Nanoethics (2023) 17:7
https://doi.org/10.1007/s11569-023-00442-5

ORIGINAL RESEARCH PAPER

Nano-hydroxyapatite Before the Science Court

Frederick C. Klaessig

Received: 30 March 2019 / Accepted: 9 April 2023 / Published online: 8 May 2023

Abstract In October 2015, the European Union's Scientific Committee on Consumer Safety issued a Preliminary Opinion on Hydroxyapatite (nano). Past industrial experience with this material and participation in ISO/TC-229, Nanotechnologies, led me to submit comments on the Committee's interpretations of physico-chemical properties, especially solubility, that in retrospect were also probing of the Committee's collective understanding of nanomaterials. The Committee's responses are examined against a background of other Opinions issued in the same time period. The expert's role and responsibility, whether as an individual or a group member or in representing a scientific discipline, are examined through the concept of epistemic community taken from the public policy literature. A central theme is the Committee's framing of chemical narratives such that its administrative procedures are projected onto the nanomaterial safety literature that is itself undergoing considerable investigation and revision. Inherent to this analysis is the singular role of toxicologists in the regulatory process. A related exchange by Australian and New Zealand colleagues is examined for its parallels to the SCCS actions, and there is a cursory discussion of later SCCS Opinions regarding Hydroxyapatite (nano).

Keywords Scientific Committee on Consumer Safety · SCCS · Nanomaterial · Solubility · Biopersistent · Standing

Introduction

The European Union's (EU) Scientific Committee on Consumer Safety (SCCS) is part of an administrative process that utilizes an independent panel of experts to advise the European Commission (EC) on the health and safety risks of ingredients found in non-food consumer products. SCCS members are compensated for their part-time committee work and are drawn primarily from the toxicological fields, e.g., for the hydroxyapatite Opinion, ten had toxicology backgrounds and one each were from pathology, biochemistry, chemistry and physics [1]. The Committee operates under rules of procedure [2] administered by a Commission staff, the Secretariat, that ensure adherence to legal requirements, precedent and harmonization with other EU agencies and their advisory committees ([2], pp. 24 and 25).

The Committee's ability to frame a chemical narrative arises from its governmental status. The broader community of non-experts (the European Commission, the European Parliament and through

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11569-023-00442-5.

F. C. Klaessig (✉)
Pennsylvania Bio Nano Systems, LLC, Doylestown, PA 18901, USA
e-mail: fred.klaessig@verizon.net

them the public) have decided that safeguarding the public welfare is well served through a review by independent experts that complements actions by EC regulators. There is nevertheless the potential for misalignment and misunderstandings, where administrative procedures might set boundaries on the independent expertise or when experts might not communicate risk effectively. The nature of an advisory committee's collective expertise has been examined by science and technology studies (STS) authors, e.g., Sheila Jasanoff [3] and Harry Collins [4]. Less studied is the role of experts when progress in their own field, here the biological sciences, is also being driven by rapid developments in another, here nanotechnology, and therefore, where new findings in allied fields may upend standardized interpretations. In this paper, inconsistencies involving a combination of legal, procedural, and technical matters are noted and are taken to be indicative of misalignment.

Considering the EU's routine use of committees in governance, whether involving member states in comitology or independent experts in regulatory contexts, the unit of analysis in this paper is the public policy field's concept of epistemic community, described by Peter Haas as 'a network of experts' having a 'shared set of normative and principled beliefs' including 'shared causal beliefs'; 'shared notions of validity'; and 'a common policy enterprise' [5]. Authors from public policy tend to examine the epistemic community's proximity to policy-makers and the nature of their learning relative to policy objectives [6]. From that perspective, the SCCS can be viewed as a 'designated' epistemic community that must balance an established role in assessing ingredient safety with a newer, non-routine responsibility for nanomaterials. Learning in this context first entails identifying pertinent new knowledge and then informing the regulated community (industry and stakeholders) of the appropriate inferences and burdens of proof [7, 8]. Yet, there may be limits to learning, if, as suggested by Shapiro and Guston [9], the administrative measures are also formulated to ensure the continuance of political compromises embedded in the enabling legislation, i.e., to limit epistemic drift. Viewing SCCS Opinions through the perspective of Haas's epistemic community is meant to decouple the Committee from its established, legally oriented routine in order to examine the non-routine challenges to incorporating an emerging field's new knowledge. A second purpose is to identify remedies that Committee members might pursue without compromising their regulatory role.

It should first be acknowledged that the SCCS's Opinions are noteworthy, refreshing and even disarming, which is noteworthy because other jurisdictions are not so transparent. The United States Environmental Protection Agency (USEPA) may publish its actions in the Federal Register, but the scope of information is frequently limited by claims of confidentiality and unpublished consent orders. Further, USEPA actions occur at the time of marketplace introduction, while SCCS Opinions cover findings that may forestall commercialization, e.g., unsafe and insufficient information decisions. The SCCS Opinions are refreshing in their comprehensiveness at the case level, thereby informing readers of issues likely to be under discussion in other regulatory forums. And, the SCCS Opinions are disarming as it is almost impolite to criticize colleagues who are so open and so dedicated.

Background

The Committee's procedures ensure comparable rigor across individual submissions, a widespread regulatory practice that has been described as 'regulatory objectivity' [10]. Comments venturing beyond the Committee's stated purpose, its role and procedures ([2], p. 50) will be viewed as irrelevant to the draft Opinion under consideration even if pertinent from a broader scientific perspective. An illustrative example occurred in a 2012 exchange between social scientists and several European Food Safety Authority (EFSA) advisory board members. The social scientists [11] had argued that the EC 'fails' to 'confront the normative dimensions embedded in risk-based science for policy' when considering risk analysis separately from risk management. The EFSA advisory board members [12] responded that the article by Wickson and Wynne 'contains omissions, errors, misunderstandings and misinterpretations' regarding the advisory board's role, to which Wickson and Wynne rejoined that the EFSA advisory colleagues were 'defending …procedures' without addressing the 'normative commitments inevitable in risk assessment.' Applied to the current work, participating in the public commentary demonstrates the awareness

of procedure that is needed later when examining the SCCS as an epistemic community grappling with its assigned, non-routine subject matter.

In terms of physical chemistry, the SCCS has a unique 'designated' responsibility of providing meanings to the terms solubility and biopersistence. In the EU's Cosmetics Directive ([13], chapter I, article 2(k)) a "'nanomaterial' means an insoluble or biopersistant… material…on the scale of from 1 to 100 nm" where insoluble and biopersistent are not found in the Commission's interim definition of nanomaterial [14]. Additionally, the EC was quite explicit about the ambiguity surrounding their definition, "An upper limit of 100 nm is commonly used by general consensus, but there is no scientific evidence to support the appropriateness of this value" ([14], paragraph 8), allowing for regulatory bodies to change the 50% threshold ([14], paragraph 11) and even exclude "certain materials from the scope of application of specific legislation or legislative provisions even if they fall within the definition." ([14], paragraph 16). Clearly, the SCCS had some interpretive flexibility with definitions.

Unlike solubility that can be measured, biopersistence is a term of art encompassing both chemical degradation (digestion, dissolution) and physical removal, as illustrated in an International Agency for Research on Cancer monograph on fibers [15], "Biopersistence is a function of the solubility of the fibre in the lung, and the biological ability of the lung to clear the fibre from the lung." The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), with one SCCS member participating, provided a more nuanced interpretation in an Opinion footnote ([16], p. 20), which reads, "However, the main tenet is that biological systems cannot deal with a biopersistent material through normal processes, e.g., digestion, metabolism, excretion, elimination etc." It is therefore arguable that particles passing through the GI tract are either digested (dissolved) or excreted and are therefore not nanomaterials, as they are not 'biopersistent.' The SCCS appears to recognize these distinctions stating that this 'definition covers only materials in the nano-scale that are intentionally made, and are insoluble/partially-soluble or biopersistent (e.g., metals, metal oxides, carbon materials, etc.), and it does not cover those that are soluble or degradable/non-persistent in biological systems (e.g., liposomes, emulsions, etc.)' ([1], p. 5). Unfortunately, this clarification assigns gradations to chemical composition rather than to empirical measurements utilizing standardized techniques, media, elapsed times, and associated test details. Of particular importance is the extent of dissolution occurring within the elapsed time of a toxicological test, which may mean the particle has dissolved completely or has reached a solubility limit. In the former case, testing of the dissolution products is indicated, while in the latter case, there may be a mixture of particles and dissolution products present. Understanding these terms and informing the regulated community on measurement techniques and interpretations should follow directly if the SCCS is to advise the European Commission fully on nanomaterial safety ([13], chapter IV, article 16(4)) and consumer product labeling ([13], Chapter VI, article 20(2)).

Hydroxyapatite (HAP) is a component of bones and teeth, and its dissolution products, calcium and phosphate ions, are physiological species. The bulk version of HAP has a long history of use, e.g., toothpaste, without incident and is generally recognized as safe (GRAS). The Commission's referral of nanoscale hydroxyapatite implicitly raised the issues of solubility and biopersistence. HAP solubility varies with acidity, being low in saliva, much higher in the stomach and low again in the intestines. Any re-precipitation in the intestines would transform the manufactured HAP particle into one with a physiological HAP surface [17]. The draft HAP (nano) Opinion was an appropriate opportunity to offer comments on the Committee's use of terms, their possible definitions and the challenging solubility characteristics of HAP. Proposing that the SCCS consider HAP (nano) in the physiological context of the gastrointestinal tract, the gut, was intended to direct the Committee's attention to these issues when deciding on testing requirements.

The Commission referred nanoscale HAP to the SCCS after receiving 35 notifications of its use in cosmetic products, specifically, "the ingredient is used in nano uncoated form both in leave-on and rinse-off oral cosmetics products including toothpastes, tooth whiteners and mouth washes" ([1], p. 5). While Applicant identities are not found in the Opinion, a reasonable candidate would have been the UK firm Periproducts Limited, a supplier of toothpastes, tooth whiteners, and mouth washes sold under the Ultra-DEX® brand name. The firm has worked closely with

academic colleagues at the Queen Mary University of London [18, 19] and holds a patent [20] covering oral care compositions that "inhibit caries, promote remineralization of teeth and treat dentine hypersensitivity, gingivitis and periodontal disease." The nanoscale HAP functions as a source of calcium and phosphate, i.e. dissolving in localized environments, and as a physical barrier or seed for in vitro occlusion with dentin tubules, i.e. acting as a biomimetic scaffold [18]. There are other companies with similar products and product claims: the Canadian OralSciences with Remin® toothpaste, the German Dr. Kurt Wolff with BioRepair® and the U.S.-based Carifree® with CTx4 Gel 1100 toothpaste. A significant issue for the Committee was the presence of needle-like HAP particles, which in part led to its decision that there were insufficient data to arrive at a conclusion on safety. A second submission occurred in 2019 leading to a 2021 Opinion [21], and a third submission led to a 2023 Opinion [22]. The later Opinions offer some resolution to the issues raised in 2015.

The Commission also referred various forms of nanoscale silica (SiO_2) to the SCCS. Like HAP, silica is a ubiquitous material that is the major skeletal component in sea urchins and related species. Unlike HAP, there are forms of particulate silica that exhibit significant toxicity. Inhalation exposure to crystalline silica, quartz, is implicated in the industrial disease silicosis. The nanoscale silica that was referred to the SCCS, however, is synthetic amorphous silica, a form that is not associated with silicosis. It is manufactured in large quantities and finds many industrial, food and cosmetic uses. In this case, the Applicant raised the issue of solubility, arguing that the material eventually dissolves completely. As with HAP (nano), the SCCS had the opportunity to address the related concepts of solubility and biopersistence.

Methodology

In this article, concepts from one science, physical chemistry, are used to probe the actions of a regulatory community whose members are predominantly from another science, the toxicology-related life sciences. The Committee communicates to a broader regulated community, those interacting with regulators, through published Opinions that are preceded by a public consultation at the draft stage. The simple methodology of posing comments and then examining SCCS responses would not be sufficient. The comment must be specific to the Opinion and the SCCS has latitude in responding. A more structured engagement was pursued, but one quite different from conventional scientific discourse conducted through conferences, presentations and published papers. While SCCS members are expected to incorporate developments in their specialties into the Committee's deliberations, the SCCS procedures focus them onto the immediate task of responding to a specific Commission referral and to do so in a timely manner. Legal requirements lead to administrative procedures comprising: a referral, consultations with Applicants, a Preliminary Opinion, a public commentary, and a final Opinion that may be published as part of the Cosmetics Directive's Annexes or as a journal publication.

In this article, probing the Committee's actions also probes the Committee's procedures, especially should they act as constraints to incorporating new knowledge. The structured engagement therefore utilizes a topic central to the Cosmetics Directive's very specific definition of nanomaterial. The Committee's responses to comments on Preliminary Opinions are interpreted in the context of the 58 SCCS Opinions from the 2013 to 2016 time period, which also provides the basis for comparing Opinions on routine ingredients with those involving non-routine nanomaterials. The discussion considers technical issues that illustrate the influence that routine administrative procedures have on the Committee's ability to act as a 'designated' epistemic community in Haas's sense, which in turn leads to suggested remedies.

There are four facets to the expertise operating within this methodology. There is personal expertise as a physical chemist regarding solubility and dissolution phenomena. There is the claim that this technical expertise is pertinent to the SCCS's legally oriented process and a second claim that a composite chemical narrative representing community practice can be discerned. Finally, there is the third claim that the chemical narrative is a valid basis for comparing SCCS actions to Haas's expectations for an epistemic community. Literature citations can be offered to support the first facet, the claim to technical expertise [23–25]. The fourth facet is straightforward if the interactions with the SCCS and the review of its Opinions are correctly interpreted, as the concept

of epistemic community is simply a framework for examining the Committee's practice for potential epistemic constraints.

The second facet, expertise in a legally oriented process, poses challenges. Due to the SCCS's procedures, experts from even the same field must communicate through a legal style that adds an interpretive layer, one that is analogous to the interactional expertise described by Collins and Evans [4]. The result is to create the roles of 'inside' and 'outside' experts communicating through an intermediary, the SCCS staff ('inside'), to reach the SCCS members who are 'inside' when sitting as a Committee, but who are "outside" in their everyday activities. The legal style and format reflect that the SCCS is an extension of the regulatory framework such that its deliberations encompass legal, procedural and technical considerations. The following sentence illustrates the net effect: Recognizing the implications for product labeling ('legal'), the public expert ('outside') proposes that the Applicant's data set ('inside') are incomplete ('technical') to which the SCCS ('inside') responds that the matter has been considered ('procedural').

The literature addressing such situations is relatively sparse. Shuy [26] compared his experience as a consulting forensic linguist with that of his academic contemporaries. The challenges for the 'inside' expert were: less time for considering case details; greater restrictions on what can be said and when; greater restrictions on what can be written and how (style); and maintaining an objective, non-advocacy stance in a forum structured for advocacy. He spoke from experience in trials where the expert's role is circumscribed. In the U.S. and British contexts [26, 27], the lawyers present the facts, which are circumscribed by the case particulars, i.e., the crime. The lawyers also constrain experts through their questions, prompting them to express opinions in the form of guidance to the jury, who decide if it applies. As noted by Scheffer [27], the 'modern criminal procedure accumulates certified facts throughout the pretrial and trial.' And, as noted by Lynch and Cole [28], there is also the initial hurdle of the expert being recognized as such, which in Cole's case led to a Court ruling that his STS expertise was 'junk science.'

A number of analogies can be drawn to SCCS procedures. The topic, the specific issues to decide and the completion date are found in the EC mandate. The facts are decided in private exchanges between an undisclosed Applicant and SCCS members and staff (all 'inside' experts). The Opinion is written in a specific style that reports on the SCCS determinations and not necessarily on all of the Applicant's arguments. The public's comments ('outside' experts) are limited to reviewing the reported facts. The procedure 'accumulates certified facts.'

Expertise in the legally stylized nature of these interactions involves a layer of interpretive skill even for physical chemistry phenomena that are unlikely to be considered proprietary information. In order to support the paper's methodology, the discussions of technical issues are supplemented with background information examining the legal and administrative processes for their potential to act as epistemic constraints. An example of the SCCS stance on defining nanomaterial by Volume Specific Surface Area (VSSA) is used as a validation exercise to illustrate the interplay of legal, procedural and technical issues. An example of a separate agency, Food Standards Australia New Zealand (FSANZ), addressing HAP (nano) in infant formula is used as a validation exercise to demonstrate that these epistemic challenges are not unique to the SCCS.

Results: HAP (nano) Comments and SCCS Response

In my submitted comments, themes were first discussed in paragraph form followed by five 'specific suggestions' that are summarized in Table 1. (The full exchange can be found in the Supplementary Information.) The comments first addressed two physicochemical properties, VSSA and zeta potential, that were used in the Opinion to distinguish between the toothpaste and mouthwash HAP (nano) and forms found in literature articles. It was suggested that the Committee's interpretations were misplaced. The comments then addressed solubility in terms of biopersistence (suggesting the Committee meant biodurability) and in terms of a fuller physiological context (suggesting the Committee should address the overall gut in detail at the same time as it emphasizes the oral cavity). The SCCS colleagues (or staff) responded in the order of the explanatory paragraphs, leading me to transpose them for the purpose of Table 1.

There were seven stakeholder comments [29]. My submission followed a format used in ISO

Table 1 Suggested actions and SCCS responses

Suggested action	SCCS responses
1. Discontinue VSSA as a specification in light of recent analyses by the Joint Research Center (JRC) and others	Your comments regarding the use of VSSA have ignored the fact that it was never proposed as the main 'defining' criterion for a nanomaterial
2. Re-examine the use of zeta potential measurements in characterizing particles	Similarly, zeta potential provides important information on the surface characteristics of a material and hence this information is essentially required for safety assessments as recommended by numerous bodies dealing with safety of nanomaterials
3. Consider biodurability rather than biopersistence as the concept coming closest to the Committee's interests	..but their [SCCS] concerns have been over the possibility and the (yet unknown) extent of absorption of HAP in nanoparticle form through the mucous membrane in the oral area
4. Indicate that..there are pertinent issues regarding HAP chemistry in a physiological context… especially cellular and gastric solubility	Your suggestions about the potential dissolution/ solubility of HAP in the GI tract are appreciated. The SCCS is however already aware of these aspects..,
5. Acknowledge that HAP is a physiological particle.. …ingested HAP poses a modest incremental risk	Not addressed

Table 2 Summary of SCCS actions for 2013–2016 period

	Hair dye	Cosmetics	Fragrance	Nano-material	Other	Statements
2013	6	9	0	4	0	2
2014	5	9	1	1	1	2
2015	10	8	2	3	2	3
Total	21	26	3	8	3	7
# Inorganic	1	2	0	6	n/a	n/a
# Insufficient	4	2	2	3	n/a	n/a
# Minority	0	0	0	0	0	0

deliberations, an explanation followed by a suggested action. Its gist was that the SCCS should frame its comments in a physiological context, i.e. gastrointestinal tract, which would have led them to address HAP(nano) solubility and biopersistence. The range of themes and suggested actions may not have been in the SCCS's preferred format, which may explain their administrative response of outlining roles and responsibilities and advising me to communicate directly with the industry, "As such it is the responsibility of the Applicants to provide (and they do provide) scientifically based evidence from all relevant angles in support of safety of their materials/products. Your suggestions should therefore be more appropriate to be directed to the industry who may find them helpful in preparing a better case for future assessments." There are similarities to the exchange between Wickson and Wynne [11] and Perry et al. [12]. Further, it should be repeated that participating in the public commentary demonstrates an awareness of procedure.

Results: SCCS Opinions for Context

As is readily visible in Table 1, the SCCS responses are brief. There is engagement, which acknowledges that the issue has some relevance, but there is no exchange of views as the public commentary comes quite late in the SCCS process for that specific Opinion. For a broader context, the individual Opinion should be examined relative to other SCCS actions, which is done in Table 2 for the years 2013 to 2016. The categories (hair dye, etc.), time period and associated Opinions are taken directly from the SCCS website. The Committee's template has space for minority opinions, which allows for a simple counting. Insufficient information (also expressed as

'inadequate data') means that the phrase was used to indicate that the Committee did not have the necessary basis for arriving at a decision of either safe or unsafe. Finally, one category is introduced to draw a distinction between chemical substances that are inorganic in nature, present as particulates and ions when in a solution, and organic substances, present as covalently bonded molecules when in a solution.

There were 28 actions in 2015; 19 in 2014; and 21 in 2013. The Committee's website refers to many activities beyond Opinions, such as brochures, plain language fact sheets and stakeholder initiatives. The actions in Table 2 encompass a broad range of chemical substances and intended uses. These include scheduled reviews of past actions that incorporate updated information, or dossier re-submissions responding to earlier SCCS Opinions, or new submissions for chemical substances in uses not considered before. 'Nano-materials' represent 14% of all Opinions, 27% of those with a decision of insufficient information and 67% of those involving inorganic substances. Of the ten inorganic substances, whether 'bulk' or 'nano-material,' four led to a decision of insufficient information. In this time period, an Applicant with a nanoscale inorganic ingredient had a one in three chance that their data set would be viewed as incomplete/insufficient/inadequate despite the SCCS's considerable efforts in providing guidance on the necessary testing. In these cases, the Applicant would need to obtain additional test results and repeat the SCCS process with an augmented dossier.

In 2019, there was a second mandate leading to a 2021 Opinion [21]. It was one of five nanomaterial mandates (HAP, Cu, ZnO, Au, Pt) active during 2020. The SCCS requested 'further information' during their deliberations, but laboratory closures due to the COVID pandemic led to delays. The 2021 HAP (nano) Opinion also arrived at an insufficient data conclusion, as did the Opinion for Copper (nano); it appears that the other referrals were withdrawn. It is noteworthy that the HAP (nano) Applicant had the benefit of a 2016 Opinion and yet still had to conduct laboratory studies during the review period, which raises questions about the effectiveness of Applicant-to-SCCS communications. A dynamic is present where the overall SCCS guidance is in some fashion unclear or that the underlying knowledge base of both Applicants and the SCCS is evolving to the point that guidance documents become quickly outdated.

Against the backdrop of 58 Opinions, the 2016 HAP (nano) Opinion contains an unusual statement: 'There is a huge body of literature on hydroxyapatite….' ([1], p. 7) that introduced an extensive listing of scientific journal articles ([1], p. 26, Annex, and Table 2). The statement and action are unusual in that the standard procedure would be for the Applicant 'to provide (and they do provide) scientifically based evidence from all relevant angles,' as communicated to me. With HAP being the primary constituent of teeth, enamel and bones and with its use as a transfection aid in biological testing, there is a reasonable basis for the statement. Comparing the 22 citations in the Opinion's text with those in the Appendix indicates that 13 were likely provided by the submitters and nine likely uncovered by the SCCS. One citation on page 25 (cited as Fan et al. 2011) does not appear in either the Opinion's Sect. 6 or Table 2. It is reasonable to assume that the SCCS members, knowing that HAP has a 'huge body of literature,' had expected the Applicants to provide more citations and took the extra step of conducting their own literature search.

The 2016 and 2021 HAP (nano) Opinions demonstrate that a tension exists between a procedural reliance on the Applicant for providing the requisite information (studies and explanations) and the Committee obtaining information from other scientific sources. In mid-2019, the SCCS added the following statement to its website for those intending to make comments on Preliminary Opinions: 'This publication intends to enable Applicants, but also other interested parties, to provide clarification/comment, if any, about the evaluation, interpretation, and incorporation of the submitted set of data in the SCCS preliminary Opinion.' And: 'Please note that this is NOT a public consultation process whereby new evidence or comments on the scientific basis of the preliminary Opinion are submitted for consideration in order to finalise the Opinion, nor is it an opportunity for the Applicant concerned to submit a totally new set of data that would lead to a new submission and mandate.' This statement stands in contrast to a 2020 EC mandate [30] requesting that the SCCS address situations where decisions of 'insufficient information' do not provide the Commission with a legal basis for taking regulatory action. Further, the requested SCCS Opinion should be made 'regardless of the data previously submitted by the respective applicants,

should be based on the available scientific literature and SCCS' expert judgement..' The 2020 mandate mentions nanomaterials as a category 'in light notably of their nano-scale dimension, bio-persistence and insolubility,' repeating the definition of nanomaterial in the Cosmetics Directive [13]. Evidently, there are legal implications when the regulator invokes the precautionary principle in that the potential for risk 'shall be more than hypothetical and based on a scientific risk assessment as thorough as possible.' Once again, there is a tension, this time between SCCS's stance on the Applicant's role and the regulator's requirement that SCCS Opinions be based on 'available scientific literature' regarding potential risk. The 'inside' SCCS experts are to be 'as thorough as possible' while not welcoming the public, 'outside' expert's contribution to understanding 'the scientific basis.'

Consistent across all categories in Table 2 is the absence of any minority opinions. If viewed from the vantage point of a single chemical substance, e.g., HAP (nano), the absence might imply unanimity or a significant consensus among the independent experts. When viewed from the vantage point of 58 SCCS Opinions, the absence is more indicative of other dynamics being present. For example, SCCS procedures encourage consensus (strive to reach common conclusions), but Opinions are arrived at 'by an absolute majority of their members' ([2], p. 19). A name on the front page, therefore, indicates participation and not necessarily full agreement. Minority opinions, on the other hand, 'can only be expressed by members and shall be attributed accordingly' ([2], p. 19). Attribution therefore becomes one dynamic whereby SCCS members would be singled out were they to propose alternative interpretations. The absence of minority opinions may also simply express a limit to SCCS transparency, which though exemplary relative to other regulatory agencies, must still accommodate legal formalisms. Minority opinions might detract from the certainty desired for a decision that might later be appealed or even litigated, e.g., as with the 2020 EC mandate requesting clarity for 'insufficient data' Opinions [30]. Minority opinions might undercut the Committee's status and authority in others' eyes [31]. Both of these factors would contribute to a relative homogeneity in member viewpoints [32]. The absence of minority opinions reflects another dynamic, this time an internal social dynamic, acting upon SCCS deliberations.

The interplay of technical, procedural and legal factors identified in the earlier methodology discussion are readily visible when examining the SCCS's 2013–2016 Opinions in Table 2. The number of 'insufficient data' Opinions is higher for nanomaterials than other categories, which in turn reflects the challenges Applicants experience in providing an acceptable data package and the difficulties regulators confront when invoking the precautionary principle. The SCCS response was to repeat its stance regarding roles, responsibilities and procedures that were founded on a legal practice developed primarily for covalently bonded organic molecules. Legal processes, however, place constraints on expertise [26–28], which may have unexpected consequences when imposed prematurely onto a subject area that is undergoing significant development. Recasting the SCCS as a 'designated' epistemic community is an opportunity to identify options that might address these dynamics while remaining consistent with the SCCS's regulatory role.

Discussion Overview

The SCCS's Opinion on nanoscale HAP [1] has three voices: one is procedural (transparency); one is toxicological (a meta-analysis of the studies viewed as pertinent); and the third responds to the Commission's terms of reference, for which the SCCS merges the toxicological meta-analysis with the consumer's likely exposure from the Applicant's intended use. Together, the three voices become a chemical narrative demonstrating that the Committee has met its administrative responsibilities. All three voices are examined, the first two through the alignment between the SCCS's obligations regarding safety and its practices taken from other fields, e.g., primarily law. The third voice is addressed using Haas's concept of epistemic community as the unit of analysis. Some issues involve legal concepts where my knowledge reflects US law, which may be expressed differently in Europe.

Solubility and Non-Knowledge

There are unavoidable implications surrounding particle dissolution that are not being explicitly addressed in the 2013–2016 Opinions, the simplest involving HAP (nano), where the SCCS Opinion suggesting a repeat oral dosage study is at odds with their knowledge that HAP particles might dissolve substantially under gastric conditions ([1], pp. 17 and 35). A second and more complex implication is the causal ambiguity surrounding particle toxicology with dissolution products present, i.e. the adverse effects due to particle size, shape and surface chemistry when there is also a toxicity contribution from the dissolution products [33]. To gauge the Committee's overall stance on solubility, the full set of 58 Opinions in Table 2 were reviewed and a great diversity was noted in reporting formats for solubility, examples being: less than 0.001%; miscible; partially; 0.05% at pH 9; > 247 g/L; < 55%; < 50 mg; and 0.0015 w/w%. It is likely that the Committee members (probably the Secretariat) simply transcribed the information provided by Applicants who in turn may have only intended to document that the ingredient was fully soluble in the applicant's product formulation (routine ingredients) or was insoluble (non-routine nanomaterials). As there is little method to the data reporting format, we can also assume that the Committee's attention to solubility is occasional, episodic, and case specific.

In 2018, nanomaterial solubility was a significant regulatory theme. In January, the Commission issued a mandate for the SCCS to examine the solubility of silica relative to the dossier deficiencies noted in the 2015 Silica (nano) Opinion, which in turn led to a 2019 Opinion on silica solubility [34]. In May, the Organization for Economic Co-operation and Development (OECD) issued a report on biodurability, a term encompassing dissolution in biological media [35]. In June, the European Food Safety Authority (EFSA) issued a nanomaterial guidance in which 'quickly dissolving' is defined in terms of particle persistence rather than the amount dissolving. Persistence was defined as > 12% remaining after 30 min of simulated intestinal digestion ([36], p. 39).

The Commission's Silica (nano) Solubility mandate is most pertinent. It probably arose from the silica industry's post-Opinion representations to EC regulators. The silica industry, as part of a broad industry consortium [24, 37], has proposed that a solid with a water solubility > 100 mg/L should be viewed as 'soluble.' It was a likely industry argument during the 2015 SCCS-to-Applicant communications as it would have obviated any SCCS-requested testing such as found in the 2015 Silica (nano) Opinion [38]. This is an example of how the Applicant can use their 'inside' status to advocate a concept favorable to their product, synthetic amorphous silica, even if disadvantaging other silica forms such as silica fume, quartz and colloidal silica. As the industry argument is not mentioned explicitly in the first Silica (nano) Opinion [38], the public does not know if the Committee disagreed with the proposed 100 mg/L value or viewed a 'soluble' nanomaterial as still requiring some level of testing.

There are two troubling aspects to the intervening history. Firstly, there were parties (the silica industry, myself and perhaps others) drawing the SCCS's attention to dissolution as it pertained to at least two Opinions, HAP (nano) and Silica (nano). It was primarily the silica industry's standing as an Applicant and its persistence that led the Commission to mandate that the SCCS attend to this issue. Secondly, the SCCS response to my comments ('The SCCS is however already aware') means the SCCS (members or the staff or both) have a knowledge and are presumably utilizing that knowledge without communicating that knowledge in the Opinions. Effectively, the Committee's Opinions are best interpreted as selective narratives intended to support the Committee's conclusions.

A more nuanced interpretation of the Committee's stance emerges when differentiating organic materials from inorganic ones. The Methylene bis-benzotriazolyl tetramethylbutylphenol (MMBT) (nano) Opinion serves to illustrate. MBBT is present as a discrete molecule both in the solid and in solution. There are nine endpoints in the MBBT (nano) Opinion [39] that note 'No studies provided with nano-sized material. For studies with MBBT: see annex 2.' The endpoints include acute oral toxicity and teratogenicity. Further, the margin of safety calculation for nanoscale MBBT uses the no effect level for 'bulk' MBBT ([39], note b to NOAEL in the Table on page 53) likely based on a read across argument (read across is the practice of filling data gaps using the value from a closely related material). For HAP (nano), there are no referrals to 'bulk' HAP endpoints, no margin of safety

calculation based on the GRAS 'bulk' HAP material and no consideration of read across. It appears that the Committee viewed the MBBT molecule as an intermediary between the nanoscale and 'bulk' forms, but did not do so with HAP. Perhaps, traceability is the issue. MBBT is a synthetic organic molecule and any exposure to it can be traced back to either 'bulk' or nanoscale MBBT. HAP, however, dissolves into Ca^{+2} and PO_4^{3-} ions both of which are already present physiologically and therefore adverse effects could not be ascribed solely to the HAP (nano) particle. Effectively, the Committee became reliant (and insistent) on biological testing for phenomena that might be better examined through abiotic solubility testing. This interpretation is perhaps also an explanation for 40% of the inorganic materials leading to 'insufficient information' Opinions. Of course, the intended MBBT and HAP (nano) uses differ, but any reliance on the molecule for toxicity calculations overlooks particle effects arising from size, shape, and surface coating.

An argument can be made, a quite reasonable one, that full knowledge of HAP (nano) solubility would not have changed the Committee's Opinion, i.e., solubility data cannot replace missing biological testing. However, there is also a counter-argument that the Committee's (or the staff's) understanding of solubility was overly focused on the dose–response results from biological testing, while overlooking the surface chemistry implications. Restated, the particle as a chemical reservoir is conflated with it being an entity with properties that can be affected by the test medium, such as dissolution rate and the influence of adsorbed species on surface chemistry [23, 33]. Substantiation of this point can be found in the Committee's questioning of HAP particle identity for those studies taken from the open literature ([1], Sect. 3). For all 15 of the open literature studies, the SCCS questioned 'whether the tested material belongs to the materials covered by the submission' or commented that the zeta potential 'is not comparable' to the Applicants' materials. Any HAP dissolution in the stomach, however, erases the particle's history by removing the surface-as-manufactured, and any precipitation in the intestines [17] generates a new HAP surface with a 'new' zeta potential. The Committee's questioning of particle identity is indicative of an unease with surface chemistry separate from particle composition. If so, the SCCS narrative becomes a source of non-knowledge, meaning that there is an implicit assurance to any SCCS Opinion that there is sufficient knowledge to support the Opinion's statements. If not, the Opinion's narrative substitutes collective belief for knowledge and simultaneously creates a hurdle to an 'outside' expert's comments (see Table 1 for the SCCS's response to zeta potential).

At this point, three types of applicants have been discussed: the individual firm (BASF for MBBT); the trade association for synthetic amorphous silica (the Association of Synthetic Amorphous Silica Producers, ASASP); and two undisclosed firms acting in loose coordination for HAP (nano). The SCCS's approach to solubility and dissolution varies with material. One explanation may well be that each Applicant has likely advocated their proprietary, product-specific views in a privatized setting. A physical chemistry concept becomes subordinated to toxicology in that the privatized exchange is about required testing or the interpretation of test results. Differences in material properties are amplified, e.g., HAP dissolves more readily in acids, silica in bases. By the time the Preliminary Opinion is drafted, the SCCS has come to a firm conclusion, and it becomes difficult for the 'outside' expert to suggest a unifying perspective such as the physiological context documented in Table 1. Absent such a perspective, the SCCS's approach on a physical chemistry concept wanders between a reasonable accommodation with MBBT to a dismissal of the 'outside' expert with HAP. In the middle is the situation with the ASASP where its position is not explicitly mentioned in the Silica (nano) Opinion [38] and would not have been addressed without the Commission's 2018 mandate and the resulting silica solubility Opinion [34].

The Committee's approach to solubility has not been particularly methodical, which allows for the inference that the use of solubility in their Opinions is the narrower, occasional, albeit more direct one of interpreting the dose–response relationships of dissolved species in biological testing. Further, the Committee did not view defining solubility as a special responsibility, one arising from the Cosmetics Directive's definition of nanomaterial, until it was mandated to do so by the Commission. Solubility and dissolution are therefore useful bridging concepts between the knowledge the Committee assumes it has and that which it should know. The Committee members may have a tacit knowledge and

not communicate it explicitly ("The SCCS is however already aware') or the Committee may not be aware that there is knowledge to be gained if a more methodical accounting of solubility were pursued. In this regard, the SCCS is well situated to be analyzed as a 'designated' epistemic community with non-knowledge as a consideration.

Validation Exercises

As noted in the methodology section, there is an added layer of interpretation when analyzing SCCS actions. This was described earlier as 'inside' and 'outside' experts communicating through a legally oriented style administered by the SCCS staff. Two test cases illustrate the style as well as provide some validation for the methodology used in this article. One is the SCCS's use of a physical chemistry concept other than solubility in specifying nanomaterials, and one is a review of the Food Safety Australia and New Zealand (FSANZ) response to needle-like HAP (nano) being found in infant formula. The FSANZ case involves their interpretation of the SCCS Opinion on HAP (nano). In both cases, the new information encounters a background narrative that deflects from a more comprehensive analysis of the issue at hand.

VSSA as a Physico-chemical Measure

The EU's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) proposed volume specific surface area (VSSA) as a means for characterizing particle size [40], and it eventually became a secondary parameter in the Commission's 2011 interim definition of nanomaterial [16]. When first adopted, VSSA was thought to be a simple combination of the specific surface area (BET (m^2/g)) that is regularly measured for powders and of the literature value for particle density (g/cm^3) [41], which was to be compared to a 60 m^2/cm^3 threshold that was then considered 'a universal cut-off boundary for different types of materials at any size distributions.' Subsequently, the EU-funded NanoDefine project (budgeted at 9.3 million euros) demonstrated that (1) the upper cut-off value is shape dependent (60 m^2/cm^3 for spheres, 40 m^2/cm^3 for fibers and 20 m^2/cm^3 for plates); (2) the cut-off value should be adjusted for surface roughness and porosity; and (3) the analytical methods should be expanded to include electron microscopy for shape and helium-pycnometry for 'skeletal' density [42]. In an interlaboratory study employing the resulting protocol, NanoDefine authors found that seven of the 25 test samples (28%) remained 'borderline' and would require even further analysis to determine particle size [42].

The SCCS has frequently utilized VSSA to differentiate one Applicant's nanoscale material from others of the same composition, as was done in the HAP (nano) and SiO_2 (nano) Opinions. My 2015 comments cautioning against this practice are found in Table 1. The reasons were twofold. Industry does not use VSSA in product specifications, which implies that the concept is not 'universal,' and further, the HAP (nano) Opinion reported an incorrect VSSA. The 440 m^2/cm^3 found on page 7 [1] was not calculated from the specific surface area on page 7 (147 m^2/g) being multiplied by the density reported on page 8 (1.1–1.2 g/cm^3), which would be ~ 160 m^2/cm^3. It is likely that the density reported on page 8 is for the mouthwash formulation, not the HAP ingredient, while an undisclosed literature value for the toothpaste HAP was used when calculating the VSSA on page 7. In responding, the Committee was not open to reconsidering its use of VSSA stating: 'Your concern about the adequacy of VSSA seems to be based on the assumption that it is used in isolation whereas in reality it provides important additional information and is used in conjunction with other size defining criteria.'

Comments to the SCCS regarding VSSA continued into 2018. Applicants intending to use nanoscale silver in toothpastes and skin care products had not provided VSSA data, leading the SCCS to note that 'VSSA must be provided for each material (see Kreyling et al. 2010 for calculation of VSSA)' [43]. It appeared that the Committee was unaware of ongoing EU projects, specifically NanoDefine, which led me to repeat the earlier technical comments with the recommendation that the Wohlleben et al. article summarizing NanoDefine results be the primary reference for VSSA test methodology. The SCCS response was that Wohlleben et al. [42] had been added to the Opinion as a supplemental reference, but that Kreyling et al. remained the 'primary reference.'

The EC had a stated intention of reviewing the 2011 interim definition as early as 2014, and though a review was initiated in 2013, it did not conclude until 2022. In the 2022 EC definition [44], the 2011 view of VSSA as a 'proxy indicator in identifying a nanomaterial' is characterized as 'not appropriate and should be removed from being a qualifier in the definition of a nanomaterial.' It cites the 2015 deliverable report from the NanoDefine project that is part of reference 42. The accompanying staff working document [45] cites the JRC report mentioned in Table 1. In the case of VSSA, an unexpected source, an'outside' expert, had informed the SCCS twice of a pertinent issue.

The initial expectations of the SCENIHR authors (primarily experts in the biological sciences) had not been substantiated in later EU-funded projects. Evidently, the NanoDefine recommendations had not been communicated to the SCCS. In contrast EFSA, which is less insistent in its use of VSSA, cites the NanoDefine decision-flow scheme ([36], Appendix). The response to an 'outside' expert raising the point was a procedural one in that revising the Silver (nano) Opinion's references would not have changed the Committee's overall position that 'the SCCS is not in the position to draw a conclusion on the safety of nanosilver when used in oral and dermal cosmetic products.' Nevertheless, the comment was timely and substantive, but evidently not circulated or reviewed with knowledgeable colleagues at the JRC or at NanoDefine. SCCS's use of VSSA in its narrative continued.

HAP (nano) in Infant Formula and the Food Standards Australia and New Zealand Response

An exchange among Australian colleagues regarding nanoscale HAP found in commercial infant formula provides additional perspective on the force a narrative has when addressing information from unexpected sources. Academic social scientists [46] had examined 'the regulatory responses to the presence of previously undetected and unlabelled nanoparticles in the Australian food systems.' Several nanoscale food additives (TiO2, SiO2 and HAP) were involved, but the exchange focused on nanoscale HAP, some portion with a needle-like shape, in infant formula. With parallels to Wickson and Wynne and the EFSA experts, the CEO of Food Standards Australia New Zealand (FSANZ), responded [47] that "the authors do not appear to understand the role of FSANZ" and then provided a counter narrative that FSANZ actions had not been 'out of step' with the SCCS opinion on HAP (nano) as that opinion was 'not relevant to a consideration of the safety of small amounts of HA in infant formula, which will dissolve to calcium and phosphate.' From Booth's perspective, Lyons and Smith had taken the SCCS opinion 'out of context' and should have consulted with FSANZ before publishing.

FSANZ is an independent statutory agency responsible for managing and developing food standards with enforcement conducted by a separate function, which in Australia are the state and territorial agencies and in New Zealand the Ministry for Primary Industries. Within Australia, FSANZ has additional, primarily networking roles for labeling, for monitoring the safety of the food supply (including emerging food safety risks) and for coordinating food recalls. One example from its website of an emerging food safety risk is microplastics for which FSANZ pursues a "watching brief" while offering an interim opinion: 'However, our view remains that plastic contamination of the food chain is unlikely to result in any immediate health risks to consumers.' FSANZ clearly has a broader range of roles, tools and responsibilities than the SCCS. However, both face the same challenge, especially with emerging technologies, of interrupting their planned activities to consider information that arises from unusual or unexpected sources.

The FSANZ stance on nanoscale materials is that those 'that may present safety concerns' would undergo 'a comprehensive scientific safety assessment before they can be legally supplied.' Website statements are supplemented by a publication authored by staff members [48], which cites Klaessig 2006 [23] and a FSANZ-funded external study [49]. However, a public report on nanoscale materials being present in infant formula challenged the narrative's procedural expectations in which a potential supplier would be the first to approach FSANZ thereby initiating an evaluation that would include confidential product information and probably cite regulatory actions from other jurisdictions. With HAP (nano), FSANZ was informed in a very public fashion by a non-governmental organization (Friends

of the Earth, FoE) who had submitted samples to academics [50] and was using the results in fund-raising. For FSANZ, the SCCS Opinion was the only prior regulatory review on nanoscale HAP, but in the FoE report, it was used as evidence that FSANZ should be conducting a product recall. In the academic article [46], the FSANZ response became an example of 'governing with ignorance.' The inconclusive nature of the SCCS Opinion was prominent in this exchange. Eventually, the SCCS Opinion was not considered relevant (from the FSANZ website): 'the studies were specifically focused on dental applications, and don't consider the solubility of the material in the gut' and 'the data used is not directly applicable to ingestion.' The two apparent pivot points for the FSANZ response were HAP dissolving in the stomach to calcium and phosphate ions and the stated FSANZ interpretation that only materials 'that may present safety concerns' would undergo 'a comprehensive scientific safety assessment.'

Dissolution, especially in the stomach, is a recurrent FSANZ theme and presaged the recent EFSA guidance [36]. The emphasis on the stomach as the starting point for analysis is reasonable. For adults, a food morsel is in the mouth for a short time before swallowing and mechanical forces during mastication center on the teeth (a form of HAP). Further, the senses of smell, taste and even oral irritation are safeguards signaling that the food morsel should not be swallowed. In meshing this knowledge of food products with the SCCS Opinion, FSANZ could reasonably consider that it applied to adults and that the products' ingredients would not be swallowed. Further, the SCCS had not explicitly addressed HAP solubility in the gut (stomach and intestines), though as noted in Table 1 'The SCCS is however already aware of these aspects.' In terms of the FSANZ dissolution narrative, it is reasonable that the amount of HAP (nano) reaching the gut would be considered inconsequential and would readily dissolve.

The importance of dissolution in the FSANZ narrative is clear, but their stance regarding exposure is more difficult to fathom when distinguishing between adults and infants. The SCCS had expressed concerns about the effects of HAP (nano), especially the needle-like form, on buccal cells during the short contact times of gargling with a mouthwash and brushing with a dentifrice. Additonally, an adult's exposure to cosmetic products is minor relative to their total dietary intake. An infant, on the other hand, might be bottle-fed 4–6 times a day with each feeding lasting roughly a half hour and involving mechanical stresses between the infant's gums (buccal and lingual epithelia) and the bottle's rubber nipple.[1] The SCCS's concerns should have had sufficient institutional merit to draw FSANZ's attention to the potential that buccal cell studies of needle-like HAP (nano) might be relevant to an infant's consumption of formula. Further, infant formula is the full dietary intake and might occur in quantities that alter the stomach's pH level. In this light, it is unfortunate that Booth misinterprets the other source of information (Schoepf et al. [50]), as stating that HAP (nano) is soluble 'at gastric pH,' when those authors expressed surprise that dissolution did not exceed 60–75% in simulated gastric fluids and that the data 'indicate that the dissolution of HA in the simulated gastric fluids may have kinetic limitations or differences in solubility products for different aspect ratio HA or presence of non-crystalline forms of calcium phosphate solids.' As noted earlier with SCCS opinions, the FSANZ's dissolution narrative obscures attention to new details including that of the one FSANZ-cited external expert who found the presence of 'needle shaped hydroxyapatite in infant formula significant since there is growing scientific evidence that the cytotoxicity of hydroxyapatite is shape and cell-dependent' and recommended that FSANZ 'setup comprehensive guidelines.'

Throughout this article, there is an attempt to identify the influence that administrative processes may have on the deliberations of technical experts. The combination of process and expertise leads to narratives that are communicated in Opinions. FSANZ chose to interpret the SCCS Opinion on HAP (nano) within its food product dissolution narrative which contributed to its decision that HAP (nano) did not 'present safety concerns' and thereby forestalled any further "comprehensive safety assessment.' FSANZ

[1] One reviewer commented that buccal cells are constantly turning over, which is why injuries to the mouth heal rapidly, and that they even slough off due to the bottle's rubber nipple. Harm to the infant would therefore be implausible as low concentrations of a nanoscale material would not add significantly to abrasiveness. This argument was not raised publicly by FSANZ, nor is it in the SCCS Opinion for adults using mouthwash.

might have chosen instead to use its Australian coordinating responsibilities for labeling and food recalls [51] to approach trade groups such as the Infant Nutrition Council with their access to retain samples in order to pose questions such as: has a product containing HAP (nano) been sold in Australia?; if so, for what time period?; how was it labeled?; was the formula manufacturer aware of the HAP (nano)?; if not, had the manufacturer's supplier been aware of HAP (nano)?; and what corrective actions should be taken? The answers arising from this quality control type of approach would have dispelled the speculations regarding motives found in Lyons and Smith, Booth and even Schoepf et al., i.e., the HAP (nano) was intentionally added [46] or was not intentionally added and engineered [47] or simply represented a new bottoms up manufacturing process intended to increase the rate of dissolution [50]. Also, the FSANZ would have tangibly demonstrated its role in monitoring emerging technologies and in safeguarding food safety.

Clearly, the FSANZ colleagues grasped quickly the importance of dissolution when considering nanoscale HAP. However, where the 2016 SCCS Opinion stresses effects in the oral cavity and is silent on dissolution in the stomach, FSANZ stresses the stomach and is silent elsewhere. Like the SCCS, the FSANZ projects a narrative based on a linear submitter-to-chemical-approval path, which places others, 'outside' experts, at a disadvantage in gaining FSANZ attention. These elements underly the concept of 'undone science,' which describes those topics that are left underfunded, incomplete or generally ignored when setting the research agenda [52]. In the retrospective account above, FSANZ had four opportunities to reconsider its dissolution narrative: an academic publication on the surprising presence of particles that did not dissolve as expected; the SCCS Opinion regarding buccal cells and mouthwash; the FSANZ external expert (albeit a minority opinion); and approaching infant formula manufacturers directly. Missing completely is a food industry response to what was at minimum an embarrassing lack of awareness about an ingredient's physico-chemical properties, for the infant formula manufacturer's product stewardship responsibility is to assure compliance to food standards and labeling for both itself and its supply chain.

In its use of available resources, the FSANZ response supports Lyons and Smith's claim of 'governing with ignorance.' Lyons and Smith propose neoliberalism as an underlying explanation for this form of non-knowledge, whereas Espeland and Stevens would emphasize that the loss of information is one outgrowth of commensuration ([53], p. 315). In terms of Haas's epistemic community, FSANZ did not make full use of its available resources, which in turn points to procedural issues becoming epistemic constraints when not offset by an articulated purpose that causes the community to reconsider, reflect, and revise the assumptions present in its narrative.

Regulatory objectivity [10] is nevertheless injured when one regulatory community views nanoscale HAP as safe in infant formula (FSANZ), while a second does not accept its use in mouthwash (SCCS), and a third is silent (the U.S. Food and Drug Administration, FDA, which has cautioned that GRAS status for bulk materials does not carry over to the nanoscale form). An administrative explanation for these diverse responses might simply be the ability to control their own agenda. The FDA has not had to respond to outside prods; the SCCS responds to Commission referrals; and FSANZ was taken by surprise. The absence of a gastrointestinal (GI) tract physiological context contributes to uncoordinated responses.

Opinions as Legal Formalism

An SCCS Opinion is not intended to be a *verbatim* recounting of the Committee's deliberations, nor is it a comprehensive scientific review. Rather, it is a purposeful document, much like a legal opinion, containing a narrative explicating the decision. The SCCS style differs from EFSA's more comprehensive accounting of the scientific literature, as illustrated by comparing the SCCS decision on titanium dioxide in sunscreens [54] with the EFSA decision on its use as a food colorant [55]. The SCCS narrative has the Cosmetics Directive as its framework with roles and responsibilities distributed among the SCCS experts, the Commission staff and the commercial Applicant (submitter): Committee experts validate or contest study findings; the staff oversees the process; and the Applicant prepares the dossier and responds to questions. The resulting narrative, i.e., Opinion, is

the allowable public version of what is likely a much more complicated internal record.

An analogy can be drawn between an SCCS Opinion and a judicial one. In U.S. practice, a judicial opinion contains both *dicta* and the holdings that support the legal decision. *Dicta* are authoritative contextual comments, while holdings are the material facts that are combined to form the *ratio decidendi* that underlies the decision. It is the *ratio* that expresses the principle that future courts should consider binding. Legal analysis requires that there be a decision if one is to distinguish the *dicta* from the holdings, or if one is to use the *ratio decidendi* for guidance. Applied to the SCCS actions in Table 2, there is a gradation in SCCS comments. All are authoritative, but their full value as *dicta* or as holdings is clouded when the 'common conclusion' is an indeterminate 'insufficient information.' A tangible example of this dilemma 'with inconclusive SCCS opinions' is the Commission's 2020 mandate [30] stating that it 'is not in the position to take potential regulatory measures' without a clearer SCCS holding regarding the potential risk to human health.

SCCS Opinions follow a template [56] where a robust summary of each study is accompanied by an SCCS comment. The studies considered pertinent are reviewed in the Discussion, which leads to the Conclusions specific to the Commission's terms of reference. An authoritative comment on a study, even a quite definitive one, may not appear in the Discussion or the Conclusion, effectively becoming *dicta*. The adept reader utilizes the determinate Opinions, those leading to safe or unsafe decisions, as guidance to the factors that the Committee considers significant. What may be *dicta* for a sunscreen additive, may be a holding for a food additive, reflecting differences in the *ratio decidendi* and terms of reference. Therefore, the SCCS Opinion favoring the rutile phase of TiO_2 over anatase does not contradict EFSA's acceptance of both anatase and rutile when evaluating TiO_2 as a food colorant.

It is only the EU's policy of transparency that allows readers to undertake a detailed, case-specific analysis. In other jurisdictions, the government scientists likely encounter similar hurdles in merging proprietary studies with published articles, but we have less insight into their reasoning. Even within a jurisdiction, the decisions of different agencies will reflect distinctions in their respective statutory law, practice or precedent. Each Opinion is a closed, circumscribed, self-referencing system of thought arising from a policy abstraction rather than being a holistic description of scientific phenomena. This was, in part, Wickson and Wynne's point [11] in that the regulatory abstraction of separating risk assessment from risk management does not encompass their concerns for the environment.

If a chemical substance is found to be safe for the specified use, the SCCS Opinion will likely be incorporated into the Cosmetics Directive's Annexes and even be published as a journal article, e.g., titanium dioxide (nano) appeared in all three forms [54, 57, 58]. Committee Opinions are viewed as 'closed and not subject to revision for a period of 3 years," ([2], p. 51), which parallels the U.S. legal concepts on the preclusion of the claims (*res judicata*) and of the topic (collateral estoppel) once there has been a judicial decision and all appeals are exhausted. Effectively, the SCCS acts as if it were a court, a science court, with procedural rules, evidential requirements, and the *dicta* and holdings found in an Opinion. Indeterminate Opinions pose interpretive difficulties. There is no means for differentiating *dicta* from holdings; there is certainly no *ratio decidendi*. It is in these circumstances that the Committee's potential role as a 'designated' epistemic community is most visible as there is an opportunity to consider new approaches so as to reach determinative decisions.

Stakeholder 'Standing'

The legal concept of 'standing' provides additional insight regarding stakeholder roles and responsibilities, those of scientists in general, those of scientist-applicants and those of scientists in a 'designated' epistemic community. Simply having a grievance or a strongly held opinion is not the basis for initiating a legal action. Consuming legal resources is constrained to concrete situations where there is a causal relationship among the parties such that resolution leads to finality regarding the immediate dispute (collateral estoppel) and to greater clarity for resolving future disputes. In one prominent case before the US Ninth Circuit ([59], pp. 8–13), the legal considerations were phrased as: 'The "gist of the question of standing" is whether the plaintiff has a sufficiently "personal stake in the outcome of the controversy" to

ensure that the parties will be truly adverse and their legal presentations sharpened. […] Because standing is "an indispensable part of the plaintiff's case," it "must be supported in the same way as any other matter on which the plaintiff bears the burden of proof, i.e., with the manner and degree of evidence required at the successive stages of the litigation."'.

The importance of standing, especially in ensuring that the resulting 'presentation' is 'sharpened,' is illustrated by comparing the SCCS Opinions on aluminum [60] and MBBT [39, 61]. For aluminum in cosmetic products, there is no apparent Applicant as there are no notifications spurring the review. Noteworthy points are: (1) the standard template is not used (there would have been many blank entries); (2) 23 aluminum substances are treated as a class; (3) there are only minor and very general statements on physical chemistry; (4) the SCCS restates reviews by other European agencies, giving them '*standing*'; and (5) the Special Investigations section is used to address reputed negative associations with aluminum (breast cancer and neurogenerative diseases), which the SCCS found to be inconclusive. For aluminum, the SCCS had no Applicant to sharpen their review.

In the case of nanoscale MBBT, BASF, one of the few firms with a toxicological laboratory, is the unnamed Applicant. MBBT is a UV absorber that is a relatively insoluble, covalently bonded organic material marketed as Tinosorb® M. In 2013, the SCCS Opinion [61] could draw 'no conclusion' on the material' safety 'since there was no appropriate data on genotoxicity.' In 2015, there was a re-submission with accompanying genotoxicity data, and the second SCCS Opinion concluded that MBBT was safe [39]. In effect, the SCCS viewed MBBT through the lens of those who had standing (the Applicant) and guided them to the testing that the SCCS considered necessary. However, in this process, MBBT was in a sense 'privatized' where all representations regarding chemistry and hazard reflected the submitter's wherewithal in responding to SCCS inquiries (to 'bear the burden of proof'). For MBBT, the SCCS had a cooperative, credible Applicant.

A scientist working for an Applicant has 'standing,' as do SCCS members. Other scientist stakeholders do not and are confined to offering commentary on Preliminary Opinions. These drafts will have already arrived at one of the three possible conclusions: safe, unsafe or insufficient information. In the case of a determinate decision, safe or unsafe, it is unlikely that the comments of public stakeholders will alter the decision. The Applicant will have likely submitted proprietary studies along with supporting literature; the SCCS members and staff will have arrived at interpretations; the Opinion summarizes the outcome and exerts an intended normative viewpoint. It is unlikely that a public stakeholder would have access to a study not already considered. Further, for topics within their expertise, the 'outside' expert may have a valid point that anticipates future Opinions without intending to overturn or contradict the Committee's position on the current Opinion, especially for those aspects that are beyond their expertise. The SCCS's responses to public comments nevertheless view the Opinion as a whole that must be considered as a whole.[2]

The situation becomes opaque when the SCCS does not arrive at a clear determination. Indeterminate may not necessarily mean indecisive. The SCCS must rely on those with 'standing' to provide information, but its ability to insist may be limited by the dynamics formed in privatized settings. A dynamic may form where the SCCS questions the Applicant's abilities or where the Applicant has a different perspective on evaluating safety. Examples from the 2013–2016 Opinions are provided in Table 3.

The dynamic revolves around credibility, for standing narrows the dialog to be that between the Applicant and the Committee. With MBBT, the applicant had credibility and resources that led to a re-submission and a second Opinion. This was evidently not the case with nanoscale HAP as indicated by the extra step of conducting a literature search. The Committee's Opinions in such a case may well be documenting the impasses that arose during technical exchanges and the resulting view the SCCS members (and staff) have formed of the Applicant's credibility (see [32] p. 196 for a medical example).

[2] For one anonymous reviewer, there would have been greater clarity if my arguments were explicit in disagreeing with the SCCS Opinions as a whole. The 'outside' expert is disadvantaged in such a case. The concept of epistemic community is used to gauge the Committee's acceptance of new information.

Table 3 Applicant credibility

Material	Applicant	Actions	Comments
MBBT [39, 61]	BASF	Insufficient and later Safe	○ Applicant is conversant with bulk MBBT and its properties ○ Applicant conducts and interprets toxicity tests ○ Applicant's strategy is to be responsive
Silica [38]	Association of Synthetic Amorphous Silica Producers	Insufficient later becomes a Commission Mandate on solubility	○ There is no direct bulk version; there are other forms of silica such as quartz, sand, flint, and diatomaceous earth ○ Applicant interprets third party inhalation testing in terms of synthetic amorphous silica dissolving over time, i.e., not biopersistent, relative to crystalline quartz that is biopersistent ○ Applicant's strategy is consistency with ~ 75 years of studies and responses to regulatory inquiries
HAP [1]	???	Insufficient	○ There is bulk HAP; Applicant is not conversant with its properties ○ Applicant interprets third party proprietary test results ○ Applicant is pursuing an innovative use

The case of nanoscale silica (SiO_2) may reflect an impasse, one where a credible Applicant differs with the Committee's views on the required testing. The ASASP, the silica trade association, represents products with a ~ 75-year production history and a projected 2014 market volume of 254,000 metric tons in toothpastes and cosmetics, growing at 4.6% yearly [62]. The products' many uses and markets co-evolved with (and in many cases even preceded) the founding of regulatory frameworks to the point that current industry practice encompasses a historical understanding of risk assessment and risk management. The SCCS, on the other hand, follows a linear administrative process where completing the nanomaterial template is a pre-requisite for deciding on appropriate risk management. It can be argued that any SCCS request for new testing ignores the established risk management approach, which is Wickson and Wynne's stance [11] regarding the influence that risk management has on the interpretation of risk assessment. Further, the silica industry's experience with lung inhalation testing has led it to the interpretation that the 23 synthetic amorphous silica products act as a class in that each member of that class will dissolve to the point that they should not be viewed as biopersistent. There are therefore two potential outcomes: one requiring the industry to accept the SCCS view on testing and one requiring the SCCS to accept the industry view on solubility. The Silica (nano) Opinion refers obliquely to the impasse ([38], p. 60): "… these issues had already been pointed out to the Applicant by the SCCS in the preliminary comments on the original submission in 2014."), but without an explanation tying silica solubility to the definition of nanomaterial. The mandate in early 2018 on silica solubility likely reflects an Applicant's successful appeal to the Commission for reconsideration, which led to a Silica Solubility Opinion [34]. As stated before, each SCCS Opinion is a narrative that is transparent for the issues that support the Committee's conclusions and less so for matters raised by the Applicants.

The SCCS's potential role as a 'designated' epistemic community is more prominent when there is a finding of insufficient information, especially should Applicants not be in the position to bear 'the burden of proof, i.e., with the manner and degree of evidence required at the successive stages of the litigation.' These are situations involving a social dynamic in addition to an expert evaluation of technical issues. The Committee's Opinions then become status reports overlaying impasses. Considerations such as these illustrate the SCCS's balancing of roles, one as a science court serving as a prerequisite for regulation and one as a 'designated' epistemic community for nanomaterials. As Martin states when examining the science court concept: 'Similarly, the science court must not adopt the rigidity of res judicata and collateral estoppel found in the legal model, although some kind of finality must be maintained so that policy decisions can in fact be made.' [63].

Discussion of the SCCS as a 'Designated' Epistemic Community

Examining the SCCS as a 'designated' epistemic community is an opportunity to revisit Haas's distinctions relative to '*other groups*' (disciplines, professions, social movements, bureaucracies and interest groups). Haas ([5], pp. 18–20) traverses an international relations landscape examining exigencies involving 'the three dynamics – uncertainty, interpretation, and institutionalization—' and proposing that the policy-maker should navigate according to a 'state interest' derived from expert advice. His model epistemic community was distinguished by its 'principled approach from the issue at hand' whereas the 'other groups' acted on conventional professional codes and disciplinary interests. It should be noted that Haas provides little insight on the epistemic community's composition, background, diversity or disciplinary training. Rather, the epistemic community is noticeable as an 'administrative empowerment of specialized knowledge groups,' because the policy-maker recognizes that the 'state interest' being negotiated may well lead to a realignment in the status, political clout and economic viability of 'other groups',

For the SCCS to act as a 'designated' epistemic community, it would need to anticipate that some elements of its own procedures might act as constraints on their deliberations. Test methods, test interpretations, roles, and responsibilities that are effective with routine additives, primarily covalently bonded organic molecules, might not carry over to non-routine nanomaterials that are the subject of on-going research investigations. If not a full realignment of procedures, then the SCCS might augment them on an ad hoc basis to encompass issues that go beyond the specifics of individual Opinions. If not in the legally oriented procedures, then the SCCS might at least reconsider the roles regarding 'inside' and 'outside' experts and the scientific disciplines that they represent. For these reasons, the SCCS's external experts are first examined as a group of individuals, leaving the privileged status of toxicologists to a separate discussion on disciplines.

Though the SCCS members are nominally non-governmental agents, their community is an established component of an administrative process, i.e. members are chosen for an expertise pertinent to evaluating the safety of non-food ingredients. For them, the pre-determined 'state interest' is the legal framework underlying the Cosmetics Directive, which is reinforced by an agenda set by Commission referrals. When carried over to a new class of materials, nanomaterials, these factors translate into a general strategy of commensurability. Commensuration is a pragmatic approach, used by the USEPA, for gaining knowledge incrementally, on a case-by-case basis, with the expectation that appropriate categories, alignments, and adaptations to current practice will be found and thereby minimize the proliferation of exemptions, special cases or the passing of new law [64–66]. An additional condition imposed by the Commission is the definition of nanomaterial, which creates a cleft between past studies, conducted without the knowledge of such a size boundary, and the SCCS's routine requirement that studies in the dossier should pertain to the material in the referral, the nanomaterial.

Table 4 Abbreviations on agents and purposes

Abbreviation	Agent and purpose
SCCS-expert	SCCS extending knowledge
SCCS-def	SCCS defining nanomaterials
Com-legal	Commission influence due to legal considerations
Com-def	Commission defining nanomaterials

Examining the SCCS as if it were a 'designated' epistemic community is also an opportunity to address two interacting deliberative processes and two abstract concepts. The deliberative processes are: (a) the SCCS members extending their collective knowledge to incorporate nanomaterials and (b) the SCCS members responding to the Commission's procedural requirements (the legal 'state interest,' the strategy of commensurability and the awareness of nanoscale ingredients entering commerce). The two abstract concepts are: (1) Haas's description of an epistemic community functioning to identify 'state interests' and (2) the current European interest in responsible research and innovation (RRI). Rephrased as questions, "Does the legal framework protrude into SCCS deliberations such that the Commission is directing and channeling the experts' knowledge?' and 'Does SCCS progress in defining the 'state's interest' in nanomaterial safety provide guidance to those pursuing innovative materials and uses?'.

The intertwined nature of these separate purposes can be highlighted by revisiting the discussion so far using the roles and purposes in Table 4. The SCCS's members extend their knowledge through access to proprietary reports (SCCS-expert), but can only present that knowledge in summary and narrative forms due to confidentiality (Com-legal). The SCCS experts realized that the nanoscale HAP (nano) dossier was limited in extent, perhaps by the Applicants' resources, leading them to conduct a literature search (SCCS-expert), but SCCS requirements surrounding particle identity, size, testing protocols, and the definition of nanomaterial (Com-legal and Com-def) precluded them from fully utilizing the results. With VSSA, the SCCS augmented the Commission's interim definition. However, the SCCS members (or Secretariat) appeared to be unaware of EU-funded projects, e.g., NanoDefine, (Com-def) or may have wished to defer to other EU authorities (SCCS–expert and Com-legal) in order to meet their primary role of responding to Commission mandates (Com-legal). Deference to EFSA (Com-legal) may account for the SCCS hesitancy regarding non-food ingredients that nevertheless enter the GI tract (SCCS-expert). How the interplay of these purposes actually influences SCCS deliberations is unknown to the outside observer except to note that three of these factors (SCCS-expert, SCCS-def, and Com-def) are not present when evaluating conventional non-food ingredients. The potential for misalignment exists between the general strategy of commensuration and the safety determinations found in individual Opinions or between the SCCS experts' pursuit of new knowledge on nanomaterial safety and the Secretariat's commitment to the legal framework as the primary 'state interest.'

The concepts of solubility and biopersistence have immediate RRI implications. If safer-by-design is to be realized through early regulatory involvement in a company's stage-gate management processes, then the SCCS should address the meaning of those terms and relate them to dossier requirements. The indeterminate 'insufficient information' for HAP (nano) illustrates two RRI limits: (1) SCCS Opinions are not necessarily informative (as demonstrated by the later EC mandate [30]); and (2) they may even lead the reader to question the safety of the bulk counterparts ('huge amount of literature' for a GRAS material is not found to be informative). The value of SCCS Opinions to RRI is doubtful when the 'state interest' in nanomaterial safety becomes mired in an administrative procedure as with the SiO_2 (nano) Opinion impasse. Further, RRI proposals for all stakeholders to have a voice in the innovation process leads to all stakeholders having standing, which is not found in current law (Com-legal) and returns us to Shapiro and Guston's suggestion that one 'state interest' might be to limit epistemic drift [9]. RRI and Haas's concept share a sense of impetus and direction in that a public issue causes individuals to coalesce into groups (stakeholders, epistemic communities) in order to interact with administrative process (stage-gate, regulatory framework). The SCCS, in contrast, simply added some new members to address the non-routine ingredient (nanomaterials) within a framework of procedures established for routine ingredients. The individual expert's experience in terms of group interactions differs between the two approaches, in particular over the 'state interest' in legal procedures.

At the 1943 annual meeting of the American Sociological Society, Robert K. Merton reflected on the intellectual's role in a public bureaucracy [67]. The dramatic growth in the number of social scientists involved with the war effort, as well as earlier in the New Deal, formed the basis for his understanding of a new governmental role relative to traditional career expectations. Three roles were identified: (1) accommodation to 'the values of the policy-makers'; (2) 'seek to alter prevailing policies'; and (3) a 'schizoid dissociation between his own values and those of the bureaucracy.' The third response he labeled the 'technician role' taken when implementing policies at variance with one's own judgements. The stresses he observed on the individual expert are familiar: indeterminacy in one's findings; the tenuous relation between expert and client where confidence affects expert selection; the difficulty in appraising achievement; and policy-makers possessing their own considerable knowledge. Merton's insights parallel those of Espeland and Stevens [53] in their frequently cited article on commensuration as a social process, which "condenses and reduces the amount of information people have to process" thereby "simplifying decision-making" and making "possible more mechanized decision-making" involving "a system for discarding information and organizing what remains into new forms."

These authors are describing experts responding to social constraints. For Merton, it was the new career path in government where policy sets boundaries to the individual's contribution. With Espeland and Stevens [53], strategic direction supplants policy. Whether or not perceived as such by the individual expert, the importance of these factors is heightened when the Applicant, the SCCS experts and the Secretariat are in effect negotiating the causal ambiguities of nanomaterial safety. Each set of experts becomes aware of their respective limitations in terms of data availability, resources, knowledge, persuasiveness and ability to control, which in turn influences their future expectations about their own role.

Social dynamics were already offered as possible explanations for absent SCCS minority reports and for impasses leading to 'insufficient information.' It is reasonable that procedures, templates and acceptance criteria that are well suited to evaluating routine ingredients (itself a challenge) may be a rather indifferent means to uncovering the attributes of a new class of materials. A form of non-knowledge is generated if decisions incorporate knowledge that is not explicitly noted (such as being 'fully aware' of HAP solubility). If noted and not resolved, then there is an argument for the 'technician role' and 'mechanized decision-making' becoming the norm. This is a different dynamic to the one described by Haas, which is one of policy-makers relying on an expert group that has an intuitive grasp of a 'principled approach from the issue at hand.' The SCCS would nominally fulfill Haas's descriptive criteria, but less so his operational one that 'they also serve as brokers for admitting new ideas into decision-making circles of bureaucrats and elected officials' ([5], p. 31). Effectively, an epistemic community must demonstrate that its causal beliefs demonstrate and reinforce the need for its own existence. Using Haas's concept for an analysis of the SCCS, therefore, hinges on the distinction between a routine pursuit of conventional knowledge and an intuitive grasp of the '*issue*' that is expressed explicitly by regularly incorporating new knowledge. In this respect, the SCCS is not an epistemic community.

The SCCS and Disciplinary Capture

There is a necessary and rational time delay from the first literature report of an advance and its use in a regulatory submission: there is confirmation by other investigators to establish relevance; and there is method standardization to ensure reliability. These steps have been formalized under the OECD's *imprimatur* in the form of test guidelines to be conducted according to Good Laboratory Practice. (GLP certification was introduced to prevent a repetition of the 1970's fraudulent data scandal ([68], p. 8).) The OECD initiatives are the basis for the mutual acceptance of data [69] and are utilized in the 2016 HAP (nano) Opinion (see SCCS comments at 3.3.1.1, 3.3.2.1, 3.3.3, and 3.3.5.1 [1]).

The overall goal is having a systematic method for evaluating regulatory health and safety studies that ensures regulatory objectivity [10] and, should there be litigation, is a basis for defending regulatory decisions. One can also view this systematic method as a distinctive 'disciplinary style' as outlined by Jasanoff in her study of science and regulatory agencies. Noteworthy is her description of independent experts on an advisory panel reviewing the FDA's proposed approval of an antiarrhythmic drug, propranolol (trade name Inderal), "The major difficulty from FDA's point of view was the committee's refusal to review the available studies en masse, as the agency's experts were prepared to do….physicians on the committee adopted a case-by-case approach to reviewing methods and conclusions …. Predictably, this style of scrutiny persuaded the panelists that none of the studies was methodologically sound…" ([3], pp. 156 and 157, underlining added). The FDA's question to its advisory panel may well have been expressed as 'have we overlooked an issue?' rather than the one the advisory panel answered ('did we follow the accepted method?'). Jasanoff's use of an EPA pesticide example reiterates the dynamics involved, 'Thus the panelists—in particular the toxicologists—felt no qualms about insisting that each animal study should either meet the state-of-the-art standards for bioassays or be rejected as inadequate' ([3], p. 150, underlining added). A disciplinary style emerges, one that generates an essential tension between standardization and new knowledge and between current and past standards. This style underlies many of the indeterminate Opinions where an Applicant relied on open literature studies, which the SCCS found deficient.

Against this background, the SCCS's success as a 'designated' epistemic community, not its success as an administrative process, is measured by

adjusting routine practice to incorporate pertinent new knowledge. It is in this respect that the Commission's 2018 mandate on silica solubility is significant, as it includes terms of reference on solubility and particle identity ('Can the SCCS indicate to which kind of Silica this solubility applies?' [34]). The core issue was chemical grouping. What the ASASP considered a single group with 23 members, the SCCS chose to categorize 'On the basis of the different synthesis methods' and then pose that they were separate entities due to the 'large variation' in experimental values for VSSA, solubility and densities. (Please note the difference with the SCCS's handling of aluminum.) The issues involve particle identity. For a molecule-in-solution, the molecular identity leads to a set of specific properties, and the manufacturing technique is reflected in the impurities and residual catalyst levels. For particles, identity encompasses composition (expressed as a molecular identity) and a range of properties, especially those influenced by surface chemistry, e.g., zeta potential. Retrospectively, the SCCS was unprepared for chemical grouping of particles based on solubility, a knowledge that it was to have gained through the strategy of commensurability.[3]

It is noteworthy that there is a vibrant dialog on new biological test methods in the SCCS's Working Group on Methodologies (with industry, academic and Joint Research Centre participants), but not a corresponding effort on particles in the Working Group on Nanomaterials. There are no discussions in their minutes of the progress made in EU projects such as NanoDefine (9.3 million euro budget), NANoREG (50 million euro budget) or ProSafe (3 million euro budget), all focused on translating academic results into useful regulatory actions. From the outside observer's perspective, the SCCS does not have visible mechanisms for gaining new knowledge on particle chemistry beyond its privatized dialog with Applicants as demonstrated when directing a member of the public (me) to go directly "to the industry who may find them helpful in preparing a better case" (see "Results" section).

If so, the SCCS combines a 'disciplinary style' that restricts acceptable test results with a 'legal style' that limits participation. While each style has its justifications, the picture of an entrenched collective belief emerges, one that is closer to Haas's 'other groups' than to his epistemic community. Collective belief is the tendency of individuals to defer to group decisions even when not fully reflective of their own personal beliefs. It is actively debated [70–73], but the authors tend to agree that the concept is most applicable to normative circumstances where group members follow an agreed upon decision-making process. Clearly, the SCCS with ~20 Opinions each year would meet that requirement. The absence of minority opinions and the implied withdrawal of staff support should a member pursue one ('can only be expressed by members') may demonstrate that the SCCS procedures include a latent potential for rebuke, a significant factor in Gilbert's analysis [70].

There are alternative articulations: disciplinary capture [74] and disciplinary imperialism [75]. Disciplinary capture occurs in the context of interdisciplinary research where, in one example, the principal investigators use their administrative positions to ensure that their 'constellation of epistemological commitments dominates methodological decisions.' Disciplinary imperialism, as the name implies, is a more assertive interaction where practitioners in one discipline apply their insights to topics conventionally associated with a second discipline. (The term was actually coined by economists from the Chicago School when applying rational choice theory to diverse fields such as geography and neuroscience.) Both concepts describe a hierarchy of disciplines leading to misdirection in either gaining or communicating findings from a subordinated discipline: misallocation of resources; missed opportunities due to distraction in responding to the dominant discipline; and mismatched epistemic criteria. These are also the elements associated with non-knowledge, knowledge that exists or might readily exist were it not for the misdirection.

Disciplinary capture and disciplinary imperialism, however, do not encompass the presence of three recognizable parties, viz. the independent SCCS experts, the Secretariat staff and the Applicants, that share similar disciplinary backgrounds [30]. The SCCS

[3] Grouping particles of the same composition on the basis of solubility was pursued in the EU-funded GRACIOUS project (7 million euro budget) active between 2018 and 2021 and generating 20 peer reviewed publications (https://cordis.europa.eu/project/id/760840/results; accessed 15 February 2023). The resulting GRACIOUS Framework supports the ASASP's 2015 arguments as found in reference 37.

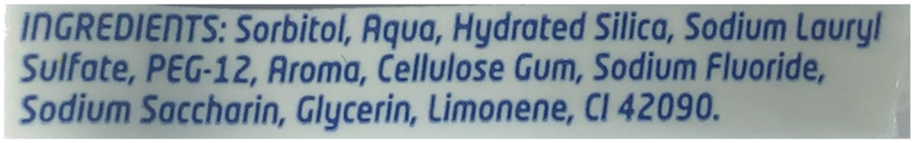

Fig. 1 Ingredient listing for toothpaste purchased in Europe in 2018

experts have limited control over their agenda, must accommodate the Secretariat's legally oriented adherence to procedure and protocol [32] and must validate, sometimes contest, the Applicant's assertions. This is a contested landscape privileging the toxicological sciences, as it is their findings that will be the basis for any regulation. Other disciplines and their contributions become subordinated to the dominant group's eventual narrative despite the interdisciplinary rationale for selecting SCCS experts.

Addressing knowledge generation in interdisciplinary collaborations, Piso et al. [76] noted three sources of sub-optimal epistemic performance: (1) 'identity-based ignorance,' where a dominant discipline leads the group to 'endorse certain norms that uncritically privilege particular perspectives,' i.e., the disadvantaged disciplines' voices are unheard; (2) 'imposed ignorance,' where external actors, institutional contexts and historical moments influence team priorities; and (3) 'complacent ignorance,' where the disadvantaged disciplines acquiesce in the 'service of constructing a solvable problem.' Each of these elements are present in the SCCS practice and may partly explain why Haas distinguishes the epistemic community's 'principled approach from the issue at hand' from the actions of 'other groups.' Non-knowledge is created whenever a peripheral concept, one lying in the no-man's land between disciplines, is left unexamined because it has implications for the group's routine interpretations and its full evaluation would require resources beyond the group's control.

According to Haas, the epistemic community's ultimate purpose is to influence policy-makers in their public roles, which for the SCCS would encompass both nanomaterial safety and consumer product labeling. It is therefore noteworthy that major toothpaste manufacturers in Europe do not list the silica abrasive in their products as silica (nano). In Fig. 1, the hydrated silica is a 'synonym for the 'water-based production process' for precipitated silica and silica gel where the surface is covered by sylanol groups,' [77] and is part of the SCCS Opinion on Silica with 26 notifications and where toothpaste is a rinse-off use [38]. Yet, there is no 'hydrated silica (nano)' in Fig. 1 or other toothpastes surveyed. There are qualifications: the toothpaste manufacturer is responsible for the label and was not a party to the SCCS Opinion; normally, the supplier's communications with customers on interpreting regulations are business confidential; and not all hydrated silica need be nanoscale. (Please note the parallels to infant formula manufacturers and FSANZ.) In the case of hydrated silica, however, the silica suppliers [78] did take a public position that synthetic amorphous silica was neither insoluble nor biopersistent. Whatever explanations will eventually be offered for toothpaste labeling, the SCCS has not considered the implications that their decisions have on labeling and the SCCS knowledge is therefore neither visible nor authoritative to policy-makers and marketplace actors. Once again, the SCCS is not functioning as an epistemic community.

Suggested Remedies

Upon being 'designated,' the SCCS members were still expected to engage with Applicants using procedures developed for routine cosmetic ingredients, even though their deepening understanding of nanomaterials might lead them to consider adjustments. Commercial firms face analogous challenges when introducing a novel technology. The product may require new marketing, pricing, and sales approaches to reach emerging customer niches, which in turn would lead to reconfigured supply chains. For the commercial firm, the marketplace, not the regulator, is the arbiter. For colleagues in STS, the commercial firm's adjustments constitute the 'social construction of technology' [79]; for those in innovation studies, they are identifying the 'dominant design" [80]; and for those in economics, they are the substance

of evolutionary economics [81]. These descriptions overlap significantly on the need to decouple from traditional relationships (customers, market niche, supply chain) in order to establish new ones. Restated, there is a competitive response involving 'de-alignment' and 're-alignment' [82]. For the SCCS, the analogy would be the deliberate review of routine procedures through a strategy of balancing commensuration with finding a 'principled approach from the issue at hand.' Some internal tension with the Secretariat's role of ensuring adherence to procedures and precedent might result; yet, the underlying history of these administrative procedures and of past SCCS actions indicates there is some flexibility in incorporating new knowledge. There are four immediate and two longer-term opportunities for de-alignment/re-alignment cycles. The immediate ones are the following:

1. Instituting a regular dialog with the EU's Nano-EHS (Environment, health and safety) projects;
2. Providing for comments and SCCS responses to Preliminary Opinions to become public;
3. Considering a draft guidance relating particle identity to chemical grouping for use in filling data gaps; and
4. Reevaluating the Committee's position on the use of zeta potential for particle identity.

For the longer-term suggestions, it should be noted that indeterminate Opinions have often involved materials that have been in commerce for some time (hydroxyapatite, silica) where an 'insufficient information' Opinion may create a perceived risk for both the nanoscale and bulk material. Both the Applicant and the SCCS are disadvantaged by missing actors, i.e., those (and their data) who decided hydroxyapatite was GRAS. In these situations, there is a valid argument for extending participation through a form of third party standing, which in US law is " allowed when the third party's interests are "inextricably bound up with the activity the litigant wishes to pursue"; when the litigant is "fully, or very nearly, as effective a proponent of the right" as the third party; or when the third party is less able to assert her own rights).' [59].

There would be challenges both in identifying third parties and in incorporating their input, especially without undercutting the Commission's legal basis for promulgating regulations. These challenges were outlined in a recent revisiting of Kantrowitz's 'science court' [83] and in a call for greater pluralism in establishing public policy relevance and reliability [84]. With these cautions, the SCCS's objective would be to have a forum beyond the 'privatized' individual Opinions to be a means for reflecting on procedures. Themes that might be considered are:

1. There is presumably a core set of toxicological endpoints that are of interest to all of the EU's regulators and would best be approached on a combined basis, e.g., genotoxicity. Here, the third-party would be the EU's other advisory panels.
2. There are topics surrounding particle chemistry that could be tasked to EU-funded research consortia leading to a report and public commentary. One such topic would be distinguishing between the parameters needed to define an applicant's material and those that may contribute to toxicity. Here, the third party would be academic and industrial colleagues.

Both sets of suggestions leverage the Committee's limited resources. The first suggestion builds on the SCCS's acceptance of EFSA statements on aluminum genotoxicity [60], which was not done with SiO_2 (compare ([38], p. 58]) with ([85], p. 16), and ([77], p. 40)). The second suggestion separates the general learning process from the specifics of a chemical substance Opinion. The goal would be to create separate forums allowing for third party participation without detracting from the SCCS's primary task of reviewing mandates. Clearly, the Committee would be taking on an administrative burden, but would also benefit greatly by expanding the range of disciplines and knowledge being considered.

Revisiting the eight years of HAP (nano) Opinions provides some measure of the value of these suggestions. In the first Opinion [1], the SCCS concluded that the published toxicity studies were insufficient, but that some studies pointed to local uptake into buccal cells and systemic effects after oral exposure. The extensive literature search in the Appendix was unusual. In the second Opinion [21], the SCCS was more specific about local exposure (oral mucosa) as the submitted data on nano-HAP solubility had reduced concerns about systemic exposure via ingestion. The

Committee's request for new testing during its review was unusual as was the additional four pages of text between the Opinion's draft and final versions. In the third Opinion [22], the submitted genotoxicity data were accepted and the HAP (nano) found to be safe in toothpaste and mouthwash. The suggested remedies would target additional resources to those issues the Committee is confronting.

Concluding Remarks

Administrative processes, like their manufacturing counterparts, have design features. For an oil refinery, the design is centered on a preferred crude oil slate, water content, production throughput, steam generation and such. There are plant engineers monitoring the process, making control adjustments, scheduling maintenance, and identifying bottlenecks and related optimization tasks. It is management's responsibility to exercise discretion, professionalism and good sense in minimizing process excursions before they become noticeable production incidents. The analogy has its limits, but whether an industrial process or an administrative one, process failure has similar implications: loss of output; of productivity; of reputation; and significantly, of safety.

As a European Commission advisory panel, the SCCS follows internal procedures that organize the workload to match the Committee's purpose, i.e., advising the Commission on safety. Identifying process excursions is difficult as there is a mix of scientific styles and administrative practice, but examples may well be: (1) a disconnect between SCCS Opinions and subsequent product labeling; (2) the delay in addressing solubility (requiring a Commission mandate); (3) inconsistent treatment of particle identity and chemical groups relative to molecules leading to frequent indeterminate decisions; (4) "insufficient information" findings creating a perceived risk about 'bulk' GRAS materials; (5) non-uniformity with decisions by other agencies (genotoxicity and EFSA; anatase preference differs with EFSA and FDA); and (6) an initially unclear boundary with EFSA (and FSANZ) between the oral cavity and the stomach.

Identifying the source of what is depicted above as disconnect, delay, inconsistency, non-uniformity and unclear boundaries is equally difficult, but some guidance is possible using Haas's concept of epistemic community. He describes a transition in role as the 'network of experts' engages with policy-makers to arrive at 'state interests'. In this paper, the concept is a tool for reconsidering formal procedures for their epistemic value, their level of inconvenience and their presence as hurdles. For the SCCS, there is no transition, but rather a combination of legal formalities (standing, Opinions in legal format, absence of minority reports), developing science, and the interaction of independent experts along disciplinary lines. When exercising state authority, it is of course a challenge to separate the regulatory framework from considerations of any one scientific discipline's proper role, its state-of-the-art methods and its stature relative to other disciplines. However, the privileged position of toxicology and its disciplinary style are significant factors in SCCS Opinions. The SCCS comes to act as a science court where legal formalities limit participation and toxicological style limits the evidence. The resulting Opinions do provide the desired legal basis for regulatory action, but they are also narratives utilizing stylized public facts that were certified during privatized discussions. Causal ambiguity is created when concepts peripheral to training in toxicology are obscured and remain unresolved. The proposed remedies are to expand participation (third party status) and to enhance the credibility of experts from fields other than the biological sciences by allowing for unprogrammed, unexpected sources of information to be heard and possibly found to be pertinent.

As nanotechnology became prominent, the toxicological community responded constructively, realizing that timely action would avoid repeating past experiences with asbestos, DDT and more recently PFOS. Rather than being the bearers of bad news, there was the potential of guiding nanotechnology development towards today's safer-by-design and responsible research and innovation concepts [86]. The field might even evolve to become 'the science of safety' [87]. The SCCS record indicates that a sub-optimal epistemic performance can occur when topics at the boundary between the life and physical sciences are handled without a deliberate effort to balance toxicology's central role with the subordinate status of other disciplines. Otherwise, the Committee mistakes its authority for knowledge. Rephrasing Justice Jackson in Brown

v. Allen on the finality of Supreme Court decisions, the Court is not last because it is right, it is right because it is last.

Acknowledgements Past employment, at Bio-Rad Laboratories, Betz Laboratories and Evonik-Degussa, contributed greatly to my understanding of hydroxyapatite and silica chemistry. Aspects of the manuscript were presented and comments received at the Society for New and Emerging Technologies meetings (2017 Phoenix and 2018 Maastricht) and the 12th International Conference on the Environmental Effects of Nanoparticles and Nanomaterials conference in Birmingham. Special thanks to Professor Sharon Tsai-hsuan Ku (University of Virginia) for continuing STS discussions. The manuscript benefited greatly from several anonymous reviewers and the journal's editor.

Authors' contributions The author has read and approved the final manuscript.

Declarations

Competing interests The author declares he has no competing interests.

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