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ORIGINAL PAPER

Sunscreen Safety: The Precautionary Principle, The Australian Therapeutic Goods Administration and Nanoparticles in Sunscreens

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Abstract The 'Precautionary Principle' provides a somewhat ill-defined guide, often of uncertain normative status, for those exercising administrative decision-making power in circumstances where that may create potential risks to human health or the environment. This paper seeks to explore to what extent the precautionary principle should have been and was in fact utilised by the Australian Therapeutic Goods Administration (TGA) in its decision to approve the marketing of sunscreens containing titanium dioxide (TiO_2) and zinc oxide (ZnO) in nanoparticulate form. In particular, this article assesses to what extent better application of that principle might have altered the TGA's decision that TiO_2 and ZnO ENPs in sunscreens do not require new safety testing, because they are considered to be functionally equivalent to their bulk counterparts.

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Introduction

Engineered nanoparticles (ENPs) can already be found in sunscreens sold to Australian consumers. The Australian Therapeutic Goods Administration (TGA) has noted that of the 1,200 sunscreens authorised by that Agency for supply as a therapeutic good in Australia in 2005, 70% of the sunscreens containing titanium dioxide (TiO_2) and 30% containing zinc oxide (ZnO)—both of which are common ultraviolet ray blocking agents—contained these insoluble metal oxide particles in a nanoscale form [54].

When reduced to nanoscale dimensions TiO_2 and ZnO become increasingly translucent which consequently provides sunscreens greater transparency when applied to the skin [29]. The advent of nanotechnology has been a boon for sunscreen manufacturers, allowing them to produce products with greater cosmetic appeal and hence offering attendant skin cancer-protective benefits through increased usage [28].

The change to using TiO_2 and ZnO nanoparticles in sunscreens has not gone unnoticed by government bodies [47, 55] and concerned community groups [33]. This has resulted in, for example, a coalition of eight non-government organisations with interests in

consumer, health and environmental issues filing formal legal petition in May 2006 with the US Food and Drug Administration (FDA) [20]. The petition called on the Agency 'to address the human health and environmental risks of nanomaterials in consumer products' ([23]: 335). The petition specifically addressed the increasing use of TiO_2 and ZnO nanoparticles in sunscreens, and requested that the FDA, 'declare all current available sunscreen drug products containing engineered nanoparticles of zinc oxide and titanium dioxide as imminent hazard to public health…' ([20]: 3). The FDA was still reviewing the petition at the time it released its Task Force report on nanotechnology [15]. In Australia, pursuant to the *Therapeutic Goods Act* 1989 (Cth) and the *Therapeutic Goods Regulations* 1990 (Cth), the TGA is responsible for ensuring the quality and safety of sunscreen products prior to their supply in Australia, as well as post-market monitoring the safety of these products so as to ensure that they do not pose a risk to human health [5, 6].

This paper tackles four central questions. (1) In general terms what are the basic elements of the precautionary principle as it has applied in international and national legal context? (2) What should be the nature of the precautionary principle as it applies to decisions of the TGA in Australia? (3) To what extent has the precautionary principle underpinned Australian regulatory actions to date, particularly including those of the TGA in relation to ENPs in sunscreens? (4) What benefits would arise from altering the regulatory system to encourage greater use of the precautionary principle by agencies such as the TGA in relation to nanoparticles in cosmetic and other therapeutic products?

The Precautionary Principle in International and National Legal Context

The precautionary principle emerged as a popular theme of regulatory policy in Germany during the 1970s [13]. It rapidly spread through the international policy arena as a philosophical challenge against traditional approaches that demanded an often unrealistic level of scientific certainty about risks before recommending or implementing health and environment protection measures [2, 21, 58]. Majone [30] has stated that, 'the precautionary principle is an idea (perhaps a state of mind) rather than a clearly defined concept, much less a guide to consistent decision making…' and has eleven different meanings within Germany alone.

One well known international enunciation of the precautionary principle is found in Principle 15 of the *Rio Declaration on Environment and Development* (1992):

> *'In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation'* [51].

Variations of the precautionary principle have since then been incorporated into regulatory decision-making in a number of specific fields of environmental and human health protection. Such fields include the protection of ozone layer, climate change, biological diversity, fisheries management and safety of genetically modified (GM) food [3, 10, 11].

The development and application of the precautionary principle has never been free from criticism, especially, one could argue, from those ideologically opposed to any component of regulation that overly inhibits rapid profit-making. Some commentators maintain, for example, that the precautionary principle does not provide a robust or reliable foundation for regulation, because there are a number of different versions without consensus on what it actually means [44]. Ambiguity of the concept, for example, as to what level of risk is acceptable and what type of action is required, has also been criticised for allowing an arbitrary and capricious application of the principle [31]. Moreover, others warn that a precautionary measure may have adverse effects, rendering protective measures hazardous in themselves to the environment or human body [7, 16]. It is even pointed out that it may well result in preventing development of new technologies that may serve to alleviate the environmental harm [19, 48].

It is thus worthwhile to note that the precautionary principle, on any rational analysis, does not express some incontrovertible, monolithic regulatory truth, but rather sets a framework within which precautionary measures practicably may be taken. The extent

and manner in which the precautionary principle applies often depends on the correlation between evidence of the nature and seriousness of the risk, as well as the kinds of remedies to be made available. [40] For example, if the potential risk meets a reasonable threshold for establishing serious and irreversible threats to human bodies and environment, strong regulatory measures (such imposing a ban on the production of a dangerous chemical) readily can be justified even in the face of ongoing scientific uncertainty about such risks. On the other hand, if the potential risk appears to be not so serious, or if there is a competing interest whose significance is equivalent to, or greater than, that threatened, a less stringent or onerous regulatory measure may warranted. ([37]; 77–79) Yet considerations of the seriousness of risk faced may be supplemented by a variety of other formulae in statutory formulations of the precautionary principle [30, 40].

The introduction of the precautionary principle into Australian legislation is a relatively recent event, corresponding to its emergence in the international regulatory arena in the 1990s. While the principle has since been embraced widely both in Australian statutory and judicial settings, its application has been restricted in at least in three significant respects.

First, the precautionary principle generally has been conceived of as a general principle concerning the prevention of environmental damage, not as a legal requirement to ensure its substantive application in a wider context of human safety. The *Gene Technology Act* 2000 (Cth) (GTA) provides such an example. The precautionary principle was a last minute inclusion to the GTA to ensure its passage through Parliament [38]. Section 4 of the GTA [6] states that:

> 'The object of this Act is to be achieved through a regulatory framework which:
>
> (aa) provides that where there are threats of serious or irreversible environmental damage, a lack of scientific certainty should not be used as a reason for postponing cost effective measures to prevent environmental damage.'

Whilst the precautionary principle is specifically mentioned in the GTA, there is little detailed guidance about, or firm requirement for, its application to decisions made by regulators of gene technology for environmental protection, much less for safety of human bodies. Peel [38] suggests that the other duties required of regulators under the GTA would restrict application of the principle.

Second, the precautionary principle has been predominantly adopted into Australian regulation in the context of risk management, not at the stage of risk assessment. There are various State and Commonwealth laws and policies that require administrative decision-makers to consider the precautionary principle when exercising their power.[1] One example, the Intergovernmental Agreement on the Environment (IGAE) includes a definition of the precautionary principle that closely adheres to the version found in the Rio Declaration. Section 3.5.1 of the IGAE states that,

> 'Where there are threats of serious or irreversible environmental damage, lack of full scientific certainty should not be used as a reason for postponing measures to prevent environmental degradation. In the application of the precautionary principle, public and private decisions should be guided by:
>
> 1. careful evaluation to avoid, wherever practicable, serious or irreversible damage to the environment; and
>
> 2. an assessment of the risk-weighted consequences of various options' [18]

The precautionary principle has also been applied in instances not explicitly defined within Australian Commonwealth and State regulations. One such example in which the Australian Government agency has supported the use of the precautionary principle within the context of an administrative policy may be found in the *Environmental Health Risk Assessment Guidelines for Assessing Human Health Risks from Environmental Hazards*. Within this context, the Federal Department of Health and Aging has recognised the precautionary principle as being 'particularly relevant' to management of risks following risk assessment [8].

Third, the Australian judiciary have in some cases factored whether the precautionary principle was

[1] See for instance, s391 *Environment Protection and Biodiversity Conservation Act* (1999) (Cth); s30(1)(c) *Fisheries Management Act* (1994) (NSW).

applied into their appraisal of the merits of an administrative decision, even in cases where the application of the principle was not explicitly mandated by legislation [50]. Yet they have been more comfortable with talking about a cautious approach as a matter of common sense, as opposed to the precautionary principle as a principle of law.[2] In the appeal case of *Leatch* v *National Parks and Wildlife Service (NSW)*,[3] for example, Justice Stein held that,

> *'the precautionary principle is a statement of commonsense and has already been applied by decision-makers in appropriate circumstances prior to the principle being spelt out… Its premise is that where uncertainty or ignorance exists concerning the nature or scope of environmental harm (whether this follows from policies, decisions or activities), decision-makers should be cautious.'* [50]

Such reasoning indicates that it is possible to invoke the precautionary principle in Australia, as in Canada,[4] to facilitate a contextual approach to statutory interpretation in the case where a statutory provision is ambiguous in its meaning.

The Precautionary Principle and the TGA

Under the *Therapeutic Goods Act* 1989 (Cth) (the Act) the TGA is responsible for regulating therapeutic goods in Australia, and in doing so ensuring the 'quality, safety, efficacy and timely availability of therapeutic goods' (s.4 of the Act). Pursuant to the Act, a 'therapeutic good' (as defined by s.3 of the Act), cannot be supplied in Australia—with the exception of exempt and excluded goods—before it is entered on the Australian Register of Therapeutic Goods (ARTG) (Therapeutic. Goods Administration 2005). As provided for by Schedule 4 of the *Therapeutic Goods Regulation 1990*, sunscreen products with a sun protection factor (SFF) of four or above (as defined in Australian/New Zealand Standard Sunscreen products—Evaluation and classification (AS/NZS 2604:1998)) are considered to be 'low risk' or 'listed goods' for the purposes of being entered onto the ARTG. In undertaking a human risk assessment of 'listed' sunscreen products for the purpose of entry onto the ARTG, the TGA is therefore required to only assess the sunscreen on the basis of its quality and safety, but not efficacy. Under this framework, evaluation of potential risks to human health posed by listed goods, including sunscreens, by the TGA must therefore occur after the product has been entered onto the ARTG, supplied in Australia, and only then in response to, for example, concerns relating to the product's safety in relation to human health. The regulatory requirements for sunscreens and their ingredients in Australia are further described in the TGA's [52] *Australian Regulatory Guidelines for OTC Medicines.*

There is no specific mention of the precautionary principle within the Act. The question thus arises whether and to what extent the TGA's regulatory obligation to ensure the safety of the therapeutic goods is capable of embracing and is likely to be enhanced by the precautionary principle as it has arisen elsewhere in the Australian legal system.

The TGA has made no official statement regarding use of the precautionary principle in its decision making process. The absence of any such reference to the precautionary principle could well be ascribed to the general and loose understanding of the principle, which seen it generally emphasised in the environmental regulatory context.

However tacit acknowledgement by the TGA of the applicability of the precautionary principle may be observed from the structure of the report it released in 2006. The report titled, *Safety of Sunscreens Containing Nanoparticles of Zinc Oxide or Titanium Dioxide*, directly addresses the elements of the precautionary principle. It assesses whether TiO_2 and ZnO ENPs are a danger to human health and if there is scientific uncertainty about the risk posed (Therapeutic Goods Administration [54, 55]). The extent to which the precautionary principle should be applied by the TGA in relation to such an issue requires a careful examination, bearing in mind the ambiguous and generally restrictive understanding of the precautionary principle in the overall legal context in Australia.

[2] The distinction was articulated in *Friends of Hinchinbrook Society Inc v Minister for Environment and Others* (1997) 142 ALR 632, 677–678.

[3] [1993] NSWLEC 191.

[4] *Janet Fletcher v The Corporation of the City of Kingston* (2004) 240 DLR (4th) 734, 754 para 86.

The Application of the Precautionary Principle to Nanoparticles in Sunscreens

The TGA has set concentrations of TiO_2 and ZnO that are permitted as active ingredients in sunscreens listed on the ARTG [52]. Under this framework, the ARTG does not differentiate between listed ingredients such as TiO_2 and ZnO on the basis of their size. Originally this was because the quality and safety of these ingredients in molecular form had been established and no smaller forms were available. The development of ENPs and publicity surrounding their potential toxicity however, has required the TGA to assess whether the use of TiO_2 and ZnO now requires further regulation [28]. If ENPs used in sunscreens were found to have different properties from their bulk counterparts according to TGA policy they would have required separate safety assessment by manufacturers in keeping with their status as new active ingredients [52].

The TGA has taken the position that sunscreen products containing active TiO_2 and ZnO ENPs do not require their own quality and safety review (TGA 2006; [33]). The rationale for this approach has been that the ENPs in question do not pose any new risks to human health. A 2006 review by the TGA states, 'there is no evidence that sunscreens containing these materials pose any risk to the people using them' (TGA 2006).

This position may be contrasted to that of the view of the European Commission's Scientific Committee on Consumer Products (SCCP), who at the request of the European Commission delivered an opinion on the safety of nanomaterials in cosmetics products [46]. Under the terms of reference, the SCCP was 'requested to review, and if appropriate, to amend its notes of guidance for the testing of cosmetic ingredients and their safety evaluating as concern cosmetic ingredients in the form of nanomaterials…'. Pursuant to the Cosmetics Directive, a sunscreen product is considered to be a cosmetic product for the purposes of the European regulatory framework, and as such, came within the scope of the Committee's Opinion.

In their final Opinion, released in December 2007, the SCCP conclude that 'there are large data gaps in risk assessment methodologies with respect to nanoparticles in cosmetic products.' In relation to the use of insoluble metal oxide nanoparticles in cosmetic products, such as TiO_2 and ZnO, the SCCP stated that while,

> *'Current investigations of nanoparticle penetration into the skin using static imaging technology are unable to detect small fractions of nanoparticles reaching the dermis, vascular bed of the dermis, and hence, the blood stream. However, if the dose of nanoparticles is very large, as is the case for TiO2 in sunscreens, even fractions as small as 10-4 may cause accumulation and subsequent inflammation in secondary target organs'* ([47]:34)
>
> ….
>
> *'should they become systemically available, translocation/transportation and eventual accumulation in secondary target organs may occur'* ([47]: 35)

Based on this uncertainty, the SCCP ([47]:6) went on to conclude that, 'it [is] necessary to review the safety of nanosized TiO_2 in the light of recent information and to consider the influence of physiologically abnormal skin and the possible impact of mechanical action on skin penetration.'

A. Factor I: Probability of Exposure to Risk

In its 2006 report the TGA concluded that light illumination of TiO_2 and ZnO ENPs may cause harmful effects to living cells. Nevertheless it was stated that the inclusion of these ingredients in sunscreens was considered unproblematic because, the 'weight of current evidence is that they remain on the surface of the skin and in the outer dead layer (stratum corneum) of the skin' (TGA 2006). The 'current evidence' referred to in the 2006 report included eight studies addressing dermal penetration of normal skin by TiO_2 and ZnO nanoparticles.

Six out of seven studies investigating dermal penetration found no evidence of TiO_2 and/or ZnO nanoparticles within living skin cells (TGA 2006). One study, by Tan et al. [49], found that microfine (ENP) TiO_2 were absorbed below the stratum corneum. However the TGA raised doubts about the validity of this study (TGA 2006).

The study by Tan et al. involved application of a TiO_2 sunscreen preparation twice daily for a period between 2–6weeks to the skin of thirteen patients with a mean age of 71years, who were to undergo surgical

removal of the skin due to lesions. Once excised the concentrations of TiO_2 in the skin was measured and compared against controls. The control specimens were obtained from the hip area of cadavers, an area of skin unlikely to have been exposed to sunscreen containing TiO_2. After adjusting for the confounding effect of a single outlier control result a statistically significant difference in the concentration of TiO_2 in the dermis of controls and patients was observed [49].

The TGA questioned the 'value' of the study conducted on patients with aged and diseased skin (TGA 2006). The TGA legitimately suggested that these factors could have impacted on the absorption properties of the tissue samples. However such an observation does not automatically detract from the overall value of the research. Sunscreens are not always used under ideal conditions. Consumers of these products are not limited to young people with non-diseased skin or physically uncompromised skin, resulting in unimpaired skin barrier conditions. Indeed people with cancerous or pre-cancerous lesions are more likely to be specifically advised by their doctors to use sunscreens when out in the sun. Understanding the potential dermal absorption pathways for nanoparticles when applied to abnormal skin would appear to be of particular importance, with the SCCP ([47]: 27) noting that despite 'there is not yet published information available on the potential penetration of nanomaterials through atopic or sunburnt human skin'.

The TGA report suggests that problems with study design invalidate the 1996 findings of Tan and co-workers. These problems included that there was no matching of the cadaver controls to patients in terms of age or lesions near the skin sample. Additionally, no analysis was conducted to determine if the microfine TiO_2 was localised within follicles in the lower epidermal and dermal layers (TGA 2006). These factors certainly cast doubt upon the extent to which the size of TiO_2 particles impacts on their absorption and distribution in skin. However they are not determinative of the accuracy of the study results. As the researchers noted, to disprove the ability of TiO_2 ENPs to penetrate into living cell layers further investigation is required [49].

Of the six other studies referred to by the TGA, three reported no evidence of penetration of TiO_2 and/or ZnO nanoparticles below the upper layer of the stratum corneum [9, 22, 45]. These studies accord with the findings of early research conducted by Lansdown and Taylor [27]. However, similar to the Lansdown and Taylor study, at least two of the studies reviewed did not take account of variables such as increased and repetitive skin movement on absorption of the nanoparticles [9, 27, 45] (the third report by Kertesz et al. [22] did not state methods of application). A study by Tinkle et al. [56] found that beryllium ENPs (0.5–1 μm) applied to skin can penetrate into the dermis following skin flexion. Rouse et al. [42] also demonstrated dermal absorption of 35nm amino acid functionalised fullerenes in a porcine skin model after 90min of flexion. The potential for flexion to influence absorption is particularly relevant to the use of ENPs in sunscreens. People will often apply sunscreens before spending long periods of time outdoors performing physical activity. Simple tasks such as gardening or swimming could potentially facilitate absorption of TiO_2 and ZnO nanoparticles.

Three remaining studies addressing dermal absorption were referred to by the TGA with each identifying TiO_2 ENPs at levels lower then the upper stratum corneum but localised within hair follicles [24, 25, 39]. Lademann et al. [25] took up the challenge of investigating the findings of Tan et al. [49]. The 1999 study demonstrated that TiO_2 ENPs (around 100nm in size according to Lademann et al. [26]) in sunscreen preparations applied to the skin of human volunteers did not penetrate through interfollicular stratum corneum to lower living cell layers. However the same study also detected TiO_2 in deeper areas of the stratum corneum within an individual follicle hair channel. Lademann et al. [24] obtained similar results with one in every ten hair follicles containing microfine TiO_2 and no TiO_2 observed in surrounding tissue. Using tape stripping and transmission electron microscopy Pflucker et al. [39] also found that TiO_2 particles (20–50nm) applied to porcine skin were isolated within hair follicles.

In its review of Lademann et al. [25] the TGA comments that, 'penetration of TiO_2 through [the fibrous sheath of a hair follicle] would probably be unlikely, since no TiO_2 was found in either the epidermal or dermal tissue surrounding the follicle (TGA 2006). Such a conclusion appears precipitate given that the TGA referred to only three studies that

demonstrated TiO_2 presence isolated within follicles. Furthermore in none of the studies was the permeability of the fibrous sheath to ENPs specifically investigated. Indeed, recent research indicates that ability of TiO_2 to penetrate hair follicles into viable perifollicular tissue cells may simply be related to the size of the nanoparticles. In research published in 2006 by Lademann et al., absorption of ENPs (below 100nm) from hair follicles into surrounding capillaries is touted as a potential avenue for drug delivery [26]. Another recent study [43] showed that quantum dot ENPs (14–35nm) (not used in sunscreens) can penetrate the stratum corneum to enter the epidermis and dermis.

Nanoparticle use in vaccines has also been investigated by Vogt et al. [59], who demonstrated using flow cytometry that when topically applied to skin ENPs less then 40nm were able to penetrate the epithelium lining follicles and be taken up by Langerhans cells. Interestingly, while manufacturers of sunscreens are currently under no obligation to provide information concerning the size of ENPs being used in sunscreens [33], Advanced Nanotechnology Limited [1] has reported that the ZnO nanoparticles that they mill for cosmetic products have a particle size distribution of 30nm, with a standard deviation of 4nm (Advanced Nanotechnology 2006). It is thus possible that consumers may have been exposed to TiO_2 ENPs that can enter antigen presenting cells and capillaries surrounding skin hair follicles.

It is thus at very least a reasonable interpretation that the evidence of penetration of TiO_2 and/or ZnO nanoparticles below the upper layer of the stratum corneum is inconclusive in relation to skin with real-life stressors such as flexion. Many studies indicating that TiO_2 and ZnO cannot descend to lower levels of the stratum corneum appear inconclusive from a safety point of view, as they were conducted in the absence of such real-life stressor. Flexion, for example, has been associated with increased ENP penetration of skin. Recent research also indicates that very small nanoparticles may be able to traverse epithelium lining hair follicles into living skin layers. Further studies need to be conducted using TiO_2 particles below 100nm and 40nm in size are required so as to ascertain their potential to cross into viable tissue. The scientific uncertainty about the risk of ENPs under such circumstances, provides in our submission a sufficient basis for the application of the precautionary principle (see for example *Pfizer Animal Health SA v Council of the European Union* (Court of First Instance) (T-13/39) [2002] ECR II-3305, para 142) particularly if the harm that might result is serious or irreversible. It is to this issue that we now turn.

B. Factor II: Gravity of the Harm

The cellular hazards of TiO_2 and ZnO in nanoparticulate form are generally considered well established [12]. Ultra violet irradiation of crystalline TiO_2 has been found to produce reactive oxidative species (ROS) damaging to cancer cell lines and human fibroblast cells [57]. Manufacturers coat TiO_2 with inert substances to decrease the potential for ROS generation due to irradiation [57]. In [17] Gurr et al. reported that ultrafine TiO_2 (10 and 20nm) induced oxidative stress in human bronchial epithelial cells in the absence of light irradiation. On the other hand, inhalation of ZnO may cause respiratory distress, neurological and visual disturbance [35]. In Australia, state governments have imposed restrictions on the means of disposal of ZnO and zinc by-products produced in sunscreen manufacture [14]. One paper claiming that in vitro toxicity studies on nanoparticulate forms of TiO_2 that show oxidative cell damage and genotoxicity should be interpreted ‘with caution’, ‘since such toxicities may be secondary to phagocytosis of mammalian cells exposed to high concentrations of insoluble particles’, was co-authored by two employees of the L’Oreal cosmetic company [34]. The same paper is uniquely unequivocal in its claim that nanoparticulate forms of $Zi0_2$ and ZnO used in sunscreens ‘pose no risk to human skin or human health’ ([34]: 272).

A draft report released in 2005 by the National Institute for Occupational Safety and Health (NIOSH) concluded that low concentrations of inhaled TiO_2 were an unlikely cause of cancer in humans. However high concentrations of inhaled TiO_2 have been found to induce neoplasias in rats by promoting pulmonary inflammation. It is currently unknown if the same mechanisms also exist in humans. On this basis, NIOSH stated it was unable determine if high concentrations of inhaled TiO_2 are carcinogenic to humans [36]. The potential toxicity of TiO_2 and ZnO to human cells was not disputed by the TGA. Given that premise, the TGA had it applied the precautionary principle more thoroughly, was surely required to

obtain unequivocal evidence that ENPs in sunscreens are not under the conditions of normal use able to penetrate into living skin layers. As discussed above, we doubt that standard was met.

C. Factor III: Inadequate Legal Direction

Although the TGA referred in its 2006 report to elements of the precautionary principle, the TGA has in fact proceeded as if the precautionary principle has no bearing on its decision to classify these therapeutic products as functionally equivalent to their bulk counterparts. The generally restricted endorsement of the precautionary principle in the Australian legal context seems to have contributed to this. In particular, it may have influenced the TGA's apparent reluctance to differentiate between traditional sunscreens and those incorporating ENPs, for the purposes of risk assessment. There are several possible reasons for this reluctance.

First, the TGA's legislative obligation to ensure the safety of therapeutic goods in relation to human health, provides few specific guidelines as to what that safety is to be measured against. This may be contrasted to subsequently drafted legislation concerning environmental protection, which more thoroughly embraces the precautionary principle.

Second, the applicability of the precautionary principle to nanotechnology in general has been a subject of debate due to the paucity of data about its risks to human health and safety [32, 41]. There is also the fear that no technology at its inception can satisfy the precautionary principle, so the principle becomes a formula for doing nothing [19]. No specific statutory guidelines are provided to the TGA about what to do to address the human health risks of the products containing ENPs.

Third, the TGA follows its existing regulatory framework is utilising what it refers to as a 'risk management approach' to monitoring the safety of therapeutic goods [53]. Yet the TGA's 2006 report on the use of nanoparticles in sunscreens relies heavily on a limited number of studies conducted in the absence of real-life stressors, including for example, skin flexion, and shows limited appreciation for the role that risk assessment plays as the basis for the application of the precautionary principle. While it is contentious whether the precautionary principle should apply equally to both risk management and risk assessment, the WTO Appellate Body has held in the *Beef Hormones* case that the concept of risk assessment should address,

> *not only risk ascertainable in a science laboratory operating under strictly controlled conditions, but also risk in human societies, as they actually exist, in other words, the actual potential for adverse effects on human health in the real world where people live and work and die.*[5]

Conclusion

One explanation for the TGA's apparent reticence to apply the precautionary principle in this context could be that the TGA procedures for identification and appraisal of evidence of risk are too narrow. Alternatively, the TGA might consider that adding the precautionary principle to its regulatory processes might be unduly burdensome in relation to the benefit likely to be achieved. In either case, the clarification of the scope and extent of the application of the precautionary principle will assist the TGA in addressing the human health risks associated with the use of nanoparticles in sunscreens.

If the TGA was required explicitly by its legal framework to apply the precautionary principle in risk assessments such as this and that was considered a feasible task, the question would still remain what could have been done in this instance to better ensure public safety in relation to use of TiO_2 and/or ZnO nanoparticles in sunscreens. How practical, for example, would be measures such as: (1) a total ban on the use of metal oxide ENPs in sunscreens, (2) a requirement under which ENPs must be deemed to be new ingredients for evaluation purposes, (3) the placement of a labelling system which notifies consumers of sunscreen products containing ENPs, or (4) the implementation of a specific post-market monitoring regime for sunscreens containing ENPs [4]?

If legislative reform did seek to provide specific guidance on the precautionary principle in the TGA's decision-making processes, it would need to address the breadth of risk assessment that needs to be conducted, its time frame and how competing considerations should be transparently and thoroughly balanced.

[5] *EC Measures concerning Meat and Meat Products (Hormones)*, WTO Doc WT/DS26/AB/R, WT/DS48/AB/R (16 January 1998), paras187, 194.

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