Environmental Sciences Europe

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The implementation of the substitution principle in European chemical legislation: a comparative analysis

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Abstract

Background The substitution of hazardous chemicals with safer alternatives is an important objective in European chemical policy, but implementation has been slower than expected. We conduct a comprehensive analysis and comparison of the implementation of the substitution principle in European regulations for pesticides, biocides, and industrial chemicals. Specifically, we examine and compare the criteria and processes associated with the identification of candidates for substitution and the assessment of alternatives.

Results We find only minor differences in the criteria applied to identify candidates for substitution amongst pesticides, biocides, and industrial chemicals, but larger differences concerning the processes used. While all substances that are to be approved as a pesticide and biocide are systematically evaluated against the established criteria for substitution, the substitution process for industrial chemicals only focuses on those substances identified as substances of very high concern. The main reason candidates for substitution remain on the market is the lack of identified safer chemical alternatives and the insufficient consideration of non-chemical alternatives, caused, at least to a large extent, by the comparatively weak incentives provided by current regulations.

Conclusions The systematic approach for the identification of industrial substances of very high concern (SVHC) under ECHAs "Integrated Regulatory Strategy" is much welcome. However, no final conclusion on SVHC properties or the need for regulatory action has been drawn for approximately 90% of the REACH-registered substances, as often even basic hazard and exposure data are missing. Hence, at least a screening-level evaluation of SVHC properties should become a mandatory part of the substance registration under REACH. To reduce the risk of strategic behaviour in the search for alternatives to industrial chemicals identified as SVHC, a setup in which regulatory authorities play a larger role as information and knowledge brokers should be considered. Investments in innovation as well as improved sharing of information and a better distribution of the workloads amongst European authorities might also improve the identification of safer alternatives. However, without stronger incentives, making it more costly for companies to continue using hazardous substances relative to safer alternatives, initiatives to promote substitution are likely to have limited success.

Keywords Hazardous chemicals, SVHC, Biocide, Pesticide, Plant protection product, Chemical risk management, Chemicals strategy for sustainability, Substitution principle

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Background

The substitution of hazardous chemicals with safer alternatives is an important objective in current European chemical policy [1]. The substitution principle is defined by the European Chemicals Agency [2] as "the replacement or reduction of hazardous substances in products or processes by less hazardous or non-hazardous substances, or by achieving an equivalent functionality via technological or organisational measures". The principle is included in several European regulations and a number of initiatives support companies in substituting hazardous substances, primarily by improving access to information about regulations and alternative substances.[1]

However, effectively implementing the substitution principle poses significant challenges. Identifying and assessing substances of concern as well as safer alternatives require substantial expertise and resources within companies and regulatory authorities. Limited and unevenly distributed information on hazards and risks associated with both the substances of concern and their potential alternatives further complicates the decision-making process. As a result, decisions about chemical substitution often occur under significant uncertainty [3], with risk–risk trade-offs being common and the distinction between hazard and risk-based decision principles not always easily discernible [4], see also Löfstedt's [5] critique of the substitution principle and the ensuing commentaries [3, 6–12].

Despite substantial efforts to support the identification of safer alternatives, substitution of hazardous chemicals has progressed at a slower pace than anticipated [2, 13, 14]. Moreover, there have been numerous instances where hazardous substances were replaced with alternatives with a different or unknown hazard profile, which later has been shown to be hazardous [15]. This so-called regrettable substitution has been documented for a variety of hazardous substances, including chlorinated solvents [16], phthalates [17, 18], bisphenol A [19–21], brominated flame retardants [22, 23] and chlorofluorocarbons [24, 25].

European chemical regulation is primarily organised based on the intended use of chemicals. The substitution principle is included in European regulation for plant protection products (pesticides) mainly regulated under the Plant Protection Product Regulation (EC) 1107/2009 (PPPR), for biocides under the Biocidal Products Regulation (EU) No. 528/2012 (BPR) and for industrial chemicals under Regulation (EC) No. 1907/2006 (REACH). Other chemical regulations, such as Regulation (EC) No. 1223/2009 on cosmetic products, Regulation (EC) 1935/2004 on materials and articles intended to come into contact with food and Regulation (EC) 726/2004 on medicinal products for human and veterinary use, also set conditions for substance approval but lack mandatory provisions to encourage the search for safer/less hazardous alternatives. The substitution principle is also part of the European occupational health and safety legislation. Art 6 of the Chemical Agents Directive 98/24/EC provides the minimum requirements for the protection of the health and safety of workers and prioritises the substitution of hazardous chemicals with less or not hazardous chemicals or processes. The Carcinogens and Mutagens Directive 2004/37/EC obligates employers to reduce the use of substances that are carcinogenic, mutagenic, or toxic for reproduction at the workplace, by replacing them, as far as technically possible (Art 4). Regulation (EU) 2019/1021 on persistent organic pollutants (POPs) aims at eliminating or restricting the production and use of POPs as defined in the Stockholm Convention. In addition, there are several regulations which can contribute to substitution but do not explicitly refer to substitution. Important examples include Regulation (EC) No. 1272/2008 on the classification, labelling and packaging of substances and mixtures (CLP Regulation) and the Water Framework Directive 2000/60/EC.

This paper analyses and compares the implementation of the substitution principle, from a public health and environmental perspective, across the regulations governing pesticides, biocides, and industrial chemicals in Europe. These three regulations cover the bulk of chemicals on the European market and contain explicit provisions for substitution of hazardous chemicals with safer alternatives. Specifically, we examine the criteria and processes associated with two key elements for operationalising the substitution principle in these regulations: the identification of candidates for substitution (CfS) and the assessment of alternatives. Based on our analysis, we aim to identify the strengths and weaknesses of the current approaches used in these regulations and propose recommendations for enhancing the implementation of the substitution principle.

Materials and methods

The analysis is based on a review of published and grey literature and a detailed comparison of the PPPR, BPR and REACH regulatory texts. We also retrieved and analysed data from publicly available databases to assess the effectiveness of each regulation in substituting hazardous substances. Table 1 lists the databases used and all

[1] See for example the information portals on substitution by the European Chemicals Agency (ECHA) (https://echa.europa.eu/substitution-to-safer-chemicals) and by the German Federal Institute for Occupational Safety and Health (https://www.subsportplus.eu). See also Green Screen for Safer Chemicals (https://www.greenscreenchemicals.org/) and the CHEMSEC Marketplace (https://marketplace.chemsec.org/) for examples of private sector and non-governmental organisations' initiatives.

Table 1 Databases used

Phase I: identifying CfS or SVHCs	Phase II: assessment of alternatives and authorisation
Pesticides	*Pesticides*
European Pesticides Database (v3) [78]	France: ANSES E-Phy Platform [79]
	Germany: BVL's Plant Protection Register [80]
	Sweden: KEMI's Pesticide Register [81]
Biocides	*Biocides*
Information on Biocides Platform [44]	Information on Biocidal Products Platform [44]
Industrial chemicals	*Industrial chemicals*
Registered Substances Platform [82]	Adopted Decisions and Consultations on Applications for Authorisation [83]
Registry of SVHCs intentions until outcome [84]	
Candidate List [85]	
Authorisation list [86]	
Substances restricted under REACH [87]	

the data are available in Additional file 1. The data collection occurred between January and April 2023, except for industrial chemicals restricted under REACH, where data was retrieved in October 2023. Our analysis focused on the period between January 2008 and December 2022. To assess the identification of CfS under PPPR and BPR, we collected information about the substances (e.g., name and CAS number), current status (e.g., approved, pending, withdrawn), approval and expiry dates. From REACH lists, we retrieved intention, inclusion and first published dates. Under REACH, substances of very high concern (SVHC) are included simultaneously in the SVHC intentions, Candidate and Authorisation lists. To avoid double counting, we portray these lists as mutually exclusive.[2]

In the absence of publicly available data on the volumes of hazardous chemicals used in Europe, we analysed whether the number and the share of CfS-containing products have decreased over time. In the absence of a European-wide database for plant protection products, we chose France, Germany, and Sweden as case studies. Each country represents one of the zones in the zonal system implemented under PPPR. For industrial chemicals, we collected information on the applications for authorisation submitted under REACH. In addition, we analysed key reports from European authorities on substitution activities, such as ECHA [26–29] and EFSA [30].

[2] For example, chromium trioxide is found in the SVHC intention (Intention date: 18/12/2009), Candidate List (Inclusion date: 15/12/2010) and Authorisation list (Inclusion date: 17/04/2013). In our analysis, chromium trioxide is included in the SVHCs intention list for the time between 18/12/2009 and 14/12/2010, in the candidate list between 15/12/2010 and 16/04/2013, and the compound is then finally included in the authorisation list since 17/04/2013.

Regulatory frameworks for identifying candidates for substitution

All three European frameworks identify CfS based mainly on the hazard profile of the evaluated substance, i.e. its intrinsic properties relevant for human health and the environment (Table 2). A substance is defined as a CfS, if at least one criterion in Table 2 is met.

Pesticides

All pesticides on the European market have undergone an authorisation process following the rules provided by the PPPR (Art 28 and 29), including an assessment of alternatives. Active substances—chemical(s) that work against pests/plant diseases—undergo a European-level approval driven by the European Food Safety Authority (EFSA), the competent authorities of the EU Member States and the EU Commission's Standing Committee on Plants, Animals, Food and Feed (SCoPAFF). Following a favourable opinion from SCoPAFF, the Commission takes the final decision. If a chemical is approved as an active substance for a pesticide product, it is included in the EU list of approved active substances [31].

Pesticide products, in the form in which they are supplied to the user, are only allowed to contain active substances from this list and, additionally, undergo a national authorisation process according to the PPPR (Art 29). The EU is divided into 3 zones (North, Central and South) to facilitate the process and EU countries assess applications on behalf of other countries in their zone. Authorisations are only given for a specific use, i.e. a defined crop that is to be protected against a defined pest.

An active substance is only approved if its efficacy is demonstrated in a pesticide product against the target pest. Furthermore, risks for the environment and human health must be assessed by the EU Member State

Table 2 Criteria to identify candidates for substitution

Criteria	PPPR (Art 24, Annex II)	BPR (Art 10)	REACH (Art 57)
Mutagen Class 1A or 1B[a]	Cannot be authorised	✓[b]	✓
Carcinogen Class 1A or 1B[a]	✓[c]	✓	✓
Toxic for reproduction Class 1A or 1B[a]	✓[c]	✓[b]	✓
Endocrine disrupting properties[d]	✓[c]	✓[b]	✓
Lower ADI, ARfD or AOEL than the majority of approved substances[e]	In the same group of substance/use category	In the same product-type and use scenario	Not applied
Persistent, Bioaccumulative and Toxic (PBT)[f]	2 of 3 criteria	2 of 3 criteria	3 of 3 criteria
Very Persistent, very Bioaccumulative (vPvB)[f]	Not applied	✓[b]	✓
Respiratory sensitiser properties[g]	Not applied	✓	✓
Significant proportion of non-active isomers or impurities	✓[h]	✓	Not applied
Other concerns associated with critical effects in combination with use/exposure patterns, in particular risks to groundwater	✓	✓	Not applied
Equivalent level of concern linked to probable serious effects to human health or the environment[d]	Not applied	Not applied	✓

[a] According to Regulation (EC) No. 1272/2008

[b] Substances with those properties can only be authorised as a biocide if risk is negligible, the substance is essential to prevent or control a serious danger or if not approving the substance would have a disproportionate negative impact on society (Art 10 and 5(2) of Regulation 528/2012)

[c] Substances with those properties can only be authorised as a pesticide if exposure is negligible and residue levels do not exceed the default according to Regulation 396/2005, Art 18(1b) (Annex II Point 4 of Regulation 1107/2009)

[d] Pesticides: according to Regulation 2018/605; biocides: according to Regulation 2017/2100; industrial chemicals: according to Art 57(f) and Art 59 of Regulation 1907/2006

[e] ADI—Acceptable Daily Intake, ARfD—Acute Reference Dose, AOEL—Acceptable Operator Exposure Level

[f] Pesticides: according to Regulation 1107/2009, Annex II, Point 3.7.2., Biocides: according to Regulation (EC) 253/2011, Industrial chemicals: according to Regulation (EC) 253/2011

[g] According to Regulation (EC) No. 1272/2008

[h] Regulation 1107/2009 (PPPR) only considers the proportion of non-active isomers

Authorities as being acceptable in accordance with the principles laid down in Art 29 of the PPPR. In addition, the active substance must not be identified as a persistent organic pollutant (POP), must not have PBT/vPvB properties[3] and must not be identified as a potential carcinogen, mutagen, as being toxic for reproduction (CMR) or considered as being an endocrine disruptor in humans (Annex II, PPPR). The first approval of a new component as an active substance is typically given for 10 years and a renewal can be granted for up to 15 years. Low-risk pesticides that fulfil additional criteria (point 5, Annex II, PPPR) are put on a fast-track for approval and are initially approved for a period of 15 years.

Active substances flagged as CfS are approved for a maximum of 7 years, instead of the usual 10 years. EU Member States are required, when assessing an application for the authorisation of a pesticide product containing an active substance identified as a CfS, to evaluate whether they can be substituted by another pesticide product or a non-chemical alternative.

Biocides

Similar to the approval of pesticides, also the approval system for biocidal products follows a two-step approach: first the active substance is evaluated on the EU level, and the full biocidal product that is sold to the user is then evaluated in individual member states. The European Chemicals Agency (ECHA) drives the process of approving the active substances, following the rules and criteria set forth in the BPR (Art 4 and 5). Approved active substances are listed in the Union list of approved active substances.[4] Active substances are approved for a maximum of 10 years, after which the approval can be renewed.

Substances that have either CMR or PBT/vPvB properties or are endocrine disrupters will, in principle, not be approved (Art 5(1), BPR). However, such compounds might still be approved if emissions to the environment are considered negligible, the active substance is essential to prevent or control a serious danger to the environment, or if the consequences of not using the active substance are disproportionate to the risk avoided (Art 5(2), BPR). Under these conditions, the active substance is immediately considered a CfS (Art 10 (1), BPR) and

[3] PBT/vPvB—Persistent, Bioaccumulative, Toxic or very Persistent, very Bioaccumulative.

[4] Formerly known as Annex I of the Biocidal Products Directive 98/8/EC.

may only be approved for an initial period of maximum 5 years (Art 4(1), BPR).

Similar to pesticide products, formulated biocidal products also require a separate national and/or EU-wide authorisation. The criteria for identifying biocides as CfS (BPR Art 10) go slightly beyond the criteria listed for the identification of pesticides as CfS (see Table 2). In addition to the criteria listed above, a biocide is also considered a CfS if it is classified as a respiratory sensitiser or a mutagen (Cat 1A or 1B) according to the CLP Regulation. Also risks to groundwater are specifically mentioned as a CfS criterion for biocides.

Biocides that are identified as CfS are approved for a maximum of 7 years. Their presence also triggers a comparative assessment during the authorisation of biocidal products. As a result, if another biocidal product or a non-chemical method exists whose application results in a significantly lower overall risk for human health, animal health and the environment, is sufficiently effective and presents no other significant economic or practical disadvantages, the biocidal product that contains a CfS as its active substance will be refused authorisation (Art 23, BPR).

Industrial chemicals

For most industrial chemicals regulated under REACH, there is only a requirement to register the chemical prior to putting them on the European market. For chemicals produced in Europe and/or imported into Europe at a total volume of at least 1 ton/year and which are present in the final product with a concentration exceeding 0.1% (w/w), the registrant must provide the information necessary for the SVHC classification. In contrast to the procedures described above for pesticides and biocides, this approach implies that an evaluation of the need and possibilities for substituting hazardous chemicals is initially restricted to a fraction of the industrial chemicals on the market. For example, only industrial chemicals manufactured or imported in volumes of 10 tonnes or more are systematically checked for PBT properties, which means that PBT substances in lower volumes can be initially registered.

The competent authorities of all EU Member States and ECHA prepare the dossiers for flagging substances as possible SVHC. The substance is then listed in the Registry of SVHC intentions until outcome. If a chemical is finally identified as a SVHC (according to the criteria in Table 2), it is placed on the EU *Candidate list of substances of very high concern for authorisation*, in accordance with REACH Art 59(10). Inclusion in this list has the following legal consequences for the manufacturer and/or importer: (a) a safety data sheet must be made available, (b) the registrant must respond to consumer requests for information whether the product contains an SVHC within 45 days and (c) the registrant must notify ECHA if an article they produce contains an SVHC above a concentration of 0.1% (w/w). Other than that, substances listed on the candidate list can be freely marketed and used. ECHA then selects substances from the candidate list for inclusion into the final authorisation list (Annex XIV of REACH), and shall according to article 58(3) in REACH prioritise compounds with PBT/vPvB properties, wide dispersive use and/or high production volumes. A chemical listed in the authorisation list cannot be produced, imported, or used in the EU after its sunset date (i.e. last date to place a chemical on the EU market), unless an authorisation for a specific use is granted.

Finally, the marketing and use of a substance can be restricted, if a Member State or ECHA (at the request of the Commission) concludes that there might be an "unacceptable risk to human health or the environment" (REACH Art 68). The dossier proposing the restriction also contains a discussion of the alternatives to the substance. However, even if no alternatives are available, a substance might still be subject to restriction if the risks are deemed unacceptably high.

Identification of candidates for substitution in practice

Looking at available data from 2008 to 2022, we find that the number of active substances approved (or registered in the case of REACH) and the total number of active substances identified as CfS have increased over time in all three Regulations (Fig. 1). It should be noted that the PPPR went into force in 2009 (building on the older Directive 91/414/EEC), the BPR went into force in 2012 (building on the older Biocidal Products Directive (98/8/EC), while the REACH authorisation process only started in 2013 without having a predecessor.

(See figure on next page.)

Fig. 1 Number of pesticides (**A**), biocides (**B**) and industrial chemicals (**C**) on the EU market and candidates for substitution. For biocides (**B**), some active substances are included several times due to their use in different product types. For REACH-registered substances (**C**), the earliest date between first published date and last modified date has been used as a proxy for registration date. The REACH-registered substances show only chemicals with a full and active registration under REACH. Note that a logarithmic scale is used for REACH-registered substances. Data Sources: Pesticides—European Commission [78], Biocides—ECHA [44], Industrial Chemicals—ECHA [82, 84–87]

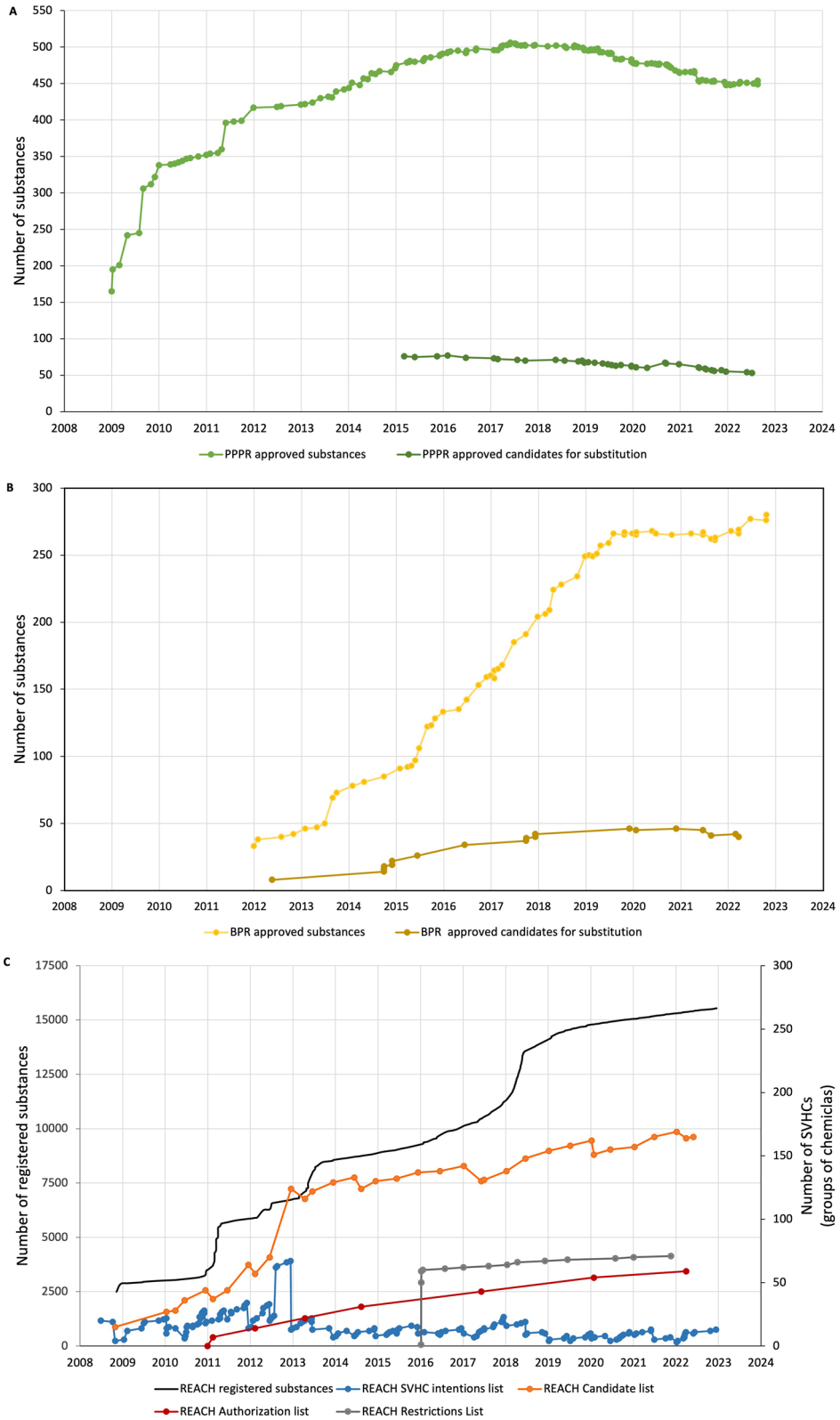

Fig. 1 (See legend on previous page.)

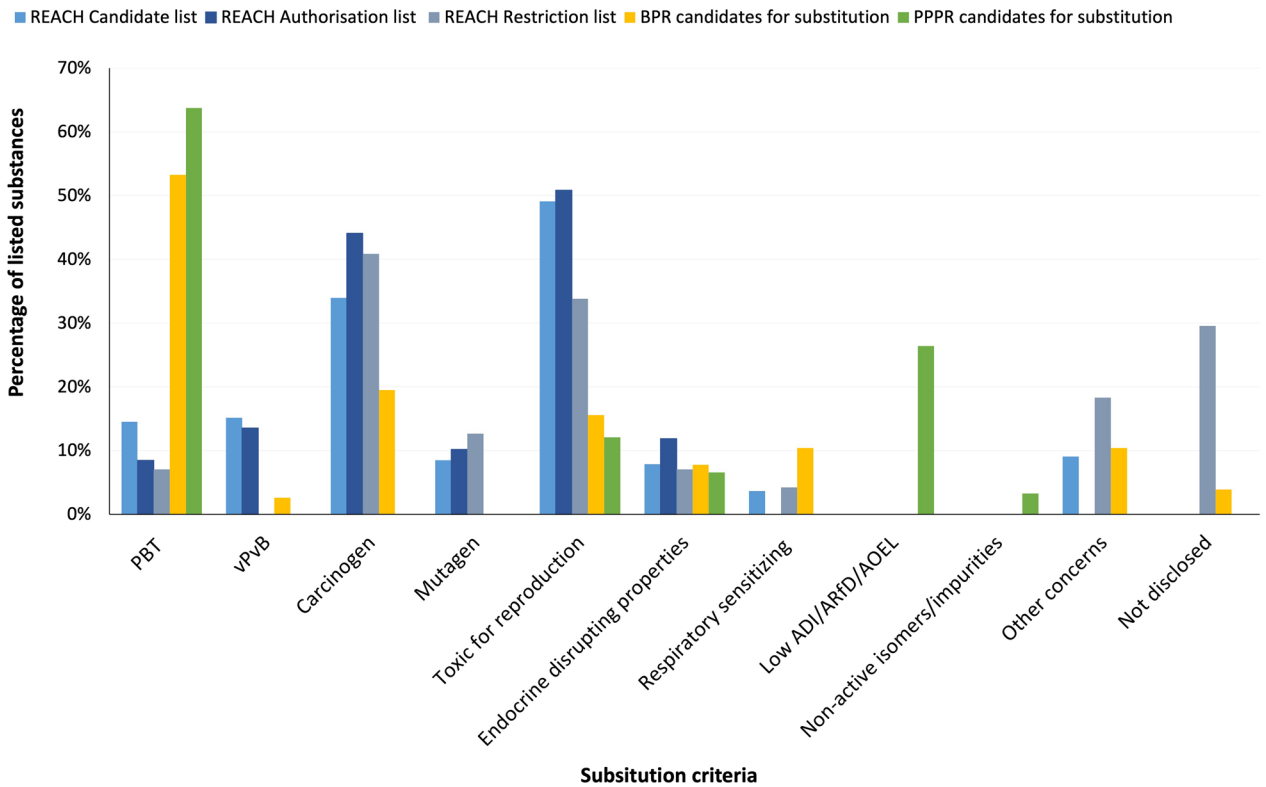

Fig. 2 Percentage of active substances meeting the substitution criteria for each indicated list. Some of the active substances fulfil several of the substitution criteria. Note that the REACH Candidate list does not include the indicated substitution criteria for low ADI/ARfD/AOEL and non-active isomers/impurities. Data Sources: Pesticides—European Commission [78], Biocides—ECHA [44], Industrial Chemicals—ECHA [85–87]

For pesticides there has been a small decrease in the number of approved active substances since 2017, as well as in the overall number of approved CfS. As of December 2022, 454 pesticides and 280 biocides have been approved, out of which 53 and 40 substances, respectively, have been approved and identified as CfS. For pesticides, the share of approved-CfS identified substances has decreased from 16% in 2015 to 12% in 2022 and for biocides from 26% in 2014 to 14% in 2022.

Over 23,500 industrial chemicals had been registered under REACH by December 2022, out of which 15,544 chemicals were full and active registrations. The REACH candidate list included 165 (groups of) chemicals, which had not been included in the authorisation list. The authorisation list included 59 (groups of) chemicals, while the restriction list included 71 (groups of) chemicals. The SVHC intention list included 13 (groups of) chemicals in addition to those on the candidate list. Accordingly, the share of registered substances classified as SVHCs is very low, around 1–2%. The share of substances on the candidate list that have been included in the REACH authorisation list has increased from 10% in 2011 to 28% in 2022.

Figure 2 displays the criteria that have triggered the identification of an active substance as a CfS under PPPR (91 substances), BPR (77 substances) and REACH (Candidate: 165 groups of chemicals; Authorisation: 59 groups of chemicals; Restriction: 71 groups of chemicals), respectively. For pesticides, the most common criterion that triggers an identification as a CfS are PBT properties, with 64% of the CfS fulfilling at least two of three PBT criteria. Low ADI/ARfD/AOEL is also a relatively common substitution criterion, with 26% of the approved pesticides fulfilling at least one of these criteria. For biocides, similar to pesticides, 53% of those that have been classified as CfS meet at least two of three PBT criteria. Carcinogenicity and repro-toxicity are also common criteria with 19% and 16% of the CfS fulfilling at least one of these criteria, respectively. 50% and 34% of the substances identified as CfS amongst the industrial chemicals are toxic for reproduction or carcinogenic, respectively. PBT, vPvB or mutagenic properties have triggered SVHC classification in 8–15% of the total number of substances on the candidate list. Among the substances placed in the REACH authorisation list, there is a larger fraction of compounds identified as carcinogens (44%) and toxic

for reproduction (52%) compared to the candidate list, indicating that these are important decision criteria for the European Commission. Similarly, carcinogens (41%) and toxic for reproduction (34%) are the main criteria to place groups of chemicals in the REACH restriction list.

The initial list of pesticide CfS was published on 11 March 2015 [32], almost 1.5 years after the deadline set by Art 80(7) of the PPPR. As the criteria for identifying a compound as an endocrine disrupter was not established at the time, substances identified as carcinogens (Cat 2) and toxic for reproduction (Cat 2) were preliminary classified as having endocrine disrupting properties [30]. Since the publication of criteria for endocrine disruption for pesticides [33], seven new active substances have been classified as CfS in 2020 and it is expected that the new criteria will increase the number of pesticides identified as CfS [34].

Also, the identification of CfS under the BPR has been affected by the slow process of approving new active substances and evaluating active substances already on the market [26]. By the end of 2019, only 35% of the active substances in the "Biocidal Product Review Program" had been evaluated [35]. The reasons for the delay include inadequate resources at EU Member State Authorities to deal with the often complex technical questions involved as well as delays by applicants in submitting additional data required for the evaluations [36].

The Council of the European Union established the "SVHC roadmap" in 2013 to identify all relevant currently known SVHCs by the end of 2020. ECHA reports that it has achieved this goal with the listing of 211 substances and substance groups as SVHCs on the Candidate list [37]. However, many of the REACH-registered chemicals could not be evaluated for SVHC status, as the necessary hazard data are still missing from the registration dossiers. This lack of adequate hazard information in the REACH registration process has been a major obstacle to the SVHC identification [2, 14, 38].

To overcome this shortcoming, ECHA is implementing an "Integrated Regulatory Strategy" (IRS) which aims to systematically collect, evaluate and compare the information available for all REACH-registered substances. The aim is to have "full clarity" by 2027 ECHA [39]. In the most recent IRS report [13], ECHA lists a total of 22,371 REACH-registered substances, of which 11% (2446) are in the groups of "Regulatory risk management ongoing" or "Currently no further action proposed". Hence, almost 90% of the REACH-registered chemicals are classified into groups that indicate data gaps or ongoing regulatory evaluations ("assessment of regulatory needs", "data generation", and "regulatory risk management under consideration"). In other words, the final assessment of the SVHC properties or its regulatory consideration is still ongoing for 90% of the REACH chemicals. This simply shows that the sheer number of industrial chemicals registered for the EU market, together with a heterogeneous data basis, is one of the main obstacles for the systematic SVHC identification and regulatory consequence analysis.

Regulatory frameworks for the assessment of alternatives

Pesticides

The assessment of alternatives forms part of the authorisation process of pesticide products conducted by Member State Authorities. Any pesticide product containing a substitution candidate is subject to a comparative assessment during which safer alternatives are actively searched for (Art 50(1), Annex IV, PPPR). The overall aim of the assessment of alternatives is to ensure that "substitution should be restricted to cases in which the benefit is evident" [40], which is specified with respect to potential risks for the environment as a difference of a factor of 10 or more between toxicity/exposure ratios (TER values) for similar ecotoxicological endpoints.

The comparative assessment of the pesticide product containing a CfS and its potential alternative is performed in accordance with the guideline provided by the European and Mediterranean Plant Protection Organization (EPPO) standard PP 1/271 [41]. It is restricted to a comparison between fully formulated products that are authorised for the same application scenario (crop, target organism, application type, etc.). Furthermore, risks to the environment should not be compared to risks for human health.

Biocides

The comparative assessment of biocidal products is also based on weighing up the risks and benefits in accordance with Annex VI of the BPR for the substitution candidate as well as for the identified alternatives. Similar to the comparative assessment of pesticide products, this is done separately for human health and the environment. Additionally, impacts on animal health are also considered. In each case, a substitution becomes mandatory, if the alternative has a "significantly lower overall risk" (BPR, Art23(3)). However, in contrast to the alternative assessment for pesticides, no operationalisation of the term "significantly lower" is provided by the BPR. In fact, the Technical Guidance Note explicitly requests to make use of expert judgement to evaluate the significance, see also discussion in Coors et al. [42].

When searching for an alternative biocide, the CfS and its alternative must belong to the same product category (e.g., PT19, repellents and attractants), have identical uses (e.g., repellent), the same target organisms (e.g.,

mosquitos), field of use (e.g., indoor), category of users (e.g., general public) and application method (e.g., spraying). Comparative assessments should also be conducted in a way that ensures a high level of protection, promotes innovation, harmonises the internal market, and avoids unnecessary testing on animals [43].

Industrial chemicals

An analysis of alternatives must be included in the application for authorisation submitted by the applicant (i.e. the producer, importer, or downstream user of a SVHC). The analysis shall identify alternative substances to the SVHC and evaluate their technical and economic feasibility (Art 60 and 62, REACH). If a viable alternative is identified, but the transition to a new chemical or technology takes time, the applicant must develop a time plan for substitution before authorisation can be granted. If the assessment of alternatives fails to find a viable alternative, the applicant must "provide information on what would be required to make possible alternatives suitable and available within an estimated time scale" (Art 61(1), REACH).

If the applicant demonstrates either adequate control of the risk to human health or the environment from use of the SVHC or that the socio-economic benefits outweigh the risk, and no suitable alternatives are available, the European Commission grants a use-specific authorisation (Art 60, REACH), taking into account the ECHA opinion[5] on the application for authorisation and the member states views.

An authorisation is granted with a time limited review period, where the length of the review period depends on the quality of the application and the prospect to find alternatives. The authorisation can be reviewed at any time if new information on alternatives becomes available (Art 61(2), REACH). During the review period, authorisation holders are obliged to continuously search for suitable alternatives, and, in order to continue using the SVHC, they must submit a review report and an updated assessment, at least 18 months before the end of their review period.

Assessment of alternatives in practice

Pesticides and biocidal products

Biocidal and pesticide products undergo a very similar authorisation process and are therefore discussed together in the following. If the substitution principle was effectively implemented, we would expect to see decreasing CfS numbers and use volumes on the European market as well as a reduction of the risk associated with the use of these substances. However, the lack of publicly available data on use volumes of individual hazardous chemicals on the European market makes it impossible to evaluate the actual development. We instead compiled the publicly available information on the share of pesticide and biocidal products containing substances classified as CfS, as well as the total number of authorised products with and without CfS in the period 2015–2022, for 3 selected countries (Fig. 3). For biocidal products we also report the average figures for the EU-27. It should be noted that the number of CfS does not necessarily correlate with the use volumes, as a CfS will remain on the list as long as there is one remaining approved use.

The share of pesticide products decreased by six percentage points to 24% in France during 2015 to 2022. We also observe a small decrease in Germany (from 23 to 17%), but a small increase in Sweden (10–15%) in this period. There was also a decrease in the total number of authorised pesticide products with CfS in France from 494 in 2015 to 393 products in 2022, but an increase in the number of pesticide products with CfS in Germany (from 243 to 292 pesticide products) and Sweden (from 44 to 61 pesticide products). It should be noted that the use of pesticides containing CfS identified substances is concentrated to specific compounds and uses. In France, for example, a third of the pesticide products that contain a CfS include one or more of the following three active substances: copper compounds (57 products), tebuconazole (45 products), and diflufenican (36 products).

The share of biocidal products containing CfS decreased from 38 to 22% from 2015 to 2022 in the European Union (Fig. 3d, see also "Appendix"). The large increase in the total number of authorised biocidal products in the EU (from 1700 to 4100), was not accompanied by an increase in the number of biocidal products containing CfS. The number of biocidal products containing CfS remained relatively stable during the period. Also, the use of biocides containing CfS are concentrated to specific uses, such as propiconazole (Product Type 08—Wood Preservative) which was used in 946 biocidal products and the two rodenticides (Product Type 14): brodifacoum (562 products) and bromadiolone (552 products) [44].

The assessment of alternatives conducted by the authorities in the approval process for pesticides and biocides seem to have played a marginal role in the observed decrease in the share of pesticide products with CfS in France and Germany as well as in the decrease in the share of biocidal products containing CfS in the EU. According to an EC (2018) study, 278 comparative assessments of pesticide products with CfS did not manage to identify even one viable safer alternative which would have triggered a substitution.

[5] Based on evaluations by ECHA's Risk Assessment Committee (RAC) and Socio-Economic Analysis Committee (SEAC).

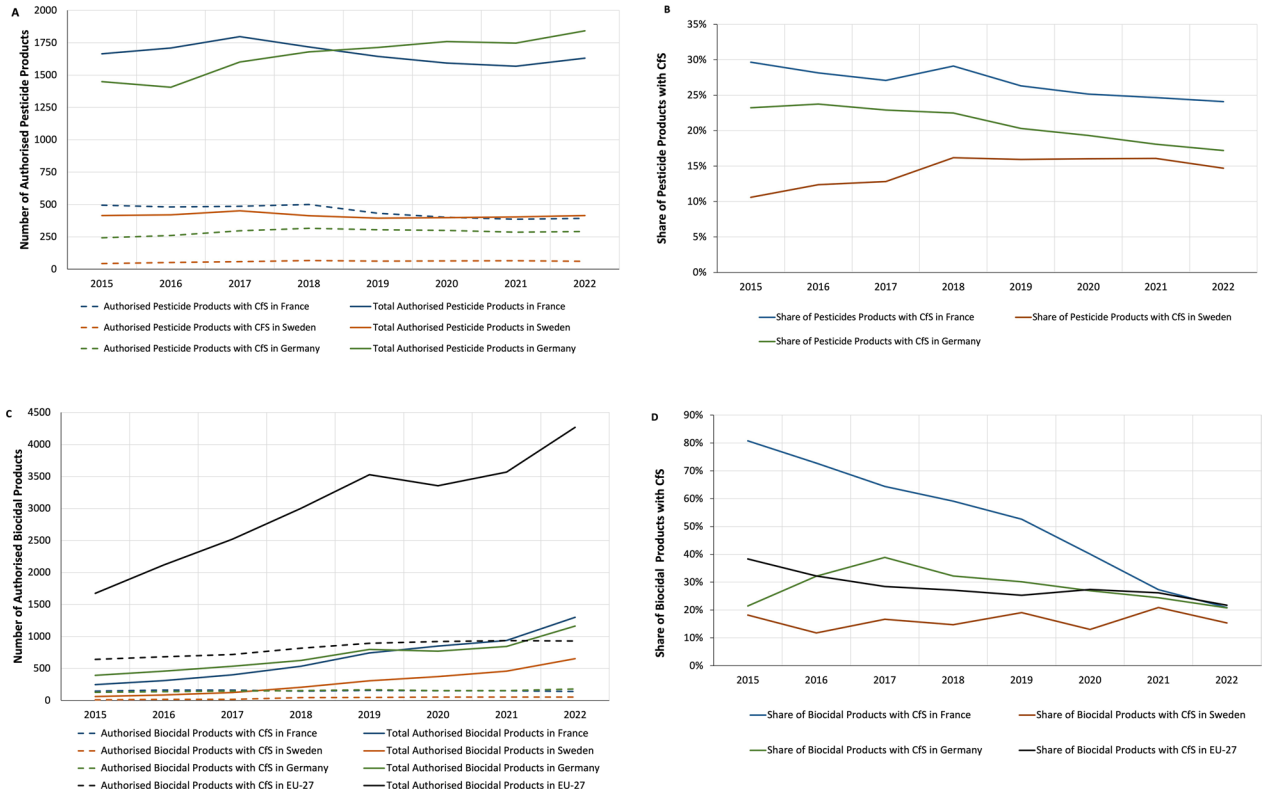

Fig. 3 Total authorised pesticide and biocidal products, shares, and authorised products with candidates for substitution. The time series for each country shows the end approval date. Note that some plant protection products and biocidal products with CfS might be available in the market after the end approval date. Data sources: Pesticide Products—France [79], Germany [80], Sweden [81], Biocidal Products—[44]

Also, for biocidal products, 92% of the 1,394 comparative assessments conducted between 2013 and 2019 did not identify viable alternatives, leading to authorisations being granted for products containing CfS without restrictions [36]. The reduced fraction of pesticide and biocidal products containing CfS is caused by the continuously declining number of CfS that are still approved as active substances. This, in turn, is a result of CfS losing market authorisation, as companies do not apply for re-authorisations [45, 46], which is likely the result of the ongoing substitution process implemented by the companies previously marketing the CfS-containing products.

Assessing alternatives under the PPPR and BPR is challenging, as the alternative product needs to target the same pest, must be efficacious in the same scenario as the original product containing the CfS, while at the same leading to a tangible reduction in hazards and/or risks for human health and/or the environment. The alternative product (and its active substance(s)) needs to be authorised itself, for the purpose at hand, and it needs to be economically competitive with the CfS-containing product. All of this results in a large number of complex comparative assessments, leading to a substantial workload for authorities, which also causes substantial delays [36, 45–47].

Member States authorities have stated that a lack of viable authorised alternatives, a general lack of knowledge and the unavailability of data on the efficacy of non-chemical alternatives have hampered the substitution of CfS-containing products [36, 45, 46]. Even public consultations generate only very limited relevant information on possible alternatives [26, 33]. Finally, the lack of a European-wide inventory of the biocidal and pesticide products on the EU market severely limit the search for alternatives.

Comparative assessments under PPPR and BPR are obliged to consider the number of modes of action available to combat a specific pest, in order to minimise the risk for resistance development. Common practice is to require a minimum of 3 or 4 modes of action for every scenario [41, 42]. This criterion is a major obstacle for the identification of substitution-triggering non-chemical alternatives, as these are only considered if there are at least 3 synthetic pesticides with different modes of action available for a given scenario [48]. Furthermore,

it is not clear whether different microorganisms, that are approved as active substances, are considered as different modes of action [42]. As a result, this criterion limits the ability of comparative assessments to identify suitable alternatives. For example, between 2015 and 2018, 21 comparative assessments for pesticides performed by the French authority were stopped because of the importance of the corresponding active substances in pest resistance management [45].

The example of neonicotinoids

Neonicotinoids comprise the most common insecticide class, used worldwide to protect a broad variety of crops against phytophagous insects. All members of this group function as agonists of the neuronal nicotinic acetylcholine receptors (nAChR) receptor and thereby block neurotransmission in the nervous system especially of insects. Due to the resulting toxic side-effects on beneficial insects, in particular pollinators, most neonicotinoids, except for acetamiprid, are no longer approved for use in biocidal products in European agriculture. Acetamiprid is, together with dinotefuran, imidacloprid and thiamethoxam, also approved to be used as an active substance in biocidal products.

The concerns about the environmental impacts of neonicotinoids on beneficial insects resulted in efforts to develop alternatives and a range of novel nAChR agonists with different chemical structures are in different stages of development. Two of those compounds (sulfoxaflor and flupyradifurone) are already approved in the EU. However, evidence is emerging that sulfoxaflor and flupyradifurone might indeed constitute yet another example of a regrettable substitution, as there is little reason to believe that the ecotoxicological profiles of novel nAChR insecticides, in particular the impacts on pollinators and other beneficial insects, should be substantially different from neonicotinoids. In fact, Siviter and Muth [49] concluded in a systematic review of the ecotoxicological profiles of flupyradifurone and sulfoxaflor, that both substances also have significant sub-lethal impacts on beneficial insects under realistic exposure conditions. As a result, the EC restricted the use of sulfoxaflor to permanent greenhouses in 2022. EFSA also recently reviewed the ecotoxicological profile of flupyradifurone [50] and requested a dedicated assessment of its impacts on solitary bees but concluded otherwise that there is no reason to reconsider its approval.

A systematic study of neonicotinoid alternatives by Jactel et al. [51] found that in 98% of the 2968 analysed cases, a chemical alternative was available, often comprising pyrethroid insecticides. Some of those compounds are substitution candidates themselves (e.g., cypermethrin). However, the authors also found that in 78% of the investigated application scenarios, at least one non-chemical alternative was available, in particular for insects that feed on leaves and flowers. These findings support the notion that non-chemical alternatives should be systematically evaluated when exploring possible alternatives for substitution candidates, which also supports the aim of the Sustainable Pesticide Use Directive according to which non-chemical alternatives are to be preferred.

The example of rodenticides

Rodenticides are biocides used to kill rodents, mainly rats and mice, in order to prevent disease transmission to humans, soiling and spoilage of food and feed as well as damages to properties and infrastructure. The main group of rodenticides currently used in the EU, the so-called anticoagulants, are classified as reprotoxicants and/or PBT/vPvB chemicals and cause high risks of primary and secondary poisoning in non-target organisms. Many of them are well-known environmental pollutants (e.g. [52, 53]).

Anticoagulants therefore fail several of the standard requirements for being authorised under BPR (see above). However, the EC concluded already in 2017 that no suitable alternatives are at hand, that non-chemical alternatives are not proven to be sufficiently efficacious and that the two generations of anticoagulants on the market, together with the few alternative non-anticoagulant rodenticides are necessary to manage resistance development in rodents [54, 55]. It was therefore concluded that substituting anticoagulants would have had a disproportionate negative impact on society [55]. In June 2021, EU Member States extended the authorisation for anticoagulants, until 1 July 2024, and are currently in the process of deciding whether to renew approvals once again.

The major problem is that no new and less hazardous anticoagulants have entered the market over the last years, although non-chemical alternatives seem to be on the rise over the last years (see discussion in Hohenberger et al. [56]). Also, efforts to minimise use and exposure to anticoagulants are implemented in European countries and elsewhere (e.g., U.S. EPA [57]). For example, the Danish EPA has published a guide that aims to minimise the use of anticoagulants by guiding a use through a flow diagram that begins rodent control with the least hazardous anticoagulants [58]. Also, the German Federal Environmental Agency recently updated the FAQ on rodenticide use which emphasises the use of non-chemical alternatives and various risk management measures [59].

Despite the need for developing innovative alternatives, competent authorities have, prior to the introduction of the Chemicals Strategy for Sustainability and the

"safe and sustainable by design" (ssbd) framework [60], described the situation as "not requiring urgent action" [54]. Following the approaches outlined by the ssbd framework, a systematic way forward for developing rodenticides with less hazardous characteristics has been outlined by Hohenberger et al. [56] and a novel decision support system (COMBASE) that is supposed facilitate the systematic identification of alternatives has been recently introduced by Blázquez et al. [62]. It remains to be seen whether those efforts will indeed facilitate the identification and subsequent market entry of rodenticides with less problematic properties.

Industrial chemicals

By December 2022, ECHA had received 283 applications for authorisation, covering 471 different uses of SVHCs beyond their sunset dates. The applications were unevenly distributed across the 59 substances on the authorisation list. While there were no applications for authorisation for 29 of the listed substances, there were more than 70 applications for authorisation for chromium trioxide alone, covering 192 uses [63]. By December 2021, the European Commission had made decisions on 145 out of the 246 applications for authorisation received.

Often the authorisations were granted with shorter review periods than applied for. Once the European Commission grants an authorisation, it is extremely rare that the authorisation will be revoked. In fact, until now, there has been only two instances where an authorisation has been revoked. This followed upon a decision of the EU Court of Justice, which found that the European Commission had failed to identify existing and suitable alternatives to the use of lead chromate pigments (case T-837/16) and that an adequate assessments to evaluate the potential human health and environmental impacts of continued use of chromium trioxide had not been conducted (case C-144/21).

As it is not possible to access time series data on SVHC production, consumption, import and export, it is challenging to assess quantitatively to what extent substitution of SVHCs has taken place. However, several studies indicate that substitution of SVHCs has taken place and that the REACH authorisation process has been an important driver. ECHA [29] finds that the use of SVHC on the authorisation list has declined by 600 000 tonnes (45%) between 2010 and 2021, although the alternative chemicals used are largely unknown. In a more limited study using Swedish data, ECHA [28] finds that companies reduced their use of SVHCs requiring authorisation by about 40%, compared to those SVHCs not requiring authorisation. Also, Sackmann et al. [18] finds that the use of plasticisers on the authorisation list had decreased significantly in Scandinavia, compared to the use of unregulated plasticizers.

In contrast to the assessment of alternatives under PPPR and BPR which is conducted by the national authorities, the company that applies for the authorisation of using an SVHC from the authorisation list must submit the analysis of alternatives. As an authorisation is only granted if no suitable alternatives are available, applicants have limited incentives to show that there are suitable alternatives available [16]. REACH therefore stipulates that ECHA must, upon receiving an application for authorisation, announce this on their website, so that interested parties can submit additional information on alternatives before a decision on authorisation is made (REACH art 64). ECHA is also required to organise a public consultation on the documents submitted by the applicant, so that producers of alternatives and other stakeholders can provide additional information and can comment on the information provided by the applicant. However, the outcomes of these public consultations have often been poor in terms of identification of alternatives [64] and, as alternatives are specific for particular uses, it is challenging for authorities to evaluate the accuracy of the information provided by the applicants [65]. The assessment of alternatives is also often limited to substances that can be used in the technical equipment that is in place for managing the SVHC. Alternatives that require more fundamental changes in a company's material flows or processes are typically not included in the analysis of alternatives [65].

The example of trichloroethylene

Trichloroethylene (TCE), perchloroethylene (PER) and methylene chloride are chlorinated solvents used in high volumes, mainly as cleaning solvents in the metal industry. Due to its proven carcinogenic properties, Trichloroethylene (TCE) was included in the REACH Candidate List in June 2010 and in the Authorisation list in 2013. The EC has granted authorisations for 18 uses to 11 companies, some involving several hundreds of users of TCE for metal cleaning. Closure or relocation of the production to outside EU were stated as a likely non-use scenario in 13 of the applications for authorisation. The use of TCE has been reduced by around 95% from approximately 53 000 tons in 2010–2650 tons in 2022 [66].

Despite the existence of several non-chlorinated solvents and methods for metal-degreasing, including aqueous cleaning and alcohols, most companies have substituted from using TCE to PER, the closest available drop-in alternative [16]. PER and methylene chloride have similar hazardous properties as TCE, but as they are classified "only" as "suspected to be carcinogenic" within

the European Union they are not included in the REACH candidate list.

The regulatory process for TCE illustrates that inclusion in the authorisation list of a substance can lead to a sharp reduction in use. It also illustrates, similar to the neonicotinoids, the limited effectiveness of a substance-by-substance approach in chemical substitution, where companies can fulfil their substitution obligations by switching to substances with similar hazard and/or risk characteristics.

Discussion

In this paper, we compare the setup and operationalisation of the substitution principle in three major European chemical regulations, governing the market approval for pesticides, biocides, and industrial chemicals. The implementation of the substitution principle follows the same two-step approach in all three Regulations: (1) the identification of CfS, followed by (2) the assessment of alternatives for those compounds that are identified as CfS. A chemical is only taken off the market if it is identified as a CfS *and* a suitable alternative is available.

While substances that are to be approved as a pesticide and biocide are systematically evaluated against a set of mainly hazard-based criteria, industrial chemicals do not undergo a similar detailed assessment by authorities before gaining market access. Although ECHAs Integrated Regulatory Strategy aims to evaluate the whole REACH "universe of chemicals" for particular problematic chemicals (including SVHCs), this work is only performed *after* the registration of a substance and based on the industry-submitted information. Because of that and given the vast number of substances registered under REACH, it is not surprising that a significant majority of REACH-registered chemicals (90%) is not finally evaluated yet—either because the necessary hazard and/or exposure data are missing, or because the regulatory option analysis is still ongoing. It seems unclear how long it will actually take before all REACH substances are fully evaluated for their SVHC properties.

It must therefore be considered a major shortcoming that only biocides and pesticides are systematically evaluated against CfS criteria before gaining market access. The process of selecting REACH-registered substances as SVHCs is driven largely by member state authorities and the decision-making process is not always transparent. It has even been argued that the identification of substances of very high concern is at least partly driven by political and economic considerations in the national competent authorities of the member states [67].

Hence, a more systematic approach is needed for industrial chemicals, in which at least a screening-level evaluation of CfS properties would become a mandatory part of the substance registration under REACH. Such a screening-level evaluation could make use of new assessment methodologies, such as modern high-throughput assays and in silico tools [68, 69]. For pragmatic reasons, these evaluations could start with chemicals that are put on the European market in intermediate-to-high tonnages. Similar to biocides and pesticides, an evaluation of producer-submitted data would need to be performed by a competent authority (e.g. ECHA), in order to ensure consistency and quality. Higher penalties for non-compliance with data requirements could also be considered in this context.

Especially the hazard-based elements that are evaluated during the CfS identification (Table 2) invite an implementation of the "one substance, one assessment" principle [1], i.e. a coherent strategy for identifying CfS across different pieces of chemicals legislation. The hazard-based elements also provide a good starting point for group-wise assessments (see e.g. [70] for suggestions on criteria that may be used), reducing the number of evaluations that need to be performed.

The CfS identification process for industrial chemicals could also be combined with the essential use concept which is to "ensure that the most harmful chemicals are only allowed if their use is necessary for health, safety or is critical for the functioning of society and if there are no alternatives that are acceptable from the standpoint of environment and health" [1]. There is a discussion to be had whether CfS that are not critical for society shall remain on the market, even if no alternatives are available. Such a discussion, however, hinges on an agreed operationalisation of the "essential use" concept, in legal as well as in economic terms.

While there is still some room for improving, and especially harmonising, the identification of CfS, our analysis shows that the main reason hazardous chemicals remain on the market is the lack of identified safer alternatives. As a consequence of the lack of alternatives, even identified CfS often remain on the market. The lack of alternatives is at least partly due to the enormous complexity of comparative assessments, which need to be conducted separately for each CfS, CfS-containing product, and use/exposure scenario. The aim to keep a certain "chemical diversity" on the market for pesticides and biocides, in order to reduce the risk of resistance development, makes it problematic to consider non-chemical alternatives.

A more even distribution of the comparative assessments between the member states as well as improved coordination on the methodologies used could potentially reduce the workload of strained member state authorities. Systematic and reliable comparative assessments, however, require knowledge on hazard and risk profiles of the potential alternatives that are already on the EU market. For this purpose,

an EU-wide database on composition, use, hazards and risks would be an essential prerequisite, which could be made accessible for competent authorities only, in order to account for concerns regarding intellectual property rights.

The insufficient incentives for companies to identify safer alternatives to identified CfS is a fundamental concern. The few minor additional administrative demands that are put on companies that use CfS seem to provide insufficient incentives for substitution, although it has been argued that the mere presence of CfS could trigger information requests from downstream users, which is supposed to create a market demand for more benign chemicals [27]. Vague reputational benefits and the "green mindset" of innovative companies might not always be sufficient to counteract these economic concerns. In fact, a review by ECHA concluded that the substitution to safer alternatives yielded no competitive advantage [26].

Companies submit their own analysis of alternatives as part of the REACH authorisation process. Obviously, it is not always in the interest of a company to identify alternatives to economically valuable chemicals and products, which might then, as a consequence, loose market access. Non-chemical alternatives might also have a distinct disadvantage in this setup, as such alternatives usually do not have dedicated stakeholders who will flag it to the competent authorities during the stakeholder consultation of the search for alternatives. Therefore, there might be an argument to be had that regulatory authorities should play a larger role as information and knowledge brokers in the alternative assessment of industrial chemicals. Governments can also foster safer alternatives by funding innovation, thereby addressing the issue of knowledge spill-overs, which reduce innovators' incentives [71]. This can be achieved through research and innovation programmes, or by providing tax credits for expenses related to research and development. The 'Safe and sustainable by design framework' initiated by the European Commission [60] is a promising initiative in this direction.

However, in order to create a stronger demand for safer alternatives it must be made more costly to use hazardous chemicals. A stricter implementation of the Polluter Pays Principle [72]—so that companies would bear the full cost of the negative impacts from production, use and disposal of products containing hazardous substances—would create incentives to reduce the use of such substances on the European market. Taxes on hazardous pesticides, for example, motivate farmers to use products with lower risk [73]. Fees on the use of CfS could have a similar effect and reduce the demand for CfS-containing products. A change of relative prices in favour of less hazardous chemicals would also lead to a higher return of investments, in favour of innovation in alternative technology [74].

Revenues from taxes or fees on hazardous substances could be used to support research and innovation as well as substitution programmes targeting specifically challenging sectors or substances, such as chromium plating or rodenticides [75]. Experiences from toxic use reduction programmes in the U.S., where companies using hazardous substances pay small fees that finance information campaigns and demonstration facilities have provided promising results (California Air Resources [76, 77]. Revenues from taxes or fees could also be used to finance the work of authorities with substance evaluation and the implementation of the substitution principle in general.

Conclusion

The substitution principle is a cornerstone of the EU Chemicals Strategy for Sustainability and the ambition of a non-toxic environment. A generally accepted framework for identification of hazardous substances and alternative assessments has been established through the regulations on pesticides, biocides and industrial chemicals. There is emerging evidence that the listing of substances of concern on the REACH authorisation list has contributed to a reduction in the use of these substances in the EU. However, the lack of public data on individual hazardous chemicals is a major obstacle for evaluating the impact of regulations on production volumes and use patterns. This lack of data also makes it impossible to assess the substitution choices of individual actors.

Our review also points to considerable challenges in the implementation of the substitution principle. Substitution has progressed slower than anticipated, there are still large knowledge gaps around the hazard and risks related to many substances on the European market, and even for identified substances of concern, safer and technically feasible alternatives are many times not identified or used. To address these challenges, it would be of particular importance to implement a more proactive and systematic approach for the identification of industrial substances of very high concern and to provide stronger incentives for the identification and use of alternatives to substances of concern. Without stronger incentives, making it more costly for companies to continue using hazardous substance relative to safer alternatives, initiatives to promote substitution are likely to have limited success.

Appendix

See Fig. 4.

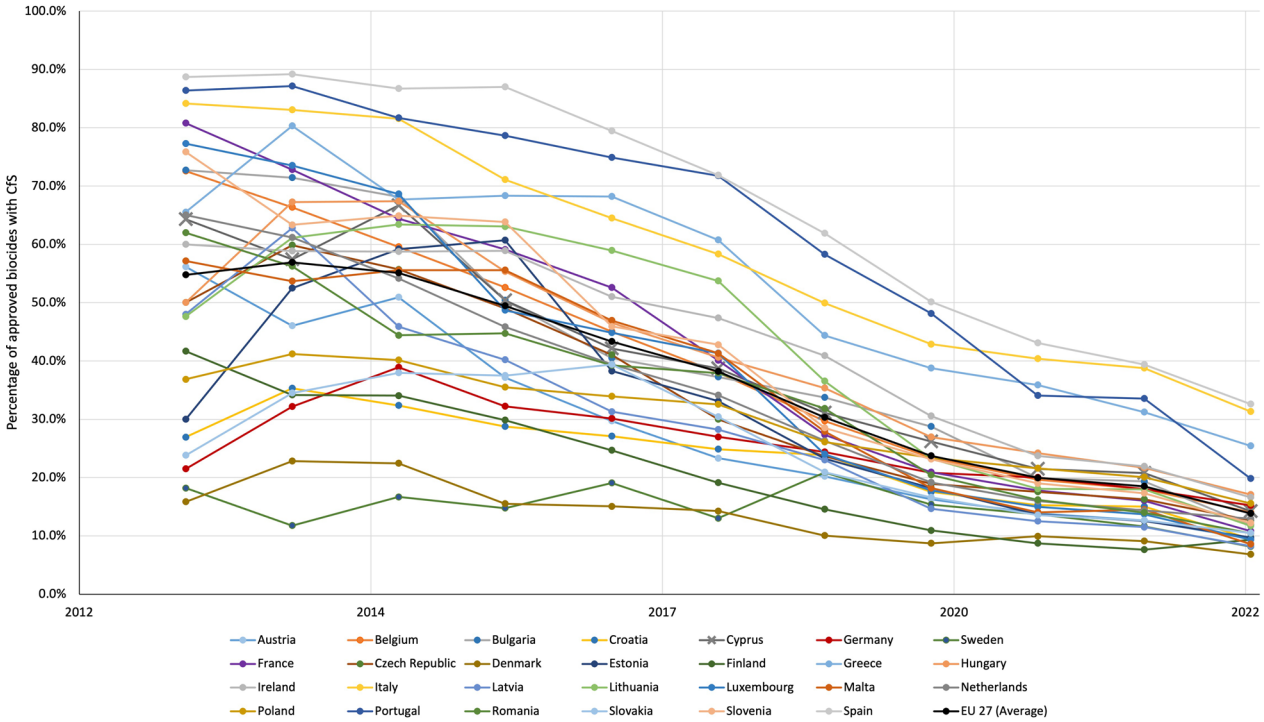

Fig. 4 Share of approved biocidal products with Candidates for Substitution in the European Union over time. The time series for each country shows the end approval date. Note that some biocidal products with candidates for substitution might be available in the market after the end approval date. *Date Source:* ECHA [44]

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12302-023-00817-1.

Additional file 1. Data Sources.

Acknowledgements

Funding from the Swedish Research Council FORMAS and the Centre for Future Chemical Risk Assessment and Management (FRAM) at the University of Gothenburg, is gratefully acknowledged.

Author contributions

D.S.: conceptualisation, methodology, investigation, writing—original draft, writing—review and editing, project administration, funding acquisition; M.M.: formal analysis, investigation, visualisation, writing—original draft, writing—review and editing; L.L.**:** investigation, visualisation, writing—original draft, writing—review and editing; T.B.: conceptualisation, methodology, investigation, writing—original draft, writing—review and editing project administration, funding acquisition. All authors read and approved the final manuscript.

Funding

Open access funding provided by University of Gothenburg. The study was funded by the Swedish Research Council FORMAS, Reference Nos. 2016-01238 and 2020-00920, and the Centre for Future Chemical Risk Assessment and Management (FRAM) at the University of Gothenburg. The funders had no role in the design of the study, the collection, analysis, and interpretation of data or in writing the manuscript.

Availability of data and materials

All data generated or analysed during this study are included in this published article and its Additional file 1.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

T.B. is an unpaid member of the EU Commission's Committee on Health, Environmental and Emerging Risks (SCHEER). T.B. is also an unpaid member of the board of the International Panel on Chemical Pollution (IPCP), a Swiss foundation working on global issues related to chemical pollution. T.B. is also an unpaid member of the board of the Food Packaging Forum (FPF), a Swiss foundation working on chemicals in food contact materials. M.M., L.L., and D.S. declare no conflict of interest.

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Received: 8 August 2023 Accepted: 18 November 2023
Published online: 05 December 2023

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