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Empirical analysis of regulative risk assessment processes of nanomaterials under the Toxic Substances Control Act (TSCA) and European Union regulation concerning the Registration, Evaluation, Authorization and restriction of Chemicals (REACH)

Mirella Miettinen

UEF Law School
P.O. Box 111
FI-80101 Joensuu, Finland

E-mail: mirella.miettinen@uef.fi

Abstract. An empirical analysis of regulative risk assessment processes of nanomaterials under the Toxic Substances Control Act (TSCA) and Regulation (EC) No 1907/2006 of the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) was performed. Risk assessment that has regulatory applicability must be based on legally binding norms, and “process” refers here to the approach taken by the regulatory bodies in the U.S. and the EU to implement those norms. Data consisted of the number of notifications/dossiers for the nanomaterials or the substances that contain also nanoform received by the Environmental Protection Agency (EPA) and the European Chemicals Agency (ECHA), and decisions of the Agencies. The data was analyzed using descriptive statistics and classification. The analysis focused on the challenges in detection of nanomaterials and information collection that are the core functions of risk-based regulation and may create dissimilar compliance requirements for companies. The results show that a loophole in detection of nanomaterials and information collection on them exists in the EU under the REACH, and that regulative risk assessment processes performed by the ECHA and EPA under the REACH and the TSCA, respectively, may result in different compliance requirements for companies. The differences arise partly from the legal provisions that determine the authority and obligations of the Agencies, but also from the decision making practices adopted by the Agencies.

1. Introduction

Nanomaterials have challenged risk governance, i.e., legal and institutional decision making processes in the United States (U.S.) and the European Union (EU) [1]. The main reason for the challenges is that engineered nanomaterials (ENM) [2] have been produced at exponential pace by wide range of industries for diverse and often novel applications. This induces a variety of uncertain and, due to global commerce, often transboundary risks. Generally, risk assessment of chemicals has been considered as an appropriate approach to evaluate the risks posed by the nanomaterials. It consists of hazard identification, dose-response assessment, exposure assessment and risk characterization [3, 4]. Hazard identification “examines whether a stressor has the potential to cause harm to humans and/or ecological systems, and if so, under what circumstances”, dose-response assessment “examines the numerical



relationship between the exposure and effects”, exposure assessment “examines what is known about the frequency, timing, and levels of contact with a stressor”, and risk characterization “examines how well the data support conclusions about the nature and extent of the risk from exposure to environmental stressors” [5]. Absence of standardized test methods and appropriate characterization data, however, results in unrepeatability in the hazard identification of nanomaterials. Exposure assessment of nanomaterials is affected by the same deficiencies, and furthermore, by the lack of information about the products that contain nanomaterials and by difficulties in monitoring the exposure at the workplaces and in the environment. In addition, toxicity of the nanomaterials can be mediated by other physicochemical characteristics than mass (e.g., particle number, surface area, morphology, and chemical composition) that complicates performing the dose-response assessment. Consequently, compared to conventional chemicals, additional properties (e.g., particle size distribution, agglomeration state, surface to volume ratio, and surface chemistry) have to be looked at when performing risk assessment of nanomaterials [3, 6]. The Organization for Economic Cooperation and Development (OECD) has long worked with guidelines for the testing of ENMs but the inconsistencies in testing procedures and reporting of the resulted data still exist [7, 8].

Transnational efforts in the risk regulation of nanomaterials have been mostly limited to technical issues (for example test guidelines formulated by the OECD) and control of more political issues on market entry regulations and reporting rules have been left to authorities of individual jurisdictions [9]. Registration of nanomaterials or chemical substances that contain also nanoforms is relatively new phenomenon, especially in the EU. Many companies operate in both the U.S. and the EU and have to comply with legislations of both jurisdictions. This may create dissimilar compliance requirements for companies in the U.S. and the EU. In this study, regulative risk assessment processes of nanomaterials under the Toxic Substances Control Act (TSCA) [10] and Regulation (EC) No 1907/2006 of the Registration, Evaluation, Authorization and restriction of Chemicals (REACH) [11] are analyzed and the reliability of the processes to detect nanomaterials is inspected. Orders, restrictions, and information and test requirements that have been set during the processes are compared to discover possible differences. In addition, policy factors behind the observed differences in the processes are discussed. Possible stricter national or state legislations are not considered here. In addition, self-regulation by industry associations is not in the scope of this study. To the best of my knowledge, empirical analysis of the regulative risk assessment processes of nanomaterials in the U.S. and the EU has not been performed before.

This article is organized as follows: after the introduction, section 2 illuminates theoretical background of the study and describes the risk assessment processes under the TSCA and REACH, section 3 presents research data and methods applied in this study, section 4 contains the results of statistical and case analyses with accompanied discussion, section 5 discusses the policy factors behind the observed differences in the processes, and in section 6 conclusions are drawn.

2. Theoretical background and regulatory framework

2.1. Theoretical background

This study represents empirical regulatory studies. Under the “better regulation” debate, being active during the last two decades within the EU and on broader international stage embraced for example by the OECD, risk-based and more data-intensive regulation has been called for [12]. This means to control of relevant risks in a way that justifies selective regulatory actions with rational data analysis. The steps of risk-based framework, however, require regulators to make judgements on, for example, prioritization and definition of risks. The regulator has to identify its objectives and the risks that the regulatees may pose to those objectives, and to develop a scoring system to prioritize the risks. This may create a political challenge to the regulator and hinder the use of risk-based framework as a purely technical instrument. Consequently, other theories such as compliance, deterrence, and prevention-based regulation, as well as really responsive regulation have been suggested to complement risk-based regulation [12–14]. Compliance approaches prefer measures that do not include prosecution, whereas

deterrence approaches use prosecutions to prevent prospective infringements. Prevention-based regulation requires the comparative assessment of alternatives with respect to the relevant criteria, such as health and environmental impacts, technical feasibility, and costs. Really responsive regulation means applying a variety of regulatory instruments in a manner that is flexible and sensitive to key factors such as the behavior, attitudes, and cultures of regulatory actors; the institutional setting of the regulatory regime; the interactions of different regulatory tools and strategies; the regimes performance, and changes in these factors. In addition, the regulator should take into account the variation in implementation challenges: detecting, responding, enforcing, assessing, and modifying [12, 13]. Detection and associated information collection are the core functions of the risk-based regulation, and choices that the regulator make, such as deterrence-based enforcement, may affect adversely the compliance of the regulatees. In addition, the reliability of detection processes dictates the coverage of the regulation [12].

Risk-based approach is adopted in the REACH (Article 1(3)) and has been a policy principle for decision making concerning regulation of nanomaterials in the U.S. [15]. Empirical analysis of regulative risk assessment processes of nanomaterials presented here is particularly related to the challenges in detection of nanomaterials and information collection that may also create dissimilar compliance requirements for the companies.

Risk regulation approaches and the rules formulated in each jurisdiction are not independent of the legal culture and antecedent as well as current environmental politics [16]. Previously, for example, transformation in regulatory state [17] in the U.S. and the EU has been studied using the regulation of global environmental and safety risks as an indirect research subject [18]. In this work, policy factors behind the observed differences in the regulatory risk assessment processes are also discussed.

2.2. Risk assessment processes

2.2.1. New chemical substances under the TSCA. In the U.S., manufacturers or importers of new chemical substances have to file a pre-manufacture notice (PMN) or a significant new use notice (SNUN) to the Environmental Protection Agency (EPA) 90 days prior to the manufacture/import of the chemical or a significant new use of an existing chemical (15 U.S.C. § 2604(a)) (Figure 1). In addition, the TSCA contains some limited exemptions for the PMN and SNUN in which an exemption notification has to be submitted to the EPA (15 U.S.C. § 2604(h)).

The EPA determines the chemical substance based on its molecular identity, i.e. the types and number of atoms and chemical bonds in the molecule, and the connectivity and spatial arrangement of the atoms in the molecule. The physical form of the substance does not merely result in its classification as new chemical substance. Nanoscale materials with the same molecular identity as a chemical substance already in the TSCA chemical substances inventory are considered existing and do not require the PMN. Nanoscale forms of chemical substances that are not in the inventory are new substances that require reporting using the PMN [19].

Information that has to be provided in the PMN and the SNUN includes the chemical identity, available test data regarding environmental or health effects, the uses or intended uses, production volume, byproducts, disposal practices, and estimate on human exposure (15 U.S.C. § 2604(d)). Pre-manufacture testing is not required for the PMN or the SNUN but during the review process the EPA can require to conduct testing by a rule, order, or consent agreement (15 U.S.C. § 2603(a)).

The EPA has to make affirmative determinations on the PMNs or SNUNs it receives (15 U.S.C. § 2604(a)(3)). Consequently, the burden of proof to ensure that the substance does not have adverse effects on health or environment is on the EPA. There are five possible endpoints in the EPA's decision making framework: (1) information is sufficient to conduct the evaluation and the substance does not likely present unreasonable risk, (2) information is sufficient and the substance presents unreasonable risk, (3) the substance is or will be produced in substantial quantities, or there is or may be significant or substantial exposure, (4) in the absence of sufficient information, the substance may present unreasonable risk, and (5) information is insufficient to conduct the evaluation (Figure 1) [20]. In

addition, the EPA can determine that the proposed use of the chemical substance is a significant new use and formulate a significant new use rule (SNUR) (15 U.S.C. § 2604(a)(2)).

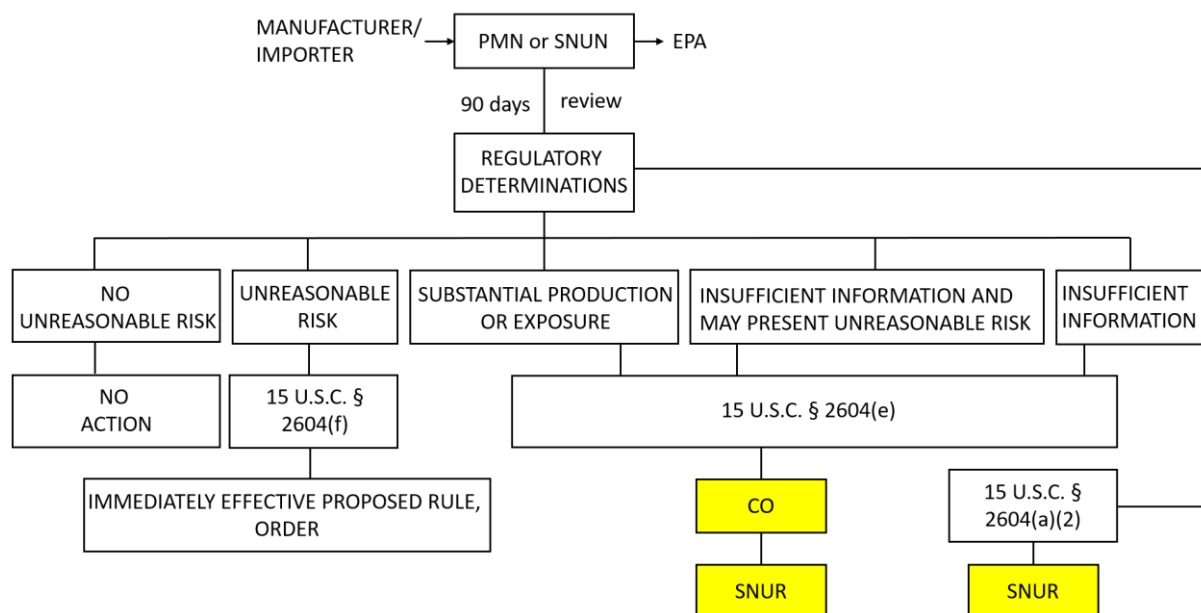


Figure 1. A schematic of the regulative risk assessment process under the TSCA. Consent orders (CO) and significant new use rules (SNUR) analyzed in this study are marked in yellow.

If the substance does not likely present unreasonable risk, the EPA takes no action but notifies the submitter of its decision and publishes the findings in the Federal Register (15 U.S.C. § 2604(g)). If the substance presents unreasonable risk, the EPA shall take the actions required in 15 U.S.C. § 2604(f). The EPA may propose a directly effective rule or give an order that will be operative after the review period to impose restrictions on the substance. In all the other cases, the EPA shall take the actions required in 15 U.S.C. § 2604(e). The EPA may issue a consent order (CO) that is negotiated with the submitter and typically includes toxicity or environmental fate testing requirements once a certain production volume or time period is reached, use of personal protective equipment, new chemical exposure limits for worker protection, hazard communication language, distribution and use restrictions, restrictions on releases to water, air and/or soil, and recordkeeping [21]. The COs are binding only on the original submitter and therefore the EPA usually formulates an associated SNUR that binds all other manufacturers and importers.

2.2.2. Chemical substances under the REACH. In the EU, burden of proof to ensure that the substance does not have adverse effects on health or environment is on the manufacturers and importers (Articles 10–14). Manufacturers and importers have to collect or generate data on the substances that they produce or import, and consequently use the data for assessing the risks related to the substances, and to develop and recommend risk management measures to control these risks. These obligations are verified by the requirement to submit a registration dossier to the European Chemicals Agency (ECHA) (Figure 2).

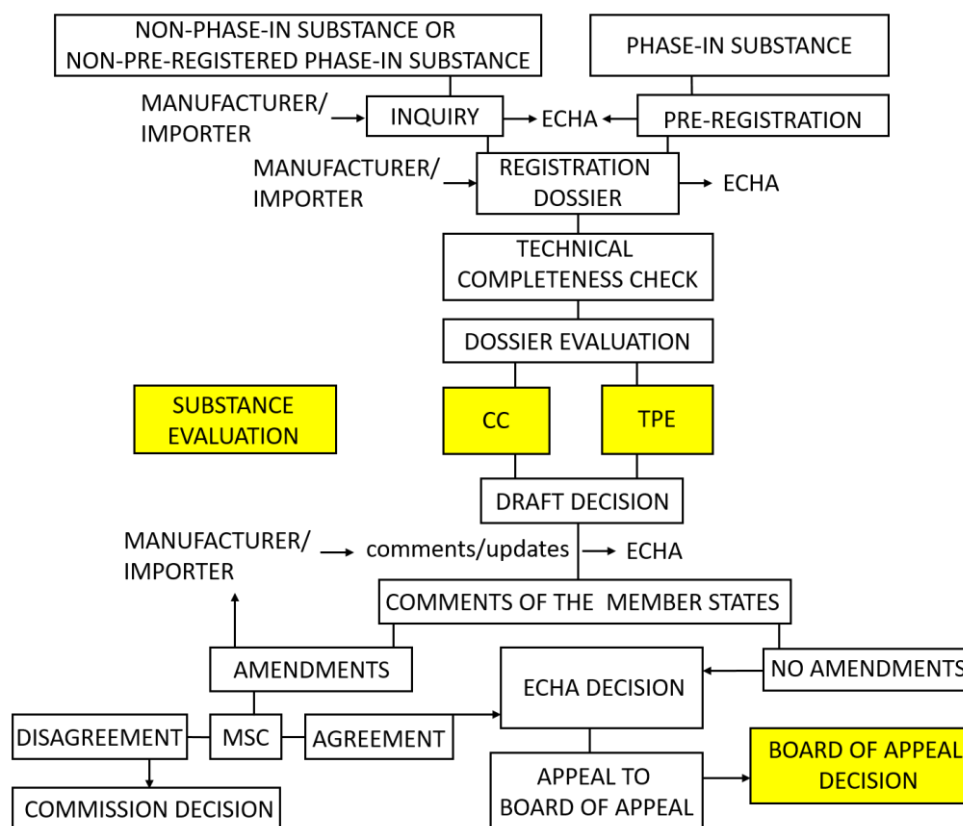


Figure 2. A schematic of the regulatory risk assessment process under the REACH. Decisions analyzed in this study, i.e., compliance checks (CC), testing proposal examinations (TPE), substance evaluations, and decisions of the Board of Appeal are marked in yellow.

In general, registration is obligatory only for substances that are manufactured or imported over one tonne per year per manufacturer or importer (Article 6(1)). Similar to the TSCA, the REACH contains the exemptions from the scope of registration. The exemptions are not considered in this study. For new chemical substances (non-phase-in substances) or for non-pre-registered existing (phase-in) substances the registration procedure has to be passed before the market entry. Pre-registered phase-in substances have been registered in steps, the last phase-in deadline (for the substances manufactured or imported 1–100 tonne per year) ended 31 May 2018. If the registration of phase-in substance has not been performed by the deadline, the substance cannot be manufactured in the EU or placed on the EU market before it has been registered (Article 5) [22].

Information requirements depend on the volume of the substance (Article 12). If the substance has more than one composition or form (including nanoforms), the information provided or generated must cover all the compositions/forms [22]. Specific information requirements for nanomaterials are presented in the appendixes of the “Guidance on information requirements and chemical safety assessment” [23]. A registrant is responsible on his own initiative to update the registration dossier without undue delay with relevant new information (Article 22). In addition, the REACH requires that before the registration, the substance must have been pre-registered (phase-in substances) (Article 28) or the registrant shall inquire from the ECHA whether a registration has already been submitted for the same substance (Article 26). These requirements ensure data sharing.

Dossier evaluation is divided to compliance check (CC) and testing proposal examination (TPE). Both follow the same decision making framework presented in Figure 2. The ECHA examines all testing proposals (Article 40) but the CCs (Article 41) are performed only for a part of the registration dossiers [24]. The ECHA has to prepare a draft decision for the TPE on non-phase-in substances within 180 days

of receiving a registration (Article 43(1)). For the phase-in substances that should have been registered by 1 June 2018, a draft decision deadline is 1 June 2022 (Article 43(2)). In the TPE decision, the ECHA may require the registrant(s) to perform the proposed tests and submit the study summary in given deadline, modify test conditions, require additional tests if non-compliance exists, or reject the testing proposal (Article 40(3)).

In the CC, the ECHA has to prepare a draft decision within 12 months from the start of the CC with 1) conclusion with no action or 2) information requirements and time limits for the submission of the updated dossier (Article 41(3)). The registrant(s) have right to comment the draft decision within 30 days (Article 50). The ECHA has to notify the competent authorities of the member states of its draft decision together with the possible comments from the registrant(s), to facilitate possible amendments (Article 51(1)(2)). If no amendments are provided within 30 days, the ECHA shall take the decision (Article 51(3)). If amendments are provided, the ECHA shall refer a draft decision with the amendments to the member state committee (MSC) within 15 days of the end of the 30-day commenting period (Article 51(4)). A new 30-day commenting period has to be noticed to the registrant(s) (Article 51(5)). If the MSC reaches a unanimous agreement within 60 days, the ECHA shall take the decision accordingly (Article 51(6)). If the MSC disagrees, the Commission makes the decision (Article 51(8)). The registrant(s) can file an appeal against the ECHA's decision in the Board of Appeal.

In addition to the dossier evaluation, a substance evaluation process exists in the EU. It is a concern driven procedure with the aim to clarify whether a particular substance poses a risk to human health or the environment [25]. The ECHA shall, in cooperation with the member states, develop criteria for prioritizing substances to further evaluation and compile the community rolling action plan (CoRAP) (Article 44). A member state may choose substance(s) from the CoRAP list to evaluate it. The ECHA has to coordinate the process and ensure that all the substances on the CoRAP list will be evaluated (Article 45). As an output of the substance evaluation, a draft decision requesting further information from the registrant(s) can be made by the evaluating member state competent authority within 12 months of the publication of the CoRAP on the ECHA's website for the substances to be evaluated that year. The decision making process after the draft follows the dossier evaluation process presented in Figure 2 (Article 46(1)).

3. Data and methods

The research data consists of the number of notifications/dossiers for the ENMs or the substances that contain also nanoform received by the EPA and the ECHA, and decisions of the Agencies. Neither of the Agencies use term "engineered nanomaterial". The EPA refers to "nanoscale materials" [26] and the ECHA refers to the Commission recommendation on the definition of nanomaterial [27] that does not differentiate natural, incidental or manufactured nanomaterials [28]. The decisions are COs and SNURs issued by the EPA, CC and TPE decisions of the ECHA, substance evaluation decisions of the MSC, and the final decisions of the Board of Appeal (from now on collectively 'decisions of the EPA' and 'decisions of the ECHA'). The number of notifications under the TSCA until 31 March 2018, and the COs and SNURs included in this study were provided by *Jim Alwood* from the EPA's Chemical Control Division. Other data was obtained from the ECHA's public webpages that were followed until 20 March 2018.

The data was analyzed using descriptive statistics and classification. Orders and information requirements issued in the decisions were grouped to eight groups (G0–G7) to present incidence. The following grouping was formulated: G0 identifiers; G1 worker protection orders; G2 application/distribution restrictions; G3 disposal/release restrictions; G4 physicochemical properties; G5 release parameters/studies; G6 toxicity parameters/studies, and G7 reference to OECD guidelines. The parameters included in each group are listed in Appendix (Table A1).

In addition, two case studies from the EU and three from the U.S. were selected for more detailed (qualitative) examination of information and test requirements. However, because of confidentiality claims on both sides of the Atlantic and a small number of identified cases under the REACH, the

comparison of information requirements set for exactly the same substance under the TSCA and the REACH was not possible in this study.

4. Results and discussion

4.1. Statistical analysis

Numbers of notifications/dossiers received and decisions issued by the EPA and the ECHA are presented in Table 1. Until 31 March 2018, the EPA had received 210 notifications for nanomaterials, of which 138 were PMNs and 72 other notifications (SNUNs and exemptions). Of the PMNs 90 are for carbon nanotubes (CNT), nine for fullerenes, and six for quantum dots (*Alwood*, personal communication). In consequence of the PMNs, EPA has issued 121 SNURs and 85 COs. Both the CO and the SNUR have been issued for 75 substances. The issued SNURs and COs comprised 62.4 % of the total number of notifications and 94.9 % of the PMNs received by the EPA. Because of confidentiality claims, of the 138 PMNs 80 were available for the further analysis.

Table 1. Number (pcs) of notifications/dossiers received and decisions issued by the EPA and the ECHA concerning nanomaterials. The total number of identified cases and the percentage (%) of the actions taken of the total number of identified cases are presented as well.

EPA	pcs	ECHA	pcs
PMN	138	Voluntarily registered	21
SNUR	121	TPE	3
CO	85	CoRAP	2
Other notifications	72	CC	12
Total identified	210	Total identified	31
Percentage (%) of SNURs and COs of the total identified notifications	62.4	Percentage (%) of TPEs, CoRAPs, and CCs of the total identified dossiers	54.8
Percentage (%) of SNURs and COs of the PMNs	94.9		

Until 20 March 2018, the ECHA had received 21 registration dossiers containing nanospecific information [29]. TPE decisions were issued for three of those substances (silver, EC No 231-131-3; nickel 5,5'-azobis-2,4,6(1H,3H,5H)-pyrimidinetrione complexes and melamine, EC No 939-379-0; calcium carbonate, EC No 207-439-9) [30]. Two of the registered substances (silver; silicon dioxide, EC No 231-545-4) have been evaluated under the CoRAP and the Board of Appeal has given two decisions of the evaluation of silicon dioxide [31–33]. In addition, the ECHA has completed 12 CCs on the dossiers with nanomaterials [29, 34]. Two of the CCs were related to the substances that have been voluntarily registered to contain nanoforms (aluminum oxide, EC No 215-691-6; titanium dioxide, EC No 236-675-5). Five appeals concerning the CCs have been decided by the Board of Appeal [35–39]. Consequently, altogether 31 dossiers were reported or considered to contain nanoforms in the EU under the REACH. The issued CC decisions, TPE decisions, and completed substance evaluations comprised 54.8 % of the total number of identified dossiers.

The results of the analysis of the orders and information requirements issued in the decisions of the EPA and the ECHA are illustrated in Figure 3. Over 85 % of the decisions issued by the EPA contained worker protection orders and restrictions on application, distribution, disposal, and release (G1–G3) whereas in the decisions of the ECHA, incidence in those groups was zero. The difference arise from the 15 U.S.C § 2604(e)(1)(A)(ii), which requires the EPA “—issue an order — to prohibit or limit the manufacture, processing, distribution in commerce, use, or disposal — to the extent necessary to protect against an unreasonable risk of injury to health or the environment —”. For identifiers (G0) the incidences were the closest to each other, being requested in over 45 % of the decisions of the ECHA and in almost 39 % of the decisions of the EPA. Release parameters/studies (G5) and toxicity

parameters/studies (G6) were required in 40 % and 85 % of the decisions issued by the EPA, but only in 6.5 % and 13 % of the decisions of the ECHA, respectively. For physicochemical properties (G4) the incidences were 80 % for the EPA and 48 % for the ECHA. OECD guidelines (G7) were referred to in over 86 % of the decisions issued by the EPA, versus only in 9.7 % of the decisions issued by the ECHA. The observed differences plainly indicate that regulative risk assessment processes of nanomaterials under the TSCA and the REACH performed by the EPA and the ECHA, respectively, may result in dissimilar information requirements and restrictions for the companies in the U.S. and the EU.

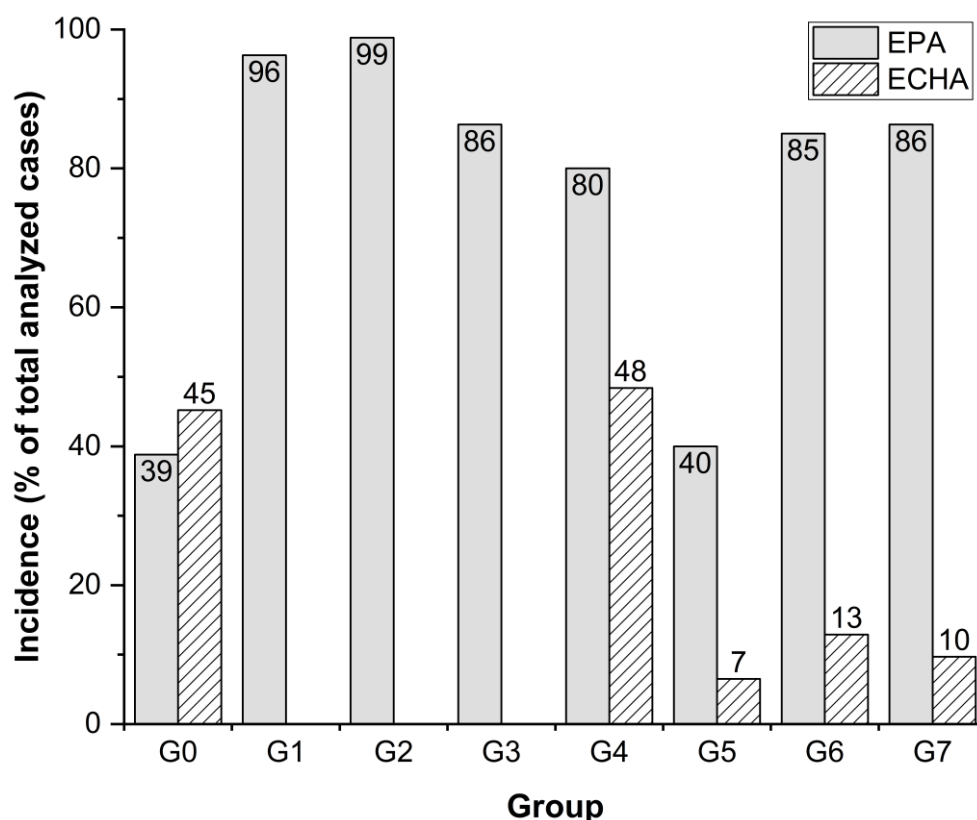


Figure 3. Incidence (% of total analyzed cases; N = 80 for the EPA, N = 31 for the ECHA) of the orders and information requirements in groups G0–G7. The groups are: G0 *identifiers*; G1 *worker protection orders*; G2 *application/distribution restrictions*; G3 *disposal/release restrictions*; G4 *physicochemical properties*; G5 *release parameters/studies*; G6 *toxicity parameters/studies*, and G7 *reference to OECD guidelines*.

The statistics in Table 1 and Figure 3 reveals also the challenges in detection and collection of information that the ECHA has encountered because of shortages in the REACH with regard to nanomaterials. Since 2005, the EPA has been able to identify almost sevenfold amount of cases including nanoforms under the TSCA than the ECHA under the REACH since 2007. The existing legal text of the REACH does not contain specific requirements for nanoforms of a substance and industry bodies have been reluctant to voluntary reporting [35, 36]. The ECHA has struggled years to ensure the applicability of the REACH to nanoforms of substances without explicit legal basis, but after the two decisions of the Board of Appeal in March and June 2017 [33, 35] was forced to admit that the framework does not work satisfactorily without the revision of the REACH annexes [40]. On 3 December 2018, the European Commission adopted a regulation that revises the annexes of the REACH to clarify registration requirements of nanomaterials [41].

4.2. Case analysis

The REACH cases selected for more detailed examination were Case A-011-2014, *Huntsman P&A UK Ltd v ECHA*, decision of the Board of Appeal of 2 March 2017, and Case A-015-2015, *Evonik Degussa GmbH and Others v ECHA*, decision of the Board of Appeal of 30 June 2017. The former case was related to dossier evaluation and the latter to substance evaluation. Next, the information required in each of the cases and the contents of disputes as well as the consequents of the decisions of the Board of Appeal are expounded, starting with dossier evaluation.

In the Case A-011-2014, *Huntsman P&A UK Ltd v ECHA*, the appeal was directed against a CC decision concerning the substance identity information for titanium dioxide (EC No 236-675-5). The ECHA requested information classified in the current study in the groups G0 (identifiers) and G4 (physicochemical properties). More precisely, the required parameters were:

- name, molecular and structural formula or other identifiers
- composition
- crystalline phases
- forms
- purity
- constituents
- surface treatment
- description of the analytical methods.

In essence, the core of the dispute was that the ECHA was claimed to act outside its competence because some of the requested parameters were not included in the list of information required for a registration under section 2 of annex VI of the REACH (third plea of the claim). The parameters listed in the section 2 of annex VI of the REACH are:

- name or other identifier of each substance
 - name(s) in the IUPAC nomenclature or other international chemical name(s)
 - other names (usual name, trade name, abbreviation)
 - EINECS or ELINCS number (if available and appropriate)
 - CAS name and CAS number (if available)
 - other identity code (if available)
- information related to molecular and structural formula of each substance
 - molecular and structural formula (including SMILES notation, if available)
 - information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)
 - molecular weight or molecular weight range
- composition of each substance
 - degree of purity (%)
 - nature of impurities, including isomers and by-products
 - percentage of (significant) main impurities
 - nature and order of magnitude (... ppm, ... %) of any additives (e.g. stabilizing agents or inhibitors)
 - spectral data (ultra-violet, infra-red, nuclear magnetic resonance or mass spectrum)
 - high-pressure liquid chromatogram, gas chromatogram
 - description of the analytical methods or the appropriate bibliographical references for the identification of the substance and, where appropriate, for the identification of impurities and additives.

The Board of Appeal stated that the list is comprehensive as regards its application to the facts of the case, and because neither explicit provision for substance identity information on crystalline phases and/or nanoforms nor an openly worded information requirement is included, it must be interpreted literally as enacted by the legislature. The Board of Appeal noticed that if the terms ‘nanoforms’ and ‘nanomaterials’ were mentioned elsewhere in the REACH, there could have been a stronger argument to apply a contextual or teleological interpretation. In addition, from the Board of Appeal point of view, a CC of the toxicological and ecotoxicological information submitted rather than substance identity information only as in the current case, will allow the ECHA to consider whether all the required information regarding the human health and environmental effects of the substance have been submitted [35].

The case underlines the prevailing lack of legal basis of the ECHA to require information on substance identity during the CC. This, obviously, is directly linked to deficient detection of nanomaterials. In addition, the ECHA’s practice to target CCs only at the substance identity may partly explain the observed lower incidence in the groups G5 (release parameters/studies) and G6 (toxicity parameters/studies). The ECHA has stated that after the decision of the Board of Appeal, designing of a CC requesting hazard information covering all different nanoforms in the dossier in a targeted and proportionate way has become very challenging and complex [40]. The decision of the Board of Appeal given about substance evaluation, examined next, further limits the ECHA’s authority to request information.

In the Case A-015-2015, *Evonik Degussa GmbH and Others v ECHA*, the appeal was directed against a substance evaluation decision of silicon dioxide, in particular four types of synthetic amorphous silica (SAS): pyrogenic SAS, precipitated SAS, silica gel, and colloidal SAS. The decision required the Appellants to submit the following information:

- information on the following physicochemical properties of each individual SAS form (excluding surface-treated forms) (*first request*)
 - granulometry, which shall include primary particle size, aggregate/agglomerate size, and particle size distribution (number-based)
 - specific surface area (by volume)
 - hydroxylation state
 - water solubility
 - density
 - dustiness
 - point of zero charge
- sub-chronic toxicity study (90-day) in rats via the inhalation route with the following four pyrogenic SAS forms (excluding surface-treated forms) as manufactured that represent: (*second request*)
 - the lowest specific surface area with the lowest number of hydroxyl groups
 - the lowest specific surface area with the highest number of hydroxyl groups
 - the highest specific surface area with the lowest number of hydroxyl groups
 - the highest specific surface area with the highest number of hydroxyl groups
- information on the uses of each individual form of SAS (excluding surface-treated forms) (*third request*)
- information on the following physicochemical properties of each individual surface-treated SAS form (*fourth request*)
 - granulometry, which shall include primary particle size, aggregate/agglomerate size, and particle size distribution (number-based)
 - specific surface area (by volume)
 - hydroxylation state

- surface treating agent(s), including chemical identity (IUPAC name and numerical identifiers (CAS and EC)) and type of reaction with the SAS surface
- water solubility
- density
- dustiness
- point of zero charge
- all toxicological information on surface-treated SAS as manufactured, imported and/or placed on the market as available to the Registrant(s) (*fifth request*).

One part of the dispute was a claim that the substance evaluation decision was unlawfully based on a concern related to the fact that SAS is a nanomaterial. The Board of Appeal found that the fact that SAS is a nanomaterial was clearly a major factor in adding silicon dioxide to CoRAP, but not the only reason considering SAS to pose a potential risk for human health or the environment. Being a nanomaterial do not alone justify a potential concern. The Board of Appeal declared that the ECHA had not demonstrated a potential concern with regards to precipitated SAS, silica gel, and colloidal SAS. Consequently, information requirements set out in the first and third requests were annulled in this respect. In addition, the Board of Appeal stated that the ECHA failed to identify a potential concern with regards to surface-treated SAS and annulled the fourth and fifth requests in their entirety. The Board of Appeal outlined that the ECHA must be able to demonstrate a specific concern (in relation to the substance at issue, not based on general concern regarding surface-treated substances that are also nanomaterials) that needs to be clarified and how the information and/or testing required will help to clarify that concern.

Another part of the dispute were claims that the ECHA had exceeded its competence by requesting information on different ‘forms’ and breached the principle of proportionality. The Board of Appeal stated that under substance evaluation, based on the Case A-011-2014, *Huntsman P&A UK Ltd v ECHA*, paragraph 72, the ECHA can request information on forms of a substance if it can demonstrate that the information will assist to clarify of the potential concern identified and the request satisfies other legal requirements such as principle of proportionality. The Board of Appeal found that the ECHA failed to demonstrate how the requested physicochemical information will be used to clarify the concern for inhalation toxicity of pyrogenic SAS (concerning the other SAS types the information requirements were already annulled above). The cost of generating a potentially large amount of data of different forms of SAS is therefore disproportionate. Consequently, the Board of Appeal annulled the first request in its entirety. In addition, the Board of Appeal annulled the third request in its entirety as breaching the principle of legal certainty due to vaguely defined term ‘SAS form’. Instead, the appellants’ claims concerning the second request were dismissed in their entirety, because the ECHA was able to demonstrate the potential concern and clearly defined the forms to be tested by reference to surface area and hydroxylation [33].

The case outlined that information requirements shall be directly linked to the evidently identified potential concern of the substance at issue, and that being a nanomaterial or lack of hazard data, *per se*, do not justify potential concern. In this case, the ECHA required information that was classified in the current study in the groups G4 (physicochemical properties), G5 (release parameters/studies), and G6 (toxicity parameters/studies). Only the requirements related to toxicity studies of four pyrogenic SAS forms (second request) were held in the Board of Appeal. The ECHA has stated that this decision significantly limits its authority to request information on different nanoforms in substance evaluations to identify the substance specified potential concern [40].

The TSCA cases selected for more detailed examination were the COs issued based on the PMNs number *P09-188* [42], *P15-487* [43], and *P17-244* [44]. The substances (generic) targeted in the first and the second COs were ‘multi-walled carbon nanotubes’ (MWCNT) and in the third CO ‘metal oxide

reaction products with cadmium metal selenide sulfide, and amine'. For the first two cases, the associated SNURs have been issued [45, 46]. In all the cases, the COs were issued pursuant to 15 U.S.C § 2604(e)(1)(A)(ii)(I). Next, the information required in the COs is examined, starting with MWCNTs.

The PMN number *P09-188* was filed for a substance that is only imported to the U.S. The PMN identified four different forms of the substance (powdered, liquid polymer, solid polymer, the last form was claimed confidential). The CO required the company to:

- submit to the EPA certain toxicity testing on the powder form of the PMN substance before exceeding either the specific production volume or a specified time period
 - 90-day inhalation toxicity study
- before exceeding a specified time period, submit to the EPA certain material and physicochemical data on the PMN substance in the powder form
 - particle size of the catalyst used in the manufacturing of the PMN substance
 - shape
 - particle size (average and distribution)
 - surface to volume ratio
 - agglomeration
 - surface area
 - dustiness
 - six parameters were claimed confidential
- require workers to wear personal protective equipment including gloves, chemical protective clothing and goggles in the work area whenever reasonably likely to be dermally exposed to the PMN substance in the work area
- require workers to wear a NIOSH-approved respirator specified in the CO whenever workers are reasonably likely to be exposed to the PMN substance by inhalation, except when the PMN substance is in the following form
 - in a liquid polymer form with a concentration of the PMN substance equal to or below 7 %, provided the activity does not generate a vapor, mist, or aerosol
 - embedded in a solid polymer form with a concentration of the PMN substance equal to or below 30 %, provided the activity does not generate a dust
- use and distribute the PMN substance only for the applications specified in the CO
- not use the PMN substance for commercial or consumer use, or in a consumer product (quantities of PMN substance that are completely reacted, cured, or embedded as described in the order may be used for commercial or consumer use, or in a consumer product)
- not manufacture the PMN substance in the U.S.
- submit a one gram sample of the PMN substance to the EPA upon request
- distribute the PMN substance only to a person who agrees to follow the same restrictions (except testing requirements) and to not further distribute the PMN substance until after it has been completely reacted (cured), incorporated into a polymer matrix that itself has been reacted (cured), or embedded into a solid polymer form with a concentration of the PMN substance equal to or below 30 %
- not release the PMN substance to the waters in the U.S. except where the PMN substance is embedded in a solid polymer form with a concentration of the PMN substance equal to or below 30 %
- maintain certain records specified in the CO.

In addition, the following additional information was recommended for the liquid and solid polymer forms:

- release of MWCNTs after landfill disposal

- release of MWCNTs during the burning
- release of MWCNTs after exposure to sunlight
- release of MWCNTs during shipping and use (solid polymer form only) [42].

The CO issued regarding the PMN number *P15-487* required the company to:

- conduct a medical surveillance program
- submit a one gram sample of the PMN substance to the EPA upon request
- require workers to use impervious gloves and chemical protective clothing when dermally exposed to the PMN substance
- require workers to use a full-face NIOSH-approved respirator specified in the CO
- use the PMN substance only in the applications specified in the CO
- incinerate or landfill all wastes
- not release wastes to water
- not use application methods that generate a dust, mist, or aerosol unless such application method occurs in an enclosed process
- distribute the PMN substance only to a person who agrees to follow the same restrictions (except testing requirements)
- maintain certain records specified in the CO.

In addition, the following additional information was recommended:

- a 90-day inhalation study (pulmonary effect)
- a two-year inhalation bioassay (carcinogenicity)
- ecotoxicology studies (fish, daphnia, algae) [43].

EPA stated in the COs that though the COs did not require the submission of the recommended information at any specified time or production volume, the restrictions of manufacture, import, processing, distribution, use, and disposal of the PMN substance will remain in effect until the CO is modified or revoked by the EPA based on the submission of that or other relevant information.

The requirements in these two cases were classified in the current study in the groups G1 (worker protection orders), G2 (application/distribution restrictions), G3 (disposal/release restrictions), G4 (physicochemical properties), G5 (release parameters/studies), and G6 (toxicity parameters/studies) reflecting, as regards the groups G1–G3, the obligations set to the EPA in 15 U.S.C § 2604(e)(1)(A)(ii). The cases show that information and test requirements issued by the EPA are decided on case-by-case basis, and may vary for the same (generic) substance class depending on the specific properties and associated potential risks of the substance at the issue. In the case *P09-188*, the requirements were different for different forms (as identified in the PMN) of the PMN substance. The CO and associated SNUR also prohibit domestic manufacture of the PMN substance without a SNUN submitted to the EPA beforehand.

The third case examined under the TSCA was for ‘metal oxide reaction products with cadmium metal selenide sulfide, and amine’. The CO issued based on the *P17-244* required the company to:

- submit to the EPA certain toxicity testing before manufacturing (including import) a total of (claimed confidential) kilograms of the PMN substance
 - a 90-day inhalation study with a 60 day recovery period
 - hydrolysis test as function of pH
- provide personal protective equipment to its workers to prevent dermal exposure

- label containers of the PMN substances and provide safety data sheets or material safety data sheets and worker training in accordance with the provisions of the hazard communication program section of the CO
- manufacture, process and use the PMN substance only as a down-converter for an optical filter as provided in the PMN, and not in applications that generate a dust, mist or aerosol
- for workers potentially exposed to the solid form of the PMN substance a laminar-flow hood or glove box will be used to reduce or eliminate inhalation exposure, workers who may still be exposed by inhalation will use a NIOSH-approved respirator specified in the CO
- distribute the PMN substance only to a person who agrees to follow the same restrictions (except testing requirements) and to not further distribute the PMN until it has been incorporated into an article
- dispose of the PMN substance only by incineration in a permitted hazardous waste incinerator
- maintain certain records specified in the CO.

In addition, the following additional information was recommended:

- indirect photolysis
- aerobic microbial mobilization of metal ions [44].

The requirements in groups G1–G3 were mainly similar to the previous cases, except a hazard communication program in the group G1 and different release parameters/studies in the group G5. Physicochemical properties (G4) were submitted with the PMN and the EPA did not request any additional physicochemical characterization in this case. In this case, as well as in the case *P09-188*, various release parameters/studies (G5) were requested to assess environmental fate of the PMN substances. In addition, all three cases required to perform toxicity studies (G6), namely a 90-day inhalation study. Based on the statistics presented in subsection 4.1., there was a clear difference between the EPA and the ECHA in requesting information on parameters in groups G5 and G6. This can be partly explained by the ECHA's practice to target CCs only at the substance identity as discussed earlier in the current section, whereas the EPA appears to request release and toxicity studies almost by rule. On the other hand, difficulties, due to deficient detection of nanomaterials, to determine the substance specified potential concern to justify generation of hazard information in substance evaluation further limit the ECHA's possibilities to establish such requests after the decision A-015-2015 of the Board of Appeal, analyzed above. The difference in reference to OECD guidelines (G7) can also be partly explained by the different incidences in the groups G5 and G6, because many of the required studies in these groups were accompanied with a reference to test guidelines provided by the OECD.

The experimental analysis presented in section 4 reveals that regulative risk assessment processes performed by the ECHA and EPA under the REACH and the TSCA, respectively, may result in different compliance requirements for companies. This may increase compliance costs of the companies in spite of the agreement of mutual acceptance of data (MAD) in the assessment of chemicals [47–49]. The differences arise partly from the legal provisions that determine the authority and obligations of the Agencies, but also from the decision making practices adopted by the ECHA and the EPA.

In the next section, a short excursion to the development of the TSCA and the REACH in the U.S. and EU, respectively, will be taken to get an impression of the policy factors behind the observed differences in the regulative risk assessment processes.

5. Policy factors behind the differences in the processes

David Vogel presented a framework to explain development of EHS regulations in the U.S. and the EU that can be applied also here to examine the effect of policy factors on regulative risk assessment processes applied in the U.S. and the EU [18]. The framework consists of three interacting elements: (1) the extent and intensity of public pressure for more stringent or protective regulations, (2) the policy

preferences of influential government officials, and (3) the criteria by which policymakers assess and manage risks. Typically, periods of regulatory stringency are characterized by strong public pressure for strict rules, by the policymakers who favor more stringent regulatory controls over business, and by decision making criteria permitting the adoption of highly risk-averse regulations. On contrary, periods with less stringent regulations are characterized by weaker public pressure, by the policymakers opposing to expand the scope or stringency of the EHS regulations, and by decision making criteria that make it more difficult to adopt highly risk-averse regulations.

In 1976, the TSCA was enacted in the U.S. after a series of “alarm bells”, which increased public pressure (first element) towards more stringent chemical regulation [18]. At that time, there was also considerable bipartisan support (second element) for stronger environmental regulation in the U.S. As Vogel stated, much of the regulatory policy is carried out by appointed officials, which enjoy a degree of discretion in drawing up risk management decisions (third element). When the TSCA was enacted, the policymakers and industry in the EU were worried about, e.g., its broad scope and substantial discretion that the TSCA granted to the EPA. Although many policies in the U.S. before 1980 were positive to regulate in the face of scientific uncertainty, the EPA based its risk management decisions on case-by-case, risk-based evaluation [19].

The EPA determines the chemical substance based on its molecular identity as described in the subsection 2.2.1., and the burden of proof to ensure that the substance does not have adverse effects on health or environment is on the EPA. Because the EPA uses the same identifier for nanoscale materials and other chemical substances, it has avoided the lack of authority related to the terminology used in the legal text of the REACH encountered by the ECHA. In addition, because the EPA has an authority to make a judgement on whether a substance has a molecular identity that is identical to an existing substance it can mostly avoid the problem of reluctance to identify, but only as regards new chemicals. Shortages related to the EPA’s authority concerning existing chemicals under the TSCA are not discussed here. Furthermore, U.S. federal courts have frequently scrutinized the rules issued by regulatory Agencies [18], which, to my opinion, increases the legitimacy of the future rulemaking in the U.S. from the point of view of the industry and the public.

In the EU, the public concern (first element) about the harmful effects of chemicals did not take center stage in environmental politics until in the late 1990s [18]. Vogel argued that since around 1990, the U.S. policymakers avoided unnecessarily stringent regulations as a response to overregulation, while the EU policymakers have prioritized more stringent regulations as a response to underregulation. In 2001, the REACH, strongly influenced by the precautionary principle adopted by the Commission [50] and supported by a powerful coalition of member states (second element), was proposed in a white paper of DG Environment [18]. However, registration, evaluation, and authorization requirements of the REACH were intensely opposed by the chemical industry on both side of the Atlantic. Furthermore, the change in the policy preferences after the installation of a new Commission in 2004 resulted in a compromised REACH finally entered into force in June 2007.

The REACH reversed the burden of proof on industry, eliminated distinction between new and existing chemicals, and established the ECHA as a new regulatory body [18]. However, the means available to the ECHA in drawing up risk management decisions (third element) concerning nanomaterials are very different from that of the EPA’s. First, tonnage limitations that mainly arose from the policy factors described above narrowed the scope of the REACH. In addition, the responsibility to identify chemical substances is on manufacturers and importers, and the ECHA has no legal basis to require information outside the list of information required for a registration under section 2 of annex VI of the REACH, as discussed in section 4. Furthermore, because the ECHA refers to the Commission recommendation on the definition of nanomaterial [27] but neither the term ‘nanomaterial’ nor ‘nanoform’ are mentioned in the legal text of the REACH, it lacks the legal authority to request information and has been criticized for using vague language, the criticism fallen once on the TSCA by European policymakers and industry [18]. While it has been stated that the REACH reversed the stringency between the chemical regulations in the U.S. and the EU [18], the results of this study indicate that in regards to nanomaterials this currently does not hold up. Today, the EPA is more capable to

detect nanomaterials and collect information on them through the case-by-case evaluation of the PMNs under the TSCA than the ECHA, bound to limited authority to request information, under the REACH.

6. Conclusions

Detection and associated information collection are the core functions of the risk-based regulation. It is obvious from the statistics presented in section 4 that a loophole in detection of nanomaterials and information collection on them exists in the EU under the REACH, diminishing the coverage of the regulation. The ECHA has stated that “– – in the current situation ECHA cannot effectively and systematically verify whether safe use of nanomaterials in the supply chain is demonstrated, and whether additional regulatory risk management measures are needed.” [40]. Unfortunately, because of reluctance of industry to voluntary reporting the state of affairs will probably not change a much before the amendment of the REACH annexes shall be applied from 1 January 2020 [41].

The experimental analysis revealed also that regulative risk assessment processes performed by the ECHA and EPA under the REACH and the TSCA, respectively, may result in different compliance requirements for companies, which may lead to increased compliance costs. The differences arise partly from the legal provisions that determine the authority and obligations of the Agencies, but also from the decision making practices adopted by the ECHA and the EPA. The future will show whether the disparity increases after the amendment of the REACH annexes. Regulatory cooperation between the policymakers (including regulatory officials) in the EU and the U.S. should be intensified to decrease legal uncertainty and increase social legitimacy of regulative risk assessment frameworks for nanomaterials.

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APPENDIX. CLASSIFICATION OF PARAMETERS

Table A1. Parameters included in the groups G0–G7.

Group	Parameters
<i>G0 identifiers</i>	name molecular formula structural formula molecular weight composition purity description of analytical methods used for the identification
<i>G1 worker protection orders</i>	workplace exposure monitoring use of personal protective equipment (gloves, clothing) use of personal protective equipment (respirator) recordkeeping medical surveillance program hazard communication program
<i>G2 application/distribution restrictions</i>	manufacture, process or use the substance only in a liquid formulation manufacturing process incorporates the substance in the pellets only no use of application methods that generate dust, mist, or aerosol restricted application limited distribution no domestic manufacture
<i>G3 disposal/release restrictions</i>	no release to water disposal by incineration in a permitted hazardous waste incinerator disposal only by landfill or incineration
<i>G4 physicochemical properties</i>	aggregation/agglomeration state morphology crystalline phase density grade/form aspect ratio shape particle size particle size distribution specific surface area surface to volume ratio surface charge surface treatment surface chemistry spacing between the layers chiral or twist angle chirality distribution and tube diameter quantitative data of constituents defects chemical composition of the encapsulating materials description of manufacturing process/reaction conditions
<i>G5 release parameters/studies</i>	hydroxylation state hydrolysis test as a function of pH water solubility dispersibility dissolution rate dustiness release studies (e.g. after landfill disposal, due to sunlight, during shipping and use) indirect photolysis aerobic microbial mobilization of metal ions electrokinetic properties uses
<i>G6 toxicity parameters/studies</i>	metabolism and pharmacokinetics pre-natal developmental toxicity sub-chronic inhalation toxicity study (90-day) two-year inhalation bioassay combined toxicity/carcinogenicity testing of respirable fibrous particles ecotoxicology studies (fish, daphnia, algae) information on the known hazards long-term toxicity to aquatic/terrestrial invertebrates effects on soil micro-organism long-term toxicity to terrestrial plants all toxicological information on surface-treated forms
<i>G7 reference to OECD guidelines</i>	

References

- [1] Malloy T F 2011 Nanotechnology regulation: A study in claims making *ACS Nano* **5** 5–12.
- [2] National Institute of Environmental Health Sciences. Nanomaterials [Internet]. [last visited 9 December 2018]. Available from: <https://www.niehs.nih.gov/health/topics/agents/syn-nano/index.cfm>.
- [3] Hristozov D and Malsch I 2009 Hazards and risks of engineered nanoparticles for the environment and human health *Sustainability* **1** 1161–94.
- [4] U.S. Environmental Protection Agency 2007 Nanotechnology white paper 1–120. Available from: https://www.epa.gov/sites/production/files/2015-01/documents/nanotechnology_whitepaper.pdf.
- [5] U.S. Environmental Protection Agency. Risk assessment [Internet]. [last visited 9 December 2018]. Available from: <https://www.epa.gov/risk/human-health-risk-assessment>.
- [6] Hristovski K D 2012 Scientific challenges of nanomaterial risk assessment *Jurimetrics J.* **52** 359–70.
- [7] Organization for Economic Cooperation and Development 2010 Guidance manual for the testing of manufactured nanomaterials: OECD's sponsorship programme; First revision, ENV/JM/MONO(2009)20/REV 1–92. Available from: <http://www.oecd.org/env/ehs/nanosafety/guidancemanualforhetestingofmanufacturednanomaterialsoecdsponsorshipprogrammefirstrevision.htm>.
- [8] Organization for Economic Cooperation and Development 2017 Alternative testing strategies in risk assessment of manufactured nanomaterials: Current state of knowledge and research needs to advance their use, ENV/JM/MONO(2016)63 1–36. Available from: [http://www.oecd.org/officialdocuments/displaydocument/?cote=ENV/JM/MONO\(2016\)63&doclanguage=en](http://www.oecd.org/officialdocuments/displaydocument/?cote=ENV/JM/MONO(2016)63&doclanguage=en).
- [9] Justo-Hanani R and Dayan T 2014 The role of the state in regulatory policy for nanomaterial risk: Analyzing the expansion of state-centric rulemaking in EU and US chemical policies *Res. Policy* **43** 169–78.
- [10] Toxic Substances Control Act, 15 U.S.C. § 2601 et seq. (1976).
- [11] OJ, N:o L 136, 29.5.2007, p. 3–278.
- [12] Baldwin R, Cave M and Lodge M 2012 *Understanding Regulation. Rhetoric, Strategy, and Practice 2nd ed* (Oxford: Oxford University Press) pp 227–65, 272, 281–3, 288, 318–9.
- [13] Black J and Baldwin R 2010 Really responsive risk-based regulation, *Law & Policy* **32** 181–213.
- [14] Malloy T, Trump B D and Linkov I 2016 Risk-based and prevention-based governance for emerging materials, *Envtl. Sci. & Tech.* **50** 6822–4.
- [15] Executive Office of the U.S. President 2011 Policy principles for the U.S. decision-making concerning regulation and oversight of applications of nanotechnology and nanomaterials 1–5. Available from: <https://obamawhitehouse.archives.gov/sites/default/files/omb/inforeg/for-agencies/nanotechnology-regulation-and-oversight-principles.pdf>.
- [16] Keleman R D and Vogel D 2010 Trading places: The role of the United States and the European Union in international environmental politics *Comp. Pol. Stud.* **43** 427–56.
- [17] Moran M 2002 Understanding the regulatory state *Brit. J. Pol. Sci.* **32** 391–413.
- [18] Vogel D 2012 *The Politics of Precaution: Regulating Health, Safety and Environmental Risks in Europe and the United States* (Princeton: Princeton University Press) chapters 1, 2, 5.
- [19] U.S. Environmental Protection Agency 2008 TSCA inventory status of nanoscale substances – General approach 2–4. Available from: <https://www.epa.gov/sites/production/files/2015-10/documents/nmsp-inventorypaper2008.pdf>.
- [20] U.S. Environmental Protection Agency 2017 New chemicals decision-making framework 1–5 Available from: https://www.epa.gov/sites/production/files/2017-11/documents/new_chemicals_decision_framework_7_november_2017.pdf.
- [21] U.S. Environmental Protection Agency. Actions under TSCA section 5 [Internet]. [last visited 10

- December 2018]. Available from: <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/actions-under-tsca-section-5>.
- [22] European Chemicals Agency 2016 Guidance on registration 1–120. Available from: https://echa.europa.eu/documents/10162/23036412/registration_en.pdf/de54853d-e19e-4528-9b34-8680944372f2.
- [23] European Chemicals Agency. Guidance on information requirements and chemical safety assessment. Appendixes for nanomaterials [Internet]. [last visited 10 December 2018]. Available from: <https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment>.
- [24] European Chemicals Agency 2017 Dossier evaluation 1–9. Available from: https://echa.europa.eu/documents/10162/13607/procedure_dossier_evaluation_en.pdf/362418b9-4ca1-445f-8bf6-c7c176463e27.
- [25] European Chemicals Agency 2016 Substance evaluation 1–12. Available from: https://echa.europa.eu/documents/10162/13607/pro_0023_01_substance_evaluation_en.pdf/18a85238-b0fd-4464-835e-42c8a151b349.
- [26] U.S. Environmental Protection Agency 2008 TSCA inventory status of nanoscale substances – General approach 1–7. Available from: <https://www.epa.gov/sites/production/files/2015-10/documents/nmsp-inventorypaper2008.pdf>
- [27] OJ N:o L 275, 20.10.2011, p. 38–40.
- [28] European Chemicals Agency 2017 How to prepare registration dossiers that cover nanoforms: best practices 1–21. Available from: https://echa.europa.eu/documents/10162/13655/how_to_register_nano_en.pdf/f8c046ec-f60b-4349-492b-e915fd9e3ca0.
- [29] European Chemicals Agency. Advanced search for chemicals [Internet] [visited 20 March 2018]. Available from: <https://echa.europa.eu/advanced-search-for-chemicals>.
- [30] European Chemicals Agency. Dossier evaluation decisions [Internet] [visited 20 March 2018]. Available from: <https://echa.europa.eu/information-on-chemicals/dossier-evaluation-decisions>.
- [31] European Chemicals Agency. Completed and planned REACH substance evaluations on nanomaterials [Internet] [visited 20 March 2018]. Available from: <https://euon.echa.europa.eu/completed-and-planned-reach-substance-evaluations-on-nanomaterials>.
- [32] Decision of the Board of Appeal of 30 June 2017, Case A-014-2015, *Grace GmbH & Co. KG v ECHA*.
- [33] Decision of the Board of Appeal of 30 June 2017, Case A-015-2015, *Evonik Degussa GmbH and Others v ECHA*.
- [34] European Chemicals Agency. Final decisions from REACH compliance checks on dossiers with nanomaterials [Internet] [visited 20 March 2018]. Available from: <https://euon.echa.europa.eu/final-decisions-from-reach-compliance-checks-on-dossiers-with-nanomaterials>.
- [35] Decision of the Board of Appeal of 2 March 2017, Case A-011-2014, *Huntsman P&A UK Ltd v ECHA*.
- [36] Decision of the Board of Appeal of 12 October 2016, Case A-008-2015, *Evonik Degussa GmbH v ECHA*.
- [37] Decision of the Board of Appeal of 12 October 2016, Case A-009-2015, *IQESIL SA v ECHA*.
- [38] Decision of the Board of Appeal of 12 October 2016, Case A-010-2015, *Rhodia Opérations SAS v ECHA*.
- [39] Decision of the Board of Appeal of 12 October 2016, Case A-011-2015, *J.M. Huber Finland Oy v ECHA*.
- [40] European Chemicals Agency 2017 ECHA strategy on substances in nanoforms 1–4. Available from:

- https://echa.europa.eu/documents/10162/2792271/mb_57_2017_echa_strategy_nanoforms_en.pdf/f913484f-9a21-02bc-d386-8cb68d0027a4.
- [41] OJ, N:0 L 308, 4.12.2018, p. 1–20.
- [42] U.S. Environmental Protection Agency 2010 Modified consent order and determinations supporting consent order based on PMN P09-188 1–58. Available from: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2010-0279-0059>.
- [43] U.S. Environmental Protection Agency 2016 Consent order and determinations supporting consent order based on PMN P15-487/488/489/490/491 1–41. Available from: <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2017-0166-0078>.
- [44] U.S. Environmental Protection Agency 2017 Consent order and determinations supporting consent order based on PMN P17-241/242/243/244 1–45.
- [45] 78 Fed. Reg. at 38221 (June 26, 2013).
- [46] 82 Fed. Reg. at 48639 (Oct. 19, 2017).
- [47] Organization for Economic Cooperation and Development 1981 Decision of the council concerning the mutual acceptance of data in the assessment of chemicals. 1981-C(81)30/FINAL. Available from: <https://legalinstruments.oecd.org/en/instruments/263>.
- [48] Organization for Economic Cooperation and Development. Mutual acceptance of data [Internet] [last visited 13 December 2018] <http://www.oecd.org/env/ehs/mutualacceptanceofdatamad.htm>.
- [49] Rasmussen K, Gonz  les M, Kearns P, Sintes J R, Rossi F and Sayre P 2016 Review of achievements of the OECD Working Party on Manufactured Nanomaterials’ testing and assessment programme. From exploratory testing to test guidelines *Reg. Toxicol. & Pharmacol.* **74** 147–60.
- [50] COM (2000) 1, final. Communication from the Commission on the precautionary principle.