarity.

The properties of BENPAT differ from the properties of the substances specified above. For instance, BENPAT does not hydrolyse based on an available standard study (Environment Canada and Health Canada, 2011[7]) whereas the two other substances are expected to hydrolyse (tests have been requested in Substance evaluation decisions). Furthermore, BENPAT does not seem to have chemical structures which are susceptible to hydrolysis (Environment Canada and Health Canada, 2011[8]). Thus, a different test concept is justified for BENPAT since it is used as anti-oxidant in rubber products such as tires. It will reach soil, sediment and water in tyre abrasion via runoff and deposition (OECD 2004[9]).

Proportionality of the test concept

[7] Environment Canada, Health Canada. 2011. Screening Assessment for the Challenge 1,4-Benzenediamine, N,N'-mixed Phenyl and tolyl derivatives and 1,4-Benzenediamine, N,N`-mixed tolyl and xylyl derivatives. 1-91.
[8] Environment Canada, Health Canada. 2011. Screening Assessment for the Challenge 1,4-Benzenediamine, N,N'-mixed Phenyl and tolyl derivatives and 1,4-Benzenediamine, N,N`-mixed tolyl and xylyl derivatives. 1-91.
[9] OECD 2004. Emission Scenario Document on Additives in Rubber Industry ENV/JM/MONO(2004)11

Furthermore, the Registrant(s) question proportionality of the test concept because available enhanced screening studies already show that BENPAT is degradable. In the Registrant(s)´ interpretation further tests are not needed and the test concept is disproportionate.

The pass level was not reached in the available enhanced screening test and therefore this test in combination with the other information on degradation is not sufficient to relieve the substance from P suspicion. Interpretation whether the pass level was reached or not relates to mineralisation which was very low. Metabolites were found but not identified. Thus it remains unknown if these metabolites may pose a problem.

In addition, Registrant(s) state that a CEFIC project has been initiated in the framework of the Long-Range Research Initiative (LRI). In this project the suitability of studies carried out according to OECD 308 are investigated in order to obtain robust information on persistence. The project should have ended in 2014. Registrant(s) propose to await its results. However, up to now the project is still ongoing and it is not sure whether it will end in 2015. The results will be considered when available; but as the timing is uncertain the substance evaluation process shall not be stopped to await the results.

Interpretation of Non Extractable Residues according to REACH Guidance and FOCUS[10]. REACH Guidance should be followed by eMSCA.
Registrant(s) also point out a soil study which showed a high percentage of Non Extractable Residues (NER) and argue that according to REACH guidance and FOCUS NER have to be considered as degradation. In this context they doubt that the evaluating MSCA had followed REACH Guidance.

It should be noted that this is a misinterpretation of REACH. The REACH Guidance clearly differentiates between removal and degradation. It states that NER is removal but clarifies in R.11.4.1.1 that *"...With regard to persistence, it is insufficient to consider removal alone where this may simply represent the transfer of a substance from one environmental compartment to another (e.g. from the water phase to the sediment)"*.

NER have to be considered as removed by adsorption as it is neither possible to differentiate NER fractions in those which may be remobilised or not nor to differentiate NER fractions in metabolites or parent. In addition, the provisions of FOCUS do not hold in PBT assessment as REACH guidance states in R.11 that *"For PBT and vPvB substances a safe concentration in environment cannot be established..."* FOCUS gives valuable advice, e.g. for calculating environmental concentrations in groundwater. While it may be correct to add the NER formation to the dissipation processes for this end it does not hold for persistence assessment because it is the degradation potential of a substance itself which is considered independently from predicted environmental concentrations. Thus, evaluating MSCA and ECHA followed the provisions as laid down in the REACH guidance.

Furthermore, the Registrant(s) argue that since NER represent degradation there is sufficient data available in the soil compartment already. However, as already expressed NER do not represent degradation but only removal. Hence, it is not possible to conclude on degradation on basis of the soil simulation study.

Experimental test set-up and compartment of concern

[10] Forum for the Co-ordination of pesticide fate models and their use

The Registrant(s) question the experimental test set-up. They argue that the choice of compartment of concern is wrong, that there is no clear guidance on how to interpret the results and that it is possible that the tests do not give the needed results.

ECHA came to the conclusion that both soil and sediment are compartments of concern because of the high adsorption of BENPAT. Nevertheless, as experiences show even such substances will reach the aquatic environment via runoff. Thus, also water is a compartment of concern. The substance properties let expect the build-up of a high percentage of NER in simulation tests which cannot provide the information needed in P assessment, i.e. degradation data. Thus, a test according to OECD 309 in its pelagic version shall be done.

Registrant(s) also point out that their efforts to determine metabolites in the tests done so far were not successful.

It is acknowledged that determination of metabolites is difficult. Identification of metabolites is often impeded by percentages which are too small for analysis. To enhance the possibility to identify metabolites it is recommended to use approaches established for the testing of pesticides. In addition, modelling of the metabolic pathway shall give information on the metabolites to expect. This information will help to decide which metabolites have key positions in the pathway, are most probable to expect and consequently to establish optimised analysis procedures.

Test substance
Registrant(s) argue that using BENPAT as test substance will complicate testing. Instead the constituent R-898 should be used.

BENPAT consists of three constituents which differ in methylation. With increasing extent of methylation the water solubility decreases and adsorption increases. Since R-898 is the most methylated constituent it represents the worst case. BENPAT would collectively introduce all constituents into the test system which will probably interfere with identification of metabolites because it will be difficult to differentiate between metabolites and the less methylated constituents. Hence, the evaluating MSCA followed the Registrants argumentation and agreed that R-898 should be used instead of BENPAT.

Deadline for delivering data
Referring to the substance properties and the foreseeable difficulties in tests conduction the Registrant(s) request additional 12 months in their comments on the draft decision.

ECHA acknowledges that increased test efforts need additional time. The usual timeline stipulates a deadline of 18 months for simulation testing and three months for the Registrant(s) to agree who performs the test. There are several requirements, e.g. modelling of metabolic pathway or changes in test setup, that have to be complied with before the tests start. Furthermore, data evaluation will be challenging. In view of this the usual deadline is thought to be insufficient. For completion of each of these tasks additional three months shall be added to the deadline. Hence, the deadline for delivering data shall be extended to 30 months from the date of this decision.

Based on the PfAs the Registrant(s) requested a deadline of 60 months as sequential testing as proposed by ECHA and a MSCA and additional tests proposed by two MSCAs require this timeframe. ECHA considers that a period of 30 months is sufficient to provide the information as requested in this decision even if conducted in sequence. The human health tests requested in this decision take up to 18 months. A first simulation test in

accordance with established OECD guidelines can be performed within 18 months including the development of the analytical protocol and any subsequent simulation test requires an additional 6 months to be conducted. As there is no parallel testing required any longer in the present decision the argument by the Registrant(s) that the CEFIC LRI project on parallel testing using OECD guidelines 309 and 308 became irrelevant. Due to the recommendation to prolong both simulation tests, additional three months are granted. The proposed timeline of 60 months could not be followed by ECHA.

Bioaccumulation assessment

The Registrant(s) question the assessment of BENPAT as bioaccumulative because they judge the bioconcentration study invalid. Instead the biomagnification study should be decisive which resulted in a BMF < 1. In addition, based on the BMF of this study a BCF < 2000 is estimated by the Registrant(s).

The bioconcentration study ([redacted]) has deficiencies but is not invalid. It is complemented by a publication (McLaren-Hart, 1998) in which the authors conduct a statistical assessment of the BCF data generated in Japanese carp study to calculate BCFs according to OECD concepts. They recalculate a minimum BCF of 1933 and a maximum BCF of 9640 while the majority of BCFs meets the trigger value of 2000 or lies beyond it.

ECHA comes to a different conclusion concerning the results of the Dietary Exposure Bioaccumulation Fish Test (BMF) than the Registrant(s). ECHA concludes that the BMF is not decisive but it provides supportive information. The study reports an estimated BCF of 2107 which only indicates bioaccumulation of R-898 since literature shows that estimated BCFs from BMFs mostly are considerably uncertain (Crookes and Brooks 2011). Furthermore, the study reports a lipid normalized and growth corrected kinetic biomagnification factor of 0.174. This BMF is close to BMF data which authors report for known bioaccumulative substances (Inoue et al. 2012).

Consideration of proposals for amendment

From one MSCA and ECHA proposals for amendment were received. The MSCA and ECHA proposed to tier testing of persistence. The decision was amended after discussion in the Member State Committee (MSC). As outlined already above in the introductory part to the section on 'Environment: Further information on persistence' on page 9, the Committee considered that no parallel testing should be conducted as initially suggested but a tiered approach as outlined in the present decision shall be used. A test according to OECD 309 shall be done. Depending on its result an additional test according to OECD 308 may become necessary. The MSC decided that the OECD 309 test rather than OECD 308 shall be performed first since the OECD 309 pelagic test minimises the potential for NER formation. In case the OECD 309 test does not allow a conclusion to be reached that the P/vP criterion for water according to Annex XIII, 1.1.1. / 1.2.1. of the REACH Regulation is met, an additional test in accordance with OECD 308 is required.

In an additional PfA the same MSCA proposed to rephrase the decision in order to require the Registrant(s) to justify the design of the studies and their interpretation to address the concerns, because the burden of proof is on the Registrant(s). The Registrant(s) supported this PfA. The decision was not rephrased based on this proposal because in this specific case it is necessary to specify the test design in order to allow interpretation of the data and conclude on the persistence of the tested substance. Thus, the specific test design shall be requested.

Furthermore, the MSCA proposed an additional hydrolysis study according to OECD 111 as in the MSCA´s interpretation data on hydrolysis of BENPAT are contradictory. The decision was not amended. There is evidence from a reliable study that BENPAT does not hydrolyse (Environment Canada and Health Canada, 2011)[11]. This study also reported BENPAT to precipitate and adsorb. Another study in which allegedly hydrolysis of the structural similar substance 6-PPD had been found proved to be not reliable ([redacted])[12]. Grave deficiencies were found in an evaluation of this study, e.g. no information on precipitates had been given. In addition, the substance also lacks functional groups which would be susceptible to hydrolysis. Hence, reliable data and the chemical structure both confirm the lack of hydrolysis. There is no need for an additional study. The Registrant(s) agree that a further hydrolysis study is not necessary.

In addition to their comments on the PfAs the Registrant(s) submitted general comments in which they repeated their first comments on the draft decision.

IV. Adequate identification of the composition of the tested material

In relation to the required experimental studies, the sample of the substance to be used shall have a composition that is within the specifications of the substance composition that are given by all Registrants. It is the responsibility of all the Registrants to agree on the tested material 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 tests must be shared by the Registrants.

V. Avoidance of unnecessary testing by data- and cost-sharing

In relation to the experimental studies the legal text foresees the sharing of information and costs between Registrants (Article 53 of the REACH Regulation). Registrants are therefore required to make every effort to reach an agreement regarding each experimental study for every endpoint as to who is to carry out the study on behalf of the other Registrants and to inform ECHA accordingly within 90 days from the date of this decision under Article 53(1) of the REACH Regulation. This information should be submitted to ECHA using the following form stating the decision number above at: https://comments.echa.europa.eu/comments_cms/SEDraftDecisionComments.aspx

Further advice can be found at
http://echa.europa.eu/regulations/reach/registration/data-sharing

If ECHA is not informed of such agreement within 90 days, it will designate one of the Registrants to perform the studies on behalf of all of them.

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://www.echa.europa.eu/regulations/appeals
The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

[11] Environment Canada, Health Canada. 2011. Screening Assessment for the Challenge 1,4-Benzenediamine, N,N'-mixed Phenyl and tolyl derivatives and 1,4-Benzenediamine, N,N`-mixed tolyl and xylyl derivatives. 1-91.
[12] [redacted].

Authorised[13] by Leena Ylä-Mononen, Director of Evaluation

Annex I: List of registration numbers for the addressees of this decision. This annex is confidential and not included in the public version of this decision.

[13] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.