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Guidance document for handling criteria for endocrine disruptors in the construction industry

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In cooperation with Golvbranschens Riksorganisation, Sveriges Byggindustrier, Byggmaterialindustrierna, Sveriges Färg och Lim Företagare (SVEFF), Substitutionscentrum, BASTAonline

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Summary

Safe products are important for the building and construction industry as many of these products have a long lifetime and are used in large quantities. The building and construction industry is focused on the substitution of unwanted chemical substances and needs methods to apply the EU's developed definition of endocrine disruptors to its operations. This guidance document proposes a practical method using scientifically based criteria for evaluating endocrine disruptors.

An evaluation flow chart with three main steps has been proposed to help optimize the adaptation of current knowledge and information about endocrine disruptors and to be prepared for new and updated information when it is made available. The flow chart supports robust weight of evidence evaluation of all the relevant scientific data in a transparent and holistic way and enables a quality-assured flow of information.

Proposed workflow:

- Step A: Assessed and identified as endocrine disruptor (ED)
- Step B: Other indications that the substance of interest can have ED properties
- Step C: Evaluation of the ED assessment found in step B

The robust weight of evidence evaluation of all the relevant scientific data has two possible outcomes: 1) the chemical substance is a (potential) endocrine disruptor and should be treated as such, or 2) the chemical substance has a low likelihood of being an endocrine disruptor and is therefore considered not to be an endocrine disruptor for the context of this guidance document[1]. This can be because the chemical substance has been assessed by the EU/ECHA not to be an endocrine disruptor or because there are no strong indications available that the chemical substance displays endocrine disruptive properties.

The main benefit of the proposed workflow is that it combines the strength of both regulatory assessments and non-regulatory lists while allowing for new scientific evidence to be included in case the criteria used in these lists become outdated or are refuted.

For the building and construction industry the next step would be to decide on, and start using the criteria, for instance by implementing them in systems for product evaluations.

[1] Please note that this does not mean that the substance can't be an ED, more that there is a lower likelihood of the chemical substance being an ED. An assessment as "not ED" can only be made at EU level.

Sammanfattning

Säkra produkter är viktiga för bygg- och anläggningsindustrin eftersom många produkter har en lång livslängd och används i stora mängder. Bygg- och anläggningsindustrin har fokus på substitution av oönskade kemiska ämnen och behöver metoder för att tillämpa EU: s definition för hormonstörande ämnen (ED, endokrina disruptorer), i sin verksamhet. Denna vägledning föreslår en metod, baserad på vetenskapliga kriterier, för utvärdering av hormonstörande egenskaper.

Ett flödesschema med utvärdering i tre steg har föreslagits för att optimera tillämpningen av aktuell kunskap och information om hormonstörande ämnen, och förbereda sig för ny och uppdaterad information när den blir tillgänglig. Flödesschemat stöder en robust sammanvägd utvärdering av alla relevanta vetenskapliga uppgifter på ett öppet och transparent sätt, och möjliggör ett kvalitetssäkrat informationsflöde.

Föreslaget arbetsflöde:

- Steg A: Bedöms och identifieras som hormonstörande
- Steg B: Andra indikationer på att det aktuella ämnet kan ha hormonstörande egenskaper
- Steg C: Utvärdering av bedömningen som hormonstörande från steg B

Den robust sammanvägda utvärderingen av alla relevanta vetenskapliga data har två möjliga resultat: 1) det kemiska ämnet är ett (potentiellt) hormonstörande ämne och bör behandlas som sådant, eller 2) det är låg sannolikhet för att det kemiska ämnet är hormonstörande och det behandlas därför inte som hormonstörande enligt detta vägledningsdokument[2] Det kan bero på att ämnet antingen har bedömts inte vara hormonstörande av EU/ECHA eller för att det inte finns några starka indikationer på att det kemiska ämnet är hormonstörande.

Den huvudsakliga fördelen med det föreslagna arbetsflödet är att det kombinerar styrkan i både legala bedömningar och icke-reglerande listor, samtidigt som nya vetenskapliga belägg kan inkluderas om kriterierna som används för listorna blir ändrade eller tillbakavisas.

För bygg- och anläggningsbranschen är nästa steg att besluta om och börja använda kriterierna, till exempel genom att implementera dem i systemen för produktutvärdering.

[2] Observera att detta inte betyder att ämnet inte kan vara hormonstörande, snarare att det är lägre sannolikhet för att det kemiska ämnet är hormonstörande. En bedömning som ”inte hormonstörande” kan endast göras på EU-nivå.

1 Preface

In order to obtain consensus on which substances to avoid in the building and construction industry, a number of voluntary criteria have been developed, of which BASTA's property criteria are an example.

For more than 20 years, the building and construction industry has had a focus on the substitution of unwanted chemical substances. Instead of focusing on substance lists, the industry switched early on to eliminating hazardous chemicals based on their chemical properties. This means that instead of pointing out certain substances that are of concern, the industry has chosen to limit all substances that have a certain property, for example, substances that have shown to be carcinogenic or have sensitizing properties.

Chemical substances that can have an endocrine disrupting effect on humans or the environment have in this context been a debated group. The mechanisms behind how these substances affect us are complex, which makes the group difficult to handle from a scientific, and therefore also regulatory, perspective. Endocrine disruptive substances are still not fully covered by the EU's system for classification, labelling and packaging of chemical substances and mixtures, CLP (The European parliament and the council of the European Union, EC/2008/1272).

For the industry, this has led to difficulties when it comes to working based on transparent and clear criteria. In the absence of a clear definition in the REACH legislation (The European Parliament and the Council of the European Union, EC/2006/1907), reference has been made to lists. The most widely used list in available criteria has been the European Commission's endocrine disturbing substances (EDS) database (The European Commission, 2007), which lists a number of confirmed and suspected endocrine disruptors. This has worked satisfactorily, but the list was originally intended to help prioritize the evaluation of potential endocrine disrupting substances and not to serve as a tool for eliminating endocrine disruptors from articles. The database has therefore not been updated when new scientific findings have been published.

In 2018, the EU agreed on a definition of scientific criteria for the identification of endocrine disruptors which is currently used in legislation relating to biocides (The European Commission, EU/2017/2100) and plant protection products (The European Commission, EU/2018/605).

This definition now gives the building and construction industry an opportunity to take an overall approach to endocrine disruptors and to introduce criteria that help bridge the challenges that can arise when relying on the use of substance lists alone. BASTA, as the first organization, has introduced the definition in its criteria documents. The aim of this guidance document is to describe how these criteria should be interpreted and applied in practice.

2 Introduction

2.1 Endocrine disruptors (ED)

The endocrine system is built of a network of endocrine glands (such as the thyroid and pancreas glands), which can release hormones directly into the bloodstream to control important processes such as blood pressure, metabolism, cell growth, fertility and many more.

Many naturally occurring as well as synthetic chemicals can have endocrine effects. These can include pharmaceuticals, oestrogens, pesticides, chemical substances used in plastic production and industrial by-products/pollutants. Crucial functions in humans and animals that are regulated by hormones can therefore potentially be affected by such endocrine disruptors (ED) which can in turn lead to issues in fertility, metabolism and development.

An increased prevalence of certain endocrine-related human diseases has been observed, including for instance: development malformations, reproduction related issues, increased risk of cancer and disorders in the function of the immune and nervous systems (International Programme on Chemical Safety, 2002). Other conditions which have been hypothesized to be linked to exposure to ED in humans include amongst others: IQ loss, intellectual disability, diabetes, obesity, infertility, ADHD (attention deficit hyperactivity disorder) and autism (Trasande, 2016). Endocrine disruptive effects as a result of exposure to certain chemicals present in the environment have also been observed in tests with laboratory test animals.

Endocrine disruptors can disturb the endocrine system in an organism in three ways (International Programme on Chemical Safety, 2002):

1. They partially mimic naturally occurring hormones in the body.
2. They bind to receptors in cells blocking the endogenous hormone from binding.
3. They interfere with or block how natural hormones, or their receptors, are manufactured or controlled.

2.2 The difficulty with assessing endocrine disrupting activity

Low concentrations of an endocrine active substance may be enough to trigger an effect. Scientists have not been able to agree if there is a minimum concentration when an effect risks being triggered (i.e. a threshold value) or if endocrine active substances are proportionally more active in lower amounts, resulting in a so-called non-monotonic dose response curve (International Programme on Chemical Safety, 2002). The dose-response curve that traditionally lies as the basis of regulatory risk assessments, and the experiments providing data for these assessments, might therefore not always be the most suitable for assessing risks from endocrine disrupting substances. As described in the guidance document from ECHA and EFSA however: “the likelihood of not detecting an adverse effect in the presence of a non-monotonic dose response is considered low” (European Chemical Agency (ECHA) and European Food Safety Authority (EFSA) with the technical support of the Joint Research Centre (JRC), 2018).

Exposure and effects can be difficult to link for hazardous substances due to several reasons:

1. Cocktail effects may occur, meaning that presence of other chemical substances in a mixture can increase or decrease the effects observed for the chemical substance on its own. (Kortenkamp, 2007)
2. It can be difficult to develop calculation models to predict negative effects.
3. Monitoring data can be insufficient or impossible to compare.

For endocrine disruptors this is complicated further by the fact that the time of the exposure to the endocrine disruptor can play a significant role e.g. if a baby or a fetus is exposed it might lead to delayed effects, for instance 10-20 years later which makes it difficult to prove the links between exposure and effect (International Programme on Chemical Safety, 2002). It can also be difficult to prove that the observed negative effect is a consequence of an endocrine mode of action or arises from a different mode of action. Within the research community, efforts have since been made to develop a consensus on both scientific principles for identifying ED (Solecki et al., 2017) and on defined key characteristics (La Merrill et al., 2020), defined as functional properties of agents that alter hormone action. These studies have provided key input on both research needs and on implementation of science-based hazard and risk assessments for ED in future regulatory efforts.

Although it remains difficult to link exposure to endocrine disruptors with adverse health outcomes, the potential cost to society can be high. The annual cost in the EU, due to potential effects of endocrine disruptors was postulated by a study in 2016 to be around 163 billion €, more than 1 % of the EU GDP or in Sweden 4 billion €, more than 1 % of the Swedish GDP (Trasande, 2016). While this number comes with a high uncertainty, it gives an indication of the scale of the potential issue with endocrine disruptors.

2.3 Definitions of an endocrine disruptor

The most broadly accepted definition for endocrine disruptors is that proposed by the WHO (World Health Organization) in 2002 (International Programme on Chemical Safety, 2002):

a) An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.

b) A potential endocrine disruptor is an exogenous substance or mixture that possesses properties that might be expected to lead to endocrine disruption in an intact organism, or its progeny, or (sub)populations.

In 2018, the EU included scientific criteria for the identification of endocrine disruptors in the biocidal and plant protection products regulations. The definition of an endocrine disruptor is identical for both legislations, but application and limitations vary slightly. The following is an extract from the ECHA-EFSA guidance document (European Chemical Agency (ECHA) and European Food Safety Authority (EFSA) with the technical support of the Joint Research Centre (JRC), 2018), applicable for both legislations. Note that this definition does not mention “potential” endocrine disruptors as is done in the definition by the WHO.

According to the scientific criteria for identification of endocrine disruptors (2017/2100 and 2018/605), a substance shall be considered as having endocrine disruptor properties if it meets all of the following criteria:

a) it shows an adverse effect in [an intact organism or its progeny]/[non-target organisms],which is a change in the morphology, physiology, growth, development, reproduction or lifespan of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences;

b) it has an endocrine mode of action, i.e. it alters the function(s) of the endocrine system;

c) the adverse effect is a consequence of the endocrine mode of action.

It should be highlighted that the 'endocrine mode of action' as stated in point (b) should be interpreted as 'endocrine activity' while the term 'endocrine mode of action' in point (c) covers the link between the adverse effect and the endocrine activity identified in points (a) and (b), respectively. Step c should always be assessed with respect to both humans and non-target organisms at population levels. (European Chemical Agency (ECHA) and European Food Safety Authority (EFSA) with the technical support of the Joint Research Centre (JRC), 2018).

2.4 Legislation

In 2018 the first European legal criteria for endocrine disruptors went into force through the Biocide directive (The European Commission, EU/2017/2100), which was soon followed by a similar update of the Plant Protection Products (PPP) regulation (The European Commission, EU/2018/605). The guidance document (European Chemical Agency (ECHA) and European Food Safety Authority (EFSA) with the technical support of the Joint Research Centre (JRC), 2018) completed the information from ECHA and EFSA. Endocrine disruptors are regulated in legislation before 2018, although not always in a transparent way.

The biocide and the plant protection legislations determine scientifically based criteria for endocrine disruptors. Endocrine disruptors should, in general, not be present in biocides or plant protection products. The criteria have been criticized for not being strict enough to secure safe use. On the other hand, it has also been criticized due to difficulties with missing clearly defined endpoints, increased demands of in vivo tests, i.e. animal tests and lacking validated laboratory capacity. The guidance has also been criticized for being too open ended and therefore leading to "endless" testing.

Initiatives to include endocrine disruptor criteria horizontally in applicable EU legislation are ongoing (The European Commission, 2019). The EU REACH regulation is also planned to be reviewed with regards to endocrine disruptor data requirement. This fitness check will focus on gaps in legislations, covering for instance the legislation for toys.

The OECD Guidelines are internationally accepted tools, used as standard methods, for assessing the potential effects of chemicals on human health and the environment (OECD, 2019). The OECD Guidance document 150 was revised in September 2018 (OECD, 2018). It outlines the OECD conceptual framework and provides a five-tier framework for the testing of chemicals, with standardized test guidelines, for endocrine disrupting effects. Although not a legislative document, the OECD guidance document is relevant as many regulations refer to the OECD test methods.

In the EU **REACH,** endocrine disruptors are included in the definition of substances of very high concern (SVHC) through the description: "substances — such as those having endocrine disrupting

properties or those having persistent, bioaccumulative and toxic properties or very persistent and very bioaccumulative properties", "for which there is scientific evidence of probable serious effects to human health or the environment which give rise to an equivalent level of concern to those of other substances listed" and "which are identified on a case-by-case basis" (REACH article 57f).

SVHC are first added to the candidate list for Authorisation, then evaluated for authorisation, i.e. inclusion on the Authorisation list (Annex XIV) of REACH. So far 16 endocrine disrupting substances and substance groups are on the candidate list for authorisation and 2 endocrine disruptors are on the authorization list (checked on 2019/11/16).

In the EU **CLP** (The European parliament and the council of the European Union, EC/2008/1272) there is no overall warning classification, i.e. no warning pictogram and no hazard nor precautionary statements describing endocrine disrupting properties in general. However, certain specific hazards, such as reproductive toxicity, are defined.

In the EU **Cosmetics regulation** (The European Parliament and the Council of the European Union, EC/2009/1223) endocrine disruptors are not yet explicitly regulated, but the regulation contains a paragraph stating that it will be reviewed with regard to substances with endocrine disrupting properties.

The **Water Framework Directive** (The European Parliament and the Council of the European union, EC/2000/60) (WFD) sets out "Strategies against pollution of water" and the **Directive on Environmental Quality Standards** (The European Parliament and the Council of the European Union, EC/2008/105) (EQSD) sets environmental quality standards (EQS) for a selection of priority substances in surface waters. Priority substances can include endocrine disruptors, which are defined as substances which have been proven to possess "properties which may affect steroidogenic, thyroid, reproduction or other endocrine-related functions in or via the aquatic environment" (The European Parliament and the Council of the European union, EC/2000/60).

2.5 Identifying endocrine disruptors

That chemical substances can affect endocrine systems is well known as these effects form the basis for medicines such as birth control pills and cancer treatments.

Defining which substances can affect endocrine systems in humans as well as in the environment however, is complicated as there are many different endocrine-regulated systems. Certain endocrine systems can be present in different organisms and species, allowing a certain degree of extrapolation between assessments made for different species, while others are more species specific.

It is also essential to distinguish confirmed endocrine disrupting properties and suspected (that need further investigation) from effects on endocrine systems which are not directly related to endocrinal effects, such as starvation.

The OECD Guidance document 150, with the OECD Conceptual Framework for testing of endocrine disrupting substances in a five tiers approach, presents OECD test methods available, validated and accepted for testing endocrine activities, for example OECD 231, OECD 416, OECD 421, OECD 422, OECD 440, OECD 441, OECD 443 (OECD, 2018). Another example is the US Endocrine Disruptor Screening Program (EDSP) (U.S. EPA, 2019), which includes 14 assays in a two-tiered test battery. The endocrine endpoints for these tests are oestrogen, androgen, thyroid and/or steroid (shortened EATS). There are no single endpoints evaluating the tests, where it is enough to stop testing and conclude on a positive or negative test result. Each test may only be

valid for a limited number of chemistry types or classes (e.g. domain of applicability) (OECD 2018). The need of test animals, the long time needed for performing the tests and the limited number of validated laboratories, able to perform tests, adds to the complex situation identifying endocrine disruptors.

For endocrine activities other than EATS (oestrogen, androgen, thyroid and steroid), for example in the pituitary glands, in the stomach and in the liver, there are no standardized test methods with validated tests available yet. Research and validating of in vitro tests are ongoing.

Epidemiological studies are a potential complementary method to investigate why endocrine effects in society and in the environment are increasing. Changes in family size and parents' age could for instance have a significant impact on endocrine disruptive effects (Personal Communication, 2019). However, it remains unclear how the combination of lifestyle changes in a generational perspective and exposure to endocrine disrupting substances in total might affect human health.

2.6 Building and construction industry

The long lifespan, large volumes and widespread exposure to building materials are the three main reasons as to why the presence of unwanted chemicals should be kept to a minimum in building and construction products.

The Swedish building and construction industry is recognized for its proactive approach, engaging in the voluntary substitution of hazardous chemical substances ahead of regulatory decisions. This proactive approach has its origin in several cases in which products have been placed on the market that were later shown to lead to severe health and environmental effects. Examples of such pro-active systems that are in place for the building and construction industry in Sweden include BASTA, Byggvarubedömningen and SundaHus. Aside from these systems there is also a range of certification systems such as Miljöbyggnad and Nordic Swan Ecolabel which have helped focus on the issue of hazardous substances in building and construction materials and have helped advance this field.

The risk of exposure to endocrine disruptors lies high on the agenda with real estate owners, city councils and other stakeholders. However, in the absence of a clear regulation on endocrine disruptors, the building and construction branch had to look for alternative ways to identify which substances should be excluded or phased out from their products on the ground of their endocrine disturbing potential.

Until now list based approaches have been the main tool used to substitute endocrine disruptors. For instance, BASTAOnline has used the EDS database (The European Commission, 2007) and Byggvarubedömningen and SundaHus use the ChemSec SIN list (ChemSec, 2019) for substitution of endocrine disruptors since 2019-07-01/2019-09-01 (Byggvarubedömningen, 2019). There is however a demand for a more long-term solution that takes into account, existing lists, regulatory decisions and definitions but also new scientific data.

In this guidance document, the EU criteria for endocrine disruptors in biocides and plant protection products is applied to building and construction products with the aim to support the voluntary initiatives of the industry to apply a criteria-based approach when dealing with endocrine disruptors in building and construction products.

2.7 Chemical lists and substitution

Chemical substance lists have been a popular and common way to drive the substitution of hazardous chemicals, due to their ease of use. Using appropriate lists to identify endocrine disruptors is possible but it is important to evaluate: 1) the scientific background to the lists, 2) their transparency, 3) whether they include confirmed or suspected endocrine disruptors, 4) what the intentions are with the list and 5) if the list will be kept up to date with new data.

Relying only on lists might also delay substitution if new data is presented much quicker than the lists are kept up to date. Another risk with lists, is that chemical substances that should not be listed any more, remain listed if the lists are not kept up to date or if they go against regulatory decisions.

In a review of available lists containing endocrine disruptors, commissioned by the WHO and executed by the IPCP, 10 initiatives that identify endocrine disruptors were reviewed covering 1000+ chemicals (The International Panel on Chemical Pollution (IPCP), 2017).

Of these initiatives, three lists were identified by the IPCP as being particularly robust and transparent and in line with the WHO/IPCS 2002 definition for endocrine disruptors. These include the REACH SVHC candidate list (REACH article 57f), the SIN list by ChemSec and the assessment of the proposed Danish criteria for identification of endocrine disruptors by the Danish Centre on Endocrine Disruptors. For each of these initiatives, documentation on the methodology, selection criteria and sources is available (The International Panel on Chemical Pollution (IPCP), 2017).

2.7.1 ECHA's Community Rolling Action Plan (CoRAP)

ECHA's CoRAP list compiles chemicals that have ongoing/planned assessment by EU member states. The CoRAP list is updated yearly with chemicals that will be evaluated over a period of three years. Prior to an annual update, chemical substances with priority for evaluation may be included. The first CoRAP was adopted in 2012 and was valid for 2012 - 2014.

Currently, 86 substances and substance groups are listed on CoRAP due to their potential as endocrine disruptors (check 2019-12-06).

2.7.2 The SIN list by ChemSec

ChemSec was founded in 2002 by four Swedish environmental organisations: The Swedish Society for Nature Conservation, WWF Sweden, Nature and Youth and Friends of the Earth Sweden. These NGOs are the ChemSec member organisations and are represented on the ChemSec board. ChemSec is a non-profit organisation, with financial support from the Swedish Government and non-profit organisations.

The SIN list (Substitute It Now List) was launched in 2008 and has been updated regularly with additional substances since then. The most recent update was in November 2019 (ChemSec, 2019). The SIN List currently consists of over 900 chemical substances of which 127 are listed as endocrine disruptors. ChemSecs process for adding substances to the SIN list is based on their own evaluation of scientific data combined with the criteria for Substances of Very High Concern as defined in the EU chemicals regulation REACH. Chemical substances can in principle become de-listed from the SIN list if evidence to motivate this action is supplied to ChemSec. However, while evidence has been reviewed by ChemSec for several chemical substances, no review has so far led to such a de-listing (ChemSec, 2019).

2.7.3 List of EDs by the Danish Centre on Endocrine Disruptors

The Danish centre on endocrine disruptors (CEHOS) was started in 2008 to coordinate new research into endocrine disruptors, to provide scientific advice to authorities regarding endocrine disruptors, to update authorities on relevant information regarding endocrine disruptors, to organize yearly information events and to coordinate the Copenhagen workshops on endocrine disruptors (CEHOS, 2019).

In 2012, the centre proposed Danish criteria to identify endocrine disruptors, based on the WHO definition of EDCs. These criteria were then used to assess 26 chemical substances, 22 of which were previously assessed by ChemSec as endocrine disruptors and listed on the SIN list. All but one of these chemicals that were previously listed on the SIN list were confirmed as being endocrine or potential endocrine disruptors (CEHOS, 2012a) (CEHOS, 2012b). This is the study that was reviewed by the IPCP in 2017 as being one of the three most robust and transparent initiatives to identify EDs (The International Panel on Chemical Pollution (IPCP), 2017).

In 2017, CEHOS published a report listing endocrine disrupting chemicals on request of the Danish Environmental Protection Agency (CEHOS, 2018). This is the list referred to further down in step B.

In this report, CEHOS assembled data from over 3000 unique CAS numbers, occurring in other lists of suspected and potential endocrine disruptors, and prioritized 13 suspected endocrine disruptors for further assessment. Of these prioritized chemicals, 10 were assessed to be endocrine disruptors using the scientific criteria set forth for identifying endocrine disruptors by the EU and 3 were assessed to be suspected endocrine disruptors using the Danish criteria. These assessments are clearly documented in the annex of the report.

In addition, the CEHOS also re-evaluated the chemical substances that were identified as endocrine disruptors in the report from 2012, making a distinction between substances where the data fulfils the WHO criteria and where it likely fulfils the WHO criteria but where there are limitations in the data.

The Danish list of EDs will likely be updated in the future but it is currently unknown as to when this will occur.

3 Assessing endocrine disruptors in the building and construction industry

An alternative to relying exclusively on lists is to use a criteria based assessment, that incorporates the EU's recently developed scientific guidelines on identifying endocrine disruptors (The European Commission, EU/2017/2100) (The European Commission, EU/2018/605) with the practical use of lists and introduces the possibility to include new scientific evidence when the lists become outdated or scientifically incorrect.

In order to effectively apply such a criteria-based assessment based on the EU's definition, a guidance that enables a quality-assured flow of information is needed. Such a guidance should be revised regularly so that it stays in line with new regulations and scientific findings.

3.1 Proposed workflow

To optimize the adaptation of current knowledge and information about endocrine disruptors, and to be prepared for new and updated information, a flow chart can be used.

The workflow proposed below in Figure 1, is inspired by that used for assessing endocrine disrupting properties of co-formulants in biocidal products and supports the robust weight of evidence evaluation of all the relevant scientific data in a transparent and holistic way. A step by step overview of the workflow is given in the chapters 3.1.1. to 3.1.3

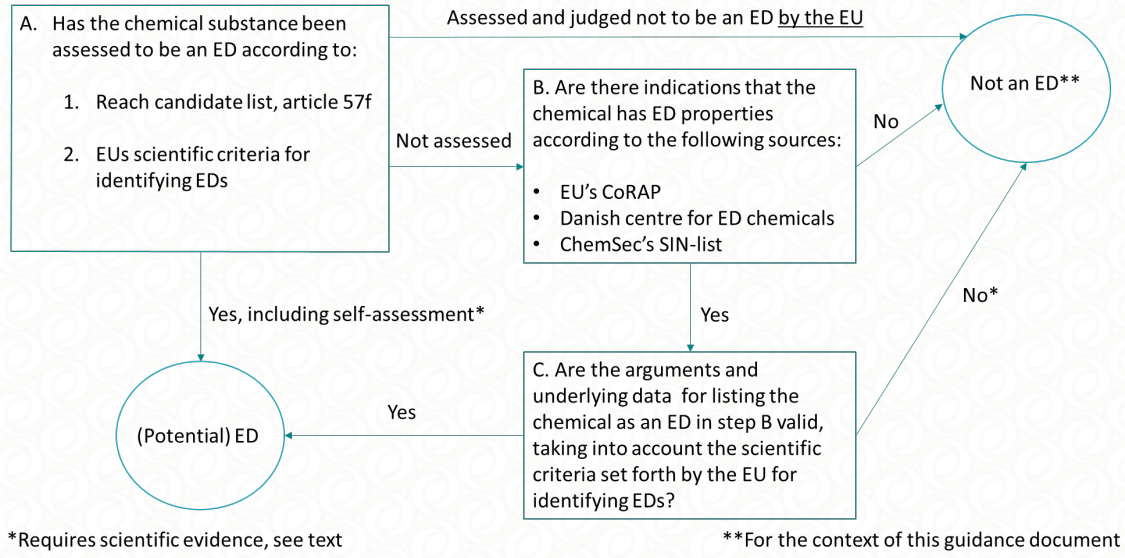

Figure 1: Workflow proposed for the assessment of endocrine disrupting properties for chemical substances used in the construction industry. The lists referred to in Step B should be kept up to date with regards to their validity. The aim with step C is not to assess if the substance is an endocrine disruptor or not, but if the arguments as to why the chemical is listed as an endocrine disruptor on the lists in step b are valid, keeping in mind the scientific criteria set forth for identifying endocrine disruptors by the EU and a weight of evidence approach.

3.1.1 Step A: Assessed and identified as ED

The first step in the workflow is to check if the substance of interest has been assessed to be a potential ED according to the REACH regulation and the EUs scientific criteria for identifying EDs. The most straight forward way to do this is currently to check:

- ECHA's Endocrine disruptor assessment list, available on https://echa.europa.eu/ed-assessment
    - Important here is that the focus here should lie on chemicals substances where the outcome is listed as "ED" or "not ED". These can be found using the filter function.

- The Endocrine disruptor assessment list currently also lists chemicals considered SVHC due to their ED activity and EDs in biocides.

- EU's Pesticide database, available on https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN

Producers' and supplier's self-assessments (according the EU-criteria) of the chemical of interest should also be considered when evaluating the endocrine disruptive properties.

An assessment by the EU that the chemical substance is an ED or a self-assessment by a supplier should lead straight to the conclusion that the chemical is a (potential) ED[3]. If the assessment by the EU states that the chemical substance is not an ED, then the chemical should be considered not to be an ED. In all other cases (i.e. when there is no assessment), step B should be pursued.

3.1.2 Step B: Other indications that the substance of interest can have ED properties

To ensure that the chemical of interest is not a potential ED, other regulatory and non-regulatory sources based on scientific data should be included. They can give an indication of chemicals that are EDs which will likely be assessed / regulated in the future.
For Step B, it is therefore recommended that ECHA's CoRAP list should be consulted as it lists chemicals that have ongoing/planned assessment by EU member states, based on their potential as EDs. The SIN list and the Danish dataset, discussed in 2.7, should also be consulted as they give an indication of which chemicals are potential EDs.

The motivation for using these three lists is based on their transparency, their use of the WHO definition of EDs and their use of scientifically grounded arguments for their selection. Each of these lists is also excluding, rather than including, meaning that there needs to be enough evidence in order for a substance to be regarded as a potential ED. While the Danish list is currently referred to by a reference to a publication (a static list), this list is also expected to be updated in the future.

Other well-known lists such as the EUs EDS database (The European Commission, 2007), or the Endocrine Disruption Screening Program for the 21st Century (EDSP21) by the US EPA (U.S. EPA, 2019) were found not be of practical use for this guidance document: 1) The EDS database is too inclusive and is not updated to include new scientific findings and 2) The EDSP21, while containing a large amount of information that can be used to assess the potential of a chemical for ED properties, is not a list of EDs where a weighted decision has been made, taking into account multiple studies.

Instructions on how to proceed with step B are as follows:

1. ECHA's Community Rolling Action Plan (CoRAP)
    - Use the search function on CoRAPs homepage, accessible from https://echa.europa.eu/en/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table to search for the chemical of interest.

[3] Please note that ED assessments are sometimes confused with assessments for reproductive toxicity. While an assessment of a chemical as ED can include reproductive toxicity, this is not always the case.

- Check if the chemical of interest is listed as “potential endocrine disruptor” or “potential ED” in the current and following years.

2. The list of endocrine and potential endocrine disrupting chemicals, as assessed by the Danish centre on endocrine disruptors
   - Download the report ” List of Endocrine Disrupting Chemicals - Final report”, which can be accessed from http://www.cend.dk/files/DK_ED-list-final_2018.pdf
   - Search through tables 8 and 13 of the report.
   - Detailed assessment are available in the annex of the report, which can currently be accessed from http://www.cend.dk/files/DK_ED-list-final_appendix1_2018.pdf .

3. The SIN list
   - Use the filter function on the homepage of the SIN list, available from https://sinlist.chemsec.org/ to look for chemicals with the variable ”Health & Environmental Concerns” as “Endocrine disruptor”.

If the chemical is found to be present on either the SIN list or the list by the Danish Centre on endocrine disruptors, go through the following steps to ensure that the chemical has not been assessed by ECHA in the meantime, by checking the Endocrine disruptor assessment list, available from: https://echa.europa.eu/ed-assessment .

If the chemical of interest has been previously assessed by the EU and shown not to have endocrine disrupting properties, the chemical substance is not to be considered as potential ED, i.e. there is no need for further evaluation (Step B and Step C). i.e. EU legislation and decisions precedes over the listing as potential ED on the lists presented above.

In the case of BASTA for example, this would mean that the chemical is not subjected to any limitation under BASTA under the criteria set forth for endocrine disruptors.

3.1.3 Step C: Evaluation of the ED assessment

3.1.3.1 Why step C

If the substance of interest was present on one of the lists in step B and there is no further information available that allows deletion from the lists, the substance should be considered a potential endocrine disruptor for which certain restrictions might have to be taken into consideration. In the case of BASTA, this would for example lead to a concentration limit of 0.1 %, which is in line with EU regulations for SVHC.

While the lists in step B are based on established scientific criteria, their findings can be challenged as the lists have no regulatory value in the EU. New scientific evidence could for example disprove some of the arguments, or their underlying data, used for listing these chemicals as potential ED.

The goal with step C is not to assess if the substance is an ED or not, but if the arguments as to why the chemical is listed as an ED on the lists in step B are valid, keeping in mind the scientific criteria set forth for identifying ED by the EU and a weight of evidence-based approach. This means, for example, that the listing of a substance in step B cannot be refuted on the ground that a study or reference included in the motivation for listing the chemical is wrong, if the overall assessment still holds without the inclusion of this study (e.g. there are other studies that are scientifically correct and which indicate the same results).

3.1.3.2 Step C, a walkthrough

- Step 1: Compile relevant information and perform assessment for challenging the arguments for listing the chemical as a potential ED, see information requirements in 3.1.3.3.

- Step 2: Send the assessment to the owner of the criteria (e.g. BASTA) before registering the product (article, substance and/or mixture) containing the chemical of interest.

- Step 3: The owner of the criteria arranges a quality assessment of the report by an independent auditor and provides feedback. The industry is responsible for their own assessment.

- Step 4: If the report is approved, the product (article, substance and/or mixture) can be registered in the system. For increased transparency, it is recommended that products (articles, substances and /or mixtures) containing the chemical substance of interest should show the name, CAS Registry Number and the concentration interval for this substance in the product. This makes it possible to identify which products contain the chemical, in case a later assessment by the EU rules that the chemical is an ED. In addition, it is recommended that a summary of the assessment is made publicly available so that the assessment does not have to be repeated multiple times for the same chemical.

- Step 5: If the criteria in the lists are updated or if new scientific data becomes available (including from self-assessments), Step C should be re-assessed, based on the new data. Note: If the chemical is registered under REACH it can be necessary to also inform ECHA regarding the new data, as outlined in article 22 of REACH (EC/2006/1907).

  If the EU comes with an assessment that the chemical is an ED, then the chemical is considered an ED. If the EU comes with an assessment that the chemical is not an ED, then step C is not needed anymore and the information requirements for the name, CAS nr and concentration range of the chemical in the product should no longer be valid.

3.1.3.3 Information requirements for step C

In order to challenge the assessment of a substance as an endocrine disruptor (as defined by the EU criteria for identifying EDs), using Step B, a clear and robust rationale should be proposed as to why the arguments used for listing the chemical as a potential endocrine disruptor (see step B) are incorrect. The basis for this assessment should be the scientific criteria set forth for identifying ED by the EU and a weight of evidence-based approach.

This rationale should be: 1) **specific** to the arguments that are addressed, 2) **clearly documented** and 3) **verifiable** in order to be comprehensible for an independent actor to be able to make an assessment.

The rationale should include:

- A summary of the assessment (which is to made public)

- A list of the arguments addressed, including a rationale for each argument as to why they are considered incorrect

- Scientific evidence, including references if referring to the literature and experimental data if referring to other studies

If a chemical is present on multiple lists, then all lists should be included in the assessment. The Danish list for example is partly based on a re-assessment of chemicals identified as potential EDs

on an older version of the SIN list and could therefore include additional criteria alongside those on the SIN list or vice versa.

3.1.3.4 Information that can be relevant to assess before collecting data

It could be valuable to start step C with checking for final opinions on chemical hazard by ECHA Committee for Risk Assessment (RAC). The RAC makes classification and labelling determinations based on observed adverse effects. RAC opinions may provide relevant information when deciding whether a listed chemical causes an endocrine pathway related adverse effect (e.g. effects to the oestrogenic pathway would be expected to cause an adverse reproductive effect if the chemical was an endocrine disruptor)[4]. The list is available from: The Registry of classification and labelling (CLH), https://echa.europa.eu/en/information-on-chemicals/annex-vi-to-clp.

Regarding chemicals that are listed under CoRAP, a study regarding their potential for endocrine disrupting activities is already planned / ongoing and it could be of interest to wait for the results from these assessments. In certain cases, these assessments by member states call for specific data / experiments to be performed in order to assess if the chemical is an ED or not. These calls should be taken into account when evaluating the ED assessment.

The chemical assessments discussed above, can be found on CoRAPs homepage available on https://echa.europa.eu/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table, by using the search function and then clicking on the "eye" symbol to the right of the chemical of interest.

It is well worth mentioning that many of the chemicals listed as potential endocrine disruptors will also have other properties of concern for which the chemical might fall under certain restrictions, e.g. several chemicals with potential ED properties will also be toxic for reproduction (e.g. dibutyl phthalate). Challenging their assessment as an ED might therefore not affect how this chemical is regulated by the owner of the criteria.

3.1.3.5 When to present the information

The assessment made in step C should be sent to the owner of the criteria (e.g. BASTA) before the registration of the product (article, substance, mixture) containing the chemical of interest, to allow time for a quality control of the report.

3.1.3.6 Who is responsible for the assessment

As in REACH, the assessment made in step C remains the responsibility of the supplier of the product (article, substance, mixture) and not that of the owner of the criteria (e.g. BASTA).

3.1.3.7 The independent auditor: role and requirements

When the owner of the criteria receives the report, it should be sent further to an independent auditor in order to assess the quality of the assessment. The focus here should be on assessing if the arguments brought forth make sense, if they are supported by scientific data and if they take into account the scientific criteria for identifying endocrine disruptors, as set forth by the EU. The auditor should have the right to ask for more information / clarification from the supplier and to discuss the case with other independent auditors if this is required.

[4] Note that the motivation for listing the chemical as a potential ED in step B can be based on more than just the effects addressed in the RAC opinion. It's important to use a weight of evidence-based approach and to address the reasons for listing the chemical in its whole.

It is important that the assessment provided to the owner of the criteria is assessed by an independent auditor with the right competence. The auditor should therefore fulfil at least one of the criteria listed below:

- Have a relevant education in toxicology (or equivalent) and have at least 5 years of experience of working with the risk assessment of chemicals or chemical products.

- Have experience of performing at least 10 risk assessments for chemicals or chemical products, together with a risk assessor with relevant education in toxicology (or equivalent) and with at least 5 years of experience.

Having experience with endocrine disruptors is seen as a merit but not a necessity as the assessment focuses on the overall quality of the report and not on performing an assessment of if the chemical is an endocrine disruptor or not.

These competence requirements are adapted from those published by Sveriges Byggindustrier for people in charge of making material inventories related to hazardous chemical substances (Sveriges Byggindustrier, 2019).

3.1.3.8 Recommended actions to take by the owner of the criteria (e.g. BASTA)

If the report is approved, the product (article, substance and/or mixture) can be registered in the system. For increased transparency, we recommend that the name, CAS Registry Number and the amount (concentration interval) of the chemical substance of interest is shown. This makes it possible to identify which products (articles, substances and/or mixtures) contain the chemical, in case a later assessment by the EU rules that the chemical is an endocrine disruptor.

In addition, it is recommended that a summary of the assessment is made publicly available so that the assessment does not have to repeated multiple times for the same chemical.

3.1.3.9 What to do when new scientific data becomes available, or if the chemical is assessed by the EU

If new scientific evidence becomes available or if the criteria in the lists are updated, step C should be re-assessed, based on the new data. This should include self-assessments made by the supplier.

If the EU comes with an assessment that the chemical is an endocrine disruptor, then the chemical is considered an endocrine disruptor. If the EU comes with an assessment that the chemical is not an endocrine disruptor, then step C is not needed anymore and the information requirements for the name and concentration range of the chemical in the product (article, substance and/or mixture) should no longer be valid.

3.1.3.10 In case the assessment is rejected

The supplier should be provided with feedback as to why their assessment has been rejected. In the case of a rejection based on an incomplete report (see 3.1.3.3) the supplier should be given the opportunity to resubmit an application.

Even though the responsibility for the assessment lies with the supplier of the products (articles, substances and/or mixtures) containing the chemical, the owner of the criteria will have a final say on which chemicals to include, based on the assessment of the independent auditor(s).

3.2 Discussion

The main benefit of the proposed workflow above is that it combines the strength of both regulatory assessments and non-regulatory lists, while allowing for new scientific evidence to be included in case the criteria used in these lists become outdated or are refuted. This criteria-based assessment is therefore in line with existing regulation, potentially ahead by including additional lists, but not contradictory to current and foreseen regulatory decisions or scientific consensus. By keeping the use of additional lists to a minimum, the workflow also becomes easier and more transparent to assess.

A potential challenge with the proposed workflow is that the research and legislation on endocrine disruptors is changing rapidly and the proposed workflow should therefore be revised when needed.

While being ahead of regulatory decisions due to the use of additional lists, the proposed workflow is still exclusive rather than inclusive, i.e. there will still be chemical substances with potential ED properties that will not be identified as such using this approach. However, the alternative would be to exclude potentially 1000s of chemical substances, for which there is no strong evidence that they have ED properties, from being used in the construction and building industry.

3.3 Industry dialogue

During the industry dialogue, tools for easier access to substance information regarding endocrine disruptors have been suggested. These are well worth to consider but are outside of the present project scope.

A transparent and quality assured process regarding drawn conclusions cannot be emphasized enough. Participants in the industry dialogue have stressed this as a most critical factor for success.

A recommendation from the project group is to use existing methods as far as possible and combine them with the suggested criteria and decision tree so as not to delay the substitution of endocrine disrupting substances. When addressing potential endocrine disrupting chemical substances, also other hazards should be included, to get a full view of the risks using the substance.

That the criteria for this guidance document are rather simple is an active choice. Substitution is key and a too bureaucratic and complicated system risks interfering with this process.

4 Outlook

The next step for the building and construction industry is to decide on and start using the criteria. A transparent and practical way to do this is to implement the endocrine disruptor criteria (section 3.1 in this document) in systems for product evaluation (for instance BASTAOnline). A transition period that does not delay substitution and which allows suppliers to report their product (article, substance and/or mixture) before the deadline of this transition is needed. A plan for a regular revision of the criteria and a guide for the independent auditor (for instance check lists) are crucial elements in the implementation phase. This guidance document in general, and step C more specifically, will need revision when scientific consensus and legislation for endocrine disruptor change.

A wanted position can be an overall knowledge and legislation level regarding endocrine disruptors that makes this document redundant. In the current situation with actions and changes, to be able to phase out endocrine disruptors, extra focus, methods and criteria is key.

There is a significant focus on potential endocrine disruptors at present. We expect actions in EU member states, at competent bodies, from scientists and NGOs. Test methods will develop and improve.

When regulatory evaluations are presented, NGO list findings may be challenged. In case lists and authority assessments are contradictory, authority assessments are superior. The suggested method must be applicable also in a future when further legislation regarding endocrine disruptors will be implemented.

To optimize the resources needed for step C, it is recommended that the owners of criteria make it public if a certain chemical has been assessed so that other suppliers using the same chemical can use this information as a basis for their own assessment. This can for instance be achieved by making the summaries of the assessment's public. Detailed assessments can likely not be made public due to issues with confidentiality.

5 Abbreviations

Abbreviations are explained the first time they are used in the guidance document. The following list is a compilation.

ADHD	Attention deficit hyperactivity disorder
BPR	Biocide Product Regulation (EU) 528/2012
CAS	Chemical Abstract Services
ChemSec	International Chemical Secretariats
CLP	The Classification, Labelling and Packaging (CLP) Regulation ((EC) No 1272/2008)
CoRAP	Community Rolling Action Plan
EATS	oestrogen, androgen, thyroid and steroid
ECHA	European Chemicals Agency
ED	Endocrine Disruptor / Endocrine Disrupting
EDS	Endocrine Disrupting Substance
EDSP 21	Endocrine Disruptor Screening Program (EDSP) in the 21st Century
EFSA	European Food Safety Authority
EPA	Environmental Protection Agency
EQS	Environmental Quality Standards
EQSD	Environmental Quality Standards Directive
EU	European Union
GBR	Golvbranschens Riksorganisation (Swedish flooring trade association)
GDP	Gross Domestic Product
H-Phrase	Hazard Phrase (from EU CLP)
IPCP	International Panel on Chemical Pollution
IPCS	International Programme on Chemical Safety
JRC	Joint Research Centre
OECD	Organisation for Economic Co-operation and Development

PBT	Persistent Bioaccumulative and Toxic
PPP	Plant Protection Products
REACH	Registration, Evaluation, Authorisation and restriction of Chemicals (EC) No 1907/2006
SIN list	Substitute It Now list from ChemSec
SIVL	Foundation IVL
SVEFF	Sveriges Färg och Lim Företagare
SVHC	Substance of Very High Concern
WFD	Water Framework Directive 2000/60/EC
WHO	World Health Organisation
vPvB	Very Persistent very Bioaccumulative

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Annex 1: Examples

Triphenylphospate, CAS: 115-86-6

A) Has the chemical substance been evaluated for ED activity according to:

- Reach candidate list, article 57f and EU criteria for identifying EDs.

No, but an assessment for ED properties is ongoing and led by France.

B) Are there indications that the chemical has ED properties according to the following sources:

1. EU's CoRAP
   Yes: https://echa.europa.eu/sv/substance-information/-/substanceinfo/100.003.739

2. Danish centre for ED chemicals
   No

3. ChemSec's SIN-list
   Yes: https://sinlist.chemsec.org/ Search for CAS-No.: 115-86-6

C) Can the arguments used for listing the chemical as an ED in B. be refuted using scientific arguments that are specific, clearly documented and verifiable?

- Optional

Conclusion: In line with this guideline document, the chemical is considered a potential ED unless its presence on the lists in step B can be refuted. Information on the CoRAP assessment by ECHA (from: https://echa.europa.eu/documents/10162/1f460a42-eeb2-c315-4eaf-7bbebea352c2), stated which dataset is needed in order to proceed with the assessment of this chemical:

"Therefore, based on the substance evaluation and in accordance with Article 46(1) of the REACH Regulation, ECHA concludes that you are required to carry out the following study using the substance subject to this decision: Fish Sexual Development Test, test method OECD 234, using Zebrafish (*Danio rerio*) and 5 test concentrations."

4-tertbutylphenol, CAS: 98-54-4

A) Has the chemical substance been evaluated for ED activity according to:

- Reach candidate list, article 57f and EU criteria for identifying EDs.
  Yes: https://echa.europa.eu/sv/substance-information/-/substanceinfo/100.002.436

Conclusion: In line with this guideline document, the chemical is considered a (potential) ED.

Resorcinol, CAS: 108-46-3

A) Has the chemical substance been evaluated for ED activity according to:

- Reach candidate list, article 57f and EU criteria for identifying EDs.
  No

But an assessment is ongoing by Finland and France for potential ED properties

B) Are there indications that the chemical has ED properties according to the following sources:

1. EU's CoRAP
   Yes, one evaluation by Finland has been concluded, indicating that the substance is likely an ED and has requested for follow-up regulatory action at EU level: https://echa.europa.eu/documents/10162/fedfa3b0-f8a2-66b4-2a08-7f686df46994 . This process is ongoing by France.

2. Danish centre for ED chemicals
   Yes, listed as potential ED but with conflicting data, http://www.cend.dk/files/DK_ED-list-final_2018.pdf

3. ChemSec's SIN-list
   Yes, https://sinlist.chemsec.org/ Search for CAS-No.: 108-46-3.

C) Can the arguments used for listing the chemical as an ED in B. be refuted using scientific arguments that are specific, clearly documented and verifiable?

- Optional

Conclusion: Potential ED, but unsure if it will be considered to be of an equivalent level of concern as SVHCs. This is what the study by France will determine. In line with this guideline document, the chemical is considered a potential ED unless its presence on the lists in step B can be refuted, in which case step C (optional) could be pursued.

Di-isodecyl phthalate (DIDP), CAS: 68515-49-1, 26761-40-0

A) Has the chemical substance been evaluated for ED activity according to:

- Reach candidate list, article 57f and EU criteria for identifying EDs.
  No

B) Are there indications that the chemical has ED properties according to the following sources:

1. EU's CoRAP
   No

2. Danish centre for ED chemicals
   Appears in the study, but not in table 8 or 13 ==> did not make it into the final selection.

3. ChemSec's SIN-list
   Yes

C) Can the arguments used for listing the chemical as an ED in B. be refuted using scientific arguments that are specific, clearly documented and verifiable?

- Optional

Conclusion: In line with this guideline document, the chemical is considered a potential ED unless its presence on the lists in step B can be refuted, in which case step C (optional) could be pursued. In the case of DIDP, an EU Risk assessment of 2006 and an ECHA evaluation of DIDP from 2013 are available online and could potentially be used in step C.

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