

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in this table as submitted by the webform. Please note that the comments displayed below may have been accompanied by attachments which are not published in this table.

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Last data extracted on 22.05.2017

**Substance name: 1,2-Benzenedicarboxylic acid, di-C8-10-branched alkylesters, C9-rich; [1] di-"isononyl" phthalate; [2]
CAS number: 68515-48-0 and 28553-12-0
EC number: 271-090-9 and 249-079-5
Dossier submitter: Denmark**

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2017	United Kingdom	British Coatings Federation	Industry or trade association	1
Comment received				
<p>The BCF does not agree that evidence in the dossier submitted justifies the classification of DINP as a reproductive toxicant according to the criteria of the CLP. The evidence does not demonstrate conclusively there are adverse reproductive effects following the exposure to DINP and therefore the British Coatings Federation proposes that classification (Cat 1B H360D) for reproductive toxicant is not required.</p> <p>Further details are given in the attachment.</p> <p>ECHA note – An attachment was submitted with the comment above. Refer to public attachment BCF comments on DINP reclassification May 17.docx</p>				

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2017	Germany		Individual	2
Comment received				
<p>Based on my professional experience in toxicology and risk assessment, recognized by being elected member of several EU-Commission Scientific Advisory bodies (CSTEE, SCHER, SHENHIR) EFSA-Panels, and WHO/FAO groups, I would like to comment on the CLH-proposal.</p> <p>The proposal to classify 1,2-Benzenedicarboxylic acid, di-C8-10-branched alkylesters, C9-rich, di-"isononyl" phthalate (DINP, CAS 68515-48-0 and 28553-12-0) as a category 1B reproductive toxicant regarding effects on development and as a Category 2 reproductive toxicant regarding effects on fertility (CLH proposal) has been submitted to ECHA. However, the CLH proposal does not follow the guidance and criteria outlined in the CLP regulation regarding requirements for classification as a reproductive toxicant. The proposal to classify DINP is not based on adverse effects as defined by WHO/IPCS but on small and inconsistent changes in some parameters observed only in some selected studies with DINP. The large database available on DINP including a two-generation reproductive and developmental toxicity study without effects on development and fertility is not further considered in the CLH-proposal and is not adequately integrated into the conclusions. Since the CLH-proposal does not rely on adverse effects as defined by WHO/IPCS and only lists a variety of</p>				

unrelated changes seen in isolated studies in support of its conclusions, the CLH proposal does not have a scientific basis for its conclusions. Based on a weight of evidence approach integrating the available database, it can be concluded that DINP does not induce adverse or permanent effects on sexual function and fertility. Thus, classification is not supported since an "adverse effect on sexual function and fertility" is required as a basis for any classification. A detailed justification of my conclusions is provided in the attached comments and further supported by copies of two recent publications that have developed a quantitative weight of evidence approach to classification and labelling regarding reproductive toxicity and applied this approach to compare requirements for classification for DINP and two other phthalates.

A proposal to classify 1,2-Benzenedicarboxylic acid, di-C8-10-branched alkylesters, C9-rich, di-"isononyl" phthalate (DINP, CAS 68515-48-0 and 28553-12-0) as a category 1B reproductive toxicant regarding effects on development and as a Category 2 reproductive toxicant regarding effects on fertility (CLH proposal) has been submitted to ECHA.

The CLP regulation (Regulation (EC) No 1272/2008) gives detailed guidance and criteria regarding points to consider when proposing classification for reproductive toxicity. As clearly stated in the CLP regulation, adverse effects (3.7.1.2) in appropriately conducted animal toxicity studies serve as the basis for classification as a reproductive toxicant both for developmental effects and for fertility. The guidance also states that weight of evidence (3.7.2.2.1, 3.7.2.3) should be applied considering consistency of the identified adverse effects over studies, including taking into account study quality, interference of maternal toxicity (3.7.2.2.2), secondary effects on reproductive endpoints due to other toxicities, and doses needed to induce toxicities. Moreover, the regulation explicitly states that small effects on a number of parameters such as small changes in the incidence of skeletal variations or small changes in sperm parameters should not trigger classification (3.7.2.3.3).

DINP is a data rich chemical with a large number of studies available for evaluation including guideline compliant reproductive and developmental toxicity studies. The large database on reproductive and developmental toxicity of DINP has been reviewed by the former ECB in 2003. The conclusion of this review, which was peer-reviewed by the responsible scientific advisory committee of the EU-commission was that classification of DINP for reproductive endpoints is not warranted based on the available database. The RAR provided the following summary of the available studies:

"Fertility assessment may be inferred from effects on reproductive organs and the two-generation study.

In the two-generation study no changes in reproductive indices are observed.

From those assays, no adverse effects on fertility may be anticipated."

Only investigative studies have been published since the ECB review in 2003 (Masutomi et al., 2003; Lee et al., 2006; Kwack et al., 2009; Boberg et al., 2011; Clewell et al., 2013a; Clewell et al., 2013b; Li et al., 2015).

The CLH proposal selectively picks effects from both the guideline studies reviewed in 2003 and the studies published after the ECB-review to justify classification. In the compilation of effects and the summary conclusions, the CLH proposal does not follow the guidance and criteria outlined in the CLP regulation.

- The proposed classification is not based on adverse effects as defined by WHO/IPCS. Conclusions on a need for classification in the CLH proposal are based on small and inconsistent changes in some parameters in selected studies with DINP.
- The CLH proposal does not adequately consider the large available database on reproductive and developmental toxicity of DINP. Consistency of observations over studies is not assessed and results from high quality studies not showing adverse effects are neglected.
- Toxicological significance of the reported effects is not considered in the conclusions.
- The CLH proposal does not perform a quality assessment on the studies used to support

its conclusions.

- The CLH proposal does not consider the well-described toxicities of DINP on other targets and/or maternal toxicity as confounders regarding reproductive and developmental effects.
- Consequently, the required weight of evidence analysis is not performed. Instead, insufficient evidence of adverse effects is compiled in the CLH-proposal with the aim of concluding “sufficient evidence” in support of an adverse effect. This is not an appropriate approach since weight of evidence in the context of CLP classification refers to sufficient evidence in support of a treatment-related adverse effect from independent reports, or several consistent observations within one report. These have to be combined to support the occurrence of an adverse effect.

A quantitative weight of evidence (QWoE) analysis based on well-defined assessment criteria for both study quality and study outcome and adversity of effects reported (Dekant and Bridges, 2016 a,b) concluded “The application of the QWoE and a narrative assessment of DINP for both developmental and fertility effect assessments are in good agreement and do not support the presence of adverse effects induced by DINP in appropriately conducted animal studies. Therefore, there is no evidence to support a classification of DINP for reproductive toxicity”. A more detailed justification for these conclusions is presented below and in copies of the publications that are submitted with these comments.

Small and reversible effects on reproductive and developmental parameters without functional or pathological consequence cannot be considered as adverse as it is done in the CLH proposal.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comment DINP-WolfgangDekant.zip

Date	Country	Organisation	Type of Organisation	Comment number
15.05.2017	South Africa	The Southern African Vinyls Association	National NGO	3

Comment received

COMMENTS ON THE DANISH EPA DOSSIER PROPOSING CLASSIFICATION OF DINP BY THE SOUTHERN AFRICAN VINYLs ASSOCIATION OF SOUTH AFRICA (SAVA)

The Southern African Vinyls Association (SAVA) is the representative body for the local polyvinyl chloride (PVC) industry and through our Product Stewardship Commitment (PSC), we provide leadership and guidance towards transforming the PVC industry in relation to commerce, health and environmental issues.

SAVA is also represented on the Global Vinyls Council (GVC) and through our information sharing network we have been made aware of the fact that the Danish EPA has made its fourth re-submission in two years of a dossier proposing the classification of DINP as a reproductive agent. We have been informed that this was accepted by ECHA and the public consultation process has now been initiated.

SAVA supports peer reviewed scientific research and concur with current robust scientific data available on DINP and agree that it does not support this classification proposal by the Danish EPA. Any proposal or submission should be based on the weight of scientific evidence and not focus on a key study by Boberg and others in 2011 and 2016 (Corrigendum to “Reproductive and behavioral effects of diisononyl phthalate (DINP) in perinatally exposed rats”) where the results have been shown not be reproducible for the large part, as is the case in the most recent Danish EPA dossier.

DINP is a major plasticiser for use in flexible vinyl (i.e. car underbody sealants, cabling, sheeting, footwear and hosing) and is of high importance to the members of SAVA. Based on international trends and product stewardship programmes, the South African PVC industry voluntarily signed a Product Stewardship Commitment in 2011 to replace DEHP with DINP as a plasticiser and the replacement has been successfully concluded in the majority of PVC applications locally.

SAVA continuously review scientific data available on various chemicals including DINP and based on our research and understanding of the available peer reviewed data showing low hazards and safe use, we cannot support any proposed classification of DINP. The commitment shown by our industry to replace DEHP with DINP is based on this collection of sound and robust scientific data.

We agree with the conclusions made by various peer reviewed scientific studies that show that low phthalates (C3-C6 straight carbon backbones in the alkyl side chains) have adverse reproductive effects in animal studies and that high phthalates (C7-C13 straight carbon backbones in the alkyl side chains), do not show any adverse reproductive effects.

Given the high importance of this substance to our members, we can only support the current body of evidence based on peer reviewed and robust scientific research and urge ECHA and RAC to commit to a balanced and thorough scientific evaluation of all the relevant data on DINP.

We do not believe the classification dossier published by the Danish EPA supports any further classification of DINP or the substitution of DINP in PVC applications.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comments on the Danish EPA Dossier_DINP_By SAVA_15May2017.pdf

Date	Country	Organisation	Type of Organisation	Comment number
13.05.2017	Italy	Istituto Superiore di Sanità	National Authority	4

Comment received

DEVELOPMENTAL TOXICITY. Upon integration of the available data from different studies, there is sufficient evidence to indicate that DINP induces adverse effects on male reproductive development; such effects are not secondary to maternal toxicity and are plausibly due to the same (endocrine-related) mode of action as other phthalates, such as DEHP. Such adverse developmental effects can be elicited in experimental animals also at dose levels lower than 1000 mg/kg; whereas the available studies indicate that DINP has a weaker potency as compared to, e.g., DEHP, potency considerations are not relevant for classification. Therefore, the proposal for classification in category 1b for developmental toxicity can be supported.

EFFECTS ON FERTILITY. The available studies provide some suggestion that DINP may affect the reproductive function in both sexes. However, the evidence is too scattered and inconsistent. Two examples of potentially relevant studies that do not allow to derive any firm conclusion:

- i) the two-generation study (Waterman et al. 2000) did not find any significant adverse effects but sperm parameters (as well as estrous cyclicity, as it seems) were not assessed;
- ii) the study on juvenile rats by (Kwack et al., 2009) observed relevant adverse effects on

sperm parameters, but with concomitant effect on liver weight (increased) and body weight (reduced). Since only one dose level (500 mg/kg bw) was tested, the dose responses for the reproductive and non-reproductive effects could not be compared. Overall, the available data do not support any conclusion on a possible classification for reproductive toxicity of DINP, even in category 2. Conversely, the available data warrant performing further studies.

Date	Country	Organisation	Type of Organisation	Comment number
12.05.2017	United Kingdom	<confidential>	Company-Downstream user	5

Comment received

We are a down stream user of DINP. It is a key raw material in the production of vinyl coated wallcoverings. We are a UK manufacturer and sell our products globally with a turnover of approx £57m and employ 500 people in the UK and International division. We have tried alternative materials to DINP but the alternatives are not available in sufficient quantities to sustain supply. We moved away from DOP to DINP as the toxicology tests indicated this to be safe to use. We question the validity of the recent study as it is based upon oral toxicity in rats the dosage is excessive and is not directly comparable to the impact/risk to the human health. This test method does not reflect the likely exposure during installation or use of the wallcoverings. We therefore oppose the proposal by the Danish authorities.

Date	Country	Organisation	Type of Organisation	Comment number
12.05.2017	Belgium	IGI - The Global Wallcoverings Association	Industry or trade association	6

Comment received

IGI – The Global Wallcovering Association – does not support the Danish proposal to classify DINP as a reproductive toxin. DINP is a major raw material for vinyl wallcoverings, and approximately 50% of our member’s products include the use of vinyls, so this classification would have a serious negative effect on our business throughout the EU. Business worth €1.2 billion, and employing 26,000 workers. We have no viable alternative to DINP that is currently freely available in the quantities required. Our industry has discontinued use of lower phthalates since they were classified as reproductive toxins, and had moved to DINP following extensive evaluations that showed it to be of low hazard and safe to use. We question the value of the recent studies put forward by Denmark, as they are based on oral ingestion by rats, and we see no relevance between this and the likely human exposure by consumers resulting from the handling of vinyl wallcoverings. Indeed, the levels of oral dosage given to rats in the recent studies, is excessive and disproportionate to the levels experienced by consumer contact. In our view these levels has been used to obtain the result that the Danish EPA required for this current proposal. As previously stated, DINP is a raw material of high importance to our members, and we urge ECHA and the RAC to reject the Danish proposal, and ensure that any classification is only based on realistic and robust scientific evaluations.

Date	Country	Organisation	Type of Organisation	Comment number
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11.05.2017	Germany		MemberState	7
Comment received				
<p>The German CA does not want to question that the two substances that refer to the CAS numbers 68515-48-0 and 28553-12-0 are structurally very similar and marketed under the same name/abbreviation "DINP". The main component of 1,2-benzenedicarboxylic acid, di-C8-10-branched alkylesters, C9-rich (CAS 68515-48-0 is identical to the substance di-"isononyl" phthalate (CAS 28553-12-0). However, the only information about the concentration of the (identical) constituent can be derived from the name "C9-rich". Neither a typical concentration nor concentration ranges are provided. It is therefore not possible to assess the similarity of the two substances. We are convinced the DK CA correctly combined both substances for one harmonised C&L entry, but would appreciate to have more information about the substance identity.</p> <p>Beyond that we think that it should be pointed out in the report that two substances are covered by the proposed entry and not one substance with two CAS and EC numbers</p>				

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	United States	The Vinyl Institute	Industry or trade association	8
Comment received				
<p>"Dear ECHA,</p> <p>The Vinyl Institute is a U.S. based trade association representing the producers of vinyl resins and additives, including plasticizers. It was recently brought to our attention that a proposal is being considered to require classification and labelling for di-isononyl phthalate (DINP) plasticizer. This plasticizer is widely used in U.S. flexible vinyl applications including certain flooring, wire and cable insulation, seals and gaskets, footwear, upholstery, and many other applications, some of which are exported from the U.S. to Europe. As such, it is an important ingredient to producers and consumers alike. Thus, it is critical that the health aspects be properly evaluated, understood, and communicated. The VI recently submitted comments* to the U.S. Consumer Products Safety Commission (CPSC) on their analysis of DINP by the Chronic Hazard Advisor Panel. In these comments which are attached for your review, two key characteristics of DINP were highlighted that must be weighed heavily when assessing potential exposure of this substance : 1.) DINP has an extremely low vapor pressure, and 2.) DINP has strong molecular bonds to the PVC molecule. Both of these characteristics are responsible for the low emissions and high retention of DINP in a finished article. For these reasons, the Vinyl Institute does not support the proposed classification. Given the high importance of this substance to our members, and the data supporting its retention and low exposure to consumers, we would urge that ECHA and RAC ensure a full and thorough scientific evaluation of all the relevant data on DINP.</p> <p>*Comments of the Vinyl Institute to U.S. Consumer Products Safety Commission, RE: Estimated Phthalate Exposure and Risk to Pregnant Women and Women of Reproductive Age as Assessed Using 2013/2014 NHANES Biomonitoring Data, Docket Number CPSC-2014-0033, March 24, 2017"</p> <p>ECHA note – An attachment was submitted with the comment above. Refer to public attachment VI Comments to CPSC on CHAP NHANES Information submitted 03-24-2017.pdf</p>				

Date	Country	Organisation	Type of Organisation	Comment
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19.05.2017	Belgium	ExxonMobil Chemical Holland BV	Company-Manufacturer	number 9
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Comment received

ExxonMobil Chemical Holland BV – Comments on the CLH Report - Proposal for Harmonised Classification and Labelling of DINP

(based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2; Substance Name: 1,2-benzenedicarboxylic acid, di-C8-C10-branched alkylesters, C9-rich; [1] di-“isononyl”phthalate; [2] [DINP]; EC number: 271-090-9 and 249-079-5; CAS number: 68515-48-0 and 28553-12-0; Dossier Submitter – Danish EPA)

ExxonMobil Chemical Holland BV (hereafter referred to as ExxonMobil) is a producer of DINP within the European Union. The summary comments below represent ExxonMobil's views on the classification proposal by the Danish EPA that is the object of this consultation. As a REACH Lead Registrant for DINP we have previously consulted with all members of the DINP Substance Information Exchange Fora (SIEF), as required by the REACH regulation, to agree classification and labelling, and to include that classification in the REACH registration dossier. Based on the scientific data and prior regulatory reviews (EU RAR, ECB, 2003), all SIEF members (over 200) agreed on the conclusion of “no classification” for all relevant CLP health and environmental hazards, and this was included as part of the REACH registration in 2010. The lack of classification was further confirmed in a major REACH registration dossier update in December 2015, which took into account the outcome of the ECHA re-evaluation which concluded that no further risk management measures are needed for DINP (existing restrictions in toys and childcare articles maintained). The CLH proposal on DINP (registry of intent November 10, 2014; final submission March 29, 2017) from the Danish EPA now effectively takes the regulatory evaluation process back to square one after a 10 year EU Risk Assessment under the Existing Substances Regulation (1995 – 2006), and a 4 year ECHA re-evaluation under REACH (2009 – 2013). In the absence of any significant new scientific data supporting classification this is very hard to understand for a REACH registrant supplying to an extensive value chain of downstream customers, who now face a further major period of uncertainty. The proposal is inconsistent with any measure of regulatory predictability to support business continuity and investment in a substance which is a major substitute for an SVHC within the EU and also a substitute globally.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment ExxonMobil DINP submission_May_19_2017_Final.pdf

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	France		Individual	10

Comment received

If the DINP becomes classified as CMR our business will be drastically impacted

ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Consultation publique DINP_V3.docx

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	China	AICM	Industry or trade association	11

Comment received

DINP is one of the major substitutes for DEHP, which is a SVHC per REACH classification, in

China and Asia Pacific. Hence it is very important to ensure a thorough robust assessment of all the scientific data on DINP, as classification will have a major impact on the substitution of DEHP by DINP throughout China and Asia Pacific, with the associated implications for articles being exported to the EU.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment DINP_CLH_Summary comments_AICM comments May 2017 FINAL.docx

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Brazil	Instituto do PVC	Industry or trade association	12

Comment received

Phthalates are plasticizers largely used in the Brazilian market in flexible PVC products, and DINP is one of the most used. This scenario is a result of many scientific studies which have been carried out for decades. Among those studies, there are strict risk analyses stating that its use is safe. In 2013, the reassessment carried out by ECHA itself and confirmed by RAC (Committee for Risk Assessment) contributes to this scenario, and it has concluded that it is not necessary to impose other restrictions to the use of DINP in products designed both to children and adults besides the existing ones.

In case DINP rating under categories 1B and 2 is approved, the Brazilian market will surely have a negative impact, losing competitiveness, since many of the manufacturers of PVC flexible products follow the European guidelines and export products to that region. The replacement of a recognized safe plasticizer - which has been studied for a long time - by other ones whose effects on both human health and environment are not yet known, may bring serious future consequences. In addition, the national manufacturers of DINP will be impacted, which may cause possible plant shutdowns and unemployment in the sector. Therefore, it is of utmost importance that ECHA considers the available technical-scientific data, as well as its own ones, so that Denmark's request is not accepted, because we know these data show that the use of DINP is safe.

The Brazilian PVC Institute is a class association whose aim is to gather and promote technical-scientific knowledge on PVC, and believes PVC versatility can provide sustainable solutions to health, housing, and well-being in society. Therefore, we seek to disclose the right perception of PVC sustainability in society.

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Germany	Evonik Performance Materials GmbH on behalf of Evonik Degussa GmbH	Company-Manufacturer	13

Comment received

see attachment

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comments on CLH for DINP CAS 28553-12-0_2017-05-19.pdf

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Belgium	EuPC	Industry or trade association	14

Comment received

Classification : the proposed classification is not based on a full robust weight of evidence evaluation of all the relevant data versus the CLP detailed criteria. Rather a selective approach, using mild transient effects not justifying per se a classification or based on studies of questionable quality is being taken. Our understanding of the available evidence is that a thorough evaluation should lead to the conclusion that classification is not required.

DINP use and alternatives : DINP is one of the major general purpose plasticizer for PVC. According to European Plasticizers (www.europeanplasticisers.eu), the 3 general purpose plasticizers DINP, DIDP and DPHP represent 57% of the European plasticizer demand. We may confirm that DINP is the most commonly used plasticizer within this family. In our membership, it may be found mainly in the following applications : flooring, wire and cable, roofing/films and sheets, wall covering, coated fabrics, flexible profiles totalling close to 1 million tons. Other applications directly within the automotive industry may be considered as well.

It has been one of the main substitutes for low molecular weight phthalates such as DEHP, BBP, DBP and DiBP, based on the intrinsic properties of this alternative deemed as not classified for hazards and considered as safe for use by the EU risk assessment of 2003 and confirmed in 2013 by the Echa review . This substitution has become even more intensive since 2001 when DEHP and other low molecular weight phthalates were classified as reproductive agents and is now about complete within the European Union, although DEHP remains a major plasticisers outside the EU. Significant adaptations had to be made to processing techniques in order to achieve comparable performance. Today the only foreseeable alternative to phthalate plasticizers in the same price range is DOTP. Please note that application specific requirement may make this alternative less or not suitable in certain cases for which a more detailed assessment of suitability should be undertaken. There is currently not enough production capacity to replace this plasticizer.

Proportionality: Classification is an important risk management decision, which has broad regulatory impacts (e.g. reproductive classification triggers EU directive 92/85 EC on the introduction of measures to encourage improvements in the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding), which will need adaptation of work practices and could lead to potential discrimination of female workers (access to work). Most importantly, it will give ta signal to the market triggering requests for substitution whilst our industry has just gone through such a demanding process over the last 15 years, in replacing DEHP and other low molecular weight phthalates with DINP.

In light of the above and potential impact on industry competitiveness, it is important that the evaluation by Echa and RAC is made based on solid scientific ground relying on all relevant data enabling a proper evaluation based on weight of evidence.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 20170519_EuPC_Position Paper on the Proposed classification of DINP as reprotox 1b.pdf

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Belgium	The European Council of Vinyl Manufacturers	Industry or trade association	15
Comment received				
To manufacture flexible PVC products, the European producers increasingly use and rely on high molecular weight phthalates such as DINP and DIDP. According to the European Plasticizers association these high molecular weight phthalates represent about 70% of the European plasticizers market.				

Based on our understanding of the scientific data on DINP, ECVM does not support the proposed classification. We are aware of the established structure activity relationships for low (C3-C6 straight carbon backbones in the alkyl side chains) and high (C7-C13 straight carbon backbones in the alkyl side chains), with low phthalates showing adverse reproductive effects and high phthalates not showing adverse reproductive effects in animal studies. As a result, in the recent years the high molecular weight phthalates have undergone extensive evaluations, to confirm their safe use in numerous applications. This motivated the European PVC industry to switch massively from low molecular weight phthalates to the high molecular weight ones.

To our best knowledge, there are no suitable plasticizers available on the market which could fully replace high molecular weight phthalate plasticizers such as DINP when considering the price range and existing production volumes. Further, any substitution of such well known and highly scrutinized plasticizer by other, less analyzed plasticizer(s) could represent undesirable risks for human health and environment.

The fact that DINP is one of the phthalates restricted in toys is sometimes interpreted as a proof of hazardousness. However, the Directive 2005/84/EC clearly stipulates that this decision was based on the precautionary principle, and not on any definite evidence:

“Scientific information regarding di-isononyl phthalate (DINP), di-isodecyl phthalate (DIDP) and di-n-octyl phthalate (DNOP) is either lacking or conflictual, but it cannot be excluded that they pose a potential risk if used in toys and childcare articles, which are by definition produced for children.”

Given the high importance of this substance to our members, we would urge that ECHA and RAC ensure a full, exhaustive and, if possible, peer reviewed scientific evaluation of all the relevant data on DINP, to enable its further safe use.

Date	Country	Organisation	Type of Organisation	Comment number
18.05.2017	Belgium	ERFMI vzw, European Resilient Flooring Manufacturers' Institute	Industry or trade association	16

Comment received

ERFMI's comments on the proposed classification of DINP as toxic to reproduction 1b

ERFMI (European Resilient Flooring Manufacturers' Institute) represents the interests of the European producers of resilient floor coverings. Resilient floor coverings are based on plastics, mainly PVC, linoleum, rubber and cork. Its 17 members manufacture over 90% of the PVC floor coverings produced in the European Union and Switzerland.

ERFMI members employ close to 12.000 employees, in all EU and EFTA countries operating more than 50 manufacturing sites and a large number of sales companies. Altogether, these companies realise app. 250.000.000 m2 sales of floor coverings. The PVC floor covering market of our members represents at least €1.4 billion.

After huge efforts to substitute the low molecular weight phthalates, which had been carried out by the European manufacturers in the nearly last 20 years, DINP became a major plasticizer for the industry. The ERFMI members rely on the fact that DINP has been the subject of extensive regulatory evaluations with the conclusion that classification (Dangerous Substances Directive) is not required (EU Risk Assessment Report 2003), and that no further risk management measures are needed for children or adults (EU Risk Assessment Report - Completed 2003 (published in the Official Journal in 2006), ECHA

Evaluation Report on New Data, 2013). These assessments included full hazard characterizations including the available reproductive studies.

Given the high importance of this substance to ERFMI's members, we would urge that ECHA and RAC ensure a full and thorough scientific evaluation of all the relevant data on DINP.
Best regards

ERFMI, European Resilient Flooring Manufacturers' Institute

Drs. A. J. Pluijmert, Managing Director ERFMI

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2017-05-17 DINP statement ERFMI final.pdf

Date	Country	Organisation	Type of Organisation	Comment number
18.05.2017	France	GERFLOR	Company-Manufacturer	17
Comment received				
<p>We are a PVC flooring producer, we use DINP as plasticizer. We can't take a scientific position on the ranking and the tests which have been performed But it would be nice to clarify the situation in order to prevent demands and demands for updating DINP classification. It has to be definitively resolved, unless new data or element is coming. we would like to be sure that tests leading to the definition of reprotoxic 1B have been scrupulously followed. we would like to recall that European Commission has concluded on several occasions that There is at present no need for further information or for risk reduction measures beyond those that are being applied already. more over Based on the risk assessment in this report, it can be concluded that no further risk management measures are needed to reduce the exposure of children to DINP and DIDP</p>				

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	Germany	Arbeitsgemeinschaft PVC und Umwelt e.V. (AGPU)	Industry or trade association	18
Comment received				
<p>Wednesday, May 17, 2017 Comments by Arbeitsgemeinschaft PVC und UMWELT e.V. (AGPU) on the proposed classification of DINP as toxic to reproduction.</p> <p>AGPU is a German industry association representing companies from the full PVC supply chain from a salt mine via PVC and additives manufacturers to converters and recyclers. DINP is a major plasticiser for our industry, it is produced by some of our member companies, it is used by many of our member companies and finally it can be contained in PVC-wastes that some of our member companies recycle. Therefore, it is of high importance to our members. We have only limited access to the full reports of the toxicological studies undertaken by the plasticiser producers. However, we are constantly monitoring the scientific/regulatory topics including evaluations by ECHA, member states, independent third party experts or regulatory reviews undertaken in other regions. The evidence presented by this CLH report fails to present a sufficient justification for the</p>				

classification and labelling of DINP as toxic to reproduction.

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	United Kingdom	INOVYN	Company-Downstream user	19

Comment received

General Comments

We find that the description of manufacturing methods is covered in very little detail, presumably since this is adequately described in the EU risk assessment document. However it is important to note that different manufacturing methods exist in the plasticiser industry and these can impart different properties to the end products. It is of note that registrants of the C9 (and C10) phthalates have registered these as multi-constituent substances whereas the CLH dossier refers to DINP as a UVCB substance. Under modern analytical techniques the composition of these substances can be determined. A great deal is known about the distributions and these have been the subject of widespread intellectual property dossiers (see for example reference (1) and references cited therein). Such details have been presented to EFSA as part of the application for food contact status of these substances under EU Regulation 10/2011 (where the assigned PM Reference Numbers refer to the different CAS identities) as well as to EChA in the REACH registration dossiers. Since there is a direct link between manufacturing method and isomer distribution, and thus to physico-chemical properties, the identification of the distribution is important. We do not understand why the CLH dossier authors appear to think that these distributions are somehow "unknown" when the knowledge of them leads to the direct understanding of the properties of the molecules. The details of the composition are an important part of standardisation work and as such are well reviewed. The effects of carbon chain distribution of plasticisation properties can be seen in the well-used text of the flexible polymers industry (2). As an extreme example we can give the case of a highly branched DINP manufactured until the early 1990s (and thus not registered under REACH) which had an inherent viscosity some 25% higher than the corresponding DINP. This is well understood.

Consequences of (an unwarranted) change in DINP classification

The PVC resin industry has embarked upon numerous studies and statistical significance analysis over the past ten years to transfer its QC determination of PVC resins from DEHP to DINP since DINP is more representative of the plasticisers in use by the industry and is the nearest thing to an industry reference material. Additionally resin manufacturers had concerns as to their ability to use DEHP in QC analysis without a REACH authorisation from the DEHP supplier. Since resins are sold into flexible applications where they will be blended with plasticiser it is vital to know that the resin in question meets a series of specified properties when blended with an industry representative plasticiser. Owing to the different manufacturing technologies available for the manufacture of DINP – a fact not present for selection of DEHP in the past - the replacement has required extensive study to identify which DINP to use for QC determinations and to ensure that our methodology is statistically robust. These are linked to company's ISO 9001 registrations and link into several key markets which will use such registrations as a starting point for material qualification.

The use of DINP in the range of flexible applications has also been reviewed in the recently developed ISO 16000-33 standard (4) since it is seen as an important component of articles and as such needs to be have details of composition understood. The importance of this substance to this industry is clearly evident.

While the above two facts should not be used as reasons to reject a change in classification where the law requires it, it does stress the importance of such a decision being based on sound understanding and a review of all relevant literature. This makes this consultation different to the recent one on di-iso-octyl phthalate for which there was no market significance owing to the fact that the substance is not in commercial production.

References

- (1) References US Patent Application US 08/991,005
- (2) J.K. Sears and J.R. Darby: "The Technology of Plasticizers" J.R. Wiley and Sons, 1982
- (3) ISO/FDIS 16000-33, Indoor air - Part 33 Determination of phthalates with gas chromatography/mass spectrometry (GC/MS)

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	Germany	REHAU AG + Co.	Company-Downstream user	20
Comment received				
I have not found any new information in this CLH report compared with former versions. I cannot identify any realistic pathway to absorb or to ingest DINP-doses comparable to the doses applied in the studies quoted for reproduction toxicity. I have a suspicion that the Danish national authority is misapplying the CLH classification to make the use of DINP more difficult because they had no such success with the implementation of their national tax on phthalates.				

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	France		Individual	21
Comment received				
DINP is a major plasticiser for use in flexible vinyl and is of high importance to the members of Alkor Draka. Based on our understanding of the scientific data on DINP, Alkor Draka does not support the proposed classification.				

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	Japan	Japan Plasticizer Industry Association	Industry or trade association	22
Comment received				
Di-isononyl phthalate (DINP) is a phthalate ester used as a plasticizer of plastics consisting primarily of polyvinyl chloride (PVC). In response to and according to the CLP Regulation, the hazard category of DINP's reproductive toxicity was inferred as of 29th September 2015 (Study No. P150412). In this report, the CLP hazard category was reassessed by considering the content and classification (Repr. 1B; H360Df) of the CLH Report (Proposal for Harmonized Classification and Labelling) issued by the Danish Environmental Protection Agency on 1st December 2017.				
For DINP classification inferred in accordance with CLP Regulations, more data was thought needed for reliable assessment. Therefore, at this time, as the DINP hazard category, 'not classified' was judged more appropriate than the 1B proposed in the CLH Report.				

Working for better regulation of chemical substances in Europe and more meaningful application of CLP Rules, we have the following two comments. They are made entirely to avoid the excessive precautionary principle.

i) Judgements to regulate all chemicals should be based both on a set of MoA of endocrine disruption and the 'degree of disorder/effect' induced.

ii) According to the Hazard Statement (H360Df), DINP "may damage the unborn child" and "is suspected of damaging fertility." Since aberrations seen before birth may disappear after birth, human health should be judged by viewing through the entire life cycle as described in b, c and d above.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comments on DINP classification in CLP by JPIA (15th May, 2017).docx

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2017	Australia	Vinyl Council of Australia	Industry or trade association	23

Comment received

Comments on the proposal by the Danish EPA for harmonized classification and labelling of Di-isononyl phthalate (DINP) as a reproductive toxicant - Category 1B Developmental - Category 2 – Fertility

The Vinyl Council of Australia (VCA) is the peak association representing the PVC value chain in Australia. Our members include both local manufacturers and importers/distributors of raw materials and PVC products.

The VCA would like to provide information relevant to the Australian PVC industry for the technical consultation on the above proposal. We have concerns about the proposal and its ramifications for the global and our local vinyl and plasticiser industries. It is our view that scientific data does not support this classification proposal of DINP as a Reproductive toxicant Category 1B (Development), nor as a Reproductive toxicant Category 2 (Fertility).

DINP is a major plasticiser for use in flexible vinyl and is of high importance to the members of the Vinyl Council. We are aware of the extensive prior evaluations of DINP showing low hazards and safe use, and these evaluations have been the basis for the current use of DINP by our members.

Based on our understanding of the scientific data on DINP, the Vinyl Council of Australia does not support the proposed classification.

Under the Australian vinyl industry's PVC Stewardship Program, we constantly monitor scientific and regulatory information and developments regarding plasticisers to keep our members and Australian stakeholders well informed. We are aware of the established structure activity relationships for low molecular weight (C3-C6 straight carbon backbones in the alkyl side chains) and high molecular weight (C7-C13 straight carbon backbones in the alkyl side chains) phthalates, with low phthalates showing adverse reproductive effects and high phthalates - such as DINP - not showing adverse reproductive effects in animal

studies.

DINP has been the subject of extensive regulatory evaluations with the conclusion that classification is not required. ECHA's Evaluation Report on New Data, in 2013, found that no further risk management measures were needed for children or adults. A study by Boberg et al. (2011) that is heavily relied upon in the Danish EPA's dossier, was assessed as part of the ECHA Restriction Evaluation and did not change the conclusion that no further risk management measures were needed.

Since the publication of Boberg et al. (2011), the paper has been critiqued by peers and the statistical methods used, questioned since the results of statistical significance for the effects of DINP in animals cannot apparently be reproduced for several parameters. The dossier submitter has not included consideration of these critiques in its proposal.

It is our understanding that the dossier submitter has been selective in referring to some observations in certain studies which do not represent adverse effects warranting classification, while neglecting the extensive evidence which supports the absence of adverse effects on sexual function and fertility or on development for DINP.

A cumulative risk assessment undertaken by Australia's chemical regulatory agency, NICNAS (2012) aimed to assess public health risk from use of DINP in consumer products such as cosmetics, children's toys and childcare articles. Its conclusions did not support the need for restrictions on the use of DINP in Australia. NICNAS had identified a weak anti-androgenic pattern observed with DINP at high doses but concluded that the risks from exposure were low.

Reversible endocrine activity is not sufficient grounds for determining adverse effects.

In February 2015, NICNAS concluded that classification for adverse reproductive effects under the Global Harmonised System is not justified. In its 2015 review, NICNAS stated [1]: "NICNAS does not consider reversible effects on components of the endocrine system or reversible outcomes of these hormonal perturbations or other related measurements to be necessarily adverse. Where these changes can be shown to lead to adverse outcomes affecting the ongoing functioning of the organism, it is these adverse outcomes that are used as the driver for recommending risk management measures. The available data do not conclusively demonstrate the presence of adverse effects."

Based on the scientific evidence, we do not agree with the Danish EPA's proposal for classification of DINP. A robust weight of evidence evaluation by the ECHA Risk Assessment Committee (RAC) should lead to the conclusion that classification is not supported.

Given the high importance of this substance to our members, we would urge that ECHA and RAC ensure a full and thorough robust scientific evaluation of all the relevant data on DINP.

Please do not hesitate to contact us if you have any questions.

Yours sincerely

Sophi MacMillan
Chief Executive

[1] NICNAS Response to Public Comment, Assessment ID 1178: Human Health Tier II IMAP Assessment for diisononyl phthalates (DINPs) and related compounds.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 170516 DINP_ECHA_DK.pdf

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2017	United Kingdom	British Coatings Federation	Industry or trade association	24

Comment received

The effects of DINP are not comparable with those seen with the classified lower molecular weight phthalates (DBP, BBP, DEH and DIBP) and this point is also made in the dossier in 4.11.4.2 "In comparison with DEHP, DPB and BBP the overall evidence for effect of DINP on fertility is limited" and yet the dossier then tries to say there is correlation. There are no similar effects shown by DINP to those shown by the other classified phthalates.

Similarly in 4.11.5 (4.11.4.1 overview of data) it clearly states that "Human.... studies did not show any clear association between adult exposure to DINP and fertility measures...." This we believe was borne out by the review of all data carried out by Dekant and Bridges published in 2016 (see: <http://www.sciencedirect.com/science/article/pii/S027323001630280X>) which concludes that there is no justification to classify DINP. It is noted that this important publication is not included in the Danish dossier, which raises concerns over the selectivity of the information given in the dossier.

The Danish dossier relies on the study by Dr Boberg to support its proposal to classify DINP, however this study (in 2011) has been brought into question and Dr Boberg has herself admitted that she did not follow strict protocols or calculate statistics correctly. The data were questioned by Morfeld and this was acknowledged by Boberg.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment BCF comments on DINP reclassification May 17.docx

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2017	Germany		Individual	25

Comment received

Specific comments on effects cited as supportive for classification in the CLH proposal: The following points are listed as scientific justification for the classification of DINP as a Category 1B reproductive toxicant for development and Category 2 for fertility in the CLH proposal:

"DINP induces effects on the developing male reproductive system. Key findings in animal studies on reproductive effects of DINP are:

- a) Structural abnormalities: skeletal effects (rudimentary ribs) were seen two developmental toxicity studies (Hellwig et al., 1997; Waterman et al., 1999) (1000 mg/kg bw/day),
- b) Effect on altered growth: decreased body weight in offspring in a two-generation study (Waterman et al, 2000) (from 159 mg/kg bw/day),
- c) Functional deficiency: dose-dependent long-lasting decrease in sperm motility in rat offspring exposed perinatally (Boberg et al., 2011) (from 600 mg/kg bw/day),
- d) Structural abnormalities: increased nipple retention and decreased anogenital distance in infant or prepubertal male rats exposed perinatally (Boberg et al., 2011; Gray et al., 2000, Lee et al., 2006; Clewell et al., 2013b) (mostly from 750 mg/kg bw/day),

e) Structural abnormalities: increased incidence of permanent changes (permanent nipples, malformations of testes and epididymis, histological changes in testes and epididymides) in rats exposed perinatally (Gray et al., 2000; Masutomi et al., 2003) (at 750 and 1165 mg/kg bw/day, respectively),

f) A comparable pattern of adverse effects and of mode of action as seen for other phthalates classified as reproductive toxicants in category 1B, e.g. DEHP, DBP, DIBP and BBP (Boberg et al., 2011; Borch et al., 2004; Hannas et al., 2011; Clewell et al., 2013a, Li et al., 2015).

....Key findings for effects of DINP on fertility are:

g) reduced absolute and relative testes weights at high doses in a 2-year study in mice (Aristech Chemical Corporation, 1995) (742 and 1560 mg/kg bw/day), and at higher doses in studies with shorter durations of exposure, i.e. a 4-week study in mice (Hazleton 1991) (1377 mg/kg bw/day), and a 13-week study in mice (Hazleton 1992) (2600 and 5770 mg/kg bw/day),

h) reduced sperm count and effects on sperm motion parameters after 28 days of exposure of juvenile rats (Kwack et al., 2009) (one dose only, 500 mg/kg bw/day),

i) dose-dependent long-lasting reduced sperm motility in rats exposed perinatally (Boberg et al., 2011) (from 600 mg/kg bw/day)."

The following comments apply to the scientific justifications put forward in support of the individual points a) to j) in the CLH proposal.

a) "Structural abnormalities". Rudimentary ribs are not an "abnormality", but a variation (Carney and Kimmel, 2007; Kimmel et al., 2014). The incidence of these variations in rat offspring is variable and these changes are reversible within days after birth. Therefore, they do not represent an adverse effect as defined by WHO/IPCS that may serve as a basis for classification. Increases in the incidence of these variations usually represent delays in ossification due to maternal or fetal toxicity. The presence of such variations after very high doses of DINP thus cannot be used to justify classification as category 1B for development.

b) "Effect on altered growth". The following text is the result of the detailed analysis in the EU RAR: "These findings were considered by the laboratory as the results of maternal stress and/or direct effects of DINP via exposure through lactation. Other studies with phthalates concluded that these decreases were apparently due to decreased food consumption by the dams and changes in the quality or quantity of milk (Dostal et al., 1987). Thus the laboratory concluded that the lower body weights in the pups might have resulted from decreased milk consumption". Palatability issues are caused by the high concentrations of DINP present in food. In addition, treatment related effects on body weight were only observed after doses of approximately 1,000 mg/kg/day at PND 0 (1.5% DINP in diet) which is at the limit dose to be considered in classification. Based on the guidance and criteria of the CLP regulation, this "effect on altered growth" cannot be used to justify classification.

c) "Functional deficiency". The CLH proposal cites "decrease in sperm motility" observed in one study (Boberg et al., 2011) in offspring after in utero exposure to DINP. As discussed several times below, raw data from this study (publicly available through the US EPA Hero database) have been reanalyzed using the statistical approach outlined in the publication (Boberg et al., 2017; Morfeld et al., 2017). Several of the sperm changes (and other changes) reported as significant in Boberg et al, 2011 could not be reproduced when relying on the raw data and applying the statistical procedures described in Boberg et al., 2011. Furthermore, several additional issues question the reliability of the conclusions regarding sperm parameters after DINP-administration made in the CLH proposal. Sperm analyses in Boberg et al., 2011 examined only 1 - 3 animals per litter, changes in sperm parameters were small, and dose-response could not be established. In well-performed studies, sperm motility in controls is > 80 %, but motility in controls in Boberg et al., 2011 was only 60 %

suggesting a general issue with the applied procedures. According to the guidance Document (OECD, 2008), in general, 200 sperm should be analyzed and a minimum of 70% motility is acceptable in controls (OECD, 2008). Sperm motility in the DINP-exposed animals in Boberg et al., 2011 also remained within the historical control range of the laboratory at all DINP doses (53.1 to 66.9 %). In addition, a dose-response regarding sperm parameter effects and adverse changes in testes histology are required to determine whether an effect on sperm parameters is adverse since testes histology is considered the most sensitive endpoint indicative of adverse effects on male fertility (Mangelsdorf et al., 2003). Testes histology and weights were not changed in the DINP-exposed animals at the time point when sperm was analyzed (Boberg et al., 2011). Therefore, the information presented regarding sperm motility is inconclusive and cannot serve as indication for an adverse effect. The CLH proposal does not integrate the results of the two-generation study performed with DINP according to the respective OECD-guideline. Since no effects on fertility were observed in this 2-generation study with DINP, there is no support for a "functional deficiency" as claimed in the CLH proposal.

d) "Structural abnormalities" (nipple retention and anogenital distance). Nipple retention occurs in juvenile male rats at low frequencies and the significance of small increases in nipple retention as observed in one study with DINP is highly questionable. As the effect is reversible, it does not qualify as adverse and thus cannot be used to support classification. The changes in anogenital distance reported by Boberg et al., 2011 in the publication could not be confirmed in the reanalysis of the raw data applying the statistical methods described in the publication. Therefore, only one study (Clewell et al., 2013b) in the database (seven studies assessed this parameter) observed a small change in anogenital distance in juvenile rats exposed in utero to DINP. The magnitude of the change remained within the range of historical controls in the laboratory. The six other studies that determined anogenital distance did not observe an effect of DINP-administration. Therefore, the support for a change in anogenital distance due to DINP-exposure is highly inconsistent and a weight of evidence analysis does not support the claims made in the CLH proposal. In addition, the small and reversible (i.e. not adverse) change in anogenital distance cannot serve as a basis for classification.

e) "Structural abnormalities: increased incidence of permanent changes". Effects summarized here in the CLH proposal are inconsistent over studies for all the endpoints cited. In addition, the changes covered under this heading were not consistently observed in studies with DINP. Small increases in nipple retention were reported in two studies (Gray et al., 2000; Boberg et al., 2011), but nipple retention was not observed in another study (Clewell et al., 2013b) with higher statistical power or in Masutomi et al. (Masutomi et al., 2003). Regarding additional support for adverse effects, the CLH-proposal cites an increased incidence of "structural abnormalities" (apparently two offspring with retained nipples, one with bilateral testicular atrophy and one with unilateral epididymal agenesis) following DINP administration (Gray et al., 2000). In this study, statistical significance was only reached when the different types of effects were summed for statistical analysis. This is inappropriate. In addition, areolae incidence at PND13 (0 % to 14 % in controls) seems to have been highly variable in the laboratory (Ostby et al., 2001). Effects reported in Masutomi et al (2003) are different from those in Gray et al. 2000 and consisted of minimal to slight changes (degeneration of meiotic spermatocytes and Sertoli cells, scattered cell debris in ducts in epididymis) that reached statistical significance only at DINP-doses of > 1,165 mg/kg/day. The CLH proposal does not integrate the absence of such "permanent changes" in the two-generation study with DINP or in adult males exposed to DINP in utero (Boberg et al., 2011). Due to the inconsistent information from the studies and the remaining database on DINP, the effects reported cannot be used to justify classification.

f) "A comparable pattern of adverse effects and of mode of action as seen for other

phthalates". Several low molecular weight phthalates, for example DEHP, dibutyl phthalate and benzylbutyl phthalate, clearly showed reduced male reproductive capacity and increased incidences of malformations in multigeneration studies. It is claimed that such effects should also be observed with DINP since a decrease in testicular testosterone production is considered an early key event in the "phthalate syndrome" in rats and some studies showed a decrease in fetal testes testosterone after DINP-exposure (Hannas et al., 2012; Furr et al., 2014). However, results from DINP toxicity studies regarding testosterone production are inconsistent over studies and changes in testosterone production induced by DINP were only induced at dose levels that induced maternal toxicity. It should be noted that the liver is the major target organ for DINP. Given the important role of the maternal liver during pregnancy (providing metabolites and precursors for the developing fetuses) the effects on testosterone seen in some studies may be secondary to effects on the maternal liver (e.g. disturbance of cholesterol metabolism which provides precursors for testosterone). There also seems to be no apparent connection between the reversible reductions in testosterone induced by DINP and adverse phenotypes since, despite reducing testosterone in some studies, adverse effects on reproductive organs or reproductive performance were not seen. DINP does not impair fertility, affect the onset of puberty or male mating behavior, does not induce cryptorchidism, hypospadias, general reproductive tract malformations, and permanent nipple retention, or permanent decreases of AGD (Waterman et al., 2000; Boberg et al., 2011; Clewell et al., 2013b). These effects were observed in appropriate studies with other low molecular weight phthalate esters such as DEHP, but not with DINP (EFSA, 2005 a, b; Lhuguenot, 2009). The absence of these effects demonstrate that DINP does not cause the permanent histopathological alterations considered as hallmarks of the "phthalate syndrome" in rats (Johnson et al., 2012).

g) "reduced absolute and relative testes weights at high doses". Histopathological changes were not observed in the testes and the high doses of DINP applied caused a significant depression of body weight gain. Therefore, the testis/epididymis weights were not decreased relative to body weight. These studies cited in the CLH proposal applied doses well above the limit dose of 1,000 mg/kg bw/day for classification and several studies have shown adverse effects of DINP on target organs other than the male reproductive tract, even at much lower dose levels. These effects occurred at much higher doses than those causing hepatotoxicity (the NOAEL for liver effects of DINP has been identified by ECHA as 15 mg/kg bw/day).

h) "reduced sperm counts". In support of this claim, the CLH proposal cites Kwack et al., 2009. This publication assessed sperm parameters after administration of a number of phthalates to rats and reported significantly lowered sperm counts (app. 25 % lower as in controls) and motility of epididymal sperm after a four-week treatment of adult rats with a single dose level of 500 mg DINP/kg bw/day administered by gavage. The study suffers from the use of a single dose level of DINP and unclear reporting regarding use of concurrent controls. Testes histology and weights, which are more appropriate to conclude on an effect of DINP on male fertility (see above), were not assessed. Moreover, the changes in sperm number only had a statistical significance level of < 0.05 and general toxicity of DINP is evident from several observations in DINP-treated animals in this study. The limited information provided (Kwack et al., 2009) indicates DINP treatment-related general toxicity such as body weight reduction, increases in relative organ weights, and effects on clinical chemistry and hematology parameters. Thus, the effects on sperm count and sperm motility may be interpreted as secondary to systemic toxicity and should not be used to support the claim of "reduced sperm counts" when effects on fertility have not been observed in a two-generation study.

j) "dose-dependent long-lasting reduced sperm". This claim in the CLH-proposal is only supported by the study of Boberg et al., 2011. Issues with this study and the sperm counts reported have been outlined above under comments to c). There is clearly no dose-

dependence of the changes reported in Boberg et al., 2011 and the statistical significance of several of the reported sperm changes is not reproducible.

Conclusions

A number of studies with different study designs applying different types of DINP and using different rat strains are available for evaluation (see table 1 in attached document). The results of these studies demonstrate that DINP does not cause permanent effects considered as the hallmarks of the "phthalate syndrome". Malformations and permanent histopathological changes of the male reproductive tract were not observed in any of these key studies. Effects on reproductive organs observed after DINP administration were only transient and did not persist to adulthood. In addition, these transient effects observed occurred at doses in a range where a number of other studies have demonstrated maternal toxicity. Thus, some of the reported effects may be secondary to liver toxicity in the maternal animals. Moreover, some of the effects (sperm motility, nipple retention) in Boberg et al., 2011 are of questionable significance (see above) and only partly reproducible by reanalysis of the raw data (Boberg et al., 2016; Boberg et al., 2017; Morfeld et al., 2017). When reported in supporting studies, effects of DINP on testes weight and testicular histology and other endpoints assessed (AGD, testosterone reduction) were inconsistent.

A weight of evidence approach based on the results of the studies in table 1 concludes that DINP does not impair fertility, affect the onset of puberty or male mating behavior, does not induce cryptorchidism, hypospadias, general reproductive tract malformations, and permanent nipple retention, permanent decreases of AGD. The absence of these effects demonstrate that DINP does not cause the permanent histopathological alterations considered as hallmarks of the "phthalate syndrome" in rats (Johnson et al., 2012). Several other phthalates, for example DEHP, dibutyl phthalate and benzylbutyl phthalate, showed reduced male reproductive capacity and increased incidences of malformations in multigeneration studies (Lhuguenot, 2009).

In conclusion, as detailed elsewhere (Dekant and Bridges, 2016b), DINP does not induce permanent effects on sexual function and fertility and thus a classification is not supported since a consistently observed "adverse effect on sexual function and fertility" is required as a basis for classification by the CLP regulation.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comment DINP-WolfgangDekant.zip

Date	Country	Organisation	Type of Organisation	Comment number
15.05.2017	France	SFEC	Industry or trade association	26

Comment received

As users, we (Sfec, company) can not take a scientific position on the ranking.
 On the other hand :

- A clear position on the situation is needed. On a regular basis, the demand for the DINP classification returns. It has to be definitely settled.

Compliance with the test criteria leading to the definition of a reprotoxic 1B must be scrupulously followed.

It is recalled that the European Commission had concluded, on 2014 that: " « There is at present no need for further information or for risk reduction measures beyond those that are being applied already ».

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Date	Country	Organisation	Type of Organisation	Comment number
15.05.2017	South Africa	The Southern African Vinyls Association	National NGO	27

Comment received

COMMENTS ON THE DANISH EPA DOSSIER PROPOSING CLASSIFICATION OF DINP BY THE SOUTHERN AFRICAN VINYLs ASSOCIATION OF SOUTH AFRICA (SAVA)

The Southern African Vinyls Association (SAVA) is the representative body for the local polyvinyl chloride (PVC) industry and through our Product Stewardship Commitment (PSC), we provide leadership and guidance towards transforming the PVC industry in relation to commerce, health and environmental issues.

SAVA is also represented on the Global Vinyls Council (GVC) and through our information sharing network we have been made aware of the fact that the Danish EPA has made its fourth re-submission in two years of a dossier proposing the classification of DINP as a reproductive agent. We have been informed that this was accepted by ECHA and the public consultation process has now been initiated.

SAVA supports peer reviewed scientific research and concur with current robust scientific data available on DINP and agree that it does not support this classification proposal by the Danish EPA. Any proposal or submission should be based on the weight of scientific evidence and not focus on a key study by Boberg and others in 2011 and 2016 (Corrigendum to "Reproductive and behavioral effects of diisononyl phthalate (DINP) in perinatally exposed rats") where the results have been shown not be reproducible for the large part, as is the case in the most recent Danish EPA dossier.

DINP is a major plasticiser for use in flexible vinyl (i.e. car underbody sealants, cabling, sheeting, footwear and hosing) and is of high importance to the members of SAVA. Based on international trends and product stewardship programmes, the South African PVC industry voluntarily signed a Product Stewardship Commitment in 2011 to replace DEHP with DINP as a plasticiser and the replacement has been successfully concluded in the majority of PVC applications locally.

SAVA continuously review scientific data available on various chemicals including DINP and based on our research and understanding of the available peer reviewed data showing low hazards and safe use, we cannot support any proposed classification of DINP. The commitment shown by our industry to replace DEHP with DINP is based on this collection of sound and robust scientific data.

We agree with the conclusions made by various peer reviewed scientific studies that show that low phthalates (C3-C6 straight carbon backbones in the alkyl side chains) have adverse reproductive effects in animal studies and that high phthalates (C7-C13 straight carbon backbones in the alkyl side chains), do not show any adverse reproductive effects.

Given the high importance of this substance to our members, we can only support the current body of evidence based on peer reviewed and robust scientific research and urge ECHA and RAC to commit to a balanced and thorough scientific evaluation of all the relevant data on DINP.

We do not believe the classification dossier published by the Danish EPA supports any further classification of DINP or the substitution of DINP in PVC applications.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comments on the Danish EPA Dossier_DINP_By SAVA_15May2017.pdf

Date	Country	Organisation	Type of Organisation	Comment number
13.05.2017	Italy	Istituto Superiore di Sanità	National Authority	28

Comment received

EFFECTS ON FERTILITY.

The available data do not support per se any conclusion on a possible classification for reproductive toxicity of DINP, even in category 2. Conversely, they warrant performing further studies,

To this purpose, ad hoc protocols might be envisaged. For instance a study starting exposure in the pre-pubertal period till adulthood, and examining in detail both sexes (histopathology of reproductive organs, including quantitative measurements, sperm parameters, estrous cyclicity, hormone measurements) in comparison with endpoints of general/systemic toxicity: this protocol may provide a robust basis to conclude whether DINP specifically impairs male and/or female reproductive function.

Last but not least, the use of in vitro assays investigating mechanisms and/or functional markers (e.g., steroidogenesis) should support classification.

Date	Country	Organisation	Type of Organisation	Comment number
12.05.2017	United Kingdom	<confidential>	Company-Downstream user	29

Comment received

We question the validity of the recent study as it is based upon oral toxicity in rats the dosage is excessive and is not directly comparable to the impact/risk to the human health. This test method does not reflect the likely exposure during installation or use of the wallcoverings.

Date	Country	Organisation	Type of Organisation	Comment number
12.05.2017	Belgium	IGI - The Global Wallcoverings Association	Industry or trade association	30

Comment received

We question the value of the recent studies put forward by Denmark, as they are based on oral ingestion by rats, and we see no relevance between this and the likely human exposure by consumers resulting from the handling of vinyl wallcoverings. Indeed, the levels of oral dosage given to rats in the recent studies, is excessive and disproportionate to the levels experienced by consumer contact. In our view these levels have been used to obtain the result that the Danish EPA required for this current proposal.

Date	Country	Organisation	Type of Organisation	Comment number
11.05.2017	Germany		MemberState	31

Comment received

A former EU risk assessment report from 2003 concluded that no classification under Directive 67/548/EC for DINP is warranted. The available new data which have been published since then demonstrate developmental effects of DINP in particular on male offspring exposed perinatally. Key findings include increased nipple retention, decreased anogenital distance, histological changes in testes and epididymis, and decreased sperm motility. The observed effects show a comparable pattern as other phthalates which have been classified as reproductive/developmental toxicants and there is indication for a similar anti-androgenic mode of action (decrease of testicular testosterone production in several studies; weak-positive in one Hershberger assay). Decreased sperm counts and motility after adult or perinatal exposure furthermore indicate possible consequences for male fertility. Regarding the above mentioned effects, DINP is certainly less potent than other phthalates such as DEHP. Nonetheless, the observed effects of DINP are not considered to be secondary to non-specific toxicity. In conclusion, the proposed classification of DINP as Repr. 1B (H360Df) is supported.

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	United States	American Chemistry Council	Industry or trade association	32
Comment received				
Please see the attached comments from the High Phthalates Panel of the American Chemistry Council.				
ECHA note – An attachment was submitted with the comment above. Refer to public attachment ACC Comments re Classification and Labelling of DINP May 2017.pdf				

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	United States	The Vinyl Institute	Industry or trade association	33
Comment received				
To the VI's knowledge, DINP has not shown adverse reproductive effects in certain animal studies.				
ECHA note – An attachment was submitted with the comment above. Refer to public attachment VI Comments to CPSC on CHAP NHANES Information submitted 03-24-2017.pdf				

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Belgium	ExxonMobil Chemical Holland BV	Company-Manufacturer	34
Comment received				
Based on the extensive scientific data on DINP, ExxonMobil respectfully disagrees with the decision from the dossier submitter to propose harmonized classification (CLH). ExxonMobil proposes that no classification is required for DINP for adverse reproductive effects (development and fertility). This extensive data on DINP includes 30 animal studies of direct relevance to inform reproductive classification. While these animal studies show that a reduction in testosterone is consistently observed following exposure to DINP, the empirical evidence on DINP collectively supports that this reduction is insufficient to culminate in adverse effects, i.e. the multitude of studies on DINP consistently fail to report the adverse effects which are seen in studies on low molecular weight phthalates (i.e. those with C3-C6 straight chain backbones in the alkyl side chains), namely, hypospadias, cryptorchidism,				

under developed prostate and seminal vesicles, changes in secondary reproductive organ weights, and underdeveloped Wolffian Duct. Other observations have also been sporadically reported in the scientific literature on DINP. These observations require careful consideration as to whether they are indeed treatment related based on dose responsiveness, high variability or imprecision of the endpoint, incidence within normal range of variation and historical controls, replicability across studies and study quality; as well as careful consideration of toxicological significance based on the level of biological organization with which the observation is associated (e.g. biochemical, cellular, whole organism), severity, incidence, correlation with other in-study observations, (both positive and negative outcomes), and occurrence below limit doses. Using this type of weight of evidence approach as described in CLP (Annex I, Section 3.7.2) our conclusion is that the CLP criteria are not met and that classification is not warranted for some or clear adverse effects on reproduction (i.e. consistent and identifiable toxicologically significant changes which affect function or morphology of a tissue/organ or produce serious changes to biochemistry relevant to human health are not supported by the evidence). This conclusion is supported by the quantitative weight of evidence assessment taking into account the CLP criteria conducted by Bridges and Dekant (2016), as well as by prior regulatory reviews (ECB, 2003) and well established structure activity relationships for low and high molecular weight phthalates. Human epidemiological data is also consistent with the conclusion that classification for adverse reproductive effects (development and fertility) is not required.

With regard to the use of the CLP criteria and the legality of the dossier, the Danish decision to propose the harmonized classification (i.e. basic legal act) is legally void in our opinion because the detailed CLP criteria (re: CLP Regulation, Annex I, Section 3.7.2.) are not applied or demonstrated, formally and materially in the review of the data and in determining whether classification is required or not.

With respect to the scientific quality, the dossier has a number of serious shortcomings which could mislead the reader towards a conclusion which is not scientifically supported:

- Selective reporting of studies and study outcomes with emphasis placed on observations representing endocrine activity (e.g. testosterone change) versus the downstream negative outcomes (e.g. hypospadias, cryptorchidism)
- Lacks a clear and objective scientific explanation for concluding observed effects are treatment related (e.g. does not explain how a minimal magnitude change in AGD that is rarely observed is considered chemically mediated; does not explain why permanent nipples that are within literature control ranges and are not dose responsive are concluded as treatment related).
- Lacks a clear and objective scientific explanation for concluding why effects representing changes at low levels of biological organization are considered adverse despite a lack of occurrence of the events downstream.
- Does not transparently assess study quality and how study limitations affect conclusions with regard to classification, particularly for key studies. For example, Boberg et al (2011) – one of the main studies used to support the case for classification – the dossier does not transparently assess significant flaws in the statistical methods applied in the original paper and in a subsequent Corrigendum (<http://doi.org/10.1016/j.reprotox.2016.07.001>) published by the authors in 2016, as highlighted in a letter (<https://doi.org/10.1016/j.reprotox.2017.03.013>) to the editor sent by Morfeld et al (2017) to the journal where Boberg et al (2011) was originally published, with a rebuttal letter (<https://doi.org/10.1016/j.reprotox.2017.03.014>) from Boberg et al (2017). These two letters to the editor receive no acknowledgment in the CLH dossier presumably because they were published shortly after the time of resubmission of the dossier to ECHA. These letters are now “in press” and available via the website (links are provided in these comments) and we would respectfully request that they should be taken into account in the RAC process.

- Some of the studies cited by the dossier submitter have already been extensively assessed by regulators in the past and have been found not to support classification (EU Risk Assessment Report, ECB 2003). The effects which regulators concluded previously did not support classification are now used to support classification and no explanation or justification as to why this is now the case has been provided (e.g. testes weights in chronic mouse study – Aristech 1995).
- As already noted the dossier submitter does not refer to and evaluate the scientific data versus the detailed CLP criteria under 3.7.2., which is essential to make a determination on classification under the CLP regarding adverse effects, total weight of evidence, toxicological significance, nature, severity and consistency of effects, and effects seen below or above limit doses.
- Furthermore the dossier submitter does not objectively depict the fundamental differences in observed effects between DINP and low molecular weight (LMW) phthalates such as DEHP (see Table 1a in Part 1 of European Plasticisers comments). This lack of adverse effects for high molecular weight phthalates such as DINP and the crucial differences in this respect with LMW phthalates is well documented in the scientific literature based on structure activity relationships (Fabjan et al. 2006; OECD 2004, Saillenfait et al. 2014). In this context it is noted that over half of the 82 references in the dossier are not related to DINP, but many rather relate to low molecular weight phthalates.

The points above are further analyzed in detail in the submission by European Plasticisers (formerly ECPI) - the CEFIC sector group of which ExxonMobil is a member - to the public consultation. We would respectfully request the RAC to take the full weight of evidence on DINP into account in line with the CLP criteria, and to clearly identify what are the consistently observed effects for DINP in reproductive animal studies, and on what basis these are considered as adverse or non-adverse, and thereby ensure a thorough, robust and transparent assessment and opinion on the proposed classification of DINP.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment ExxonMobil DINP submission_May_19_2017_Final.pdf

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	France		Individual	35
Comment received				
No specific comments				
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Consultation publique DINP_V3.docx				

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	China	AICM	Industry or trade association	36
Comment received				
The evidence and rationale brought forward by the dossier submitter does not justify classification of DINP as a reproductive toxicant according to the criteria of the CLP. Based on the extensive scientific evidence demonstrating a lack of adverse reproductive effects following exposure to DINP, per the CLP criteria as detailed in section 3.7.2. of Annex I of the CLP, AICM proposes that classification for development and fertility effects is not required. This proposal for no classification is consistent with the statement in the current DINP IUCLID REACH registration dossiers (updated December 2015) which uses IUCLID				

standardized language – that is, the reason for no classification is that the reproductive data on DINP is “conclusive but not sufficient for classification”.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment DINP_CLH_Summary comments_AICM comments May 2017 FINAL.docx

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Brazil	Instituto do PVC	Industry or trade association	37
Comment received				
As representative of the Brazilian PVC production chain, we would like to declare our position against Denmark’s proposal to rate DINP under categories 1B and 2 as toxic for reproduction, development and fertility, respectively.				

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	France		MemberState	38
Comment received				
<p>There is no reporting of the quality of the studies in the tables. Could you please clarify if all the studies are considered of adequate reliability?</p> <p>Page 29: There are some discrepancies between findings reported in the table and in the text. For example, for the one generation study, reduced live birth pups and pup survival are noted in the text but not in the table. Could you please clarify?</p> <p>Page 56: For developmental toxicity, it was stated that decreased AGD occurred mostly from 750 mg/kg bw/day. However, it should be noted this effect can occurred at much lower doses since Lee et al., 2006 reported reduced AGD at all doses tested starting from 2 mg/kg bw/day.</p> <p>Page 60: Mode of action: effects on male reproductive system reported with phthalates are not only linked to an anti-androgenic effect. In particular, multinucleated gonocytes can be due to a direct effect on germ cells. Decrease of insulin like 3 can also be involved in reduced sperm production and cryptorchidism.</p> <p>Page 66: In addition to effect on sperm, the occurrence of malformations in the male reproductive system reported in the prenatal and perinatal toxicity studies can be used as supportive data to classify the substance for fertility (category 2).</p> <p>Page 67: It would have been interesting to assess the potency of DINP with the setting of SCL (specific concentration limit) for developmental toxicity by calculating ED10 for the effect considered the most sensitive in all studies and choose the resulting lower value.</p> <p>Overall, we agree with the proposed classification.</p>				

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Germany	Evonik Performance Materials GmbH on behalf of Evonik Degussa GmbH	Company-Manufacturer	39

Comment received
see attachment
ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comments on CLH for DINP CAS 28553-12-0_2017-05-19.pdf

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Belgium	EuPC	Industry or trade association	40

Comment received
<p>The dossier proposes 2 types of reproductive effects warranting classification. We herewith comment point per point the summary justifications provided in page 8 to 10 of the dossier, commenting each indent.</p> <p>1. Developmental toxicity effects</p> <p>a) Observation of skeletal effect (rudimentary ribs) found in Hellwig et al 1997 and Waterman et al 1999, such foetal variations are not per se considered significant criteria for classification as per the CLP Regulation Annex I, Section 3.7.2.2.2.</p> <p>b) Decreased weight of offspring in a two-generation study (Waterman et al 2000) is quoted, but it is not so clear what is the cause of this reduced weight : effects seen are likely related to palatability and not due to the inherent toxicity of DINP. In addition effects were only seen above the limit dose and were reversible. These effects do not meet the CLP criteria for classification.</p> <p>c) Functional deficiency decrease in sperm motility observed by Boberg et al 2011 : limited number of specimen , control rats were not fulfilling OECD quality requirements for sperm motility (minimum 70% motility), the sperm motility for rats within the same lab varied greatly and the statistical approach is questioned (Morfeld et al 2017)</p> <p>d) Structural abnormalities and anogenital distance in infant and prepubertal rats : one has to note that such changes were only transient, are of probably low biological consequence (hence not meeting CLP annex 1 section 3.7.2.3.3. : significance of effect) and furthermore occur at levels where there is a clear toxicity from other effects to mothers. It is therefore not possible to distinguish an effect different from others as required by CLP annex 3.7.2.1.1.</p> <p>e) Likewise for bullet point e, Dekant et al 2016 questions the reliability of Gray et al 2000 and also the statistical significance of the findings.</p> <p>f) Regarding similar effects of low molecular weight phthalates (mode of action), one should note that this is not consistent with known structure activity relationships showing differences between C3-to C6 phthalates and C7 to C13 (OECD SIAM 2004 and Clewell 2013b)</p> <p>Reproductive fertility effects</p> <p>g) Reduced testes weight quoted in g) occur at doses typically above the limit doses and well above those inducing toxicity for the liver (NOAEL set at 15mg/kg.bw by Echa in 2013).</p> <p>h) Kwack et al 2009 reports a reduced sperm count , but there are several flaws in the study : single dose of 500 mg.kg.bw, unclear concurrent controls, the study is of low reliability in view of inconsistent results for sperm counts and motility, for example showing effects for MEP for which other studies have clearly shown not to cause reproductive effects. Boberg et al 2011. reports dose dependent long lasting effect on sperm motility in rats exposed perinatally. For limitations of this study see above point c.</p> <p>Conclusions on classification of DINP</p> <p>EuPC would note that the CLP criteria have not been applied in the DINP CLH dossier in</p>

reviewing the data. As indicated above, when the criteria are applied the conclusion is that the criteria are not met and classification is not required.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 20170519_EuPC_Position Paper on the Proposed classification of DINP as reprotox 1b.pdf

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Belgium	The European Council of Vinyl Manufacturers	Industry or trade association	41

Comment received

Based on our understanding of the scientific data on DINP, ECVM does not support the proposed classification.

Date	Country	Organisation	Type of Organisation	Comment number
18.05.2017	Belgium	ERFMI vzw, European Resilient Flooring Manufacturers' Institute	Industry or trade association	42

Comment received

After huge efforts to substitute the low molecular weight phthalates, which had been carried out by the European manufacturers in the nearly last 20 years, DINP became a major plasticizer for the industry. The ERFMI members rely on the fact that DINP has been the subject of extensive regulatory evaluations with the conclusion that classification (Dangerous Substances Directive) is not required (EU Risk Assessment Report 2003), and that no further risk management measures are needed for children or adults (EU Risk Assessment Report - Completed 2003 (published in the Official Journal in 2006), ECHA Evaluation Report on New Data, 2013). These assessments included full hazard characterizations including the available reproductive studies.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 2017-05-17 DINP statement ERFMI final.pdf

Date	Country	Organisation	Type of Organisation	Comment number
18.05.2017	Netherlands		MemberState	43

Comment received

Several other classification proposals for ortho- phthalates have been discussed in the last period. The overall conclusion is that ortho-phthalates with a backbone length of C3-6 are associated with reproductive and developmental toxicity, whereas ortho-phthalates with a shorter (<C3) or longer (C7-C13) do not induce such effects. For these effects, a category approach has been proposed (see a.o. Fabjan et al., 2006 and Saillenfait et al., 2011). Since DINP has a backbone length of C7, classification for reproductive and developmental toxicity is unexpected. The current proposal for DINP is partly based on data for the substance itself and partly on similarities with other phthalates. In our opinion, due to the fact that DINP is a borderline case between C3-C6 and longer backbone length ortho-

phthalates, classification should be based on the observed effects with DINP and only the type of effects can be compared to other ortho-phthalates.

In general, an assessment of the observed effects in relation to the limit dose of normally 1000 mg/kg bw/day, the severity and the reversibility of the effects, and thus the relevance of the observed effects, seems to be limited. Also the consistency of the effects between the studies should be considered. Please include this in your assessment for example by providing an overview table(s) for the main effects.

Below, we will comment on the key findings as indicated in 4.11.4.1 Overview of data.

Development

a) An increased incidence of rudimentary ribs as observed in two developmental toxicity studies is not sufficient for classification.

b) When controlled for litter size, a significant reduction in pup weight is only observed in high-dose males on PND 0, in males and females of the mid and high-dose levels on PND 7 and 14 and in all treated animals on PND 21. The effects on PND 21 may be caused by direct intake of DINP by the pups and are thus not considered to be an effect on development. In addition, the weights of all F1 and F2 treated offspring were within the historical control range of the laboratory with the exception of the F2 high-dose males and females on PND 0 and the F2 high-dose males on PND 1. It can therefore be questioned whether the effects are biologically relevant. In addition, general toxicity (liver and kidney) can be expected at this dose level.

c) A significantly reduced percentage of motile sperm was observed in juveniles after exposure to dose levels ≥ 600 mg/kg bw during development in the study by Boberg et al. 2011. However, there are some questions on the methods of analysis of the sperm parameters (see Boberg 2016, Morfeld 2017 and Boberg 2017) which reduce the reliability of the data. In addition, it is noted that the percentage of motile sperm in the control animals (59%) is also very low, and even below the quality criteria of the OECD (OECD 2008), which states a minimum of 70%. Further, the decreased % of motile sperm was within the range of the historical control data. Also, the % of progressive sperm cells, which is more relevant than % motile sperm, was not significantly affected at most dose levels.

d) In contrast to what is mentioned in point d, DINP did not affect nipple retention or AGD in the study by Gray et al (2000). Decreased anogenital distance was observed in the study by Boberg, at a dose levels of 900 mg/kg bw, but only when analysed with non standard methods (see Boberg 2016 and Morfeld 2017). Furthermore, as for an effect on nipple retention (≥ 750 mg/kg bw), a very high dose is needed for the effects to occur. In the study by Clewell, a decreased AGD was only observed at a relatively high dose level (750 mg/kg bw). No effects on nipples was observed at this dose. Further, these effects are likely reversible as no effect on AGD was observed on day 90 in Boberg. In addition, nipple retention is not a relevant effect in humans as all human males retain their nipples but more an indicator of reduced systemic testosterone.

Decreased anogenital distance was observed at dose levels from 1 mg/kg bw in the study by Lee et al. However, this is inconsistent with all other available studies and ECHA already noted that no firm conclusions could be drawn from this study due to its limitations.

e) In the study by Masutomi et al., testicular histology was only slightly affected, and only at a dose level > 1000 mg/kg bw, which also induced maternal toxicity. This is not considered relevant for classification. The effects in the study by Gray et al. (malformations of testis, epididymis, accessory reproductive organs and external genitalia, 4 out of 52 pups and statistically significant, 3 out of 14 litters and not statistically significant, differences between the observed type of reproductive malformation) occur at a slightly lower dose (750 mg/kg bw) and should be considered. Could you provide information on historical control values to have an indication whether these types of male reproductive organ abnormalities occur spontaneously?

f) As already mentioned, DINP does not belong to the group of ortho-phthalates that is generally accepted to cause effects on development (and fertility), because of its backbone of C7. Whereas the observed effects are not comparable to other C7-C13 backbone phthalates (which do not cause effects on fertility or development), they are also not completely comparable to the shorter, reprotoxic ortho-phthalates with a backbone of C3-C6, which amongst others clearly show hypospadias and cryptorchidism. Therefore, DINP should be assessed based only on the observed effects.

Overall, the available data shows that DINP induces a reduction in fetal testicular testosterone production due to an effect on steroidogenesis as do other phthalates. However, the available comparisons with other phthalates show a reduced potential for DNIP. The primary effect occurs at dose levels clearly below the limit dose. Histopathological changes of the fetal and pup testis, secondary or related to the reduction in fetal testicular testosterone, occur (increased Leydig cell clustering and multinucleated gonocytes). These effects are also observed with other phthalates but the potency of DINP is lower. However, the observed fetal and pup histopathological effects are at least partially reversible as in adult rats treated in utero or peri-natal structural effects are only observed at incidences without statistical significance even at dose levels above the limit dose, small increase with a doubtful significance (Gray) and no structural histopathological testis effects (Boberg day 90), or only minimal to slight at dose levels above the limit dose (Masutomi). A possible reduction in sperm motility, but not in sperm count or sperm progression, was observed on day 90 PND after exposure from GD 7 to PND 17 is considered of doubtful biological significance as the % of progressive sperm cell (moving in a direction) is considered more relevant than the % of motile sperms (moving) and the observed changes in motility were within the historical control range of the lab. It can therefore be questioned whether these effects warrant classification in category 1B. Other phthalates show irreversible effects on the male reproductive organs such as hypospadias at dose levels at or below the limit dose. In addition, in some studies more general effects secondary to the reduction in testosterone production were observed in the form of an increase in nipple/areola retention in males (low incidence) and a decrease in male anogenital distance mainly around PND 14. These type of effects are under control of T3. However, no significant increase in nipple/areola retention was observed in adult animals exposed perinatal indicating that this effect is reversible. Also, there was no significant effect on male AGD on day 90. Therefore it is concluded that DINP induces comparable developmental effects as other phthalates but with a lower potency and without conclusive evidence for irreversible structural/functional effects on the adult male. In addition, based on the reduced potency it cannot be concluded that such effects are likely to occur at dose levels at or below the limit dose. Therefore, classification in category 1B is not considered justified. However, as there are some indications of structural/functional effects (Grey, 2000) supported by the observation of effects in line with the proposed AOP that could induce such effects classification in category 2 is warranted.

The effects on male developmental testes are considered not secondary to the general toxicity and there is insufficient evidence that these effects are not relevant to humans.

Fertility

g) Results occurring only at dose levels > 1000 mg/kg bw are normally not considered relevant for classification. Therefore, only the reduced testis weight observed at a dose level of ≥ 742 mg/kg bw in the 2 year mouse study by Aristech (1995) at dose levels also inducing a reduction in body weight could be relevant. However, since no histopathological changes in the testes were observed in this study, the results are not considered biologically relevant. In addition, no such effects were observed in repeated dose and generation studies at dose levels below 1000 mg/kg bw/day.

h) The effects of DINP on sperm count and sperm velocity were only observed at a dose

that also reduced body weight (by 12%). As the dossier submitter also indicates, this implies that the effect on sperm velocity may be secondary to a delay in general development in a sensitive period for spermatogenesis. Sperm production in rats starts at day 50 and increases up to day 100 (Robb, 1978, J. Repro. Fert. 54: 103-107). A reduction in body weight and body weight gain resulting in a delay in general developmental can therefore have a strong effect on the development of sperm production and parameters. The observed reduction in sperm count and change in sperm parameters is therefore not considered evidence of a direct effect of DINP on the testis. It is however noted that sperm motion was affected in a similar manner as by other ortho-phthalates (e.g. DEHP, DBP and BBP) and therefore, that a direct effect cannot totally be excluded. This is further supported by the study of Glass (1986, Pediatric Research 20(11)) showing that limited feed reduction does not reduce daily sperm production per gram testis and only limitedly reduces total sperm production (results day 51) but somewhat more for the day 81 results.

i) See point c. Furthermore, an effect due to peri-natal exposure would be more relevant for classification for effects on development than for classification for effects on sexual function and fertility.

In conclusion, DINP induces comparable effects on the sexual function of rodents as other phthalates. However, mainly at dose levels above the limit dose of 1000 mg/kg bw/day. The only effects observed at or below the limit dose are of questionable biological relevance or possible secondary to the general toxicity. The proposed classification in category 2 is justified mainly on the decrease in sperm counts and sperm motility in the presence of general toxicity in the study by Kwack (2009).

With regard to the derivation of an SCL it is suggested to derive ED10 values for the different effects warranting classification. If the lowest ED10 still indicates a low potency, a higher SCL than the GCL could be considered.

Date	Country	Organisation	Type of Organisation	Comment number
18.05.2017	France	GERFLOR	Company-Manufacturer	44
Comment received				
page 7/369 ECHA document DINP.				

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	Belgium	European Plasticisers	Industry or trade association	45
Comment received				
We provide attached the extensive quantitative weight of evidence report prepared by W. Dekant, J. Bridges and G.M.H. Swaen on reproductive and developmental effects of DINP, DnHP and DCHP. This project was sponsored by ECPI (now European Plasticisers).				
ECHA note – An attachment was submitted with the comment above. Refer to public attachment DINP-WOE Report-final.pdf				

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	Belgium	European Plasticisers	Industry or trade association	46

Comment received

European Plasticisers – Comments on the CLH Report Proposal for Harmonised Classification and Labelling – Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2; Substance Name: 1,2-benzenedicarboxylic acid, di-C8-C10-branched alkylesters, C9-rich; [1] di-“isononyl”phthalate; [2] [DINP]; EC number: 271-090-9 and 249-079-5; CAS number: 68515-48-0 and 28553-12-0; Dossier Submitter – Danish EPA European Plasticisers¹ represents the major producers of plasticisers in Europe (BASF, Evonik, ExxonMobil, Deza, Grupa Azoty, Lanxess, Perstorp, and Proviron). The opinion of European Plasticisers on the classification proposal is as follows:

1. Based on the scientific evidence, European Plasticisers does not agree with the proposal for classification of DINP as a Reproductive toxicant Category 1B (Development).

2. Based on the scientific evidence, European Plasticisers does not agree with the proposal for classification of DINP as a Reproductive toxicant Category 2 (Fertility).

3. European Plasticisers would note that the endpoints brought forward by the dossier submitter have not been interpreted and/or documented in the dossier versus the detailed criteria established under the CLP for effects warranting classification (see Section 3.7.2.2. – Basis for classification). In the attached comments scientists from European Plasticisers member companies have applied these detailed criteria to the data with the conclusions shown under point 5.

4. European Plasticisers would note that a key study central to the CLH dossier is by Boberg et al (2011). This study is used in four of the nine key points in the “Short scientific justification” which the dossier submitter includes to support the classification proposal. A re-analysis of the raw data from this study using the methods in the published paper (Boberg et al. 2011) has shown that the results of statistical significance for the effects of DINP in animals cannot be reproduced for several parameters (Morfeld et al., 2017²). A Corrigendum³ from Boberg et al. in 2016 and letters to the editor (Morfeld et al., 2017; Boberg et al. 2017⁴) have confirmed that the original published methods were not in fact followed and that non-standard methods are now proposed, thereby maintaining the original results. When the statistics are performed according to the original methods, the statistical significance of AGD, histopathology outcomes, and sperm parameters is lost in almost all instances, calling into question the statistical and toxicological significance of these observations. A Data in Brief article (Chen et al., submitted) and a letter to the editor (Morfeld et al. 2017) have been written by scientists from European Plasticisers member companies, which clarify the reproducibility discrepancies and their significance to interpretation of this particular study. The editor and an independent reviewer engaged by the editor confirmed in writing their agreement with nearly all of the points in the European Plasticisers letter (Morfeld et al, 2017). European Plasticisers would also note that according to the metadata in the dossier, Dr. Boberg is also the author of the classification dossier.

5. The evidence and rationale brought forward by the dossier submitter does not justify classification of DINP as a reproductive toxicant according to the criteria of the CLP. Based on the extensive scientific evidence demonstrating a lack of adverse reproductive effects following exposure to DINP, per the CLP criteria as detailed in section 3.7.2. of Annex I of the CLP and the detailed criteria in section 3.7.2.2. (Basis for classification), European Plasticisers proposes that classification for development and fertility effects is not required. This proposal for no classification is consistent with the statement in the current DINP IUCLID REACH registration dossiers (updated December 2015) which uses IUCLID standardized language – that is, the reason for no classification is that the reproductive data on DINP is “conclusive but not sufficient for classification”.

The above opinion is supported by the attached detailed comments which are provided in five parts:

Part 1 – Short Summary of the Scientific Justification for No Classification
 Part 2 – Structured Summary on Danish EPA Reproductive Classification Proposal – DINP does not fulfill the criteria of Annex I of the CLP and therefore does not warrant classification

Part 3 – Detailed comments on the dossier

Part 4 – Scientific Appendices providing detailed information relevant to Parts 1 and 2

Part 5 – Additional Background Information

The above comments (Parts 1 to 5) are provided as 5 individual pdf documents in the zip file attached to this submission to the ECHA web page.

1 www.europeanplasticisers.eu

2 <https://doi.org/10.1016/j.reprotox.2017.03.013>

3 <http://doi.org/10.1016/j.reprotox.2016.07.001>

4 <https://doi.org/10.1016/j.reprotox.2017.03.014>

ECHA note – An attachment was submitted with the comment above. Refer to public attachment DINP CLH comments pdfs May 17.zip

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	Germany	Arbeitsgemeinschaft PVC und Umwelt e.V. (AGPU)	Industry or trade association	47

Comment received

Please find hereunder our comments/rationale:

We focus our comments on the summary on page 8 (but realize that the same arguments have also been used on other places in the document).

a) "Structural abnormalities: skeletal effects (rudimentary ribs) were seen [in] two developmental toxicity studies (Hellwig et al., 1997; Waterman et al., 1999) (1000 mg/kg bw/day),"

What is the reason that DK is bringing up this topic again?

To our understanding, there is no significant difference between the evaluation criteria for effects toxic to reproduction between the old Directive 67/548/EEC, Annex I and the CLP (Regulation (EC) No 1272/2008).

The effects described in these publications have already been evaluated within the EU RAR (2001/2003) with the conclusion that no classification was warranted.

b) "Effect on altered growth: decreased body weight in offspring in a two-generation study (Waterman et al, 2000) (from 159 mg/kg bw/day),"

What is the reason that DK is bringing up this topic again?

To our understanding, there is no significant difference between the evaluation criteria for effects toxic to reproduction between the old Directive 67/548/EEC, Annex I and the CLP (Regulation (EC) No 1272/2008).

The effects described in these publications have already been evaluated within the EU RAR and concluded not to be sufficient for classification.

c) "Functional deficiency: dose-dependent long-lasting decrease in sperm motility in rat offspring exposed perinatally (Boberg et al., 2011) (from 600 mg/kg bw/day),"

Boberg et al. (2011) seems to be essential to support the CLH proposal. However, we notice that this study is not undisputed but even under massive scrutiny.

In a most recent letter to the editor, Morfeld et al. (2017) expresses serious doubts on the validity of this study. Having read the letter to the editor and the poor response of the authors, we share this view, i.e. Boberg et al (2011) seems to suffer from various flaws and therefore may be of ambiguous validity.

Further, it is hard to understand how a substance that is claimed by DK to act via an antiandrogenic mode of action leads to statistically significantly increased sperm counts at

the highest dose level.

f) "a comparable pattern of adverse effects and of mode of action as seen for other phthalates classified as reproductive toxicants in category 1B, e.g. DEHP, DBP, DIBP and BBP."

We are not at all convinced that this statement is a proper representation of the data. Low molecular weight phthalates result in cleft palates, cleft prepuce, hypospadias, mal positioned testes and testicular damage, e.g. Saillenfait (2008) describe malformations and other adverse effects as a result of DBP and DiBP dosing: "Preputial separation (onset of puberty) was delayed in male offspring at 500 and 625mg DIBP/(kg day). Hypospadias, cleft prepuce, and undescended testis were observed in males (11–12 or 16–17 weeks old) exposed in utero to 500 and 625 mg DIBP/(kg day). Histopathological lesions were also present in adult testes, mainly consisting in seminiferous tubule degeneration."

To our knowledge, none of these malformations are reported from valid studies with DINP. Page 64: "Species similarities are seen between mice, rats and marmosets in the foetal germ cell effects seen with prenatal exposure in vivo (McKinnell et al., 2009; Gaido et al., 2007)."

Again, this statement is strange as e.g. McKinnell (2009) report significant differences; their conclusion says: "Fetal exposure of marmosets to MBP does not measurably affect testis development/function or cause testicular dysgenesis, and no effects emerge by adulthood. Some effects on germ cell development were found, but these were inconsistent and of uncertain significance."

Also, the second quote, Gaido et al. (2007) , reports differences and not similarities as in the mouse, gonocyte multinucleation is not associated with decreased testicular testosterone.

g) "reduced absolute and relative testes weights at high doses in a 2-year study in mice (Aristech Chemical Corporation, 1995) (742 and 1560 mg/kg bw/day), and at higher doses in studies with shorter durations of exposure, i.e. a 4-week study in mice (Hazleton 1991) (1377 mg/kg bw/day), and a 13-week study in mice (Hazleton 1992) (2600 and 5770 mg/kg bw/day)"

The US CEHRH Monograph on DINP notes that the testicular weight decreases coincide with decreased body weights.

Further, what about limit dose aspects? The majority of effects described here are related to dose levels exceeding 1000 mg/kg bw./day – what is the reason to suggest to take them into account?

h) "reduced sperm count and effects on sperm motion parameters after 28 days of exposure of juvenile rats (Kwack et al., 2009) (one dose only, 500 mg/kg bw/day), What about the validity of this study? There are ambiguous results presented for very short chain phthalates, i.e. Dimethylphthalate (DMP) and Diethylphthalate (DEP) including the respective monoesters, which actually do not show toxicity to reproduction.

While the report cited Habert (2009) to claim species similarities, it unfortunately fails to include the more recent findings presented by Habert et al. (2014); this review should be included for discussion on the validity of data selected in the report:

Habert R. et al. (2014), Concerns about the widespread use of rodent models for human risk assessments of endocrine disruptors, *Reproduction* (2014) 147 R119–R129.

The CLH report needs to deal with the doubts regarding the relevance of the effects seen with rodents for human hazard assessment.

Already the abstract of this excellent review concludes: "...For instance, MEHP and DES

affect steroidogenesis in rodents, but not in human fetal testis. These species differences raise concerns about the extrapolation of data obtained in rodents to human health risk assessment and highlight the need of rigorous comparisons of the effects in human and rodent models, when assessing ED risk."

While this applies to DEHP, the doubts should also work for DINP.

Our Conclusion

Overall, AGPU concludes that the CLH report presented by DK has several flaws and presents a very selective view on the data with DINP.

AGPU urges ECHA/RAC to critically evaluate this report and ultimately reject the proposal as unfounded.

References:

1) Morfeld P et al. (2017): Letter to the Editor, Boberg et al. (2011) – Corrigendum (2016): Further significant modifications needed. *Reprod Toxicol*, online first:

<http://www.sciencedirect.com/science/article/pii/S0890623816303719>

2) Saillenfait, A. M. et al. (1998): Assessment of the developmental toxicity metabolism, and placental transfer of di-n-butyl phthalate administered to pregnant rats. *Toxicol. Sci.*, 45, 212–224.

3) Saillenfait A.-M et al. (2008): Diisobutyl phthalate impairs the androgen-dependent reproductive development of the male rat, *Reproductive Toxicology* 26 , 107–115

4) McKinnell C. et al. (2009): Effect of fetal or neonatal exposure to monobutyl phthalate (MBP) on testicular development and function in the marmoset. *Human Reproduction*, Vol.24, No.9 pp. 2244–2254,

5) Gaido KW et al. (2007) Mouse phthalate exposure shows that gonocyte multinucleation is not associated with decreased testicular testosterone. *Toxicological Sciences* 97, 491–503

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	United Kingdom	INOVYN	Company-Downstream user	48

Comment received

Specific Comments

Based on our understanding of the science INOVYN does not support the classification proposal and considers that no classification for DINP still remains the appropriate status. Given that the substance was extensively reviewed under previous legislation (DSD and EU Risk Assessment programmes) and recently by Dekant and Bridges (1) and found to not require a change of classification we think that, given that the studies considered in the CLH document were also considered in the previous consultations, we see no reason for a change in the classification.

Since DINP remains a very important product for the flexible polymer industry we feel that studies must be viewed in the context of an overall weight of evidence approach taking into account all robust studies, particularly those previously assessed by regulators and found to support a not classified conclusion. No measure appears to have been made by the CLH authors to review the overall quality of the studies cited (a requirement that is placed on registrants when submitting their REACH dossiers) nor do we see reference to the basis for classification as described in section 3.7.2.2. of the CLP regulation (for example, nature of adverse effects, their toxicological significance and severity, and the fact that the effects seen below or above limit doses). We are also aware that the publication of Dr Boberg (2),

regarded as significant by the CLH authors, was the subject of a corrigendum in the journal in which it was originally published since strict protocols for the calculation of statistics were not followed. Moreover the well-established relationship between alkyl chain length and degree of branching of phthalate esters and their reproductive toxicology properties has not been discussed.

Hence we conclude that the findings of the previous reviews and, including, importantly, the more recent review of weight of evidence of studies on DINP (which included the Boberg paper) (1), that no new classification is warranted, remain applicable.

(1) W. Dekant and J. Bridges, regulatory toxicology and Pharmacology, Vol. 81, November 2016, pages 397 – 406

(2) Boberg J, Christiansen S, Axelstad M, Kledal TS, Vinggaard AM, Dalgaard M et al. Reproductive and behavioral effects of diisononyl phthalate (DINP) in perinatally exposed rats. *Reprod Toxicol* 2011; 31(2):200-209

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	Germany	REHAU AG + Co.	Company-Downstream user	49

Comment received

The proposal for classification is H360 Df which refers to hazards for females. The summary for justification refers to effects on males which is very curious. I cannot understand why adverse effects of other phthalates with much lower molecular weight should be sufficient to classify this substance DINP with H360 Df even if studies performed with DINP don't lead to such a classification. Most studies were performed using rats and mice which are known to have a weakness on excretion of phthalates and their metabolites. This make most of the studies quoted worthless.

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	France		Individual	50

Comment received

We ask that the classification of the DINP is definitively established and not discussed again in the future as well as the application of the criteria which defines a reprotoxique 1B. We recall that the European Commission had concluded that:
« There is at present no need for further information or for risk reduction measures beyond those that are being applied already. »
Voir page 301/302 du DINP report.
« Based on the risk assessment in this report, it can be concluded that no further risk management measures are needed to reduce the exposure of children to DINP and DIDP »
Voir page 7/369 du document Echa DINP.

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2017	Japan	Japan Plasticizer Industry Association	Industry or trade association	51

Comment received

a) Based on the results obtained from generation reproductive studies in rats using oral exposure, DINP did not adversely affect rat reproduction (generation reproduction) because of no changes in indices of reproductive toxicity (mating index, male fertility index, female fertility index, fecundity index, gestation index, gestation length, etc.) or male reproductive system organs (organ weight, necropsy and histopathological examination) in F0 or F1 parental animals.

b) As for the developmental toxicity in rats, non-specific changes were seen in skeletal/visceral examinations of fetuses (increase in skeletal variations, etc., which are frequently seen also among control animals) and suppression of body weight gain in pups, but these changes were all considered secondary effects of maternal toxicity. In addition, nipple retention and histopathological changes of the testis observed were inferred to probably be very minor.

c) In classifying the hazardousness, although the above literature and their results were all equally valuable as weight of evidence, data seemed to be lacking to assess the hazardousness of DINP in more detail. That is, the endpoints to examine the endocrine action (AGD, nipple retention, sexual maturation, sperm function test, etc.) were not seemed to be sufficiently evaluated in generation reproduction studies.

d) To supplement this deficiency, studies assessing endocrine action were conducted; AGD, testosterone level in the testis and histopathology were evaluated. However, in order to discover if the changes seen in fetuses would remain to affect the reproductive function in adulthood, more comprehensive assessment appears to be required by conducting multi-generation reproductive studies, etc., not by examining only the adverse effects at the fetal stage.

e) Moreover, since almost all the reproductive developmental toxicity studies used rats and no studies used non-rodents such as rabbits, for example, to assess the developmental toxicity, particularly teratogenicity, the data was considered insufficient to discuss species differences.

f) In addition, toxicological effects on the testis reported from general toxicity studies were very likely secondary ones associated with other toxicological changes because many other studies did not report any findings indicating testicular toxicity.

For DINP classification inferred in accordance with CLP Regulations, more data was thought needed for reliable assessment. Therefore, at this time, as the DINP hazard category, 'not classified' was judged more appropriate than the 1B proposed in the CLH Report.

See attached in detail

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Comments on DINP classification in CLP by JPIA (15th May, 2017).docx

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2017	Italy	Polynt S.p.A	Company-Manufacturer	52
Comment received				
Based on the extensive scientific evidence demonstrating a lack of adverse reproductive effects following exposure to DINP, per CLP criteria as detailed in section 3.7.2 of Annex I of the CLP, we propose that classification for development and fertility effects is not required.				

ECHA note – An attachment was submitted with the comment above. Refer to public attachment DINP_CLH_Polynt Comments.pdf

PUBLIC ATTACHMENTS

1. ACC Comments re Classification and Labelling of DINP May 2017.pdf [Please refer to comment No. 32]
2. VI Comments to CPSC on CHAP NHANES Information submitted 03-24-2017.pdf [Please refer to comment No. 8, 33]
3. ExxonMobil DINP submission_May_19_2017_Final.pdf [Please refer to comment No. 9, 34]
4. DINP_CLH_Summary comments_AICM comments May 2017 FINAL.docx [Please refer to comment No. 11, 36]
5. Comments on CLH for DINP CAS 28553-12-0_2017-05-19.pdf [Please refer to comment No. 13, 39]
6. 20170519_EuPC_Position Paper on the Proposed classification of DINP as reprotox 1b.pdf [Please refer to comment No. 14, 40]
7. 2017-05-17 DINP statement ERFMI final.pdf [Please refer to comment No. 16, 42]
8. DINP-WOE Report-final.pdf [Please refer to comment No. 45]
9. DINP CLH comments pdfs May 17.zip [Please refer to comment No. 46]
10. Comments on DINP classification in CLP by JPIA (15th May, 2017).docx [Please refer to comment No. 22, 51]
11. DINP_CLH_Polynt Comments.pdf [Please refer to comment No. 52]
12. 170516 DINP_ECHA_DK.pdf [Please refer to comment No. 23]
13. BCF comments on DINP reclassification May 17.docx [Please refer to comment No. 1, 24]
14. Comment DINP-WolfgangDekant.zip [Please refer to comment No. 2, 25]
15. Comments on the Danish EPA Dossier_DINP_By SAVA_15May2017.pdf [Please refer to comment No. 3, 27]

CONFIDENTIAL ATTACHMENTS

1. Consultation publique DINP_V3.docx [Please refer to comment No. 10, 35]