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An academic researcher's guide to increased impact on regulatory assessment of chemicals†

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The interactions between academic research and regulatory assessment of chemicals may in theory seem straightforward: researchers perform studies, and these studies are used by regulators for decision-making. However, in practice the situation is more complex, and many factors decide a research study's regulatory use. According to several EU chemical legislations, all available and relevant studies can be used in hazard and risk assessment of chemicals. However, in practice, standard tests conducted under GLP and sponsored and provided by industry are predominantly used. Peer-reviewed studies from independent sources are often disregarded or disputed since they often do not comply with regulatory data requirements and quality criteria. To help bridge such a gap, the aim of this paper is to give an overview of the general workings of legislation of chemicals and propose a set of actions to increase the usability of research data. In the end, this may increase the use of academic research for decision-making and ultimately result in more science-based policies. From a policy perspective, useful scientific evidence comprises those studies that are sufficiently reliable and relevant. This is not in contradiction to the aims of research and generally accepted scientific standards.

Environmental impact

Science used in policy decision has the potential to solve environmental problems and impact the society in a more sustainable direction. However, reaching outside the academic sphere has proven to be difficult for researchers, partly because of a lack of knowledge of the regulatory processes. From a policy perspective, useful scientific evidence comprises those studies that are sufficiently reliable and relevant. This is not in contradiction to the aims of research and generally accepted scientific standards, but there are no direct reward mechanisms within academia for research that proved valuable for society which makes this a less desirable and clear goal for researchers. This paper presents ten actions for researchers who strive to have an impact on regulatory assessment of chemicals.

Introduction

Regulatory hazard and risk assessment of chemicals is complex, and for many chemicals assessments are hampered by data gaps and other uncertainties that need to be handled. Sometimes this results in lengthy discussions and controversies about the exact magnitude of the risk. Examples of highly debated cases include assessments of the brominated flame retardant decaBDE, the industrial chemical bisphenol A (BPA), and the herbicides atrazine and glyphosate.[1–5] For all these chemicals, the reliability (*i.e.* inherent quality) and relevance of peer-reviewed studies, and hence their usefulness for hazard and risk assessments, have been a question of debate. Atrazine was banned in the European Union (EU) in 2004, [6] but it remains the second-most widely used herbicide in the US. The USEPA has been accused of being captured by the pesticide industry after not allowing peer-reviewed ecotoxicity studies to influence the assessment.[3] For both decaBDE and BPA, discussions regarding use of peer-reviewed studies have been ongoing for several years, and recent regulatory dossiers from the European Chemicals Agency (ECHA) and the UNEP Persistent Organic Pollutants Review Committee (POPRC) include peer-reviewed studies. ECHA proposes that decaBDE shall not be manufactured, used or placed on the market, and BPA was recently listed on the EU Candidate List as it is assessed as being toxic for reproduction. POPRC has prepared a proposal to include decaBDE in the Stockholm Convention on Persistent Organic Pollutants.[7–9] The assessment of glyphosate is an emerging controversy, in which the European Food Safety Authority (EFSA) recently concluded that the chemical is "unlikely to pose a carcinogenic hazard to humans", while the

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International Agency for Research on Cancer (IARC) classifies it as "probably carcinogenic to humans".[10,11] EFSA based its conclusions mainly on prescribed data requirements by EU PPP legislation (predominantly standard tests conducted under GLP and sponsored and/or provided by industry, but not excluding open literature data that meet pre-defined quality criteria). IARC, on the other hand, used peer-reviewed literature for its assessments and judged these studies to be more reliable than EFSA did, hence the differences in classifications.[4] Even though it is not always possible for a reader of a chemical assessment to determine in detail how individual studies were allowed to influence the final conclusions, it is argued that the controversies surrounding these four chemicals demonstrate that the use of peer-reviewed studies can be improved.

In addition to management of chemicals, there are other areas within the field of environmental policy, such as management of resources, climate change, and land use, that struggle to improve the relationship between science and policy.[12–15] Previous research suggests that peer-reviewed studies are more likely to influence policy if the studies are seen as credible, relevant, and/or legitimate.[16] Still, systematic research on what influences the impact of peer-reviewed studies in policy decisions is largely missing.

In the EU, producers and importers of chemicals are responsible for providing data on human health and environmental hazards.[17,18] According to the legislations, any new (eco) toxicity study should be performed according to validated test guidelines (if such guidelines exist), such as those adopted by the Organization for Economic Co-operation and Development (OECD), the US Environmental Protection Agency (US EPA), and the European and Mediterranean Plant Protection Organization (EPPO). The use of such standards is argued to improve the reliability and reproducibility of the studies. In addition, the laboratories where studies are performed should comply with the requirements stipulated within the system for Good Laboratory Practices (GLP).[19] GLP was introduced to safeguard the truthfulness of the studies after cases of fraud.[20] Test guidelines and GLP aid in comparison and use of data across chemicals, countries and jurisdictions, *i.e.* through Mutual Acceptance of Data.[21] However, the use of GLP and test guidelines also has its drawbacks. Although GLP guarantees *e.g.* the use of the calibrated research equipment and archiving of all basic data, GLP is not a guarantee for scientific excellence,[22] and the standard test guidelines have been criticized for not addressing some of the most sensitive and relevant endpoints.[23–26]

In addition to providing the guideline studies required by the legislation, industry also has the possibility to, or for some legislations is obliged to, include available peer-reviewed studies in the information package that is submitted for the assessment of hazards.[27–29] This does not necessarily mean that the peer-reviewed study is used in the risk assessment as it may be dismissed because it is considered to be of insufficient reliability or low relevance. In practice, it is not known in detail to what extent the peer-reviewed literature is consulted in regulatory processes. For most chemicals the availability of peer-reviewed data is scarce or non-existing,[105] but even for chemicals that have been researched by independent scientists, the regulatory chemical assessments have been shown to be based primarily on toxicity studies sponsored and/or conducted by the chemical industry.[2,30,31] This is problematic for at least two reasons. First, we run the risk of making less informed decisions when excluding peer-reviewed studies. Second, there is an inherent conflict of interest in the system when the main responsibility for data gathering and risk assessments lies on the party that has economic interest in having the chemical on the market.[32–37]

Registration of chemicals is performed by the companies that import or manufacture that particular chemical, and hence the focus in this process is to comply with the regulatory demands in order to get a market approval. Science, on the other hand, can take different perspectives and may include additional aspects, beyond the specific regulatory demands in their investigations.[38] Non-standard studies can therefore provide regulatory assessments with important information not gained through the use of guideline studies, for example by using a sensitive test organism or a novel endpoint. Exclusion of peer-reviewed studies is further an inefficient and inadequate use of experimental animals and research funds.

To influence the decision-making process, peer-reviewed studies need to satisfy the regulatory requirements regarding reliability and reproducibility, and be of relevance for the particular assessment.[19] This is not always achieved. For example, peer-reviewed (eco)toxicity studies are often insufficiently reported. This will hamper, or may even hinder, the use of these studies for regulatory hazard and risk assessments.[39–41]

The purpose of this paper is to contribute to an increased awareness among academic researchers on how peer-reviewed studies can be made more useful in regulatory assessment of chemicals without compromising with the overall aims of research and generally accepted scientific standards. In particular, we aim to outline the general workings of legislation of chemicals and propose a set of actions that researchers can take to increase the usability of their research results. The suggested set of actions are generic, but our examples and experiences mainly come from the EU chemicals and water legislations. The actions have been divided into three categories, each representing a step towards increased regulatory impact: finding relevant regulatory information; increasing the regulatory usefulness of peer-reviewed data, and additional possibilities to contribute to legislation of chemicals. This is a guide aimed at academic researchers. However, we also encourage risk assessors and regulators to modify their rules of procedure with the aim to contribute to a better dialogue with academia and thereby improve the use of peer-reviewed studies in chemical legislation, and ultimately improved chemical assessments.

How academic researchers can increase their regulatory awareness and promote the use of peer-reviewed studies in decision making

Increasing the knowledge of the workings of regulatory processes among academic researchers is a step towards better

alignment between science and regulatory risk assessment. It is also a step towards increased use of peer-reviewed studies in hazard and risk assessment of chemicals. This increased 'regulatory awareness' includes an understanding of issues such as the following. What are the prerequisites for use of scientific studies in regulatory decision-making? Which factors influence regulatory decisions? What can be done to increase the regulatory usefulness of peer-reviewed studies? The following ten actions provide a starting point for academic researchers that would like to understand more about science-policy interactions in the field of chemicals and management of chemicals of potentially high concern for human, life-stock and the environment (Table 1).

Find relevant regulatory information

Action 1. Identify applicable legislation and guidance documents

Legislation of chemicals aims at identifying and managing chemicals of high concern. Examples of targeted properties are carcinogenicity, mutagenicity, and reproductive toxicity (CMR), persistence, potential to bioaccumulate, endocrine disruption (ED), and sensitization. The applicable legislation determines the regulatory data requirements and enables tracing of the regulatory assessment underpinning decisions (see Action number 2).

Chemicals are regulated depending on their intrinsic hazardous properties and/or intended use, and if used in different product types each chemical may be regulated under more than one legislation. For example, UV-filters are used in sunscreen products and in paint, and the health aspects are therefore regulated by the cosmetics regulation for sunscreen products, and by the REACH regulation for paint.[42] The provisions in different legislations differ and a chemical can be restricted for a particular use, but allowed in other applications. These differences may be due to a number of factors including dissimilar risk assessment practices, differences in data requirements, differences in the use of the chemical resulting in different exposure patterns (*e.g.* professional *vs.* general consumer use), or that the scopes and protection goals in the legislations vary.

Table 1 The suggested actions

Ten actions for increased understanding about science–policy interactions in the field of chemicals
1. Identify applicable legislation and guidance documents
2. Identify relevant regulatory procedures and their outcomes
3. Identify relevant assessments from non-regulatory stakeholders
4. Evaluate chemical assessments
5. Report studies in a way that enables regulatory use
6. Place academic studies in a regulatory context
7. Submit studies and comment on current assessments and processes
8. Create a dialogue with stakeholders
9. Write for policy makers
10. Train the next generation

The requirements within each legislation are usually explained in more detail in appropriate guidance document(s). Examples of relevant guidance documents for academic researchers working with chemical exposure and effects on humans and the environment are those intended to provide guidance for industry and authorities when testing and performing hazard or risk assessments. In addition, guidance documents describing status assessments and quality standard development under the Water Framework Directive (WFD) may also be of relevance.

The legislations of chemicals are, for the purpose of this paper, divided into different groups. Table S1 in the ESI† gives examples of legislations with publicly available assessment information.

Legislation applicable to chemicals in general. There are two legislations applicable to a broader set of chemicals: the regulation on the classification, labelling and packaging of chemicals and mixtures (the CLP regulation), and the regulation concerning the registration, evaluation, authorization and restriction of chemicals (the REACH regulation). The CLP regulation is the European implementation of the United Nations' Globally Harmonized System of Classification and Labelling of Chemicals (GHS). The CLP regulation requires manufacturers, importers and downstream users to classify the hazards of a chemical, and label it accordingly, based on available data. A hazard classification can thereafter trigger other legislations to impose restrictions, for example, ban of chemicals classified as CMR (categories 1A, 1B and 2) under the Toy Safety directive. Hazard classifications for individual chemicals and certain mixtures can be found in the Classification & Labelling Inventory database available through the ECHA webpage.

The REACH regulation insists each importer/producer to register chemicals and mixtures manufactured or imported in quantities at or above 1 tonne per year. Information requirements for the registration dossier increase with the annual quantity manufactured or imported. The registration dossier shall contain hazard information and, where relevant, an assessment of the associated risks, and suggestions for how these risks can be controlled. The REACH regulation covers in principle all chemicals and mixtures unless they are exempted, *i.e.* regulated under another specific legislation, such as the plant protection products regulation. Within REACH, chemicals posing unacceptable risks to health or to the environment can be restricted, or phased out, and companies can request authorization for continued use of "substances of very high concern" (SVHC).

Legislation regulating specific use of chemicals. Specific legislations are in place for chemicals with potentially high risks to humans, live-stock and/or the environment. These apply to chemicals designed to be toxic (*e.g.* plant protection products and biocides), designed to be biologically active (*e.g.* pharmaceuticals) and/or include widespread and long-term exposures (*e.g.* feed and food additives). These legislations generally require an approval of a chemical and/or product before being placed on the market. The authorization procedure typically includes a risk assessment of the products taking into account specific use conditions or exposure scenarios.

Product-specific legislation. Product-specific legislation related to chemicals is available for the following product groups in the EU: toys, electrical and electronic equipment, construction products, medical devices, and food packaging materials. These legislations generally build on the hazard information (*i.e.* classifications) provided by the CLP regulation. In some product-specific legislations it is specified that products may not contain chemicals classified as having specific properties, such as CMR (*e.g.* the Toys Safety directive), and other legislations restrict the use of specific chemicals in products (*e.g.* the RoHS directive on the restriction of the use of certain hazardous chemicals in electrical and electronic equipment, or the cosmetics regulation). There are also legislations that specify the allowed maximum residue levels in products (*e.g.* the Construction Products Directive). Recently, the Swedish Chemicals Agency suggested development of a product-specific legislation for textiles.[43]

Legislation based on the intrinsic properties of the chemical. Global conventions for restriction of chemicals based on the intrinsic properties of chemicals include the Stockholm Convention on Persistent Organic Pollutants (POP), the Convention on Long-Range Transboundary Air Pollution (CLRTAP), and the Minamata Convention on mercury. The Stockholm Convention aims at prohibiting and/or eliminating the production and use of chemicals that are identified as POPs. A POP is a chemical that bioaccumulates, is persistent in the environment, is toxic, and has a potential for long-range transport. The CLRTAP was the first international legally binding instrument to deal with problems of air pollution. It stipulates regulation, monitoring and evaluation of, for example, ground-level ozone, POPs, heavy metals, and volatile organic compounds. The Minamata Convention is a global treaty to protect human health and the environment from the adverse effects of mercury. It includes a ban of new and phase out of existing mercury mines, phase out of mercury in a number of products, control measures on emissions and disposal regulations. The Minamata Convention is expected to reach the number of necessary ratifications within a short period of time and will thereby enter into force.

Legislation taking the perspective of the receiving environment. The Water Framework Directive (WFD) and Groundwater Directive and Marine Strategy Framework Directive (MSFD) establish objectives to be reached in the aquatic environment. Other examples of legislation taking the perspective of the receiving environment are the Industrial Emissions Directive (IED), and the Air Quality Directive.

The WFD includes, for example, classification of the chemical status of surface water, where the goal is that the measured environmental concentrations of priority substances do not exceed Environmental Quality Standards (EQS) (listed in the Directive on Environmental Quality Standards). As part of the assessment of ecological status, river basin specific pollutants (RBSPs) are also taken into account and concentrations are compared to EQSs established at the national level. Within the MSFD assessment of good environmental status (GES), similar assessments to those within the WFD are made; the priority substances and RBSPs of marine relevance as well as observed effects are taken into account.

Legislation concerning waste. The Basel Convention is an international treaty that was designed to prevent transfer of hazardous waste from developed to less developed countries. The Sewage Sludge Directive prohibits use of untreated sludge on agricultural land and lists threshold values for concentrations of heavy metals. The Urban Waste Water Treatment Directive aims at protecting the environment from adverse effects of wastewater discharges from cities and the industrial sectors.

Action 2. Identify relevant regulatory procedures and their outcomes

The assessment procedures can be more or less transparent, *i.e.* access to assessment dossiers and the underlying data vary between legislations, and over time (ESI, Table S1†). In the REACH legislation dossiers are available for chemicals produced or imported in amounts above one tonne, and the amount of data increases with each tonnage span. In these dossiers, information and effect values from (eco)toxicity studies performed by industry may be obtained, but full access to these studies are normally not granted within any legislations. There are exceptions to this though; EFSA recently announced that they will release raw data for glyphosate to the NGO Corporate Europe Observatory and European Parliament members from the Greens.[44]

For plant protection products the EU Pesticides database provides an overview of information on all active substances that have been reviewed. It includes the formal documents for individual active substances, *i.e.* the review report and the decision from the European Commission. At the EFSA website, EFSA's conclusions are available. These include information on substance properties, exposure estimates, and the summary of the risk assessment. For some active ingredients, the Draft Assessment Report with more details on the risk assessment and its underlying studies can be retrieved. The human health and environmental risks of the active substances of plant protection products are evaluated at the EU level. Formulated plant protection products, however, are approved at the national level and the availability of information varies between countries.

A list of approved active substances in biocidal products is available through the ECHA website. The assessment report, in which the risk assessment is summarised, is available through the European Commission's website CIRCABC. The C&L Inventory is a database with information on classification and labelling of substances (and some specific mixtures) according to the CLP regulation. It includes legally binding harmonized classifications according to Annex VI to the CLP regulation as well as proposed classifications made by notifiers (producers/importers). For pharmaceutical products, a summary of the environmental risk assessments is available. However, this requirement only applies to new market approvals.

Within the WFD a small selection of assessments is prepared by member states for use at the EU-level (priority substances) or national level (RBSPs). At the EU-level, chemicals are prioritized

according to a joint prioritization activity involving the member states, industry and NGOs, and at national level according to each country's prioritization. The European dossiers are often publicly available. Because the EQSs are based on available studies, peer-reviewed studies are frequently used.

In addition to the selected assessment procedures explained above, expert groups at different global and EU authorities perform assessments more or less regularly. This may result in risk management decisions, for example, restrictions in the use of certain chemicals. The initiative for these assessments can come from the European Commission, international organizations, authorities, or member states. Table S2 in the ESI† gives examples of currently active scientific committees and other institutions that provide publically available chemical assessments.

Besides regulating chemicals, national and European agencies and authorities also publish reports that may be of interest to academic researchers. These reports provide insights into what regulators are prioritizing, current topics of interest, future legislations, and working plans. Although there are exceptions, these reports are rarely published as scientific papers and hence they do not appear in the scientific databases. Hence, to learn about them, researchers need to actively search for them. Alerts about new reports can be obtained by subscribing to newsletters from relevant agencies. Also non-English speaking countries produce reports in English.

Action 3. Identify relevant assessments from non-regulatory stakeholders

Non-regulatory actors sometimes perform assessments and make recommendations based on either current legislation, or according to their own guidelines. Consequently, they can address chemicals that are not yet regulated/assessed but may become so in the future, and they can address regulated/assessed chemicals but arrive at dissimilar results compared to the authority as a result of different assessment guidelines or different interpretations of these.

Current examples include the NORMAN network, a network of reference laboratories, research centres and related organizations for the monitoring and biomonitoring of emerging environmental chemicals that provides lists of chemicals suspected to be of environmental and/or human health concern and thereby considered relevant for environmental monitoring.[45] The non-profit organization ChemSec has currently identified 844 hazardous chemicals on the Substitute It Now-list (SIN-list)[46] based on the criteria established by the REACH regulation.[47] The list contains chemicals, which are regulated or, according to ChemSec, are likely to become so under the REACH regulation. The Endocrine Disruption Exchange produces the TEDX List of Potential Endocrine Disruptors (http://endocrinedisruption.org/). The Swedish Trade Association for the Research-Based Pharmaceutical Industry has developed a voluntary environmental classification system for pharmaceuticals, and risk assessments are available through their webpage (http://www.fass.se).[48] The guide is based on the guideline for environmental risk assessment of pharmaceuticals[49] but adjustments have been made since additional sales data are available for Sweden. In addition, the classification system uses peer-reviewed studies to a greater extent compared to the regulatory assessments performed by the European Medicines Agency.[50]

Action 4. Evaluate chemical assessments

The credibility and usefulness of available chemical assessments need to be evaluated and scrutinized,[51] regardless of their sender. In this process, it is important to recall the purpose, scope and limitations of the framework in which the assessment was produced. When evaluating assessments, the following considerations are recommended as a first step:

- What are the final conclusions of the assessment? Did the assessment result in any risk management measures, *e.g.* restrictions or mitigation measures? Did the assessment result in classification and labelling?
- Which studies were considered to provide the key evidence? How do the studies relate to the others included in the assessment? Were data gaps identified?
- Who performed the assessment, and are there possible financial conflicts of interest? Organizations with specific interests may sometimes be difficult to identify. The organization's name may give false associations, like the American Conference of Governmental Industrial Hygienists (ACGIH), which is an industrial organization that has been criticized for misrepresentation of studies.[52–54] Another example is the Center for Indoor Air Research (CIAR), which was formed by tobacco companies to divert attention away from the negative effects of second-hand smoke.[55] Even highly respected organizations like EFSA, IARC and the European Commission have been accused of biased expert groups,[56–59] but they, and also many other major organizations in the field, now have policies that aim to prevent bias and increase transparency by requiring that potential conflicts of interest are declared and scrutinized.
- When was the assessment performed/updated? Are there studies of sufficient relevance and reliability that were not included in the assessment? If not, which studies were excluded and why? Would the inclusion of these studies alter the final conclusions of the assessment? Previous studies demonstrate that even when risk assessors have access to the same studies, the selected datasets may vary among risk assessors. Such a biased study selection may influence risk assessors' conclusions.[60–62]
- How were the included scientific studies evaluated in terms of their adequacy, and was the result from this evaluation reported in a transparent manner? Are there limitations with the selected evaluation method in terms of scope and the details of the criteria? How were the results from several studies weighted and merged to arrive at a conclusion? Previous studies show that the choice of study evaluation method matters,[40] and that assessment processes may lack transparency.[63]
- Are there any controversies or unusual uncertainties discussed in the assessment? Previously developed criteria for transparency of the assessment emphasize the importance of clearly stating uncertainties.[63]

• If more than one assessment is available for the same chemical: how do they compare in terms of the bullets above? Are different conclusions the result of different purposes and scopes of the assessment, or are there other reasons? A previous study shows that risk assessors may use different studies and therefore arrive at different conclusions regarding the risk of BPA.[2] The EQS values for river basins (RBSP) within individual EU member states under the WFD show lack of harmonization with examples of EQS values that differed more than tenfold from each other.[64]

• If there is no assessment performed for a chemical, what is the reason for this?

Increase the regulatory usefulness of peer-reviewed data

Action 5. Report studies in a way that enables regulatory use

Ensuring that a peer-reviewed study is reliable, reproducible and sufficiently reported is crucial both in order to fulfil the general scientific quality standards as well as for its regulatory use. Seemingly conflicting research results, in combination with retractions and insufficient reporting of peer-reviewed studies, have triggered a debate about the reliability of peer-reviewed (eco)toxicological and biomedical studies.[39,65–68]

Common mistakes when reporting (eco)toxicity studies include lack of information regarding measured concentrations and choice of analytical technique, use of controls, statistical evaluations and statistical power, and confounding factors. This obstructs the reliability evaluation of studies and consequently excludes studies from regulatory use.[39,40] One simple way to increase a (eco)toxicity study's regulatory use is to base it on a guideline study in terms of study design and reporting of results, and then modify it according to the research need by adding endpoints and doing slight modifications that are clearly justified. In response to the discussion about the reliability of peer-reviewed studies, several recommendations have been made by academic researchers, consultancies and governmental representatives to ensure sufficient reliability and reporting of peer-reviewed studies.[35,65,69–72] However, still there is no generally agreed method for reporting of (eco)toxicity, persistence or bioaccumulation studies. For (eco)toxicity studies, reporting recommendations that cover critical aspects to be considered in the design, performance and reporting of a study have been proposed.[69,73] These recommendations are freely available at http://www.scirap.org (Science in Risk Assessment and Policy), and they can be adjusted to also be used on higher-tier studies.[74] To ensure adherence to regulatory processes, these reporting recommendations are based on currently used evaluation methods for (eco)toxicity studies and the reporting requirements as stipulated by the OECD test guidelines. To aid in this work a check-list for reporting is available from the SciRAP webpage. For analytical methods used to quantify occurrence of chemicals in humans and the environment, the Norman Network has proposed detailed recommendations for reporting of methods and results. The recommendations include: method definition, documentation of the process, general requirements, applicability domain, prevalidation, intra-laboratory performance, and inter-laboratory transferability.[75]

Besides ensuring sufficient reporting, there are also other measures concerning objectivity, independence, and transparency that can be taken to enable use of peer-reviewed studies in assessment of chemicals. Conflict of interests, with regards to financial, social, political and personal interests, should include a specification of the extent to which the funder was allowed to influence the design, performance and analysis of a study.[35,106] To counteract publication bias, negative results should be made publically available, preferably in peer reviewed papers (ESI† is one option, however results should be reported in the main paper in order to make the results searchable in scientific databases). Providing raw data increases the credibility of the results and gives risk assessors the opportunity to reuse data, provided that data are presented in accessible ways.[76–79] This is also in line with the present and future requirements of open access publication of both peer-reviewed articles and data.[80] In ecotoxicology, access to raw data makes it possible for risk assessors to calculate additional effect values other than those provided by the authors, for example, EC_{10}-values instead of the often provided NOEC-values.[81] An informative title and abstract is helpful since risk assessors may not have time to read full papers in search of suitable data. Publishing studies with open access safeguards risk assessors' access to them.[15,70]

Action 6. Place academic studies in a regulatory context

Academic researchers need to describe how a particular peer-reviewed study relates to existing or ongoing regulatory assessments. Performing research in an area of societal importance does not automatically qualify the results for inclusion in regulatory assessments. In an interview study with UK employees working with environmental and science–policy issues related to management of resources, flooding, and environmental change, the interviewees expressed concerns regarding usability of research results in decision-making, even though the research was intended to be policy relevant. The same study concluded that research results were more likely to be considered relevant for ongoing regulatory processes if the research was managed by someone familiar with policy processes.[15]

There is no agreement among regulators and researchers as to whether or not authors of peer-reviewed papers should discuss the research results in the perspective of the current regulatory assessment. Some argue that this is an unnecessary introduction of bias and values, while others argue that academic researchers are obligated to do so, especially if the research is funded by public resources. If a discussion concerning the regulatory use of the studies is included it is however important to clearly differentiate it from the results of the study.[15,35,82] The EU Horizon 2020 research programme "Inspiration", which aims at developing a strategic research agenda for soil and land use management that meets societal needs and challenges, has developed indicators for societal

relevance that can be used when evaluating research proposals, as well as when evaluating outcomes of research projects. One of these indicators is a detailed presentation from the researchers on how and where research results can directly be implemented in policy.[83]

Regardless of whether authors of peer-reviewed papers discuss the regulatory use of their studies or not, it may still be important for them to understand how their results relate to current regulatory processes. To do so, the following aspects could be considered:

- The relevance of the new results in relation to the current regulatory assessments. For (eco)toxicity studies, general relevance criteria have been developed to guide risk assessors and researchers in this process.[69,73]
- The data gaps addressed by the new results, and how the results challenge or support existing assessment(s) and/or classification(s), or the need to prioritize the chemical for regulatory action if no such assessment is yet available, or the need to perform additional testing.
- If the new results are in conflict with existing studies it should be reflected upon why this may be the case, for example, if differences in study design may explain the different outcomes and how the different designs affect the relevance of the studies.

Additional possibilities that contribute to chemicals legislation

Action 7. Submit studies and comment on current assessments and processes

Academic researchers can submit studies to ongoing or planned assessments and to databases, and engage in public consultations concerning specific chemicals and the continuous development of the legislation of chemicals. Public consultations are often used within the EU and create opportunities for the academic community to add state of the art knowledge to the chemicals legislation and chemical assessment process. This is a welcome opportunity since previous studies from the environmental field raise concerns that science is not involved early enough in policy processes.[15]

ECHA invites stakeholders to comment on draft opinions regarding authorization and restriction of chemicals, and harmonized CLP classification proposals. There is also a possibility to comment on guidance documents for chemical assessments during the revision of these. EFSA invites stakeholders to add studies to their scientific assessments and to engage in public consultations on draft versions of scientific assessments and institutional initiatives. In addition, the European Commission invites EU citizens to comment on draft opinions, as well as on future policies and legislations. The Secretariat of the Stockholm Convention invites stakeholders to comment on proposals for listing chemicals under the Stockholm Convention, and IARC welcomes data to their monographs (ESI, Table S2†, column 5).

Another way to make regulatory agencies aware of peer-reviewed studies is to include them in publically available databases used in regulatory processes. Table S3 in the ESI† lists examples of such databases.

Action 8. Create a dialogue with stakeholders

To engage in direct dialogue with regulators and other stakeholders, it is important to understand the potential societal use of research results. Here the strength of face-to-face meetings should not be underestimated.[15] A stakeholder dialogue may take different forms, ranging from presenting research results at workshops and conferences attended by stakeholders (preferably a tripartite approach like SETAC has) to co-supervising PhD-candidates, co-organizing seminars, direct correspondence, and inviting stakeholders to participate in reference councils. Such collaborations can also include a dialogue regarding formulation of research questions and the design of future studies.[15] The indicators for societal relevance related to dialogue with stakeholders produced by the research programme "Inspiration" include: involvement of relevant stakeholders in a reference network, the use of professional resources for communication of research results to stakeholders, and cooperation with stakeholders when performing the research.[83] One example of a research programme initiated by stakeholders is the Swedish programme "MistraPharma" (http://www.mistrapharma.se). A group of key persons working at different organizations with the issue of pharmaceuticals as environmental contaminants contacted relevant stakeholders from regulatory agencies, the health care sector, and wastewater management companies before contacts with appropriate academic researchers were established. The close contacts between researchers and stakeholders remained during the eight years the programme was ongoing and professional communicators were used to organize meetings. As a result, research outcomes were considered to be of societal relevance, and several spin off projects were developed by different clusters of stakeholders and researchers.[84]

Action 9. Write for policy makers

Academic researchers are trained to critically evaluate studies and to make estimates about future perspectives. It is therefore argued that these skills, in combination with peer-reviewed studies, should be used to improve management of chemicals.[38] Since policy makers and their advisers often are short of time, there is also a need to summarize policy-relevant key findings and their implications.[15,85,86]

An example of a policy initiative from academic researchers is the Madrid Statement on poly- and perfluoroalkyl substances (PFASs),[87] which has resulted in several policy-relevant interactions such as inclusion in an agency report proposing national restrictions in firefighting foam,[88] invitations to participate in various policy discussions, *e.g.* EU meeting in Brussels and in the Helsinki Chemicals Forum, and contacts with wastewater companies, down-stream users, and NGOs. Recommendations regarding improvements in the environmental risk assessment for pharmaceuticals are another example.[89] These recommendations have resulted in meetings with policy makers at both national and EU levels. Another topical example of a process

where academic researchers have made substantial contributions and clarifications concerns the establishment of criteria for endocrine disrupting chemicals within the EU.[90–93]

In addition to evaluating current policy and management decisions, there is a possibility for academic researchers to engage in expert tasks such as writing reports[94–96] and participate in scientific committees. Unfortunately, this type of work is not rewarded in academia with the currently used measurements for impact (*e.g.* the *h* factor), even though a report addressing policy-relevant issues may exceed the societal impact of a scientific paper multiple times.[97] An examination of how societal impacts of research projects are assessed concludes that measurable impact criteria are rare and that a broader impact including societal value is hard to capture.[98]

Action 10. Train the next generation

Academic researchers should pass on regulatory awareness to graduates. If upcoming academic research results are to guide future updates in legislation of chemicals, training of the next generation researchers has to include knowledge about the regulatory process and how peer-reviewed studies can contribute to decision-making. This has been identified as an important task in order to reach the Swedish environmental objective "A non-toxic environment",[99] but stands in contradiction to the advice often given to academic researchers in their early career; to concentrate on isolated activities that do not include policy considerations.[97] Hence, in order to increase the science–policy exchange and thus societal impact of research, future education programmes in environmental science need to include opportunities for students to increase their knowledge and understanding of regulatory processes, as well as opportunities to interact with relevant actors.

Discussion and summary

Recommendations for a more efficient science–policy exchange are available; these recommendations concern general aspects such as characteristics of the policy process, timing, and dialogue strategies.[100–104] However, specific recommendations for improving science–policy interactions in chemical assessments are currently missing.

There is a gap between academic research and legislation of chemicals. This gap results in unjustified low use of peer-reviewed studies in hazard and risk assessment of chemicals. Partly, this can be explained by low regulatory awareness among researchers. Some may argue that peer-reviewed studies are not intended for regulatory use. This may be true, but there is still no reason why studies should not be used if proven relevant for a particular assessment. In addition, several legislations now state that all available studies should be taken into consideration. Also, in the establishment of EQS values within the WFD, there is no demand on industry to provide data which may leave regulators completely dependent on peer-reviewed studies.

To be successful in science–policy interactions, researchers need an understanding of the complexity of policy decisions, an understanding of the present institutional barriers, and the potential limits of scientific reasoning, together with knowledge of the approaches used in assessment of chemicals. This paper lists ten actions for academic researchers that aim to increase their regulatory awareness, and thereby the possible societal impact of their work. These actions may on the one hand increase the workload of academic researchers, but may on the other hand open up additional possibilities for stakeholder collaborations and funding directed at research of societal interest, as well as saving time when writing scientific papers if reporting recommendations are used.

Research indicates that peer-reviewed studies can contribute to assessments of chemicals, and that even small adjustments in test design and reporting of studies could facilitate their use in regulatory assessments. The freedom of academic science gives researchers the opportunity to investigate aspects beyond regulatory demands and potentially add new perspectives and knowledge related to a specific chemical or exposure situation. If the scientific approach is combined with thorough considerations of the reliability and reproducibility of the study, as well as a clarification of how the research results can contribute to the current regulatory assessments, researchers can increase their impact on decision making in hazard and risk assessments of chemicals.

Conflict of interest

The authors declare no financial conflicts of interest.

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