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SINGLE CONTRIBUTION

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Abstract Carbon nanotubes (CNTs) are one of the first examples of nanotechnology, with a history of promising uses and high expectations. This paper uses the recent debate over their future to explore both ethical and value-laden statements which unsettle the notion of CNTs as a value-free nanotechnology and their regulation as purely a technical affair. A point of departure is made with the inclusion of CNTs on the Substitute-It-Now list by the Swedish NGO ChemSec, an assessment process that anticipates and complements the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) regulation in Europe. An argument map is constructed to illustrate the core contention in the debate—should CNTs be substituted or not—which follows from a systematic literature review and content analysis of sampled journal articles. Nine arguments are articulated that bolster one of two camps: the pro-substitution camp or the contra-substitution camp. Beneath these arguments are a set of three implicit values that animate these two camps in prescribing competing interventions to resolve the dispute: (i) environmental protection and human safety, (ii) good science, and (iii) technological progress. This leads to a discussion around the regulatory problem of safeguarding conflicting values in decision-making under sustained scientific uncertainty. Finally, the study suggests further empirical work on specific nanomaterials in a pivot away from the abstract, promissory nature of nanotechnology and other emerging technologies in science, technology, and innovation policy. The examination of ethics and values is useful for mapping controversies in science and technology studies of regulation, even amongst experts in cognate research fields like nanomedicine and nanotoxicology.

Keywords Carbon nanotubes · Nanomaterials · Nanotechnology · Ethics · Content analysis · Controversy

Introduction

Emerging from early nanoscale research in the 1990s [1], carbon nanotubes (CNTs) have earned a reputation for being the paradigmatic example of nanotechnology [2]. CNTs are carbon nanofibers with high aspect ratios, i.e., with much longer lengths than diameter [3, 4]. Both single-wall and multi-wall CNTs share useful properties, such as high strength, conductivity, and corrosion resistance [3], and may serve as a substitute for rare metals [3]. Since the

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2000s, CNT applications have proliferated and the material is now used across various fields, from material coatings, composites, microelectronics, and batteries [5, 6], to water purification and drug delivery [7]. In a recent review, Temizel-Sekeryan et al. [5] find production estimates between a few thousand to 20,000 metric tons in the first half of the 2020s.

This commercial success story has also been marked by scientific and regulatory disputes about the classification, standardization, and ultimate implementation of CNTs in society, which parallel longstanding discussions on the potential environmental implications of nanotechnologies [8]. These issues remain contentious and unresolved [7, 9], as is common for nanomaterials in general [10–12]. In November 2019, this contentiousness was made more acute by the publication of a *Nature Nanotechnology* article, in which the Swedish NGO ChemSec pointed to the potential hazards of CNTs [13]. ChemSec, or the International Chemical Secretariat, "[…] is an independent non-profit organization that advocates for substitution of toxic chemicals to safer alternatives", through "[…] independent research, cross-border collaboration and practical tools" [14]. These substitution efforts are targeted at corporations, with various online tools to help evaluate products that might contain hazardous chemicals.

With CNTs, a nanomaterial was added to the organization's SIN (short for Substitute-It-Now) list of hazardous chemicals for the first time [15]. This was remarkable, as the SIN list evaluates materials on the basis of the very same criteria as the European Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) regulation [13], suggesting that CNTs should become subject to future EU regulation. ChemSec implicitly supports this claim by stating that "out of all the substances that are officially regulated under REACH today, ChemSec named over 94% of them well ahead of the authorities," on their website [16]. However, the SIN list has no direct legal implication and avoiding SIN entries in products is voluntary. Still, Hansen and Lennquist [13] assert that many companies (e.g., H&M, AkzoNobel, and Scandic) are aware of and make decisions about their chemical use in consultation with SIN to highlight its industry relevance. The implications of this development might thus be significant for the CNT industry.

Following ChemSec's decision, a debate ensued in the journal *Nature Nanotechnology*: should CNTs be substituted or not? [7, 9, 13, 17, 18]. *Nature Nanotechnology* "aims to be the voice of the worldwide nanoscience and nanotechnology community" [19]. This community extends from the natural sciences to the "broader nanotechnology picture," including "funding, commercialization, ethical, and social issues" [19]. The journal promises "independence from academic societies and other vested interests," high-quality science, and lists social diversity as well as science for "positive change" as guiding editorial values [20].

The aim of this paper is first to analyze the main theses and arguments of the debate about CNT substitution. Second, this leads to an exploration of the implicit values that underpin the arguments for and against CNT substitution. This demonstrates that the debate—which is presented by protagonists and antagonists as a technocratic conflict about facts—is equally about value-laden preferences in the management of technology (cf. [21]). Swierstra and Rip [22] introduced this journal, *NanoEthics*, by presenting two models for ethical discussion about nanotechnology: the Athenian *agora* and the Machiavellian *arena*. In an agora, the forum is deliberative, and issues are resolved by reaching consensus. The arena is instead seen explicitly as a space of competing interests, "where some win and others lose." Here, the consensus is illusory, and compromise is the goal. The present work attests to the debate about CNTs as a combined agora-as-arena in the sense that the arena masquerades itself as an agora.

The focus on CNTs addresses a gap in the literature on the above social and ethical issues [21, 23] in the "broader nanotechnology picture." With various social science [24–26] and applied ethics [22] approaches investigating the nexus of nanoscience, nanotechnology, and society, there is a lack of research at the level of specific materials, products, and technologies, especially as nanotechnologies begin to mature [27].[1] Previous research has

[1] There are exceptions, such as an analysis of the Swedish popular controversy over nano-silver [28] and analyses of graphene risks perceived by experts [29, 30] and the media [20]. Regarding nano-enabled products, the Horizon 2020 project GoNano explored public engagement with nanotechnologies for three specific sectors, health, food, and energy, and analyzed the role of value mobilization by citizens [31, 32]. There is also research on the Australian controversy from the 2000s over nanoscale metal oxides in sunscreens [33].

Table 1 Scopus literature review search strategy

Last date run	Results	Complete string
2021–02-09	325	TITLE-ABS-KEY ((philosop* OR ethic?? OR legal* OR social OR governance? OR "anticipatory governance" OR "Registration, Evaluation, Authorization and Restriction of Chemicals" OR chemsec) AND ("carbon nanotube*"))

produced generalist accounts of nanoscale-to-society relations, notably building upon two principal research perspectives. One is the public and expert perception [34, 35] and engagement with nanotechnology in a broad sense [36–39]. The other is oriented towards policy-making practices for science, technology, and innovation (STI) [40, 41], often explicitly to strengthen trust and legitimacy [42]. This includes aligning research and innovation with societal values, as typified in Europe with Responsible Research and Innovation (RRI) [43], after rising lay "backlash" [44] to emerging technologies like GMOs that preceded nanotechnology in the 1980s and 1990s [45]. In contrast, this article seeks to understand the regulatory and ethical discussion about the specific nanomaterial CNT.

The article is structured as follows: after a brief methodological description (Sect. 2), the subsequent section contains a mapping of the arguments of the opposing camps in the above-mentioned debate (Sect. 3). The next section analyzes the implicit values that help explain the latent fissures of the debate (Sect. 4). The article is concluded by a restatement of the thesis and a call for further studies of the implicit institutionalization of values and ethics for CNTs and other nanomaterials.

Methods

The investigation of the debate on CNTs has been conducted through a mixed qualitative methodology. The following three sub-sections describe the methods used as an iterative, three-step process, consisting of (i) data collection, (ii) content analysis, and (iii) argument and value mapping.

Data Collection

The text sample was obtained from a qualitative snowballing approach and later joined by a quantitative literature review. After the initial text was published in *Nature Nanotechnology* [13], an update alert was placed for additional responses; the journal has to date published five pieces: four correspondences [7, 13, 17, 18] and one editorial [8]. Owing to the limited sample size and their proximate timing, this sampling was coupled with a literature review through the scientific database Scopus. Whereas the policy recommendation to constrain CNT use is novel, empirical research on their potential toxicity and environmental consequences began in the 2000s [8, 46]. Considering the prolific nature of CNTs relative to nanotechnology development, we presumed earlier normative engagement in the academic literature before the SIN listing. The final Scopus search string is provided in Table 1.

The search was designed to identify publications with a normative prescription on CNTs, modeled after the focus of the initial five papers on whether CNTs *should* be substituted (or not). In addition, a reference to REACH and ChemSec was present to capture studies related to the recent SIN listing, beyond the *Nature Nanotechnology* series. From these results, Scopus metadata, namely titles and abstracts, were imported and evaluated using the online software tool Rayyan [47]. Rayyan facilitated the initial evaluation process by organizing and visualizing the metadata, with highlighted search terms, and employed advanced tagging features to sort the papers for additional review or exclusion. This first review based on metadata led to sixteen candidates. Thereafter, a second review focused on the texts, through reading introductions, conclusions, and searching for in-text mentions of CNTs. Ten papers, culled from the initial 325 results, were ultimately selected for detailed

reading to locate any normative reasoning about CNTs that could broaden the scope of the debate. Of these, two articles were added to the corpus: Franco et al. [48], which profile three (carbon) nano-enabled products to identify European regulatory gaps, and Philbrick [49], with its review of CNT toxicology that advocates for an "anticipatory governance approach."

The final dataset thus consists of seven texts, spanning the years 2007–2020, with the five published in *Nature Nanotechnology* plus two additions identified in the literature review. The two additions from the review [48, 49] predate the episode surrounding the SIN listing, published in 2007 and 2010. However, neither article is referenced in the later debate, despite one of the protagonists, Hansen, co-authoring the earliest entry [48]. Although seven articles from a grand total of 330 candidates is a small ratio (and sample size) for analysis, it attests to the generous search criteria in Table 1 and the largely positivistic (rather than normative) approach to CNT research and innovation in most Scopus papers. Restricting the data collection to CNTs alone, instead of nanotechnology in general, indicates the relative lack of normative engagement for specific nanomaterials.

Content Analysis

At this point, the corpus consisted of three distinct phases, each uncited by their successor: Franco et al. [48], Philbrick [49], and the *Nature Nanotechnology* series [7, 9, 13, 17, 18]. The corpus was reviewed sequentially with content and intertextual analysis; this was later distilled into a dual-purpose argument map and value map. In choosing this approach, the focus was on cataloguing arguments rather than more general themes or linguistic analysis as is common in discourse approaches (cf. [50]). While potentially less nuanced and contextual, the content analysis is well suited for describing the controversy and evincing arguments.

In the content analysis, each text was reviewed separately and had its logical reasoning reconstructed from argument to argument, with supporting earlier studies and normative claims. The aim was to capture the theses and explicit evidence, most often the results from previous toxicology studies or reviews, invoked to make their cases. Franco et al. [48] do not explicitly broach the debate question or generate any arguments about the preferable use of CNTs, so it was absent in these final steps. Likewise, arguments in the texts beyond the scope of the topic were excluded from the analysis.

The identified arguments for and against the substitution of CNTs were then visually rendered and organized through mind-maps.[2] Both the insights from the initial analysis and specific quotes motivating the arguments were included in this iterative process to refine a series of mind-maps, such that the content and intertextual analyses evolved with the argument mapping described below. Two central tensions across the sample were (i) the issue of indiscriminately substituting *all* CNTs and (ii) disagreement on placing *all or only some* variants of CNTs onto the SIN list. The texts thus revealed a preoccupation with the substitution and aggregation issues.

Argument and Value Mapping

In a further analysis of the arguments, we elaborate upon the argument map technique used previously in applied ethics, as documented by Sharkey and Gillam [51]. Their work reviews the debate on whether patients with self-inflicted illness should receive lower healthcare priority. Although reviewing medical ethics and not emerging technology, the article develops a transferable outline between initial arguments (pro and con), responding counter-arguments and rebuttals which directs future discussion to overlooked aspects in the debate. Another inspiration addresses the construction of risk in a recent lay/expert nano-silver controversy in Sweden [17]. Boholm et al. review texts from different Swedish media sources, such as TV, websites, newspapers, and government documents, whereas this study is centered around the academic literature and expert disagreement. While considering different sets of actors (experts versus society at large), both approaches give attention to the underlying values at stake in the respective controversies.

This paper takes the argument map technique [51] literally in producing mind-maps, a brainstorming tool allowing hierarchical sorting of phrases or other text. Mind-maps were created to illustrate the resulting arguments in support of and against substituting

[2] The mind maps were created from MindMeister, a free use online platform. https://www.mindmeister.com/

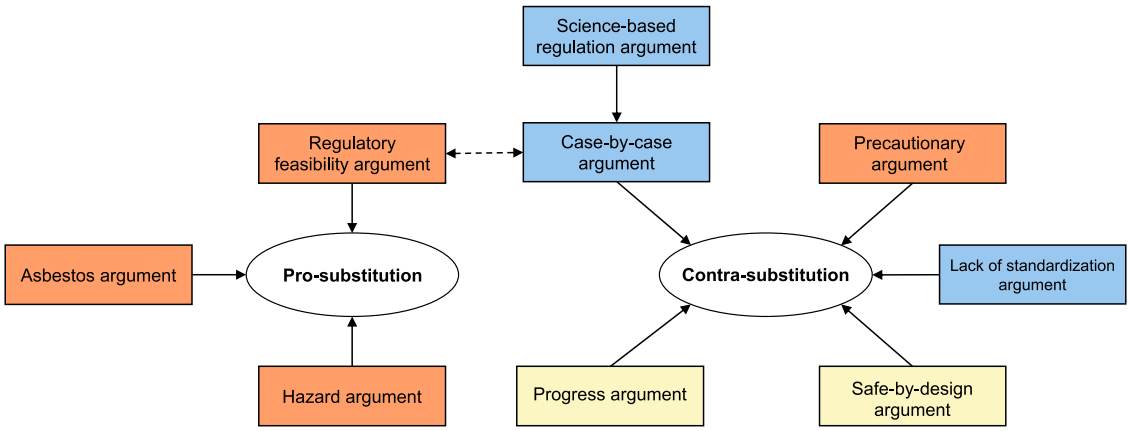

Fig. 1 The argument map showing the two camps (in ovals) and their respective arguments (in boxes). Solid arrows illustrate arguments supporting a camp or another argument, while dashed arrows illustrate counterargument relationships. The main value shown to underpin each argument is also marked: environmental protection and human safety in orange, good science in blue, as well as technological progress in yellow

Table 2 Studies in the two camps of the CNT debate

Pro-substitution camp	Contra-substitution camp
Hansen and Lennquist: "Carbon nanotubes added to the SIN List as a nanomaterial of very high concern"	Fadeel and Kostarelos: "Grouping all carbon nanotubes into a single substance category is scientifically unjustified"
Hansen and Lennquist: "SIN List criticism based on misunderstandings"	Heller et al.: "Banning carbon nanotubes would be scientifically unjustified and damaging to innovation"
Philbrick: "An Anticipatory Governance Approach to Carbon Nanotubes"	Nature Nanotechnology: "The risks of nanomaterial risk assessment"

CNTs, but moreover to demonstrate connections across and within debating positions. This flexible tool also helped to go beyond the limitations of a predefined typology, for instance, arguments, counterarguments, and rebuttals, to structure the debate in greater detail. Eventually, one stylized mind-map was refined into a flowchart diagram to display the arguments amongst the two positions (Fig. 1).

After mapping these arguments, three values were extracted by investigating their underlying motivations. Each value at stake was subsequently placed onto the argument map to address the secondary aim of expressing the ethical dimension behind this controversy. The mapping methodology thus orients the dual dimensions of arguments and values.

Results

The argument mapping is split simply into two camps—*pro* substitution of CNTs and *contra* substitution of CNTs—stemming from the polemic nature of the debate, particularly in the *Nature Nanotechnology* papers. Table 2 organizes the reviewed studies into the different camps according to the corresponding arguments. Arguments are clearly sorted by the camp they support; each paper can contain multiple arguments, which sometimes cross this divide. In total, nine arguments are identified: three in support of the pro-substitution view, and six in support of the contra-substitution view. Each camp's arguments are discussed below and are visualized in Fig. 1.

Pro-substitution Arguments

According to the pro-substitution camp, CNTs as such should be treated as a hazardous material and substituted. However, two slightly different theses harbored within this camp can be distinguished. The more absolute prescribes that all CNTs should be substituted, period. The more flexible suggests that CNTs should generally be substituted but might be used given certain conditions. The latter relies upon the more detailed assessment procedure within REACH, which is to be applied given positive hazard identification like that of the SIN listing [17]. According to this procedure, hazardous substances can still be used (i) under safe conditions,[3] (ii) when there are no alternatives, or (iii) when the potential benefits outweigh the risks to society. These exceptions, put together, suggest potentially wide use of CNTs even if proven hazardous. This said, the three arguments identified broadly apply regardless of the detailed pro-substitution thesis.

The Hazard Argument

The pro-substitution camp declares that the SIN listing means that CNTs are hazardous, such that their use ought to be limited: today with SIN, and eventually also through, e.g., addition to the candidate list of substances of very high concern through REACH [11, 12]. CNTs were added to the SIN list because of an evaluation [13] demonstrating them to be carcinogenic, toxic to reproduction, and persistent (long-lived) in the environment. Being carcinogenic or toxic to reproduction are each sufficient for a SIN listing, while persistence needs to be matched with being toxic or bioaccumulative.[4]

In the initial paper reporting about the SIN listing [13], carcinogenicity is claimed to be proven based on work by the International Agency for Research on Cancer[5] and another in vivo study on multi-wall CNTs. That in vivo study reports positive findings on pulmonary inflammation, granulomas, and fibrosis for single-wall, double-wall, and multi-wall CNTs in mice or rats. From the International Agency for Research on Cancer's work, carcinomas, bronchioloalveolar adenoma, and peritoneal mesothelioma are found for multi-wall CNTs, in vivo. Regarding reproductive toxicity, they mention the International Agency for Research on Cancer report again, specifically, in vivo and in vitro experiments with single-wall and multi-wall CNTs on mice. Finally, the criterion of environmental persistence is discussed with reference to research on CNT half-life at greater than 60 days for water and 180 days in soil or sediment—the specific Substances of Very High Concern requirement. One negative study is mentioned here but dismissed as irrelevant due to unrealistic conditions.

The Regulatory Feasibility Argument

This argument regards whether CNTs should be regulated as one entity on a group level or as several sub-types and recommends the first option. There are many varieties of CNTs, above and beyond single-wall, double-wall, and multi-wall. The regulatory feasibility argument maintains that CNTs as an entirety are the proper regulatory object, because of both expensive purification and regulatory design. First, because "consumer products containing CNTs are rarely verified to contain only one type of CNT, as purification is costly" [17], CNT nano-enabled products generally contain a mixture of types. Whatever differences in characterization that may exist between such types, the ultimate nano-enabled product exposure scenario will contain a mixture of different CNTs rather than any specific variety. Second, regulators (e.g., the European Chemicals Agency) simply do not have the capacity to create separate regulatory profiles for every possible CNT configuration. CNTs should therefore be regulated in its entirety, at an aggregated level or substance group level, due to the production and regulatory context. In addition,

[3] For example, CNT dust might not cause adverse effects in someone wearing a protective mask.

[4] The complete set of criteria is whether the substance is (i) carcinogenic, (ii) mutagenic, or (iii) toxic to reproduction (CMR); (iv) persistent, bioaccumulative and toxic (PBT); (v) very persistent and very bioaccumulative (vPvB); or (vi) of equivalent concern, e.g., endocrine disruption [52].

[5] The International Agency for Research on Cancer (IARC) is part of the World Health Organization (WHO). See: https://www.iarc.who.int/

the general policy context is to encourage group-level characterization of chemicals that foregrounds real-world exposure scenarios and not idealized laboratory-based purification profiles.

The Asbestos Argument

The third argument of the pro-substitution camp, articulated in the paper by Philbrick [49], is based on an anticipatory governance approach to address scientific uncertainty about CNT hazards and risks. Its essence is that CNTs—all CNTs—should be treated "as if" they are hazardous, with the remedy of limiting and replacing use. Just because the science is uncertain on CNT hazards, at the time of publication in 2010, does not mean that action should not be taken. Within the framework of "as if" hazard status, asbestos is proposed as a worst-case analog to CNTs, owing to similar physio-chemical properties and hazard profile [49].

Specifically, the case is made by presenting empirical uncertainty in both in vivo and in vitro toxicological methods. Three in vitro issues are (i) confounded assays, (ii) medium interactions, and (iii) surfactants [49]. The confounded assay problem refers to evidence that CNTs interfere with and compromise the reliability of cytotoxicity assay methods. Regarding medium interactions, CNTs are demonstrated to interact with other components in the medium, like vitamins, amino acids, proteins, and cytokines. This can create false positive results and challenge interpretations. Finally, surfactants are commonly used during in vitro tests to keep the CNTs from aggregating into clusters. However, these surfactants may then cause toxic effects, which can be misinterpreted as being due to the CNTs.

Considering these uncertainties and early indications of potential hazard (viz. inflammation, oxidative stress, and persistence), Philbrick writes that "the weight of the toxicological evidence to date suggests that inhaling CNTs may induce injury, and the analogies with asbestos counsel an additional level of caution. Recognizing the substantial need for additional research, this article argues that the data support treating CNTs 'as if' they are hazardous" [49]. The analogy to asbestos is substantiated by two experimental studies where CNTs are found to cause similar types of effects: Poland et al. [46] and Takagi et al. [53].

Contra-substitution Arguments

According to the contra-substitution camp, CNTs as such should not be substituted. It should be noted that they do not necessarily believe that no variant of CNTs should be substituted. Members of the contra-substitution camp clearly express that some CNTs are more hazardous than others, such as the long and rigid CNT type called MWCNT-7 [18]. Their main thesis is rather that all CNTs should not be substituted by default. As motivation, a range of arguments are employed by the members of the camp, as described below.

The Case-by-case Argument

In opposition to the regulatory feasibility argument (from the pro-substitution camp), the contra-substitution camp asserts that there is enough evidence of varying hazards for different CNT types to instead assess and regulate CNTs on a case-by-case basis [7, 18]. In other words, the regulatory classification of CNTs should be based on linking defined physio-chemical properties to hazard. As not all CNT types demonstrate hazards in the scientific literature, CNTs in their entirety should not be substituted. Fadeel and Kostarelos conclude that "CNTs should not be viewed as one material but instead as a class of materials with varying properties that may elicit distinct biological outcomes in vitro and in vivo" [18]. To this end, they elaborate upon three hazards, carcinogenicity, biological effects, and biopersistence, with mixed results.

The contra-substitution camp points out that claims about carcinogenicity are far from universal. The principal report boosting this stance comes from the above-mentioned International Agency for Research on Cancer, which concluded that the only CNT variant demonstrating carcinogenicity in animal (in vivo) studies is MWCNT-7 [18]. All other tested CNT types showed, at most, inconclusive results. Some additional CNT types might be carcinogenic, but many—or most—are probably not or the answer remains uncertain. Fadeel and Kostarelos also examine adverse biological effects based on morphology. They review the length, rigidity, and diameter of different CNTs. On CNT lengths, they conclude that "long (> 15–20 μm) and biopersistent fibers are known to induce 'frustrated' phagocytosis." On CNT

rigidity, "indeed, the rigidity of CNTs is strongly correlated with both acute and chronic inflammation." Rigidity and diameter are also relevant for potential damage to lysosomes, notable "as a general predictor of the pathogenicity of such materials" [18]. Their final consideration is biopersistence of CNTs. There is no conclusive case that CNTs are generally biopersistent, with negative findings on short single-wall and multi-wall CNTs. The discussion ends with "CNTs are not necessarily biopersistent, although the rate of biodegradation may vary depending on the specific material properties" [18].

Heller et al. go further to point out this issue in reviewing ChemSec's work, most egregiously in suggesting, "However, ChemSec decided that data from a preparation with up to 45% impurities and with lengths above 5 micrometers could accurately reflect the carcinogenicity of all single-walled carbon nanotubes" [7].

The Science-based Regulation Argument

A supporting argument to the previously mentioned case-by-case argument is the science-based regulation argument, also posed by the contra-substitution camp. The argument says that since the current scientific understanding is that only some CNTs are hazardous, while others are not. Therefore, regulation needs to happen on a case-by-case basis. Such a fine-grained regulatory strategy would require more regulatory effort than to evaluate all CNTs together as a group. Yet, the proposal of the pro-substitution camp for generalized classification does not cohere with the available science on CNT hazards. Heller et al. [7] reiterate this with "[…] conclusions of safety or toxicity have to be based on experimental data in the right context." CNT regulation thus needs to be based on the best available science and not simple regulatory convenience.

The Safe-by-design Argument

According to this argument, the use of CNTs should not be limited merely because of evidence of hazard, because actual risks of a certain CNT are situated and conditional. An evaluation outcome as hazardous should—instead of substitution—trigger a series of interventions towards safety. CNTs are not inherently risky, they just sometimes lead to risky outcomes. Hazardous CNTs can become safe CNTs by replacing questionable long or rigid CNTs with shorter types or by chemically functionalizing CNTs to diminish the hazard. Any hazards can be amended through known techniques or further research, alongside creating safe spaces where exposure is likely to be highest. In other words, CNT risk is not an essential property to be first identified and then have CNT use minimized. Rather, safe CNTs are the result of research, development, and engineering processes. Safe use of CNTs has already been shown [7, 9, 49], as in alternative CNTs, functionalized CNTs, and exposure mitigation. Even the pro-substitution camp member Philbrick admits that much can be done to make CNTs safer [49]:

> "Inthe case of CNTs, the evidence to date suggests that engineering controls can beeffective in controlling workplace concentrations, and both NIOSH and the DOEhave issued helpful guidelines in this regard. Had HEPA filters been availableand deployed in the heyday of asbestos manufacturing and usage, theepidemiological history might be quite different. It is also worthwhile to notethat engineered CNTs are not mined, but produced under controlled conditions inclosed systems, simplifying the containment problem. Useful information is alsoemerging regarding the release characteristics of various productionmethodologies, and modes of hood design and usage to minimize worker exposure."

There are three approaches mentioned to make CNTs safe in their use context, namely (i) substitution, (ii) functionalization, and (iii) preventing exposure [7, 9, 49]. The first two affect CNTs as such and the final pathway targets possible use contexts. Substitution here refers to switching to less hazardous CNT types, for instance, going away from MWCNT-7. The idea behind the functionalization of CNTs is to alter their properties to become less or non-hazardous in comparison with current formulations (cf. [42]). Fadeel and Kostarelos [18] summarize the promise of functionalization by describing studies that show functionalized CNTs behave differently, weakening the connection to asbestos.

The third approach to make CNTs safe is to address their use and exposure, for example, by "engineering controls" and "nonrespirable aggregates" [49]. First, engineering controls are designed

to limit human exposure through lessening airborne concentration, by generating more knowledge about production methods and with technologies to prevent exposure. If CNTs would reveal a comparable hazard to asbestos, their potential for pulmonary exposure within contemporary production methods would then still be lower. Second, a more direct way to prevent this exposure via respiration is with aggregation. Already in 2010, Philbrick [49] informs that the company Bayer had developed an aggregation technique that would prevent the formation and release of airborne, respirable CNTs in the initial phases of production and transportation.

The Progress Argument

Overall, assuming that CNTs are—or could be—a beneficial material, progress in their science and technology require sustained investment in research, development, and innovation. Heller et al. [7] are direct: "Human and environmental safety are a top priority; however, engineering of novel technologies progresses only through research and development." Technological progress, in this case through CNT research and development, requires financial investment. Here, the SIN listing constitutes a significant headwind and should therefore be avoided. Three notable consequences are (i) damage to the CNT innovation system, (ii) obstructing specific applications of CNTs, and (iii) creating an undesirable precedent, with effects beyond CNTs.

Investment towards CNT innovation can result in safe uses: innovation does not merely proliferate the quantity of applications but also their quality and ultimate safety. If CNTs are not already safe, then investment is necessary to promote safe innovations and to produce the necessary knowledge. This investment to (future) safety pipeline would be obstructed given a blanket limit to CNT use, which self-evidently disincentivizes that very funding. Comparisons are made to silica and iron oxide nanoparticles as previous worrisome technologies that were made safe through development [7].

Due in part to the plurality of CNT variations, illustrated by the case-by-case argument, subsequent applications of nano-enabled products and nanotechnologies are plentiful. Known uses vary: improving the strength of building materials, the development of nanomedicine with treatments for kidney disease and Parkinson's disease, molecular imaging, gene delivery, image-guided surgery, and non-invasive disease monitoring [7]. Given enough investments in technological progress, CNTs could enable an impressive array of highly beneficial cross-cutting products for the market.

Finally, if successful, the pro-substitution camp creates a challenging precedent that can travel across innovation systems. CNTs could become an early instance of many future technological innovations cut short by misguided and confusing policy interventions. Inspired by this SIN listing and its possible consequences, similar misguided fates might occur to other nanomaterials as well.

The Precautionary Argument

Instead of looking to the SIN list and any eventual substances of very high concern candidacy by considering hazards [13, 17], an alternative policy is the precautionary principle [7]. The CNT industry, according to the contra-substitution camp, is already precautionary, and any proposed substitutions should not be premised on this principle. Nanomaterial producers and importers have the burden of proving safety, and Heller et al. [7] state that "the nanotechnology field [already] subscribes to [the precautionary] principle and routinely conducts tests on the biocompatibility and potential biotoxicity of nanomaterials that are under development for medical and non-medical applications." Precaution, defined by the contra-substitution camp as a good, desirable condition, thus supplements hazard (bad, undesirable condition) in determining proper CNT use and regulation.

The Lack of Standardization Argument

The contra-substitution camp argues that because of the considerable uncertainty surrounding CNTs and their potential risks, in particular the lack of standardization [7, 9], recommending substitution is premature. The way to address lingering uncertainty about CNT hazards is through three forms of standardization: characterization methods, reporting, and safe handling.

Characterization methods have been problematic in the past and standardization is fledgling. Early studies of nanomaterials in general, but also CNTs, "[…] did

not characterize the properties of the nanomaterials, which considerably reduced their significance. Additionally, many of these earlier studies were performed with nanotubes that were long, improperly stabilized by excipients leading to aggregation, administered to animals in the microgram scale and/or contained metal catalysts" [7]. Completely non-characterized or questionable studies used to be the majority, making them ill-suited for more contemporary scientific or regulatory reviews.

The contra-substitution camp also argues that there is a lack of standardization when it comes to reporting of results. In toxicology in general, positive results (that is, some substance is toxic at a significant level or concentration) are more likely to be published than are the negative experimental studies (meaning a substance is not found to be toxic at a specific significance level). This represents a bias in the reporting entrenched by a lack of standardization. Also, even if studies showing negative (or modest) results do get published, there is a bias when it comes to subsequent attention:

> "Duringthis period, broad claims of toxicities were ascribed to carbon nanotubes,which were later found to apply only to a narrow subset of CNT preparationsand/or exposure routes. Numerous subsequent publications that reported morenuanced results were given much less attention" [7].

To avoid this situation, which persists as "a one-sided story that damages research efforts" [7], there needs to be a more balanced approach and better standardization for reporting toxicology studies—especially for CNTs.

The third aspect of standardization is in safety and material handling practices. CNTs should be evaluated across the product life cycle, from production, manufacture, shipping, use, and end-of-life. Standardized practices and procedures would develop from the nano-enabled product's hazard profile and intended use. Heller et al. explain that CNTs used in medicine are already "tightly controlled" through the use phase, in comparison with other sectors like electronics [7].

All three standardization issues—uncertainty about characterization, reporting biases, and handling procedures—imply that proper use or substitution of CNTs cannot yet be established. For the editors of *Nature Nanotechnology*, this results in a neutral position to neither encourage nor discourage CNT use [9]. However, at present, not advocating for limits to the spread of CNTs in nano-enabled products, for all intents and purposes, amounts to a tacit endorsement.

Discussion

As shown above, the two camps provide various arguments for and against the substitution of CNTs as implicated by the SIN listing. Some of these arguments to a large extent regard matters of fact, such as whether CNTs—all or some—are carcinogens. However, some of the arguments posed by the camps are not only about such technical matters of fact. The use of technologies in society—here with CNTs—is never value-free [23]. This debate thus oscillates between an explicit technical and implicit ethical dimension, as proposed by Swierstra and Rip:

> "The focus on technical questions is onlypossible when some closure of the open-ended ethical (or normative, orpolitical, or foundational) debate has occurred, and further discussion can bedelegated to technical–analytical work. Conversely, the technical discussion canbe opened up again to ethical discussion when the assumptions protecting thetechnical approach are questioned" [22].

This section will unravel how these assumptions are contested by the mobilization of values, both by the pro- and contra-substitution camps. Three intrinsic values, or final values, emerge from the arguments (as illustrated by Fig. 1): (i) environmental protection and human safety, (ii) good science, and (iii) technological progress. The pro-substitution camp largely invokes environmental protection and human safety, whereas the contra-substitution camp also relies upon the values of good science and technological progress—all three values. These intrinsic values are not made explicit, with the exception of the progress argument used by the contra-substitution camp but can be inductively derived from the arguments. Nevertheless, the debate revolves around the two camps not agreeing on the best means to safeguard such values, as developed below.

Environmental Protection and Human Safety

The pro-substitution camp sees unharmed environments (including non-human organisms) and human safety as the main value to be safeguarded, as foregrounded in the hazard and asbestos arguments. This is also clear from the emphasis on effectively functioning safety regulation, as emphasized in the regulatory feasibility argument. Regulatory feasibility is a norm to be defended even when in conflict with, for example, the scientific norms of precision (the case-by-case argument) or standardization (the lack of standardization argument). Scientific experimentation on CNTs produces the empirical evidence to inform regulatory action, but regulatory and scientific reasoning should not be conflated. Science is the means of regulatory ends to safety.

The pro-substitution camp's review of available evidence concludes that CNTs are hazardous in the regulatory sense (i.e., the hazard argument). However, the contra-substitution camp argues against a conclusion on the higher CNT level because of either (i) inconclusive or non-standardized, unreliable research (in the lack of standardization argument) or (ii) outcomes varying across CNT morphology (in the case-by-case argument). This opposing viewpoint by the contra-substitution camp uses available experimental data to tell a different story: CNTs do not merit group-level categorization and regardless, they are not demonstrably hazardous.

As both camps refer to empirical work through nanotoxicology studies, the key contention is not the availability of testing, but how to interpret results and thereafter shape regulation—a point detailed by Philbrick's paper [49] for the asbestos argument. One way to deal with this uncertainty, or "ignorance" in Swierstra and Rip's lexicon [22], is by directly taking action—developing regulation from assumed ignorance, instead of delaying under the promise of stable knowledge in the future. This rationale is akin to the precautionary principle, which encourages action to prevent or avoid potential risks in the absence of scientific certainty and the capacity to undertake comprehensive risk assessment [54]. There is a clear appeal to the precautionary principle as a way to proactively regulate under uncertainty [55–57].

However, the contra-substitution camp both (i) claims that the precautionary principle is already followed for CNTs [7] (in the precautionary argument), but at the same time (ii) dismisses it as irrelevant considering the rich availability of information about CNT properties [18]. There is thus an ambivalent view on the precautionary principle and precautionary regulation in the contra-substitution camp. On the contrary, in the pro-substitution camp, precautionary logic is frequently reiterated: uncertainty must according to them not be an excuse to delay regulatory intervention. They argue that prioritizing scientific certainty before regulatory intervention can incentivize unfortunate substitutions [13]. Producers might then switch to less studied or newer—and thus not yet regulated—substances, even if these are equally or more hazardous to humans and the environment.[6]

Good Science

The relationship between science and regulation is unsettled in the debate. Science is clearly useful or instrumental to develop and ultimately practice regulations that protect humans and the environment from toxic pollutants. This view is shared by the two camps. However, to the contra-substitution camp, quality science, presented as experimental scientific research (mostly nanotoxicology) and performed in a robust manner—precise and standardized—is a value to maintain, in and of itself. Science is therefore articulated as a virtue, in the sense of virtue ethics. The key phrase underlining this value, "scientifically unjustified", is shared in the titles by two of the responses to the SIN listing: Fadeel and Kostarelos [18] and Heller et al. [7].

A science-forward perspective, imbued across the contra-substitution camp and especially evident in the case-by-case and lack of standardization arguments, hinges upon a linear trajectory from good science, producing fundamental certainty, to best regulatory practice. For CNTs that cannot currently be easily grouped through reviewing scientific studies, and where hazards remain unclear and speculative, then hard regulation and demands for substitution are consequently premature. Further, regulatory

[6] This specific type of "race to the bottom" is explored in detail for the development of US chemicals policy in the late twentieth century through the lens of "institutionalized ignorance" with the TSCA [58], as part of a recent special issue on ignorance, the chemicals industry, and regulation [59].

norms—like high-level grouping—that challenge scientific knowledge or ignore either the unstudied variants or inconclusive work on CNT hazards, should be questioned. The right thing to do is to regulate based on the principle of good science in areas of certainty, which implies that only that which is scientifically well-studied is an appropriate regulatory object.

The pro-substitution camp suggests that because of uncertainty, empirical indications of hazards for some CNTs should be generalized to the rest. CNTs must exist as one aggregated regulatory object for practical purposes to ensure feasibility (as in the regulatory feasibility argument). Regulations should prioritize feasibility in order to safeguard humans and the environment. The burden of proof is then dissimilarity for prospective CNT producers and importers. The contra-substitution camp, on the other hand, starts from the position that the best policy is the most scientifically justified route. According to them, the current scientific evidence suggests that CNTs as a group vary widely [7, 9, 18]. The burden of proof should thus be similarity. Policy-making should prioritize the science over ease of practical implementation. The best policy is not to group CNTs together *ex ante*, but to group at a sub-type level according to empirical evidence.

This value schism between the pro- and contra-substitution camps is thus about priority. The general question remains value-laden: should scientific rigor or regulatory feasibility be the determinant? Here, it can be noted that grouping and precaution are presented as alternative approaches to good science in recent European regulatory research [4], which assumes both ignorance and practical constraints for nanomaterial innovators. This adds external support to the regulatory feasibility argument through extending these norms into research and innovation, contesting the contra-substitution camp's unilateral invocation of good science.

Technological Progress

Technological progress is a central concern for the contra-substitution camp, especially Heller et al. [7], as voiced in the progress argument. In addition to placing safety and good science as key values at stake in the debate, progress in terms of technological advancement is also seen as in jeopardy. The turn from abstract progress to tangible innovation is highlighted with both the progress and safe-by-design arguments: progress and safety happen through continued investment and prioritization of research and innovation. Safety can be achieved by modifying CNTs as suggested in the safe-by-design argument, but might also be a direct effect of progress, since CNT innovation might benefit sectors such as nanomedicine. Progress is thus understood here as deontological—the duty to advance technologically—coupled with the consequentialist assertion of beneficial applications, a recurring trope from Swierstra and Rip's [22] "patterns of moral argumentation." Instead of a sciento-regulatory divide, progress, and safety are articulated as almost inseparable. Technological progress, as described here, results in safety, and is exemplified by two initially problematic cases of nanoparticles: iron oxide, and silica [7]. This constitutes a rationale for being cautious when discussing hazards and potential regulation; continued investment is seen as the prime mover of both progress and safety. CNTs, like other emerging technologies, depend upon hype [22, 60] in order to ensure investment and fuel their progression. Regulation, and even its anticipation, puts this at risk.

This processual understanding of progress and safety pivots from the regulatory focus on hazard towards evaluations of risk, echoing elements of the longstanding debate about the role of hazard contra risk in regulation [61]. There are two positions, risk-predominant and hazard-predominant, that differentiate the pro- and contra-substitution camps.

The first position extends from earlier arguments made by the contra-substitution camp. Safety in terms of the safe use of CNTs is a process of development. Identifications of hazards—the inertia behind the debate—ought to signal substantive development of (i) safe CNTs by less hazardous formulations and (ii) safe use through lessened exposure and thus reduced actual risk. Heller et al. [7] write that neglecting risk for hazard across emerging technology regulation could threaten the linear progress paradigm: from hype to investment to innovation to safety. Without the safety-through-progress rationale, any emerging technology could struggle to secure funding, as hazards are often inherent to early research and development phases (cf. [4]). Even if CNTs would be cleared for widespread safe use in the end, it might not be relevant after this supposed initial stigmatization by ChemSec.

The second position, made by the pro-substitution camp, is aligned with the European norm of hazard identification first and risk assessment second, implemented through REACH [62]. With the hazard identification behind the SIN listing, the limitation of CNTs becomes the mantra, instead of cautious development to eliminate the hazard or minimize exposure. CNT use after hazard identification can, at least according to the weaker variant of the pro-substitution thesis, be tolerated only under exceptional circumstances and not encouraged to achieve progress. Progress can then be redefined as pursuing substances or nanomaterials which, Hansen and Lennquist [13] conclude, "[…] provide similar functionalities with less risk."

Conclusion

The researchers from the two camps arrive at different conclusions regarding the core question of the debate: should CNTs be substituted? The debate is indeed devoted to technical issues, with references to experimental studies about CNT carcinogenicity, reproductive toxicity, persistence, and other properties. It can thus appear as if the substitution of CNTs is solely a technical issue, and that its resolution requires further accumulation of data in delaying intervention in favor of stable knowledge (cf. [9]). However, despite citing similar sets of experimental evidence and shared conceptual understandings, the two camps reach opposing conclusions. This study shows that beyond matters of fact, the technical is indeed exposed as normative in contesting critical assumptions that motivate these dueling positions [22]. The regulation of CNTs—as problematized in the debate—does not only have ethical implications, but is itself an ethical issue [21].

The debate is not so much presented as a contest between intrinsic values, but on the optimal means to safeguard them. The value of environmental protection and human safety is shared by both camps, but the instrumental means of safeguarding that value are disputed. The pro-substitution camp favors the substitution of all CNTs based on evidence of hazard for some CNTs, as their preferred means to safety. The contra-substitution camp instead believes that CNTs should be made safe through research and innovation and substituted only on a case-by-case basis given sufficient scientific evidence. The value of good science is advocated by the contra-substitution camp as an intrinsic value to challenge the pro-substitution camp's prioritization of regulatory norms. Yet, good science is additionally presented as a prerequisite, a means, for environmental protection and human safety through the production of certainty.

In deciding on the future of CNTs, this ethical ambivalence adds to the case for compromise over consensus, of arena behind agora [22], in resolving the debate. At present, CNTs remain on the SIN list, but not as a Substance of Very High Concern under REACH. Substantive closure remains to be seen, with both ChemSec's decision made [13, 17] and *Nature Nanotechnology's* editorial recourse to scientific certainty [9] functioning as two dueling "temporary stabilizations" [22]. Put together, this marks an impasse for the debate, underlining the limits to a consensus-oriented, agora model.

Currently, there are at least five areas of future research that can build on the approach elaborated upon in this paper. First, the arena model above suggests a broader power analysis of these conflicting interests—both central and marginal—through stakeholder analysis [63] that captures CNT governance beyond academia and regulators. Second, this expert debate has implications for the public as well, with a need to investigate their perceptions of CNTs, risk, and toxicity [28, 35]. Third, while exposing a few inconsistencies, this methodology stops short of normative prescriptions for CNT regulation, a task for additional applied ethics research [51]. Fourth, similar studies that interrogate anticipatory practices, like the SIN list [29], could further establish the makings of promissory nanotechnologies in context, as is forthcoming with a follow-up on the institutional position of ChemSec [64]. Fifth, with the current proliferation of nano-enabled products [27], narrative studies could trace the temporalities within Swierstra and Rip's [22] postulated "co-evolution of ethics and new technologies."

Thinking beyond CNTs, it is fruitful to ask not only what and why experts argue, but, more fundamentally, to which and whose ends. As such, the debate over whether to substitute CNTs reanimates the question of whose values come to matter in the regulation of particular emerging technologies.

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Declarations

Competing interest Some of the authors (NS, KP, and RA) work concurrently with some of the researchers whose output is analyzed in the text through the above program. Notably, these include representatives from both camps outlined in this study.

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