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Antinomies and contradictions in the use of nanotechnology in agribusiness

Antinomie e contraddizioni nell'utilizzo delle nanotecnologie nel settore agroalimentare*

The development of new nanomaterial technologies and research into nanoparticles has an impact on many areas, including agriculture and food production. Despite growing interest in nanomaterials, a comprehensive and clear regulatory framework on the subject remains lacking. Regarding their application in food preparation, novel food regulations are key; however, there are some contradictions due to different licensing regimes. For example, titanium dioxide is considered hazardous to health when used as a food additive, yet it continues to be used in drug preparation. This contradiction is explained by the fact that controls and regulations for substances used in food and medicines differ. Research in the broad field of nanotechnology and nanoparticles is closely connected with the debate on the relationship between science, technology and law, as it requires constant updates on issues such as sustainability, responsibility and freedom. The author hopes for greater harmonisation in the dialogue between scientists and jurists in this area, following the model offered in the 1970s by the Asilomar Conference, which increased civil society's interest in research. It is crucial to avoid ideological barriers and the regulatory bans that often accompany new experiments. Such bans are often driven by unfounded collective fears and political motivations rather than scientific evidence, resulting in bans that are both inexplicable and unreasonable and which only hinder scientific progress.

Keywords: nanotechnology, scientific research, nanoparticles, Agriculture 4.0

Lo sviluppo di nuove tecnologie dei nanomateriali e la ricerca sulle nanoparticelle hanno un impatto su molti settori, tra cui l'agricoltura e la produzione alimentare. Nonostante il cre-

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scente interesse per i nanomateriali, manca ancora un quadro normativo completo e chiaro in materia. Per quanto riguarda la loro applicazione nella preparazione degli alimenti, le nuove normative alimentari sono fondamentali; tuttavia, esistono alcune contraddizioni dovute ai diversi regimi di autorizzazione. Ad esempio, il biossido di titanio è considerato pericoloso per la salute se usato come additivo alimentare, ma continua a essere utilizzato nella preparazione dei farmaci. Questa contraddizione si spiega con il fatto che i controlli e i regolamenti per le sostanze utilizzate negli alimenti e nei farmaci sono diversi. La ricerca nel vasto campo delle nanotecnologie e delle nanoparticelle è strettamente connessa al dibattito sul rapporto tra scienza, tecnologia e diritto, in quanto richiede un costante aggiornamento su temi quali sostenibilità, responsabilità e libertà. L'autore auspica una maggiore armonizzazione del dialogo tra scienziati e giuristi in questo ambito, seguendo il modello offerto negli anni Settanta dalla Conferenza di Asilomar, che ha accresciuto l'interesse della società civile per la ricerca. È fondamentale evitare le barriere ideologiche e i divieti normativi che spesso accompagnano le nuove sperimentazioni. Tali divieti sono spesso guidati da paure collettive infondate e da motivazioni politiche piuttosto che da evidenze scientifiche, risultando in divieti inspiegabili e irragionevoli che non fanno altro che ostacolare il progresso scientifico.

Parole chiave: nanotecnologie, ricerca scientifica, nanoparticelle, agricoltura 4.0

1. Nanomaterials in agriculture and agribusiness

In the past century, increased agricultural production and food security have relied on the use of chemical fertilisers and pesticides to provide a response to the growing demand for food. However, these factors decisive in agriculture in the past are now being strongly challenged for multiple reasons related to environmental protection and pollution reduction needs.

While on the one hand it is essential to respect the environment and limit the use of pollutants in agriculture, on the other hand, the research and technological innovation make it possible to mitigate many of the feared negative side effects. This allows for alternative uses and a more rational and correct selection of the different types of substances. While nanoelements and nanomaterials can certainly pose new risks to consumer health and the environment, they can also offer opportunities to improve production and achieve significant results[1] and improve the general conditions of nutritional requirements.

For these reasons, it is necessary not to fall into the misleading general demonisation of the use of chemicals, and rather examine more accurately

[1] L. Brazell, *Nanotechnology Law. Best Practices*, Alphen aan den Rijn 2012.

the evolution of studies in the field, fostering a dialogue between science and law. More specifically, the use of nanomaterials represents an emerging area of research that affects multiple fields, including agricultural and agribusiness sectors.[2]

In the Horizon 2020 program, nanotechnology has been categorised as Key Enabling Technology (KET) for the innovation and the creation of new products. These products are materials of small dimensions between 1 and 100 nanometers[3] which, despite having an identical chemical composition to homologous materials (*bulk materials*), exhibit completely different chemical and physical properties.[4] For example, they are highly reactive and interact

[2] A. Di Lauro, *Mercato agroalimentare e innovazione tecnologica*, in: P. Borghi, I. Canfora, A. Di Lauro, L. Russo (eds.), *Trattato di diritto alimentare italiano e dell'Unione europea*, Milano 2024, p. 782 ff.; F. Prete, *Nanofoods*, in: L. Costato, F. Albisinni (eds.), *Trattato breve di diritto agrario italiano e dell'Unione europea*, Milan 2023, p. 1137 ff.; E. Sirsi, *Biotecnologie in agricoltura. Profili giuridici*, Pisa 2003, p. 151 ff.; L. Salvi, *Diritto alimentare e innovazione tecnologica nella regolazione dell'Unione Europea. Profili di legittimità e accountability*, Naples 2017, p. 171; L. Leone, *Nanotecnologia (applicazione nella produzione di alimenti) – Nanotechnology (application in food production)*, in: *Digesto delle Discipline Privatistiche – Sezione civile: Aggiornamenti*, Torino 2016, p. 539.

[3] One nanometer corresponds to one billionth of a meter. EU Regulation 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods defines an engineered nanomaterial as an intentionally produced material that is characterised by one or more dimensions in the order of 100 nm or less, or that is composed of distinct functional parts, either internally or at the surface, many of which have one or more dimensions in the order of 100 nm or less, including structures, agglomerates or aggregates that may have dimensions greater than the order of 100 nm, but which exhibit nanoscale characteristics. A very similar definition was provided by the European Commission Recommendation 2011/696/EU of 18 October 2011 which states that the term nanomaterial should be understood to mean a natural, derived or manufactured material containing particles in the free state, aggregate or agglomerate, and in which, for at least 50 percent of the particles in the number size distribution, one or more external dimensions is between 1 nm and 100 nm. For the purpose of framing the notions of nanomaterials, see also Regulation 528/2012 of 22 May 2012 on the making available on the market and use of biocidal products, which defines nanomaterial as "an active substance or a non-active substance, whether natural or manufactured, containing particles in a free, aggregated or agglomerated state, and where, for at least 50 percent of the particles in the number size distribution, one or more external dimensions is between 1 nm and 100 nm" and Regulation 1223/2009 of 30 November 2009 on cosmetic products, which defines nanomaterial as any insoluble or biopersistent and intentionally manufactured material having one or more external dimensions, or an internal structure, measuring from 1 to 100 nm.

[4] The characteristics of materials at the nanoscale level (less than 100 nm) are different from those of the same non-nanostructured materials. Properties characteristic of the nanoscale include properties related to the high specific surface area of the materials considered and/or physicochemical properties. In the nanoscale, the force of gravity is less important than the Van der Waals forces.

with cell membranes. These properties enable multiple application but can also be risky to consumer health and the environment.[5]

In other words, the microscopic size of nanoparticles alters the characteristics of substances from what is known at the macroscopic level, thereby increasing their toxicological potential. Scientists[6] concerned with detecting such toxicological potential have distinguished between the following characteristics of nanoelements: 1) the great chemical reactivity; 2) the ability to pass through cell membranes; 3) the inability of the human immune system to recognise nanoparticles and thus activate defensive mechanisms; 4) the ability to cross the blood-brain and the blood-placenta barriers, depositing in organs and damaging health. However, these same characteristics also enable nanoparticles to be used effectively for beneficial purposes, such as, for example, to achieve the goal of combatting many oncological diseases by taking advantage of the ease with which nanoelements penetrate inside cells. Nanoparticles are also used to produce vaccines and to counteract the degenerative effects of neurological diseases. These are forms of nanomedicine that target substances to their specific site of action, reducing the side effects that more general drug therapies have on the body as a whole.

Regarding the use of nanomaterials in agriculture, it should be noted that nanoparticles can be used for the fertilisation of cultivated land. In addition, nanoparticles with antimicrobial properties can reduce the need for pesticides, while ensuring proper protection of crops from pathogens. The ability of some nanoparticles to enter hormone biosynthesis could promote greater crop resistance to diseases caused by fungi or bacteria, or even counteract the damaging effects of high temperatures or water scarcity. This would be a useful aid in combatting the negative consequences of climate change.

Technological innovation and nanomaterials research may also lead to fundamental achievements in combatting soil degradation and preserving biodiversity. This is important because we must remember that we are losing many plant species to those that are able to provide a higher yield, but

[5] These properties allow for multiple uses but could also lead to new health hazards for consumers and the environment. See EFSA, *Guidance on risk assessment of nanoscience and nanotechnology applications within the human food chain*, May 2018; L. Leone, *Nanotecnologie e alimenti tra etica e diritto prospettive della regolazione nell'Unione europea*, "Glocalism Journal of Culture Politics and Innovation" 2014, no. 1–2, p. 3.

[6] A. Elsaesser, C.V. Howard, *Toxicology of nanoparticles*, "Advanced Drug Delivery Review" 2012, vol. 64, no. 2, pp. 129–137.

increasing the quantity of production does not always correspond to maintaining the quality and nutritional intake.

Soil degradation and the loss of plant biodiversity are often accompanied by the loss of plants' ability to bind micronutrients and thus contribute to making foods that provide the correct nutrient intake for consumers. These negative effects could be countered with the use of nanoparticles that can maintain productions that ensure proper nutritional intake.

Nanotechnology can also offer numerous advantages in the agribusiness industry. In fact, nanoparticles can be used in packaging enabling the preservation of food and preserving its organoleptic qualities, but interactions with other substances would need to be more carefully evaluated and results could differ depending on the specific use. The examples of their use in packaging are numerous if we think of nanocelluloses[7] or smart nanosensors capable of detecting environmental variations or the presence of contaminants which allow to know, whether a food can be consumed or not.[8]

The issue of the use of nanoparticles in agribusiness intersects a variety of problems regarding the tightness of regulations that do not require mandatory labeling of those ingredients that are found in very small percentages and remain below tolerance thresholds, raising unprecedented questions about the appropriateness of updating accidental food contamination profiles and even the definition of substances reasonably and intentionally present in production processes.

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[7] Microfibrillated cellulose has very useful thixotropic properties because it becomes viscous, depending on the variation of impressed stresses.

[8] Among the most innovative nanotechnological materials in food preservation are the use of smart packaging materials that can detect the presence of microbes and other pathogens by counteracting their proliferation so as to slow down the perishability time of food. These are applications that gain prominence especially in policies to counter food waste because they allow safe consumption beyond the mere legal expiration date. In food refrigeration, the use of nano-silver particles with antimicrobial properties should be noted, while in agriculture nanosensors are being developed for pesticide detection, which play a very useful role in the certification of organic agricultural products because they make it possible to reveal the absence of even very low percentages of impermissible substances, as well as the use of nanofilters for irrigation that enable water purification. Nanosensors are also used to track the transport and storage of food ensuring full transparency of the production route. See: V. Sodano, M. Quaglietta, *Nanotecnologie e settore agroalimentare: applicazioni e quadro normativo*, "Agriregionieuropea" 2014, no. 36; S. Mura, G. Seddaiu, F. Bacchini, P. Roggero, G.F. Greppi, *Advances of Nanotechnology in Agro-Environmental Studies*, "Italian Journal of Agronomy" 2013, no. 8, p. 127.

2. Conflicting science and law: the model offered by the Asilomar Conference

Research in the field of nanotechnology and nanoparticles is closely connected with the ongoing debate on the relationship between science, technology, and law[9] that requires constant updating of the issues involving sustainability, responsibility, and freedom. Regarding the role of law, among the questions that remain most evident, are those related to the relationship with scientific research, as it is unclear whether law should always maintain a neutral position or whether it should, to some extent, place itself in a relationship of true subordination to science or even whether another thesis that recognises a more prominent role aimed at guiding and, where appropriate, limiting scientific research and the use of innovations should prevail.[10]

Science and law adopt methodological paths that are inherently opposed and which could be summarised as primarily descriptive (science), and predominantly prescriptive (law). These differences concern not only the different epistemological status, but also the aims pursued and the language[11] adopted. As profoundly different realities that must co-exist, their relationship should be based on mutual respect and tolerance of each other's approaches, to be understood, as far as possible, always on an equal footing. This difficult relationship has many gray areas represented by technical standards, which should be interpreted as true unifying normative containers

[9] M. Tallacchini, *Scienza e diritto. Prospettive di co-produzione*, "Rivista di filosofia del diritto" 2012, no. 2, p. 315. According to which, while the life sciences preceded biojuridical reflection, nanoscience developed "together" with "nano-law."

[10] A. Di Lauro, *Mercato agroalimentare e innovazione tecnologica*, in: P. Borghi, I. Canfora, A. Di Lauro, L. Russo (eds.), *Trattato di diritto alimentare*..., p. 782.

[11] In contrast, the opposite view is reiterated by those who argue that scientific language and legal systems must decline by following a common language, especially in the process of interpreting and adapting science to law (R. Feldman, *The role of science in law*, Oxford 2009, 4). The debate around the definition of nanomaterial represents one of the most obvious examples of the co-partnership of different epistemic communities, which has seen the interaction of institutions, research centers and numerous spaces of public consultation. About the topic discussed here, it should be remembered that the study of the complex regulatory process represents an effort to reconcile the requirements of regulatory language with the language of science. The concept of nanomaterial, to refer to a natural material containing particles of very small size, between 1 nm and 100 nm, has identified size as the general criterion for classification. The normative choice of finding a criterion for homogenising definitions around the nanoscale and especially around the concept of nano-size has thus enabled the adoption of a shared nomenclature, helping to smooth out epistemic differences between different knowledges. On this point see: M. Tallacchini, *Scienza e diritto*..., p. 326.

as opposed to partisan methodological choices. However, it is precisely in the preparation of technical standards that the greatest contrasts often occur.

In fact, regardless of which approach one wishes to follow, it must be noted that science, understood as a public expression of rationality, has always played a fundamental in legitimizing the production of legal norms.[12]

The debate is strongly conditioned by the mistrust that generally accompanies technological innovations and experimental results, although, from a historical perspective, there is no shortage of examples that can be recalled here that demonstrate the proper balance between the freedom of research and experimentation and the necessary precautions arising from the need to ensure the highest levels of public safety. In this regard, one example that may be useful to recall here concerns the debate around recombinant DNA technology. The scientific community had questioned the limits of experimentation and the need to suspend certain processes until the safety issues surrounding the development of this technology were addressed in a more coordinated manner.

It is well known that the debate over the limits of DNA research helped to design the regulatory framework that subsequently led to the 1975 Asilomar Conference in California. This conference involved numerous scientists, jurists, and physicians in determining a set of guidelines on the use of new technologies. A very similar process has also been adopted recently to address issues that have arisen around regulation in the field of Artificial Intelligence.[13]

The Asilomar Conference offered a model of self-regulation by the scientific community, helping to increase civil society's interest in biomedical research by avoiding the ideological barriers and the appearance of unreasonable regulatory bans, which very often accompany new experiments and which, in most cases, are generated more by unfounded collective fears than by scientific evidence.

[12] Y. Ezrahi, *The Descent of Icarus*, Cambridge, Mass. 1990.

[13] In 2017, during the Beneficial AI Conference, organised by the Future of Live Institute, 23 principles on the development of Artificial Intelligence Regarding the field of nanotechnology, for the call for an Asilomar Conference in this area, see the reflections of: C. Tourmey, *An Asilomar for nanotech*, "Nature Nanotech" 2014, no. 9, pp. 495–496; M. Roco, W. Bainbridge (eds.), *Societal Implications of Nanoscience and Nanotechnology*, New York 2001; eidem, *Nanotechnology: Societal Implications II: Individual Perspectives*, New York 2007; F. Allhoff, P. Lin, J.H. Moor, J. Weckert, *Nanoethics: The Ethical and Social Implications of Nanotechnology*, Hoboken, NJ 2007.

In Europe, Regulation (EC) No 1907/2006 on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), also applies to nanomaterials, which are classified according to their properties and assessed with respect to potential health and environmental risks. The framework of authorisation and control, however, is more complex because it draws the expertise of multiple authorities. Thus, for the agri-food sector, EFSA must assess the safety of all food; therefore, any nanoparticles deemed hazardous to consumers' health cannot be marketed and used in the food sector.

Under the REACH Regulation,[14] any substance manufactured in or imported into the European Union must be registered. In addition, manufacturers and importers of chemicals must declare any hazard to health and the environment, as well as provide information on how to control and contain these hazards to ensure their proper use.

In the United States, the Environmental Protection Agency (EPA) is responsible for nanomaterials and provides the specific guidelines under the context of the Toxic Substances Control Act (TSCA), but it should not be forgotten that the World Health Organization (WHO) and the Organization for Economic Cooperation and Development (OECD) are also developing international guidelines for the assessment and management of nanomaterials.

In Europe, despite the great interest in the development of nanotechnology, there continues to be a lack of an organic and comprehensive discipline. Many of the rules applied in this field are derived from other disciplines, such as EU Regulation 2015/2283, on novel foods, or EC Regulation 1333/2008 on food additives. In particular, the latter Regulation stipulates that a food additive that has been authorised but is subsequently made with different preparation methods or raw materials, including the modification of the size of the substances, using nanotechnology, makes it necessary to make a new assessment for the purpose of marketing, not being able to disregard the obligation of supplementation through additional data.

With the Recommendation of 7 February 2008,[15] the European Commission adopted a Code of Conduct for responsible research in nanoscience

[14] Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC (OJ L 396, 30.12.2006, p. 1).

[15] Recommendation 2008/345/EC of 7 February 2008, notified under C(2008) 424.

and nanotechnology. It is well known that in sources of European Union law, Recommendations do not have binding force, but the approved code of conduct is an important step toward shared directions that can guide scientific research in the future. The voluntary code of conduct aims to involve as many stakeholders as possible, ensuring the safe development and use of nanotechnology. It is an instrument that was approved, following a public consultation, and calls out seven general principles to be followed in nanoscience and nanotechnology research.

The principles are as follows:

1. Information and respect for fundamental rights: research activities must be understandable to the public, respect fundamental rights, and be disclosed and used in the interest of the welfare of people and society.

2. Sustainability: research activities must be safe, comply with ethical principles and contribute to sustainable development. Research is free, but experiments must be conducted without harming people, animals, plants and the environment.

3. Precaution: research activities should be carried out in accordance with the precautionary principle, ensuring the highest possible level of protection.

4. Inclusion: the management of research activities must be done in a transparent manner, ensuring that all stakeholders participate in decision-making processes.

5. Excellence: research activities must comply with the best scientific standards, including research integrity and good laboratory practices.

6. Innovation: the management of research activities should encourage maximum creativity, flexibility and planning capacity for innovation and growth.

7. Accountability: the researchers and research organisations involved must be responsible for the impact of their work on society, the environment, and people's health.

It is important to note that the Recommendation is not only addressed to member states, but has a general scope, involving employers and research funding bodies, researchers, and all those stakeholders participating in or interested in the development of the nanoscience and nanotechnology sector.

An additional source that needs to be mentioned is Regulation 1169/2011 which requires consumers to be informed whether purchased foods contain or consist of engineered nanomaterials. In fact, if such elements are present, it is mandatory to indicate in the list of components the name of the ingredient preceded by the prefix "nano" in parentheses.

3. The REACH Regulation, EFSA and ECHA controls

The Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation governs the manufacture, import and use of chemicals within the European Union. It stipulates that companies intending to manufacture or import chemicals in quantities above a certain threshold must register these substances with the European Chemicals Agency (ECHA), and provide detailed information on what are the risks to people's health. In some cases, additional data or safety measures may be required. In fact, the REACH Regulation allows for special restrictions on the manufacture, import, sale, and use of the most hazardous substances, and provides for the possibility of specific authorisations for companies.

The ECHA (European Chemicals Agency) is the European Union agency responsible for the enforcement of the REACH Regulation and, more generally, oversees managing the authorisation and control processes for chemicals. ECHA's main tasks may certainly include collecting information on chemicals produced or imported into the European Union and assessing their impact on the environment and human health. ECHA cooperates with national authorities in evaluating the data submitted by companies to determine whether the information rendered is to be considered sufficient or whether additional information needs to be provided to ensure safety and flag any health or environmental hazards. Chemical substances are classified according to hazard, and those of greatest concern, which require more extensive and careful monitoring are labeled as "substances of very high concern" (SVHC), based on their potential to harm health or the environment. When a substance is included in the list of SVHCs, companies must be specifically authorised to continue to manufacture and use such substances, with the understanding that ECHA may impose further restrictions on their manufacture, import, sale, or use.

The ECHA's function may also be relevant to the use of chemicals within the agricultural organisation due to the fact that this agency plays an important role in implementing the rules of Regulation (EC) 1272/2008, which aligned the classification and labeling of European chemicals with the GHS (Globally Harmonized System of classification and labeling of chemicals), as well as in implementing Regulation (EU) 528/2012 on the placing and use of biocidal products.

The tasks of the European Chemicals Agency (ECHA) and the European Food Safety Authority (EFSA) cover different areas (chemical industrial for ECHA and food for EFSA), but there may be inconvenient overlaps in some circumstances. Indeed, while the specific areas of responsibility of these independent authorities focus on different aspects of risk assessment, on the other hand, both are concerned with ensuring the safety of citizens and the environment in the European Union.

By adopting different approaches, the analysis and research conducted on a given substance, respectively, could lead to different results, because the examinations to be carried out under REACH mainly focus on toxicological and environmental effects, including long-term exposure assessments, while EFSA's evaluations focus on risks in a context that is exclusively food safety.

Thus, a pesticide authorised for agricultural use and allowed by ECHA for certain exposure levels could instead be banned by EFSA when residues in food exceed safe limits for human consumption. Divergences could also relate to the setting of tolerability thresholds for a given substance, contributing to an opaque framework, despite the need for transparency that should always characterise consumer rights.

The results could also depend on different assessments of exposure levels, since EFSA's analysis focuses on residues in food, while ECHA's tasks also include measuring the degree to which workers tolerate the use of chemicals during production processes.

However, these opposing "interpretations" of the same phenomenon, which seem to contradict each other, are equally legitimate because they remain consistent and intended for different regulatory domains. This shows that the discipline of nanotechnology involves many different scientific and production areas that are difficult to regulate in a systematic way.[16]

4. Variability in experimental results and conflicting applications: the examples of graphene and titanium dioxide

The risk management of nanomaterials follows the traditional rules regarding the controls to be performed before marketing a product that is to be considered safe for consumers' health. However, the usual testing methods in this specific field are not always applicable at substances at the nanoscale

[16] M. Tallacchini, *Scienza e diritto...*, p. 329. According to whom, in order to cope with the impossibility of an accomplished and systematic regulation on the subject of nanotechnology, an approach has been adopted through a network of heterogeneous legal instruments, with ethics played out as a soft connective tissue in a rarefied archipelago of hard rules.

have different sizes and unknown chemical and physical properties that affect their bioavailability and toxicity. For these reasons, potential health hazards are not easily detectable through traditional empirical assessment methods, because regardless their actual toxicity level determined in toxicology, the interaction of nanoparticles with human tissues and organs allows for greater penetration and easier absorption than macro forms of the same substances. This makes the results of laboratory tests highly variable and insufficiently reliable.

Furthermore, one must ask how the new rules[17] that aim to modernise the regulation of producer liability considering technological developments and changes in product production and distribution chains will affect it. The question is whether the list of justifications for producer liability with reference to, for example, the exemption of development risk can be invoked without an update that considers the uncertainties of laboratory test which, in the field of nanoelements, often provide data that are inconsistent and contradictory.

More generally, it can be observed that the toxicity processes resulting from internalisation, that is, the introduction of a nanomolecule inside a cell, are difficult to measure with certainty and can vary considerably. Thus, some tests traditionally used in *in vitro* experiments have proven to be inadequate for nanoelements, producing human immune system responses that are completely opposite to those of testing the same macro substances.

Regarding the use of nanoparticles and nanotechnology in agriculture[18] and in food production, numerous examples may certainly be given in addition to the reasoning already considered.

By way of example only, the experiments carried out on graphene[19] and titanium dioxide may be mentioned. These materials may be considered nanomaterials when their particles have dimensions in the nanometer range (1 to 100 nm). In this case, titanium dioxide has different physical and chemical characteristics than larger particles.

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[17] The reference is certainly to EU Directive 2024/2853 of the European Parliament and of the Council of 23 October 2024 on product liability, which repealed Council Directive 85/374/EEC.

[18] For a discussion of the use of nanotechnology and nanomaterials in agriculture see: S. Mura, G. Seddaiu, F. Bacchini, P.P. Roggero, G.F. Greppi, *Advances of Nanotechnology...*, pp. 127–140.

[19] For the many properties and applications of graphene, see the studies by: M. Aliofkhazraei, N. Ali, W.I. Milne, C.S. Ozkan, S. Mitura, J.L. Gervasoni (eds.), *Graphene Science Handbook: Applications and Industrialization*, Boca Raton 2016.

In the mind of Regulation (EU) 528/2012, fullerenes, graphene flakes[20] and single-walled carbon nanotubes with one or more external dimensions of less than 1 nm are considered nanomaterials. Carbon fibers are used as an additive of many materials to increase their strength and conductivity.

In the field of agriculture, the extremely thin thickness of graphene makes it particularly suitable for making molecular filters used to desalinate water.

The decision to focus on these two elements rather than a very wide range of further possible examples is justified by the fact that they represent two different and emblematic hypotheses of nanomaterials, which leads to the need to formulate opposite conclusions about their use, constituting paradigmatic cases for the discussion.

Studies on graphene have demonstrated the possibility of multifunctional uses destined to become increasingly prevalent in the future. In contrast, while there was initial enthusiasm for the extraordinary applications of titanium dioxide as a food additive, and in particular as an anti-caking agent (rubricated E171), a number of negative aspects have more recently emerged that are prompting greater caution and a reversal of the trend on the use of this substance.[21] More specifically, in the European Union, the use of titanium dioxide (TiO_2) as a food additive (E171) has been criticised[22] because of potential adverse health effects on consumers in the long term, while it continues to be used in the pharmaceutical industry as a coloring and coating agent in many drugs.[23] In food preparation, higher levels of

[20] Graphene is considered a super nanomaterial. It was isolated in 2004 from graphite and is the thinnest material so far available, consisting of a sheet of carbon atoms forming a hexagonal lattice. Among the most important characteristics of a graphene sheet are its high conductivity of heat and electricity, with performance that is superior to silicon and copper, respectively; remarkable mechanical strength, superior to that of steel; and high ductility and thinness.

[21] EFSA, based on the data collected, stated in its May 6, 2021, opinion that the genotoxicity hazards of titanium dioxide cannot be ruled out and it cannot be considered as a safe food additive.

[22] In fact, the succession of studies and trials for the application of titanium dioxide in food have been quite variable. In the past, titanium dioxide had been authorised as a coloring agent in certain foods in accordance with Annex II of EC Regulation 1333/2008. Subsequently, EU Regulation 2022/63 was passed, which intervened in the matter for a timelier update, after EFSA recommended new toxicological tests to establish the permissible daily intake, calling for a characterization of the particle size distribution and the percentage of nanoscale particles present of titanium dioxide used as a food additive, revising the maximum limits for toxic element impurities.

[23] In a document dated 8 September 2021, the European Medicines Agency (EMA) pointed out that, from a technical point of view, the substitution of titanium dioxide in authorised

caution are required and strict guidelines must be followed together with the application of the precautionary principle. Also evaluation of more specific safety data is needed.

However, this contradiction is explained not only by the fact that the controls and regulations regarding the use of substances in food and medicines differ, but also because of the stated inability of the EMA (European Medicines Agency) to find viable alternatives as substitutes.

Closely related to this reflection is then the issue of the declaration of toxicity of a substance that could be outlawed, as of a certain point in time, allowing companies to dispose of and sell products, since the volume of the products concerned and the global supply chains, imply that the immediate substitution of a specific element used in the production industry, could cause economically unsustainable negative effects on the Union market. This reasoning is explicitly referred to in recital 15 of Regulation (EU) 2022/63 regarding the food additive titanium dioxide, in the part concerning the substitution of this element in authorised medicinal products. In other words, there could be situations where reformulation of each individual product would take a very long time for global supply chains. Thus, from the standpoint of the economic analysis of the law, despite scientific findings, an element considered hazardous to health could equally remain provisionally on the list of authorised additives, pending the development of suitable alternatives that could replace it. In the case of titanium dioxide, which can be examined as an illustrative situation of this problem, without prejudice to the pharmaceutical industry's duty to make all possible efforts to accelerate research and development of possible alternatives to be used as replacements, this criterion was the basis for the decision to continue to allow the sale of medicines containing titanium dioxide.

In the food sector, on the other hand, the feasibility of possible substitution was considered more easily feasible. However, even in that different production sector, the Commission assessed the market impact and the quality, safety, and effectiveness of the ban against the costs of production and organisation of agri-food companies. For this reason, without prejudice to the removal from the EU list of food additives for use, Regulation (EU) 2022/63 identified a transitional period for the full entry into force of the measure, indicating a time frame within which products containing this element may

medicines would require very complex examinations and bioequivalence studies. In addition, considering the wide scope of use of this excipient in the pharmacological industry, any substitution in the field of drug preparation would cause worrying shortages in the European market for essential medicines.

continue to remain on the market, subject of course to the minimum shelf life or expiration date of the packaging.

Well, these two examples represent how difficult it is to find definitive general rules for substances with very different specific characteristics. Thus, while legally falling into the same regulatory category, because from the perspective of legal definitions these chemical substances are counted as "nanoelements," they inevitably need a more precise degree of refinement in their regulation. At the same time, this reflection must prompt a more flexible articulation of the debate on the subject, sifting through all the aspects involved, without slowing down research that must be guided and supported by law.

One is faced with the need for legal regulation that can function differently in relation to individual compartments, establishing good practices and useful pointers for future legislation. In a highly fragmented framework that is difficult to interpret because it is driven by uncertain empirical results, the path that has dominated European legislative choices to date is based essentially on the application of the precautionary principle. This principle continues to be an indispensable tool, but the most up-to-date thinking on the use of nanoparticles and nanotechnology seems to reiterate more strongly the need to develop regulatory hybrids that can generate heterogeneous legal instruments depending on the specific areas of application. These new forms of normativity in areas dominated by science and technology include definitions, prohibitions, and authorisations, which may change depending on the specific contexts, and it is for this reason that processes and materials that are unsuitable in one area of application may come in handy for other forms of use.

In this context, the requirements specified in the 2018 document, "Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain," continue to be key.

In conclusion, there is an enormous difficulty in regulating normatively, through general rules, products that are completely unknown or only partially known. Faced with the structural limitations of *hard law* mechanisms, most correct approach seems to necessarily postulate the use of *soft law* regulatory sources that can function even in the face of a high degree of indeterminacy in the scientific and technological data collected.[24]

[24] T.F. Malloy, *Soft Law and Nanotechnology: a Functional Perspective*, "Jurimetrics. The Journal of Law, Sciences & Technology" 2012, vol. 52, no. 3, pp. 347–358; K.W. Abbott, G.E. Marchant, E.A. Carley, *Soft Law Oversight Mechanisms for nanotechnology*, "Jurimetrics. The Journal of Law, Sciences & Technology" 2012, vol. 52, no. 3, pp. 279–312.

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