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ORIGINAL PAPER

Sunscreens with Titanium Dioxide (TiO_2) Nano-Particles: A Societal Experiment

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Abstract The risks of novel technologies, such as nano(bio)technology cannot be fully assessed due to the existing uncertainties surrounding their introduction into society. Consequently, the introduction of innovative technologies can be conceptualised as a societal experiment, which is a helpful approach to evaluate moral acceptability. This approach is illustrated with the marketing of sunscreens containing nano-sized titanium dioxide (TiO_2) particles. We argue that the marketing of this TiO_2 nanomaterial in UV protective cosmetics is ethically undesirable, since it violates four reasonable moral conditions for societal experimentation (absence of alternatives, controllability, limited informed consent, and continuing evaluation). To remedy the current way nano-sized TiO_2 containing sunscreens are utilised, we suggest five complementing actions (closing the gap, setup monitoring tools, continuing review, designing for safety, and regulative improvements) so that its marketing can become more acceptable.

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Introduction

The current debate about the impact of nanoparticles on environmental, health, and safety (EHS) issues is frustrated by the high level of discord surrounding nanotechnology [5]. Part of the confusion started with the rhetoric used to promote nanotechnology and heralding the novel technology as the next industrial revolution. After warnings from environmentalists and civil activists groups (CAGs) the tone changed and nanotechnology was portrayed not as a revolution, but more as a gradual evolution of science and engineering. Nonetheless, the novelty of nanotechnology was claimed to emerge from the unique properties of known materials at the nano-scale. This claim led to concerns that the risk profile of such material could also be unique and so additional as well as new safety measures ought to be taken. In turn, this even lead some CAGs to demand severe precautionary measures including a total moratorium on nanotechnology [2, 10]. In the middle of this debate the confusion was increased by agencies that are responsible to advice on the toxicity level of used substances. For example, the International Agency of

Research on Cancer (IARC) classified titanium dioxide (TiO_2) as a possible human carcinogen—in group 2B—[12], while the hazards of nano-sized TiO_2 in sunscreen applications were fiercely debated. However, the IARC recognised that TiO_2 particles are being used in various sizes (nano and fine-sized particles), though the agency does not make this size distinction for the given classification. The agency increased the discord further by basing the classification on the results of animal experiments and indicating in its conclusions that human epidemiological cohort studies to support this classification suffer from methodological limitations.

The discord in the current nanotechnology debate is not solely the result of communication issues such as rhetoric, mix-ups, hype, over-claiming and misunderstandings. The debate is also highly technical, heterogeneous, and plagued by uncertainty. The diversity of the field becomes apparent by comparing, for example, the buckminsterfullerene C_{60}, carbon nanotubes, silver nanoparticles and quantum dots [24]. These examples represent just a few groups of nanomaterials and already they have very varied uses and risk profiles. This diversity is further increased by the many different ways in which these various nanomaterials can be functionalised for specific applications. For example, doping or coating these nanomaterials will give them other functional properties and also different risk profiles. The diversity of the nanotechnological field is even larger than only products that contain nanomaterials. The technology can also be applied to use nanomaterials to fabricate products that do not contain nanoparticles themselves. As a result of this diverse nature of nanotechnology, it is nearly impossible to make general claims about EHS issues of nanotechnology, nor is it possible to make such claims on nanoparticle groups (such as nano-sized TiO_2 particles) due to their heterogeneity. Therefore, different nanomaterials and their applications should be analysed on a case-by-case basis.

Besides the diversity of the nanotechnological field and its applications, the debate on EHS aspects is also greatly affected by the uncertainties that surround nanotechnology. As a result of these uncertainties, it is at the moment, generally acknowledged that we do not know enough about nanomaterials to claim that they are safe. At the same time, due to the same uncertainties, the opposite claim of certain dangerousness can also not be made credibly. The general public is highly apprehensive about these uncertainties and EHS researchers are giving guarded answers due to the same uncertainties, it seems clear that most parties in the debate ask for more research into EHS issues [8, 21, 25]. However, it is still unclear how much data is needed to give a final and credible answer to these issues. Dealing with the uncertainties of the possible implication of novel technologies, such as nanotechnology, seems necessary for a more meaningful deliberation about their introduction into society.

Titanium Dioxide

The ethical aspects of the EHS issues surrounding nanoparticles in light of uncertainty will be illustrated by a case study on nanoparticles made primarily of titanium dioxide (TiO_2) used as a UV protector in cosmetic sunscreens. Nano-sized TiO_2 is different from the well-known micronized form that is used for its clear white appearance as a pigment in coatings, paints, cosmetics, paper, and food stuffs. This large-sized form of TiO_2 is known as titanium white or pigment white 6 for pigment applications, while it is often referred to as E171 in food applications. In contrast TiO_2 nanoparticles have various interesting electrical and optical properties that can be utilized in commercial applications. The photocatalytic properties of nano-sized TiO_2 are used in the photodegradation of pollutants, treatment of wastewater, and destruction of tumour cells. These applications mostly rely on the ability of TiO_2 nanoparticles to form reactive oxygen species (ROS) on its surface when excited with UV light. There are also investigations into the use of its catalytic properties for the production of hydrogen. Nano-sized TiO_2 also has photovoltaic properties which can be used in cells for producing electricity from light, while its superhydrophilicity can be applied in 'self-cleaning' windows and ceramics. The electrochromatic qualities of TiO_2 nanoparticles can potentially be applied in windows that colour when a small voltage is applied, while its ability to absorb substances has been investigated for hydrogen storage and sensing applications. Finally, the light scattering and absorption properties of nano-sized TiO_2 can be used for UV protection in applications such as paints, plastics, and cosmetic sunscreens.

For the case study in this paper, we focus on the cosmetic sunscreen utilisation of TiO_2 nanoparticles. The nano-sized particles are used in sunscreens as an alternative to existing chemical UV absorbers, such as p-aminobenzoic acid and benzophenones, which can cause allergic reactions in sensitive individuals. Sunscreen lotions are generally marketed as cosmetic products in most countries including the European Union. In the United States however, sunscreens are treated as over-the-counter (OTC) drugs under oversight of the US Food and Drug Administration (FDA).

This specific utilisation of nano-sized TiO_2 was selected since it has already been marketed for over a decade and has become one of the most widely-used examples of present (first generation) nanotechnological applications. Focusing upon such a specific case study may seem to narrow the case so that it loses the heterogeneity that is so prevailing in the nanotechnological field. However, the case still harbours the very specific diversity related to the nanotechnological field and the case-by-case approach is in line with the advocated way of approaching nanotechnological issues. The heterogeneity of TiO_2 nanoparticles for sunscreen applications can be found in the following factors:

- Particle size measures and distribution.
- Agglomeration and aggregation.
- Morphology of the particle.
- Crystal structure.
- Purity and doping.
- Use of coatings.
- Surrounding matrix.

The size measure of particles is generally used to define materials as nano-sized. This kind of definition based on a measured size seems straightforward; nonetheless it is subject to several difficulties. The first complication is the comparison of the size measure due to the different ways the particle size can be measured and calculated. Size measurements are based on a collection of nanoparticles and so the calculated average size of the collection can be represented on volume, weight, or area basis. Furthermore, the measurement devices generally use specific environments, such as hydrodynamic or aerodynamic, and require pre-treatment methods for measuring, which can lead to misrepresenting the actual size in applied circumstances. A second complicating factor is that the particle collections have a specific distribution of sizes. This distribution of particle sizes is the result of the production processes and is specific for the applied conditions [29]. So representing the collection by only an average particle-size measure does not indicate how varied that size distribution of the collection is. Thus the size measure alone does not give all the information about the used nanoparticle that is needed to differentiate between collections with potential different properties and risk profiles. For example a collection with an average particle size of 150 nm is considered not a nanomaterial under most accepted definitions that set the size limit at 100 nm. However, this collection can contain a certain fraction of particles that are smaller than 100 nm and thus contains nanoparticles. It is therefore difficult to compare used nanoparticles based on size measures alone. A third complication is caused by the fact that nanoparticles, such as TiO_2 nanomaterials, tend to agglomerate and aggregate into larger structures [9]. This assemblage into larger structures alters the actual properties of the material and can thus change the risk profile as well as the effectiveness of the application. The agglomeration and aggregation effects are also environmentally dependent and so sample preparation before size measurements is very critical to insure that the sample is a valid representation of the actual effective particle size in application conditions.

Titanium dioxide nanoparticles can also be produced in various morphologies, such as spheres, tubes, rods, and wires [7]. Furthermore, titanium dioxide can exist in various crystal morphologies of which anatase and rutile are the most prominent. These different crystal structures also give various properties to nano-TiO_2. For example, the rutile has a lower density, higher refractive index, and is less photo-active than the anatase crystal structure. Another factor of the heterogeneity of TiO_2 nanoparticles for sunscreen applications can be found in the purity of the particle. Due to production methods or intentionally contaminating the crystal structure (doping) with other metals the properties of the nano-TiO_2 can be changed [1]. This doping is for example implemented by the company Oxonica-Croda, which uses manganese to reduce the unwanted photo-activity of the nano-sized TiO_2 marketed under the name Optisol.

To utilise TiO_2 nanoparticles in sunscreens, they are normally surface coated with silica, alumina and/ or various polymers to (a) increase its stability in the lotion or cream and (b) reduce its photo-activity [22, 23]. Not only the material used for the surface coatings, but also its thickness, its chemical purity, and the use of multiple coatings, increase the heterogeneity of the utilised TiO_2 nanoparticles further. The use of coatings also raises questions about its effectiveness to reduce the unwanted photo-activity, durability of the coating layer in the whole life-cycle, and the recyclability of these particles. Another factor in the diversity of nano-sized TiO_2 is not the particle itself, but the matrix in which the particle resides. The nanoparticles can, for example, be fixated in a matrix, such as silica beads with nano-sized TiO_2 particle of Sunjin Chemical Corporation, or glued together by the used surface coating. Together these factors lead to a large diversity in nano-sized TiO_2 particles used in cosmetic sun-screens. As will be shown below, this heterogeneity results in more uncertainties, which forms a barrier to assess and manage the risks of nanomaterials.

Risk Assessment and Management

To assess the risk of technological applications, the hazards should first be identified and the exposure predicted. Then the negative effect and exposure need to be correlated in such a way that the resulting risk can be characterised and classified. The relation between the impact of the undesirable event and the probability of its occurrence is generally defined as the product between the two. In this way the hazard phenomenon is specified quantitatively into risk. It is thus clear that the assessment and management of technological risk requires knowledge of the possible effects of application, the exposure, and the relationship between the effects and the exposure. This knowledge is generally based on statistical data and toxicological studies; however such information is mostly unavailable for novel technologies due to the uncertainties that surround them during conception and initial implementation.

These uncertainties are caused by a number of underlying factors, of which (a) lack of knowledge, (b) ignorance, and (c) complexity are the most prominent. In a situation where we know the effects, but cannot attribute probabilities to the likelihood of its occurrence we speak of lack of knowledge or “known unknowns”. This knowledge gap can generally be overcome by gathering more information. However, during the conception and initial implementation of a technology, not all likelihoods can be quantified. With nano-sized TiO_2, for example, there is still no consensus about the penetration of these nanoparticles through the skin. Initial studies indicated that nano-TiO_2 particles could penetrate the skin, however these results were refuted, since the methodology could not differentiate between penetrated particles and particles trapped in hair follicles [15]. Currently, studies suggest that compromised skin—such as diseased, sunburned, or physically damaged dermis—could provide an insufficient barrier [14]. Another example of such uncertainties is the conflicting results in literature, because of the different measures for exposure doses—based on mass, area, or particle number—that are utilised and in practice hard to convert into each other [16, 20, 28]. A final illustration of this lack of knowledge is that, besides the two major routes of exposure, specifically inhalation and skin contact, also alternative exposure routes, such as penetration of TiO_2 nanoparticles dust into the brain via nasal exposure [27], were and still are only marginally investigated. It is clear that in the case of TiO_2 nanoparticles for sunscreens there are still knowledge gaps in certain areas.

In some cases we even do not know that there is a specific kind of hazard. Targeted gathering of information does not remedy the situation, because we are dealing with what can be called “unknown unknowns”. Generally this cause of uncertainty is referred to as ignorance and it clouds risk assessment and management, because it is tremendously difficult—if not impossible—to anticipate the consequences of hazards that are unknown to us. Simply put, we do not know what we have to prepare ourselves for. In retrospect, we can illustrate that such a situation has already occurred with nano-sized TiO_2 in a cosmetic sunscreen application. A few years after the introduction of these sunscreens the BlueScope Steel Company investigated the appearance of defects on prepainted steel roofs. They concluded that the defects were the result of extreme weathering, caused by TiO_2 from sunscreen lotions used by workers during installation [3].

Thirdly, uncertainty can also be caused by the complexity of causal relations. The causal relation between the agent and the specific effect can be very hard to express due to diffuse system interactions, long term cumulative effects, system adaptability, incoherent dynamics, and subject heterogeneity. The large diversity in utilised TiO_2 nanoparticles, as described above, creates such complexity and so forms a barrier for effective risk assessment and management. This problem can be illustrated by the fact that there are some issues surrounding the interpretation and relevance of toxicological studies. Many toxicological studies of nano-sized TiO_2 use P25 of Evonik Degussa as their object of research. However, the usability of these studies for TiO_2 nanoparticles for sunscreens is at least questionable, because P25 is sold as a catalyst and not for cosmetic application. Moreover P25 is not coated to reduce photo-activity and it is of the anatase crystal type, whereas almost all of the TiO_2 nanoparticles utilised in sunscreens are coated and of the less photo-active rutile type. Another issue is that most toxicological studies on TiO_2 are short term and only look for acute toxicity. For instance Griffitt et al. [11] studied the effects of nano-sized TiO_2 on Zebrafish in 48 h experiments. They concluded that it is almost non-toxic in the timeframe studied, however, they also found some alterations in the expression of genes that might lead to negative effect upon long-term exposure. A further hurdle in setting up needed causal relation is that the studies are done under laboratory conditions and on test animals, such as rats, mice and hamsters, which makes it questionable if these represent the actual circumstances in the product's life cycle and if the results can be directly translated to other species. For example, it is already established that the various test rodents have species differentiated responses to TiO_2 nanoparticles [4].

Finally, ambiguity can contribute to the uncertainties in the EHS debate. Ambiguity refers here to the type of uncertainty in the interpretation or assessment that can be given to EHS data [18]. For example, one can interpret the conclusion of a study reporting that a certain nanoparticle can cause observable harm above a certain level as a negative effect and claims that avoidance of the material would be wise. In contrast, one could also regard this nanomaterial as safe, because the level is above that of a reference material which is already used in practice. Although, these ambiguity issues raise ethical questions, the other three factors of uncertainty (lack of knowledge, ignorance, and complexity) also raise ethical issues which we discuss in further detail below.

Societal Experimentation

From the current debate about the impact of nanoparticles on (EHS) issues debate it is clear that stakeholders want to have a complete assessment of the possible risks, before the novel technology, such a nanotechnology are being introduced into the market. However, the uncertainties surrounding the novel technology make it essentially impossible to make an early complete risk assessment, because not all information can be available prior to introduction. In principle, only after its introduction the hazards of the technology can be fully assessed. In such case, the introduction would amount to a large scale societal experiment, to test the hazards of the novel technology [13].

The moral acceptability of such a societal experiment has been investigated by van de Poel [26]. He describes four *prima facie* moral conditions that are helpful to judge the acceptability of a societal experiment in the light of uncertain risks. These seemingly reasonable conditions are: (1) the absence of alternatives, (2) the controllability of the experiment, (3) informed consent, and (4) the proportionality of hazard and benefits. To these acceptability conditions van de Poel adds four responsible set-up requirements: monitoring, feedback, scale, and containment. We will use those requirements as part of the controllability condition, since that is their main aim.[1] In the case of nano-sized TiO_2 in cosmetic sunscreen we will show that the introduction and current practice do not adhere to these four conditions for the moral acceptability of societal experimentation under uncertainty.

Absence of Alternatives

The first acceptability condition is '*to require that first all other methods for gaining knowledge about the actual functioning of a new nanotechnology and its ethical consequences and hazards have been tried out before a societal experiment is carried out*' ([26]: 135). This seems a reasonable condition, because large scale societal experiments generally will pose a greater danger to society than small scale laboratory

[1] The set-up requirements have other functions besides controllability. Especially, the monitoring and feedback requirements have an additional function to ensure that data is gathered and ensure learning from the societal experiment.

tests. So the latter type of experiment is thus generally preferred to societal experiments.

We have examined over 150 laboratory scale toxicological studies that have been published about nano-sized TiO_2. Most of these studies have investigated dermal penetration, inhalation, photo-activity, and cellular damaging. Although still some questions remain on these topics, other topics have hardly received any attention. For example, only a few studies have investigated acute ecological effects or toxicity after oral ingestion. Clearly other acute routes of toxicological risks could have been investigated at laboratory scale before marketing and introducing it into society. In this case there are clearly other methods of testing besides societal experimenting and there seems to be no good reason not to employ these alternatives first. The introduction of nano-sized TiO_2 is thus at odds with the first acceptability condition. Another example is the continued discussion on dose metrics (mass, area, or particle number based) that is appropriate for risk assessment and management of nanoparticles. It seems possible to investigate this at laboratory scale, thus there seems to be no good reason to test this in a large scale societal experiment.

Controllability of the Experiment

The second moral condition that is proposed in van de Poel [26] is the controllability of the experiment. The main function of this consequentialist criterion is to prevent potential negative effects to turn into major or irreversible ramifications. To this end, a morally acceptable societal experiment (a) should be monitored, (b) ought to encompass a feedback mechanism, (c) should set up to constrain potential hazards, and (d) ought to be consciously scaled up. Monitoring is essential to control an experiment, because it is the initial step in a feedback mechanism in response to any harm resulting from the experiment. In addition: '*Responsible societal experiments also require that measures are taken to contain the hazards of the experiment.*' ([26]: 140). This can be achieved with measures such as safety factors and safety barriers to address known risks, but also guard against possible *unknown* hazards. In view of the fact that experiments are more controllable and it is easier to learn from experiments at smaller scales, is desirable to gradually scale up the societal experiment.

In the TiO_2 case there is essentially neither monitoring nor containment required by law. In Europe and the United States post marketing surveillance is virtually absent. For instance, there is no adverse effect reporting system [6]. Although, after-sales monitoring is not legally mandatory, it is questionable whether we are currently technically able to do so. Contemporary methods of detection are poor at distinguishing natural from engineered nano-sized particles. The methods are also unable to cope with the complex nature of environmental samples [19]. Another controllability issue is that in practice the TiO_2 nanoparticles are not contained after use. The nanoparticles are readily washed off during swimming or bathing and wastewater treatment facilities are poorly suited for nanoparticle removal, so the TiO_2 nanoparticles can get directly into the environment [17].

Informed Consent

In light of the fact that societal experiments involve humans, van de Poel [26] suggests the deontological restriction of informed consent. This restriction entails that an experiment using human subjects is only morally acceptable if the subject has voluntarily agreed to take part and the decision is based on a sufficient knowledge of the expected benefits and potential risks involved. Van de Poel [26] recognises that there are various issues with the specific application of informed consent to societal experiments, particularly the restrictiveness of the conditions and problems with acquiring the consent from indirectly involved subjects; nonetheless it can be argued that the underlying concern of respect for moral autonomy should be addressed in judging the moral acceptability of a societal experiment.

A major issue with the informed consent condition is that it seems an impossible task to ask all those possibly affected by a novel technology to consent to its application, especially those who are indirectly involved. So, the informed consent criterion should be formulated in such a way that it becomes workable. From a practical standpoint it seems reasonable to request that at least those who are directly affected should be informed. This practical criterion then would also need to encompass the obligation to re-evaluate who is being affected directly. So that during the experiment, when new information comes to light that point towards new group(s) of directly affected, those should immediately be informed. Another issue with the informed consent condition for societal experiments is that it remains questionable, if it is desirable that when one individual raises an objection to a certain hazard, the whole experiment should be abandoned. This is especially problematic, since novel technologies could bring large benefits to more than one individual. The principle seems to be overly restrictive in essentially giving every individual veto power. This predicament could be addressed in a practical sense by giving directly affected individuals a reasonable option to stop the experiment for themselves only. A *reasonable way* means that stopping the experiment would not put a overly large burden on that individual. In practice such a way out could be accomplished by having or keeping alternatives that achieve roughly the same function.

In the TiO_2 case, this limited notion of informing consent would result in only informing primary users of sunscreen lotions containing nano-size TiO_2 by labelling the products as such. Furthermore, the primary users should be able to stop using the sunscreen and switch to an alternative that does not contain these TiO_2 nanoparticles. In the current situation, there is no legal requirement to label sunscreens[2] in such a way that the users are being informed that they contain nano-sized TiO_2 [6]. Few commercially available sunscreens are labelled appropriately, mainly because producers expect negative consumer reaction to such labelling. As a consequence of the lack of labelling, consumers are not informed about their involvement in the societal experiment and are unable to terminate their participation in the experiment. Although, it seems at first glance that the consumers of the experimental sunscreen can straightforwardly stop using the product containing the nanoparticles, they are unable to switch to an alternative because it is unknown to them which alternative does not contain the experimental material.

Proportionality of Hazard and Benefits

As a final criterion for judging the moral acceptability of societal experiments van de Poel [26] proposes to weigh the proportionality of risks and benefits. As described above, uncertainty makes such an assessment impossible, because it is not possible to quantify risks and benefits. As a solution, van de Poel [26] suggests to weigh *expected* benefits of the experiment against the *credible* hazards from the experiment. Therefore, this criterion seems to be a way to rule out extreme experiments which provide almost no benefit or present very large hazards. However, there is a practical problem with this approach, at least in the case of TiO_2 nanoparticles. The move away from quantitative benefits and risks towards expected benefits and credible risks makes the analysis more speculative. Furthermore, in light of uncertainty resulting from ignorance, the analysis is plagued by being incomplete and the issue will often stay unresolved. A debate about the moral acceptability of the societal experiment based on this criterion will thus most likely run aground, because there is no clear distinction to show credibility of the anticipated hazards or benefits, as already shown in the description of the debates about nanomaterials. In practice, this weighting approach puts the judgement on a slippery slop, which most likely will result in a social stalemate. A possible solution is to consider the most restricted form of such a weighing; only considering quantitative risks and benefits.[3] A societal experiment should then at least provide more quantitative benefits than quantitative risks before it can be considered acceptable.

Another related problem with this criterion is that it seems to suggest that we somehow can make a well-considered decision before the introduction of a novel technology. This is a step away from what the concept of societal experiments stands for, which is to recognise that under uncertainty the implementation of technology should be monitored and continuously evaluated, since uncertainty blinds us to certain effects. So, a stronger argument could be made for continuous evaluation based on the risks and benefits that can be quantified at that time. The "absence of alternatives" condition already requires gaining as much quantitative knowledge of risks without doing

[2] This situation can change in the EU if the Commission adopts the proposed new regulation for the EU's Cosmetic Directive in which it would be mandatory to file nanomaterials in concentrations of more than one weight percent in the list of ingredients followed by the word "nano" in brackets.

[3] One could also consider other less restrictive forms of credibility criteria than scientific quantifiability, however, this should be accepted by all stakeholders to prevent the same social stalemate. Scientific quantifiability gives a prevalent way to measure credibility and provides a baseline case that at least should be obtained.

the societal experiment and the proposed criterion then sets an *a priori* burden on the proposer of the societal experiment to quantifiably show that based on current best knowledge the benefits outweigh the risks. Furthermore, during the experiment new information about the risks and benefits will emerge and the continuation of the experiment should than be re-evaluated. In the TiO_2 case there is, however, no clear post-market regulation in either Europe or the United States [6], so its introduction could be considered morally unacceptable according to this criterion as well.

From the above it is clear that the introduction and the continued marketing of cosmetic sunscreens containing TiO_2 nanoparticles can be perceived of as a morally unacceptable societal experiment, since it does not meet any of the reasonable conditions for such experiments. This is mainly the result of not considering the introduction as a societal experiment and this is still hampering better informed risk assessment and management following its introduction. Essentially, the introduction of nano-TiO_2 in sunscreens was and still is a large scale societal experiment in which no data is being gathered and no learning takes place.

Towards Acceptability

We will show in this section that the four modified acceptability conditions of societal experimenting could be used to support and guide the introduction of innovative technologies. In general this requires that novel technologies can be monitored and are flexible; so that the technology can be adapted after introduction when new information becomes available via continued monitoring and evaluation. Furthermore, the conditions can also be used to point the way for already applied technologies that could be considered morally unacceptable, such as the TiO_2 nanoparticles in cosmetic sunscreens. In the TiO_2 case one could conceive of five complementing routes to do so, knowingly: (1) closing the existing knowledge gap, (2) monitoring the societal experiment, (3) systematic evaluation of quantifiable risk and benefits, (4) designing for safety , and (5) incorporation the experimental nature of technological introduction into regulation. These five routes based upon the four modified conditions will be discussed below.

Closing Knowledge Gaps

For the nano-sized TiO_2 in sunscreens case, we have shown that there are uncertainties because we lack knowledge on specific hazards. These knowledge gaps could have, and according to the conditions should have, been resolved before introduction of nano-sized TiO_2 in sunscreens. A first step to moral acceptability is thus to close these knowledge gaps, such as the appropriateness of dose metric for toxicity, aggregation/agglomeration state of nano-sized TiO_2 in natural environments, acute oral toxicity, and short-term eco-toxicity. To facilitate these investigations, funds could be made available to support research in these specific directions; alternatively obligations could be set on producers to provide this information before products are allowed onto the market.

Monitoring the Experiment

As the introduction of TiO_2 nanoparticles into sunscreens can be considered a societal experiment, it is clear that the experimental data from this experiment should be measured and recorded. For example, the exposure to these nanoparticles should be investigated for workers, direct users, and those otherwise indirectly affected. Data on production and market volumes are also required to get a good view on possible exposure amounts and long-term ecological fate of the nanoparticles. Other examples of studies are the (bio) accumulation of the TiO_2 nanoparticles, long-term stability of particles and/or applied coatings, mobility in the environment, and chronic toxicity. Furthermore, all the results of these studies should then be combined to give insight into the complex causal relations that play a role in the possible risks associated with the use of nano-sized TiO_2 in sunscreens. It is, however, questionable if these measurements can be done directly, because currently most methodologies are ill-suited for complex samples that need to be investigated. A necessary primary step is thus to put further efforts into the development of analysis tools that can identify specific engineered nanoparticles in complex samples directly.

Continuous Review

The new data that is gained from the societal experiment by monitoring should be used to complement existing information. In turn, this data should be used to support ongoing evaluation and acted upon if necessary. In the nano-sized TiO_2 case, participants should firstly be properly informed in such a way that they at least know that their partaking in a societal experiment. Labelling sunscreen containing nano-sized TiO_2 would be a straightforward way of accomplishing this notification. Nonetheless, currently the industry has scarcely done so without obligation, most likely due to the expected negative reactions after its initial hype, similar to what occurred with genetic modification. A legal obligation to put forward this product information could possibly ensure directly-affected consumers have a way to know and provide these consumers with a possibility to terminate their use. Furthermore, reviewing procedures and strategies for terminating or altering the experiment should be put in place.

Designing for Safety

A further way to moral acceptability could be achieved by engineering design for safety in the sense of societal experimenting. In this kind of design, the experimental nature of technological introduction is taken into account during the design process. One can think of flexible production methods that can be changed when new risk information becomes available to produce a safer or completely other product. In the case of nano-sized TiO_2, this flexibility could be in the form of production units that are not narrowly dedicated, but can be modified rapidly in such a way that it can produce different particle sizes, other crystal types, incorporate different types of coatings, or even utilise a whole different metal oxide. Furthermore, one could think of alternative applications of the same particle when newly discovered traits seem to have negative effects upon the current application. In the TiO_2 case this has already been done with regard to ROS formation. The photo-activity of not coated anatase type TiO_2 nanoparticles are used in remediation of wastewater by utilising the same catalytic effect that made it less suitable for the sunscreen application. So, in a sense these flexible ways of using the novel nanoparticle apply the inherent diversity and changeability of the developing nanotechnological field. A further conceivable option could be designing the product such that it is easier to measure to facilitate the monitoring of the societal experiment, for example by adding tracers. Yet, another way to improve controllability of nanoparticles could be found in making them easy to remove after use. One could think of making the nanomaterial biodegradable or putting the nano-sized particles in a larger matrix so that the whole (nanoparticle embedded in the matrix) become removable by normal waste treatment facilities.

Regulation of Societal Experiments

As the introduction of novel technologies can be conceptualised as a societal experiment, it seems reasonable to create a framework that upholds and supports the moral acceptability of such experiments. Such a framework should not only prevent unacceptable societal experiments *a priori* by striving for sufficient pre-market studies and a proper experimental setup, but in addition should support actual experimenting and continued parallel evaluation during its execution after introduction. In the case of TiO_2 nanoparticles in sunscreens one could think of aiming at studies to close the knowledge gaps; for example toxicity test in areas that have received little attention or with nano-sized TiO_2 particles that are actually used in sunscreens. Furthermore, regulations could be beneficial in supporting post-market surveillance of the product, which is currently only meagrely picked up by the market; this is evident by the almost total lack of product labelling, limited voluntary registration in nanoproduct databases, and the unavailability of market volume data on nanomaterial containing products. Finally, regulation could also be useful in the area of setting up bodies that are able to facilitate (re)evaluation of the information gathered by monitoring the experiment and suggesting adaptations to the execution of the societal experiment.

Conclusion

The discord in the debate on the EHS aspects of nanotechnology is largely affected by the uncertainties surrounding the technology. Dealing with these uncertainties and their causes is necessary for a more meaningful deliberation about the introduction of technologies into society. We have argued that this introduction of novel technologies, such as the use of TiO_2 nanoparticles in cosmetic sunscreens, can be conceptualised as a societal experiment due to various causes of uncertainties. The moral acceptability of such an experiment can be investigated on the basis of four *prima facie* moral conditions that have been developed by van de Poel [26]. In light of the practical considerations we have proposed to modify the acceptability conditions of societal experimenting into the following:

1. The absence of alternative ways of extending the knowledge required for a complete risk assessment and management.
2. The controllability of the experiment, including monitoring, feedback, scale and containment.
3. Informing directly affected and providing the ability to terminate their personal involvement.
4. The *a priori* and continuous (re)evaluation of risk and benefits based on current and evolving knowledge.

The current practise in the nano-sized TiO_2 sunscreen case seems to violate all four acceptability conditions and so we argued that it constituted a morally unacceptable societal experiment. To remedy this situation we have agued for the following complementing actions:

a. Closing the existing information gap.
b. Setup of monitoring tools and gathering data from the conducted societal experiment.
c. Start continuous evaluation of available quantitative risk and benefits.
d. Ongoing engineering design for safety.
e. Altering legislation so that it incorporates the experimental nature of introducing novel technologies into society.

In a more general sense, it is very helpful to recognising that the introduction of a novel technology into society amounts to a societal experiment and that the moral acceptability of such an innovative technology can be evaluated from this viewpoint.

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