Evaluating Progress for the Implementation of European Union Nanotechnology Strategies for Safe Design and Responsible Innovation of Nanomaterials

by

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Abstract

This study examines the twin themes of risk governance and anticipatory governance to establish whether European Union (EU) risk governance instruments and others such as Responsible Research and Innovation(RRI) are delivering on their promises for the safe and responsible development of nanomaterials(NM). This is an empirical study that conducts semi-structured interviews with cross-sectoral experts working within nanotechnologies to examine these issues. The main findings identify critical flaws in the principal chemical safety regulations(REACH) due to the lack of specificity for NM safety testing, and the scientifically contested EU definition for NM. Both of which undermine legal authority for enforcing regulatory compliance. Secondly, critical scientific gaps are evident that prevent comprehensive nano-risk analysis of the Environmental, Health and Safety (EHS) implications of NM production. Thirdly, there are indications that the nano industry is seeking to avoid engaging with either product regulation (REACH) or the social-ethical appraisal of NM production. Finally, compounding these deficiencies, the EU does not provide a bespoke overarching EU risk governance framework to scrutinise either the EHS effects or the wider social implications of current and future nano-innovation pathways. In this study, I proposes a novel solution for such a framework centred on a 'Safety by Social Design' approach. Its purpose is to facilitate responsible innovation by the societal alignment of nano innovation within an adaptive and integrative risk governance framework. This will serve the purpose of progressing the EU towards a more anticipatory governance approach for nano innovation.

Key Words: Nanomaterials, Risk Governance, Anticipatory Governance, Responsible Research and Innovation, Safety by Social Design

Dedication

I dedicate this thesis to my family. To my wonderful wife Lyn who has been so supportive and uncomplaining of the long hours I have committed to this research. To my children Amanda and James, and their beloved baby sister Charlotte whose loving memory will always be with us .

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Finally, but by no means least, is my charming friend Indrani Mahapatra who has been a rock throughout this process, as I followed her footsteps in researching risk governance of nanomaterials. She has been a fount of information, a guide on many critical aspects for this research, and picked me up in the moments when I was down. No one has been a better friend and mentor to me during this time.

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Abbreviations

ACOP	Approved Codes of Practice
AoP	Adverse Outcome Pathways
ATS	Alternative Testing Strategies
Cefic	European Chemical Industry Council
CSR	Corporate Social Responsibility
DCA	Directed Content Analysis
D/G	Directorate-General
EA	Environmental Agency (UK)
EC	European Commission
ECHA	European Chemicals Agency
EFSA	European Food Standards Agency
EU	European Union
FSA	Food Standards Agency (UK)
HSE	Health and Safety Executive (UK)
HTS	High Throughput Screening
ICCA	International Council of Chemical Associations
IRGC	International Risk Governance Council
JRC	Joint Research Centre
MoA	Mode of Action
NGO	Non -governmental Organisation
NM	Nanomaterial
nm	Nanometre

nf	Nanoform
NP	Nanoparticle
NGO	Non-governmental Organisation
OECD	Organization for Economic Co-operation Development
QSAR	Quantitative Structured Activity Relationships
R&D	Research and Development
RTA	Real-time Technology Assessment
RI	Responsible Innovation
RRI	Responsible Research and Innovation
Ro1	Research Objective 1
Ro2	Research Objective 2
Ro3	Research Objective 3
SbD	Safety by Design
SbSD	Safety by Social Design
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SCHER	Scientific Committee of Health and Environmental Risks
SME	Small and Medium Size Enterprises
SOP	Standard Operating Protocols
STS	Science and Technology in Society
SVHC	Substance of Very High Concern

Chapter 1: Introduction

1.1 Introduction

In 2004, the European Commission (EC) published its strategy '*Towards a European Strategy for Nanotechnology*' [COM(2004)338]. I designate this policy document with its subsequent Action Plans collectively as the EC *NanoStrategy*, as it sets out how the EC wished the development of nanomaterials(NM) to proceed within the European Union(EU). The principal focus of this *NanoStrategy* is for the rapid economic development of NM, but it also clearly stated the aim for NM to be developed in a safe and responsible manner within an integrative process. The key question I consider in this study is whether this EC *NanoStrategy*, and subsequent iterations, are delivering on those promises. If not, then what approaches need to be adopted to fill any policy/scientific/regulatory/deliberative lacuna to achieve that policy goal. To assist me in this process, I examine the twin themes of risk governance and anticipatory governance. They are utilized to determine in what way the EU risk governance instruments, and its Responsible Research and Innovation(RRI) policy, have contributed towards achieving this policy goal. But before I set out how I intend to undertake this study, I provide background information as to NM biophysicochemical properties, their commercial applications, their growing politico-economic importance, and current concerns regarding potential human and environmental risks.

1.2 Background

NM are defined by the European Union as particles between 1 and 100 nanometres(nm) in size [COM (2011)275]. They can exhibit unique biophysicochemical phenomena which enable the exploitation of novel scientific and technological applications into new commercial products. There is considerable national and international support for their

development and their application within commercial products [COM (2004) 338]; EC NanoCode 2008; UK Nanotechnology Strategy 2010; HM Treasury 2014; USA National Nanotechnology Initiative 2014, 2016 & 2019;German Nanotechnology Strategy 2020, EU Horizon 2020 https://ec.europa.eu/programmes/horizon2020/en/h2020]. Some of these novel applications will bring incremental technology benefits, but others are predicted to be nothing short of being scientifically revolutionary (Gordon 2003), which may be substantial engines for economic growth (Maynard 2014, Nano-safety in Europe 2015-2025). NM are, therefore, regarded as having the potential to contribute to driving the technological and economic progress of nation states. Inshakova and Inshakova (2018) published conservative estimates that the global nanomaterials market, was valued at about USD 4.1 billion in 2015, and is expected to be worth USD 11.3 billion by 2020. Whilst the European NM market generated revenue of more than USD 2.5 billion in 2015, with projections to reach USD 9.1 billion by 2022, supported by a compound annual growth rate of 20.0% during the period 2016-2022.

The predicted influence of nanotechnologies on science and technological advancement can be summarised as two-fold. First is their capability to enhance the current range of uses of technoscientific applications, including novel physical, chemical and biological functionalities (Parandian and Rip 2012). Secondly, it is envisaged that NM technologies will converge with other emerging sciences to create brand new scientific platforms and products, such as nanobiotechnology, as foreseen in discussions on the 'fourth industrial revolution' (Schwab 2015; World Economic Forum 2016). The intention of this study is to consider the prospects for a balance between maximising the potential socio-economic benefits from NM, whilst mitigating or eliminating risks by the societal alignment of the nano innovation process.

Figure 1.1 below illustrates the breadth of scientific, technical and socio-economic applications of current nanotechnology platforms. These range from catalysts to composites, coating materials to medical devices, and aerospace to targeted drug delivery. An important feature is that NM offer the prospect of developing 'molecular machines' with future potential to undertake programmed tasks (Stoddart et al, Nobel Prize for Chemistry 2016), and enable data storage at vastly smaller scales than are possible currently (Sessoli 2017).This prospective plurality of future technoscientific applications is why the Royal Society and Royal Academy of Engineering jointly proposed the term 'nanotechnologies' rather than 'nanotechnology' as the accepted overarching term (Royal Society and Royal Academy of Engineering 2004).

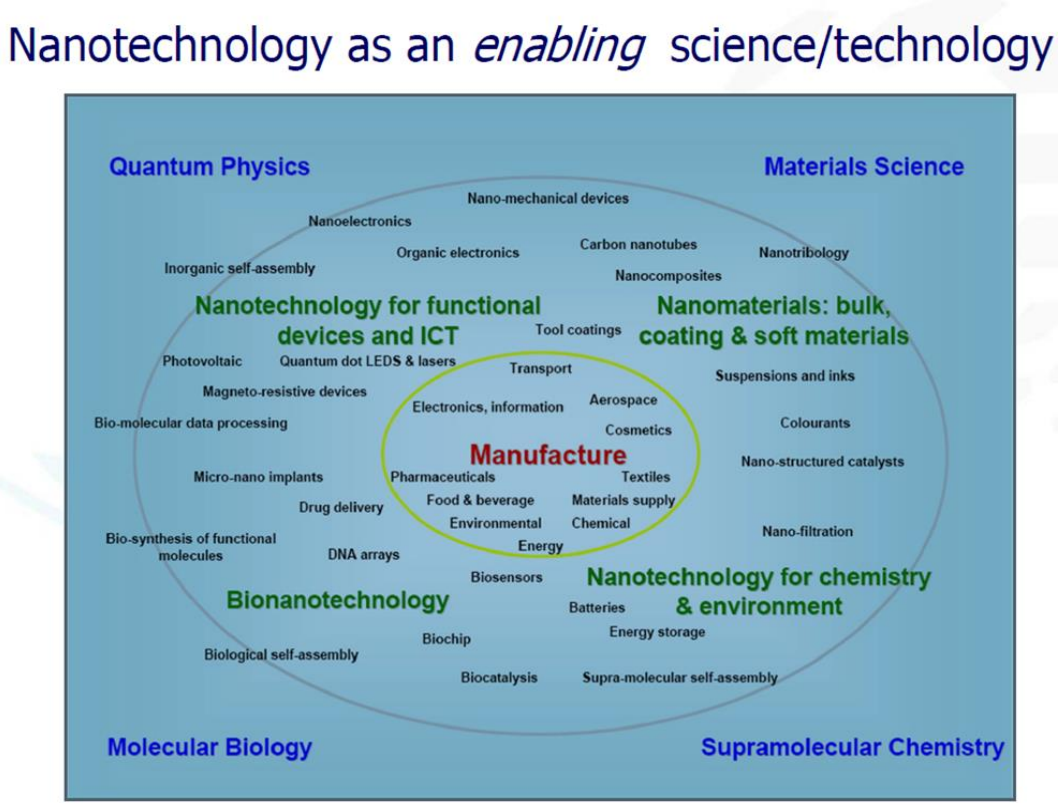


Figure 1.1: Overview of nanotechnologies applications. Source: Hankin (2012)

What Figure 1.1 indicates is the breadth of the potential for NM to offer a new era of technoscientific discovery and product applications which, in some cases, may have a profound impact on our world. In the next section I briefly discuss the biophysicochemical properties that differentiate NM from other chemical substances, and why this makes them so important for our futures.

1.3 Nanomaterials : Why are they different?

NM can exhibit unique chemical, physical and biological properties not demonstrated by their own macro versions. A good example is the chemical element gold, which at a macro level is relatively inert, but at 30 nanometres scale (30nm), can be highly chemically reactive and an effective catalyst. Separately, it also offers the potential for novel pharmaceutical applications such as acting as a drug carrier (Mahapatra 2016). The scientific explanation for these unique biophysicochemical properties has now been established. Within the 1-100nm range, unpredictable quantum effects can be endowed on the nanoparticles (see Figure 1.2) which is briefly explained here.

As the particle size reduces on the nanoscale, it exhibits a higher surface to mass ratio with more atoms at surface. The number of surface atoms increase as the nanoparticle size falls below the 100-nm level and generates greater particle reactivity (Oberdoster et al 2005). Lynch (2018) explains this concisely as the result of the consequent increase in nanoparticle surface curvature, which enhances its potential for external reactivity, as the fundamental foundation for its quantum properties. The uniqueness of this feature provides for a disproportionate number of atoms at the surface which are available for biophysicochemical interactions. This leads to dominance of the surface area over the biophysicochemical properties exhibited in its traditional macro version. Maynard (2007) believes that these

startling biophysicochemical characteristics of NM takes us into a *post-chemistry* era. This is when the established scientific rules, developed and adopted over centuries, can no longer be applied with any degree of certainty. This includes utilizing our historical understanding of the risks posed by individual chemical substances.

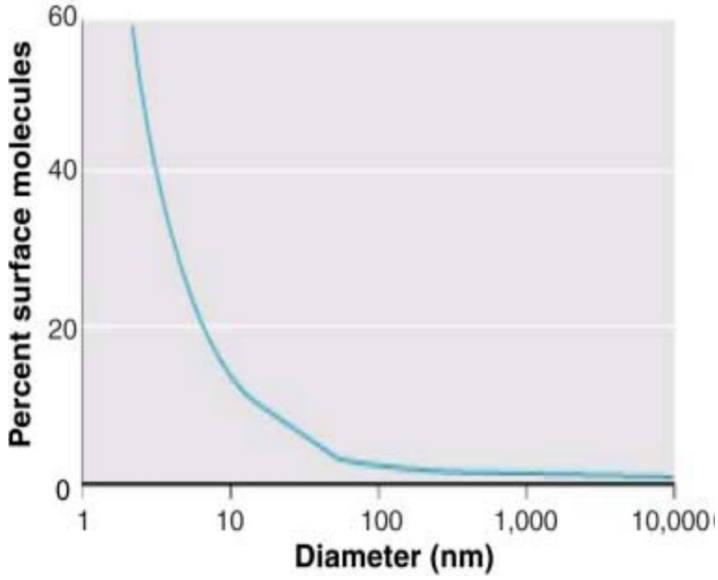


Figure 1.2: Novel physico-chemical functionality from quantum effects. Source: Oberdoster et al. (2005)

These nano quantum properties include enhanced chemical, optical, magnetic, and electrical conductivity, which cannot be readily predicted from the known physico-chemical properties of its macro-version. Not only is there the possibility of new products that are lighter, stronger, with enhanced optical, magnetic and conductivity properties (e.g. graphene), but some have the potential to be engineered to have important therapeutic capabilities. An example is the targeted pharmaceutical carriers that can be transported via the bloodstream to major organs, and to cross critical biological membranes such as the brain and placenta (Mahapatra 2016). Clearly, such penetrative capability, into the most vital organs, must be viewed with a certain level of caution and concern until any unaccounted risks have been fully examined and documented. What is clear, however, is the need for effective policy regulation of this rapidly developing area of physical science.

Consequently, in the next section I discuss the current debates, principally within the European Union (EU), on potential risks to human and environmental health and safety (EHS) posed by this new generation of NM. I will then briefly consider the EU risk governance considerations and implications for the control of those risks.

1.4 Potential Risks to Human and Environmental Health

At the same time as the EC was formulating its own *NanoStrategy* in 2004, the Royal Society and Royal Academy of Engineering jointly expressed their unease regarding the safe use of NM in commercial applications. This was in terms of the acknowledged scientific uncertainties surrounding the long-term exposure to NM, their potential adverse EHS effects, and the questionable level of public acceptance for this novel technology. Today, that unease is still evident within global scientific and policy communities. An example is found in the recently constituted European Union Observatory for Nanomaterials (EUON) report published in 2018 (ECHA /PR 18/13). It concluded that there are still substantial gaps in our understanding of the hazards and risks from nano-sized particles. More specifically, these gaps relate to the physico-chemical characterization of NM, our lack of understanding of their environmental fate and behaviours (e.g. bio-accumulative effects), their long-term EHS toxicity potential, and their risk characterizations for specific endpoints of human and environmental health e.g. carcinogenic, mutagenic, reprotoxic (Nano-safety in Europe 2015-2025). On this basis, Fadeel *et al* (2018) advises that there is still much experimental work to be done for the development of new scientific methods, tools and protocols, if these hazard and risk uncertainties are to be fully resolved. Fiorina (2010) describes this situation as reflective of the complexity now to be found in 21st century science and technology driven

problem-solving; rather than was previously found in the high-volume commodity chemicals from the mid-20th century onwards.

With traditional scientific problem-solving strategies seemingly failing to provide answers to these pressing questions, Funtowicz and Ravetz (1993) have argued for a *post-normal* scientific approach. This novel conception for the management of complex science-related problems, recommends that established policy decision-making processes are supplemented by extensive peer and lay community reviews to address risk uncertainties. By this means, *post-normal* science provides a new pathway to move beyond the triple helix of government, industry and researchers in innovation (Wiek et al 2016). The purpose is to progress towards a greater democratization of science which can assist in providing new perspectives and insights for the risk problem solving.

One stand out example of the need for post-normal scientific approaches is the major EU policy failure to engage with civil society in respect of the debacle for the introduction of genetically modified foods (GMO) in the 1990s. That public outcry and strength of opposition against GMO crops resulted in an EU moratorium in year 2000 that continues to this day. For the EU biotechnology industry, the consequences can only be described as catastrophic. This outcome from a highly orchestrated protest across the EU nations, still resonates within policy, legal, regulatory and industry circles (Von Schomberg 2013). What has emerged for EU policy makers, following this harsh experience, is the recognition that public opinion is a pivotal policy factor in the process of acceptance and diffusion of new technologies into main- stream consumer products (Bauer and Bonafadell 2002). It is better appreciated by EU policymakers that public opinion now needs to be actively engaged if new product technologies are to gain widespread acceptance. Bauer and Gaskell (2002) make the point that, following this humbling experience, EU policy makers realised that simply achieving

regulatory compliance is no longer enough. It now has to satisfy the court of public opinion on ethical as well as safety issues, and the publics need to participate actively within the governance processes.

How these experiences are reflected in the development of EU strategies for the risk governance of nanotechnologies, and how that manifests in the decisions to control risks from NM, is discussed next.

1.5 EU Strategy for the Risk Governance[1] of Nanomaterials

The European Commission published its governance strategy for nanotechnologies in the document, "Towards a European Strategy for Nanotechnology" [COM(2004)338]. This governance strategy sets out the EC policy, regulatory and economic framework for supporting and investing in the development of nanotechnologies platforms, product applications, and consumer products within the EU. It opened the discourse for the governance of NM at the international institutional level across its Member States. Further supporting Action Plans were published [COM(2005)283], European Parliament 28th September(2006),[COM(2007)505],[COM(2009)607Final] with a voluntary industry NanoCode published in 2008 [EC NanoCode 2008].

These documents are reflective of the GMO lessons, by emphasising that a narrow policy framing of nano risk solely predicated on EHS is no longer the way forward. Instead, what should become accepted practice is not simply the traditional scientific risk assessments for EHS, but also the identification and management of the ethical, legal, and socio-economic implications of nano innovation. This process to be instigated by timely and meaningful

[1] Following Klinke and Renn (2012, p.277), I define risk governance as 'the institutional structures and policy process that guide and restrain the collective activities of a group, or society to regulate, reduce or control risk problem'.

engagement with a broad range of relevant stakeholders within the research and development processes (R&D). This approach is reflective of Funtowicz and Ravetz (1993), and fitted well with contemporary thinking for a matrix framing of 'Risk Governance' by Renn (2005 p.6) who describes it as follows:

'Risk Governance sits on the confluence of all analyses and actions relative to the development of a given technology including its framing, with its technological context, assessment of the benefits and risks, evaluating specific socio-politico-economic interests, and identifying risk management and risk communication options'.

This matrix thinking is reflected in the EC *NanoStrategy* document as it sets out how it is to achieve its principal risk governance aim that '*nanomaterials are developed in a safe and responsible manner*' [COM(2004)338p.3]. This aim is to be achieved through the fulfilment of three key supporting risk governance objectives, which are summarised as follows:

EC Objective 1-Maximum use would be made of existing regulation though adjustments may be necessary.

EC Objective 2 - Existing parameters for EHS chemical safety testing may not be appropriate for the unique properties of nanoparticles, requiring new methods and tools for risk assessment, and refinement of nano scale metrology and standardisation activities.

EC Objective 3- The Risk Management paradigm to be expanded to incorporate socio-ethical considerations into the R&D process with the creation of a culture of responsibility which is participatory and inclusive.

I will discuss briefly the intentions of the three risk governance objectives and what they were expected to achieve. For the first objective, the application (retro-fitting) of existing chemical safety legislation was intended to avoid the need for the approval of nano-specific legislation. It was recognised that nano-specific regulation was likely to be a very public,

highly complex and contested political process (e.g. remembering that the GMO crops debacle was recent). Moreover, in the early 2000s, new major EU chemical safety legislation was in draft and very close to completion. These regulations are titled the *Registration, Evaluation, Authorisation of Chemical Substances Regulations* [(EC) No 1907/2006]. These regulations will be known from now on by their widely accepted acronym 'REACH'. But as Bowman (2017) points out, when REACH was finally enacted in 2008, it was entirely silent on any risk issues from NM. It treated them no differently to their macro versions.

By this critical omission, the regulations lacked any nano specificity in the published risk assessment protocols for potential hazards/risks emanating from the unique NM properties. This omission has haunted the EC ever since, and is an issue raised time and again within the literatures and in respondents interviews. The first concerns were raised by the European Parliament in 2006 (2006/200/ 187) but set aside by the EC at that time. In its first review of its *NanoStrategy* in 2008, the Commission restated its support for REACH to control, in principle, the potential health and safety and environmental risks in relation to NM (EC [SEC (2008)2036]/[COM(2008)0366]. This decision to 'retrofit' REACH to NM was subsequently endorsed by the Organization for Economic Co-operation Development (2013), as well as international chemical industry bodies and other authoritative voices (European Chemical Industry Association 2011, EC COM (2012)572, Nanotechnology Industry Association 2013). Yet as Bowman (2017) and Hanani and Dayanne (2015) point out, in their detailed reviews on EU nano risk governance, these endorsements seem perverse. This is because the capture of NM by an unadapted REACH does not give the publics the necessary assurances for the safe use of NM. Neither did it represent a joined-up approach with other relevant EU initiatives currently being developed for nano regulatory control, such as the foresight driven 'Regulatory Preparedness' policy '(Katalgariniakis 2018; NanoReG2

http://www.nanoreg.eu/; Gottardo *et al* 2017) and the new 'Sustainable Innovation Approach' (Noorlander2019; Katalagariniakis 2018; NanoReG2 http://www.nanoreg.eu/). Another significant outcome is the widespread criticism, in the literatures and from the interviews, of an over-dependency on the EU Precautionary Principle to address unresolved hazards and risks from NM. As will be seen, the Precautionary Principle has an important part to play in this study.

The second risk governance objective recognises that to underpin the EU regulatory control of NM, new scientific knowledge, methods and tools for undertaking risk analysis for NM will be crucial. Such tools and protocols are essential for regulatory sciences to be able to provide accurate risk assessments and public assurances on the safe use of NM. These deficits received formal recognition by the Commission in the *EC Second Review of the Regulatory aspects of Nanotechnology* in 2012 [COM (2012) 572 Final]. In this review, the EC accepted that the lack of specific tests for some nano risk assessments was now recognised as a significant problem. The EC promised and delivered significant research funding to develop new testing protocols which would be formally adopted as amendments to the existing REACH Annexes (with the Projects listing on the NanoSafetyCluster website https://www.nano-safetycluster.eu/).

However, current academic debates emphasise that the traditional single probalistic toxicological tests for regulatory purposes, using vertebrates or lower level organisms, can be flawed by false positives/negatives (Stirling 2016a, Jahnel 2015b). In its place, are emerging Systems Biology discoveries as a move towards scientific and regulatory preferences for novel toxicological paradigms. These offer the prospect for utilizing multi-cellular testing protocols, in combination with other multiple primary and secondary data sources, with animal testing as a last resort (ECHA 2017; Stone *et al* 2017; Hjorth *et al* 2016;

Jahnel 2015a, 2015b; Oomen 2013; Stone *et al* 2013; Nel *et al* 2013). These scientific initiatives have support at the highest policy, regulatory and scientific levels and are very relevant to the discussions later in this study. They offer a future which could progress regulatory sciences from single probabilistic testing to a multi- data sources 'weight of evidence' approach for nano risk characterization (Linkov *et al* 2018; Stone *et al* 2018; Gottardo *et al* 2017; Jahnel 2015b; Hristozov *et al* 2014; SCHENIR 2012). These techniques are in receipt of substantial EC research funding and are being extensively developed for future predictive toxicological profiling for tiered hazard and risk ranking of NM (NanoSafetyClusterhttps://www.nano-safetycluster.eu/). The major drawback is their lack of proof of concept at this time.

The current state of EU regulatory approaches to NM could thus be described as one where techno-scientific complexity and risk uncertainties for NM are currently unresolved by nanosciences knowledge and regulatory actions. Consequently, Funtowicz and Ravetz (1993) would recognise the remedy as *post-normal* scientific approaches to urgently address the shortcomings of traditional scientific methodologies. By this means, a new pathway may be constructed, beyond the limitations of the triple helix establishment previously mentioned, with progression to a democratization of innovation for a more anticipatory role in risk prevention.

This brings us to the third EC risk governance objective which is reflective of the Funtowicz and Ravetz viewpoint. It does so through the EC's tacit recognition that risk assessments alone are no longer sufficient to make sound risk management decisions, and other legitimate factors need to be taken into consideration [EC (2003) para 32 preamble]. In EC Objective 3, the critical consideration is that socio-ethical considerations must now be taken into account when making risk management decisions. There will be detailed discussions in

later Chapters as to the role that RRI might play in supporting a deliberative mechanism for delivering on this objective.

In conclusion, the construction of these objectives within the EC *NanoStrategy* offers a matrix approach, as suggested by Renn (2005) above, for achieving its key aim for the safe and responsible development of NM. It sets EU nano risk governance outside of the traditional state-centric regulatory boundaries and offers the prospect of deliberatively driven multi-level governance systems to promote a culture of responsible innovation. This was a major initiative for promoting a novel anticipatory approach, for the responsible innovation of an emerging technology, to be generated by stakeholder collaborations. However, the strategy lacked a critical policy component which is a detailed mechanism for how this deliberative[2] activity was to be undertaken, and how the outcomes could be incorporated within the risk governance decision-making.

In addition, since the *NanoStrategy* publication in 2004, a wide array of academic and policy proposals for embedding socio-ethical concerns within the nano innovation space have been published. These include well publicized concepts such as 'Responsible Innovation'(RI) (Owen *et al* 2013; Stilgoe *et al* 2013) and its EU policy equivalent 'Responsible Research and Innovation' (RRI) (Rome Declaration 2014; Horizon 2020; Von Schomberg 2013). The formal adoption of the RRI concept as a policy instrument for EU Member States is given authority by the Rome Declaration (2014). There are a number of extant definitions for RRI in the literatures, with the Declaration defining RRI '*as an on-going process of aligning research and innovation to the values, needs and expectations of society'* (Rome Declaration

[2] In this study, 'Deliberative' is defined as the social process wherein deliberators are amenable to changing their judgements, preferences, and views during the course of their interaction, which involve persuasion not coercion, manipulation or deceit (Dryzek 2002p.15)

2014.p.1). This is the primary definition of RRI for use in this study. It requires all stakeholders, including civil society, to take a shared responsibility for co-production of the outcomes of the R&D process. Nonetheless, whilst these debates provide more shape and form for the development of a culture of responsible innovation by industry, crucially, they still do not provide a mechanism by which it can be operationalized.

The current representations for RRI have it acting in an anticipatory manner to determine the positive and negative impacts of emerging technologies such as nanotechnologies. This is achieved by reflecting on the socio-ethical dimensions of nanotechnological development, with the participation of diverse actors contributing to setting the agendas for nano innovation processes (Ribeiro et al 2018; Owen 2014). Yet, many nano businesses and entrepreneurs are still largely unaware as to what specifically the concept of RRI entails (van de Poel *et al* 2017;Auer and Jarmai 2017). This continues to be the significant deficiency for the development of an industry led responsible innovation culture, which has not been given the attention within research funded projects that it deserves. In particular, the important issue of linking industry best practice to contemporary thinking on RRI, in respect of the potential for mutually beneficial outcomes from precautionary and anticipatory processes. It is an important element of this study to consider a deliberatively based mechanism, by which RRI can facilitate the bridging of socio-ethical concerns into the nano innovation process. This to be achieved by a timely and meaningful dialogue with civil and other relevant actors and, by this approach, to enable EC Objective 3 to be fulfilled.

1.6 Research Context

This study directly addresses the pressing theoretical and policy challenges framed by the EC risk governance strategy for the safe and responsible development of NM. It does so by

focussing upon the three-risk governance objectives and considering how far they offer an opportunity to break from the current, ineffectual traditional EHS risk governance framework. In the next sections, I will provide a brief overview of my research purpose, proposed methodology, supporting research objectives, and how they can make a contribution to these ongoing debates.

1.7 Research Purpose

The intention for my research is to obtain a better understanding of the continuing policy, scientific and regulatory complexities, uncertainties and ambiguities surrounding nano innovation within the EU. In particular, what has been the EU progress in developing good risk governance for NM, so as to embed an R&D culture for safe and responsible nano innovation? By gathering interview data from a variety of expert nano sectoral respondents, I hoped to build a measure for that progress. Then, from the identified policy, scientific and regulatory gaps, to also build a novel framework for delivering on the key *NanoStrategy* aim and objectives. Next, I will illustrate how these strategy objectives have been transformed into the research objectives which will underpin this study.

1.8 Research Objectives

For the purposes of this study, the Research Objectives set out below are explicit statements on what I need to know to be able to generate new insights for the issues previously discussed (Bryman 2012; Saunders et al 2012; Jankowicz 2005). By utilizing these Research Objectives, I shall then be able to operationalize my enquiries into the effectiveness of the individual EC *NanoStrategy* risk governance objectives (Saunders *et al* 2012; Jankowicz 2005).

Research Objective 1

To critically review whether the current EU chemical safety regulations (REACH) provide acceptable public environmental health assurances for nano-safety

Research Objective 2

To determine to what extent can existing and emerging scientific methods, tools and models provide for future competent risk analysis of nanomaterials

Research Objective 3

To consider the development of a deliberative model to facilitate socio-ethical considerations for safe design into nano risk management

These research objectives will be the basis for the three testable propositions that will be applied to the primary data gathered from respondents (see table 4.2, Chapter 4). In brief, they will test whether (a) the current EU regulation (REACH) can provide necessary assurances for public environmental health safety (b) that the new and developing scientific methods and tools for risk analysis will provide for future public confidence in industry and regulatory safety decision-making, (c) finally, consider the role of RRI for embedding socio-ethical values for safe design into nano innovation.

1.9 Organisation and the Structure of this study

The structure of the thesis is designed to research the key themes of Risk Governance and Anticipatory Governance, both of whose role in the contemporary management of risks from NM will emerge from the debates in forthcoming Chapters.

The Introductory Chapter (Chapter 1) has provided a broad outline as to the global socio-economic importance of nanotechnologies, together with a brief review of the rapid technoscientific development of NM and their applications. It discusses the continuing policy, scientific, regulatory and practice deficits/gaps for the implementation of an effective

EC strategy for the risk governance for NM. The research objectives are developed for the purpose of operationalizing my enquiries into the effectiveness of the EC *NanoStrategy* for delivering on its goal for the safe and responsible development of NM .

In Chapter 2, I review the EU risk policy for NM, with particular attention to the role of the precautionary principle for addressing hazards and risks. I critically examine its regulatory responses, and the continuing implications of identified deficiencies for nano-safety decisions. I review and evaluate the prospects for novel scientific methods, tools, and toxicological paradigms for nano risk assessment rapidly evolving from experimental systems biology. I consider their future significance for regulatory sciences and to the EU risk governance of NM .

In Chapter 3, I will identify the key concepts which will be applied in the process of analysis for this study such PP, RRI and SbD. The concepts are constructs that assist in the analysis of data, processes, variables and their relationships. The concepts will enable my reasoning within frameworks to facilitate logical outcomes. Though not lineal in application, they do provide for a progression in the data analysis to infer implications and conclusions that are supportive of the other concepts being applied. Not only do they allow me to infer the implications from the study findings as to theory and practice (Gallagher 2010), but they have challenged me to develop a new refined conceptual framework for EU risk governance from the gathered empirical data. (Grix 2010).

In Chapter 4, I set out the justification for the methodology for the selected exploratory research theory and design process. It will explain the reasons why semi-structured interviews of expert actors are considered the most appropriate format for the collection of data for this study. Along with the structure and selection of the sampling frame and the criteria used to select the interviewees. The data management and analysis in terms of

coding and query using *Nvivo* software is explained as well as any identified confounding factors.

In Chapter 5, a key purpose is to analyse the interviewee responses regarding the efficacy of the current EU risk governance instruments such as REACH. In addition, to identify and evaluate the novel scientific methods, tools and practices which are emerging for application within regulatory sciences. Then to consider the benefits that might accrue by replacing the current traditional scientific tools and paradigms for toxicological animal testing with assays of multi-cellular testing contributing to generate a 'weight of evidence' approach. Finally, to consider a framework for delivering their promise for future competent risk analysis for NM

In Chapter 6, the discussion will centre of how a mechanism can be developed for the embedding of socio-ethical concerns within the nano innovation process. The analysis will consider how the Precautionary Principle (PP), Responsible Research and Innovation (RRI) and Safety by Design (SbD) concepts can be applied in tandem to generate the novel concept of Safety by Social Design (SbSD). An adaptive and integrative risk governance framework is devised as the setting for SbSD, in which risk analytical data and socio-ethical concerns can be processed together. The decision outcomes of this process can then influence regulatory compliance, identify the social utility of the nanoproducts , and their commercial viability and marketability.

In Chapter 7, (*Conclusions and recommendations)* will provide an overview of the discussions of the study, the key learning points from the research, and the explanation and application of the proposed Adaptive and Integrative Risk Governance framework for NM.

Chapter 2: Current EU public policy on nanotechnologies, existing scientific and future debates

2.1 Introduction

Following on from Chapter 1, this Chapter presents a contextual examination of European Union (EU) public policies for nanotechnologies. As set out in its 2004 Strategy, the policy intention is the translation of NM into commercially viable processes and products [COM (2004) 338]. This intention underscores the EU's promotion of a competitive market for nanotechnologies, particularly for small and medium size enterprises (SMEs), across disparate manufacturing areas [COM (2004) 338]. As discussed in Chapter 1, the importance of NM derives from their unique biophysicochemical functionalities that, if successfully scaled up and applied to manufacturing and industrial processes, could potentially deliver significant socio-economic benefits (German Action on Nanotechnology Strategy 2016 & 2020; USA National Nanotechnology Initiative 2014, 2016; UK Nanotechnology 2010).

In this context, the EC 2004 *NanoStrategy* [COM(2004)338] can be described as a mechanism to catalyse discussion on the politico-economic significance of nanotechnologies amongst its member states. This is in the classic EC manner to begin to build a policy consensus and a shared sense of purpose as to how EU policy might proceed. There is also a clear recognition in the *NanoStrategy* that while it is a policy drive for nanoproducts in the marketplace that NM need to be developed safely and responsibly [COM(2004)338]. Consequently, this document recognises that industry stakeholders, traditionally engaged within the innovation process, need to consider projected societal impacts and product social utility as much as scientific and economic benefits. The *NanoStrategy*, therefore,

advocates positive engagement with a wide range of other industry, regulatory and civil society actors in a collaborative and deliberative manner. The purpose of which is to socially align the innovation process by identifying societal-ethical aspirations beyond the consequentialism of market-driven innovation [COM(2004)338], EC(NanoCode)2008; Horizon2020). The Commission's aim here seems to have been to build as wide a consensus among stakeholders as possible, to foresight unexpected problems and anticipate future developments, as a means of strategic policy planning. This was considered especially important due the disruptive nature of nanotechnologies, and their continuing scientific ambiguities, technological complexities, and risk uncertainties [COM (2004) 338].

To examine the issues arising from the Strategy, I discuss where policy responsibilities might lie for its delivery and for implementing the supporting risk governance objectives foreseen in this document. The first part of this Chapter leads with discussions on the current understandings for nano risks, how EU risk policy is currently applied through regulatory controls, and recent substantive progress made in the applied sciences. The second part considers how these policies might change and the proposed scientific changes that may accompany and support them, including anticipatory approaches. This includes discussion regarding the potential role of 'safe design' and 'responsible innovation' within new regulatory and risk governance framings for this policy area. The Chapter also addresses the pragmatic issue of where responsibilities lie for the delivery of the 2004 strategy. It does so by considering the role of key sectoral actors, and where changes might usefully be made in current arrangements to achieve the delivery of the strategy goal and objectives. Taken together, these lines of enquiry help inform the development of three research propositions that provide the framework for qualitative empirical data analysis in subsequent Chapters

of the thesis. In the next section I start the discussion with a review of the current understanding of the risks currently posed by NM .

2.2 What are the risks from nanomaterials?

Nanoparticle (NP) size is fundamentally important to its properties and hence its technological applications. It is within the metrical range of 1-100 nanometres (nm) that most unique physical, chemical and biological characteristics occur that enable novel nanoproduct applications. A cause of concern for some experimental nanoscientists is that this size range coincides with fundamental biochemical processes at human and ecological scales (Lynch 2014). By this I mean that these are the scales at which cellular metabolic processing and pathways naturally function. NPs have been proven to breach cellular protective mechanisms and cross critical biological membranes (e.g. placenta, brain) whether beneficial or not. Once inside cells, NPs may engage in cellular in- vivo circulation, with the potential to cause negative and harmful interference with essential cellular metabolic activity and pathways (Kobayashi *et al.* 2014, Lynch 2014, Nel 2014).

There is also evidence that NPs with high-energy surface areas (Figure 1.2, Chapter 1) are more likely to bind to other substances within the biological media in which they are situated. Within these bio-media, the NPs may absorb proteins/ lipids to form coatings known as bio-nano 'coronas' (Mahmoud *et al.* 2016; Nel 2014; Lynch 2014; Nel *et al.* 2009). This bio-nano interface may confer a novel biological identity on the NP that can cause it to interact in a very different way to that predicted from its known chemistry (Lynch 2018). The corona may significantly disguise and transform the NP from its original chemical-biological form, and unexpectedly alter its predicted life cycle (Lynch *et al.* 2014). This could mean that with its outer layer protein/lipid corona, the NP is disguised as a new bio-nano entity. By this

means, it could enable a 'Trojan Horse' effect, by mis-directing cell wall sensors into accepting it as suitable for importation into the cellular matrix. Thus, by evading the natural cellular gate-keeping defences, it gains the prospect of causing adverse interference of critical metabolic processes. (Lynch 2014, Lynch *et al.* 2014; Nel 2014; Lowry *et al.* 2012). Once internalized by the cell, the corona may then dissolve and deliver a toxic NP to interfere with normal cellular activity (Valsami-Jones and Lynch 2015).

Experimentation for investigating these new biochemical modes of action (MoA) has developed new scientific whole system concepts such as Adverse Outcome Pathways (AoP). They identify the interaction of toxicants, within a biochemical system, and any adverse outcome relevant to risk assessment at the biological organisational level (OECD 2012c). This concept has been proven to be equally applicable to describing toxicological processes underpinning human-relevant adverse effects (Vinken *et al.* 2014). These emerging concepts can act as a bridge to identify new ways of describing toxicological hazards based on mechanistic cellular profiling. These processes utilize hundreds of NP inoculated cell lines rather than an association with animal testing for pathological endpoints. This ground-breaking science could potentially provide the foundation for implementing mechanistic reasoning into nano regulatory safety decision-making which is discussed later in this thesis (NanoReG2 http://www.nanoreg.eu/; Whelan 2014; see Chapter 5:).

The above discussion shows that there has been substantive progress since 2004 in scientific understanding of the potential modes of action of NPs once they enter a cell. Yet, there continues to be lack of evidence to support the view that all NPs are intrinsically hazardous (German Action Plan for Nanotechnology 2020; NanoReG2 http://www.nanoreg.eu/; COM (2012) 572 Final). In fact, Donaldson and Poland (2013) successfully challenge the myth that all NPs exhibit nano-specific toxicity *per se*. Neither has a nano specific human illness,

disease, or pathology been identified (Nel *et al.*2015; Nel 2014). Though, of course, this does not mean that individual NPs cannot be toxic at appropriate dose levels and exposures, as would be the case with other non- nano chemical substances.

In conclusion, there continues to be outstanding a definitive answer as to the potential risks posed by NM, now and in the future. The reasons are the very significant and unresolved gaps in our scientific understanding of the chemistry of NPs, their modes of cellular action (MoA) and their potential for adverse EHS effects (Fadeel *et al.* 2018). These include particle physico-chemical characterization (e.g. their size, shape, morphology); their intracellular adverse MoA; their environment fate, behaviours and exposures (e.g. bioaccumulation); their long term EHS toxicological impacts; and the summation of these factors into realistic nano risk characterization profiles. Fadeel *et al* (2018) make another important point that the resolution of these problems will not occur in the short term, and much experimental nanoscience still needs to be done. Having briefly discussed the most recent advances in nanosciences , in the next section I consider how EU risk governance policy has responded to risk uncertainties based on our current understandings of NM.

2.3 EU Risk Governance policy for nanomaterials

2.3.1 The Current EC Policy Position

Beck (1992) recognises that science and innovation co-produce risks to society. The relatively straightforward risks can be dealt with technocratically but, with the globalisation of discovery and product manufacturing, more complex anthropogenic risks requiring new approaches are evident (Bennet 2016). Risk governance seeks to translate the core principles of governance into the context of risk related policy making. In simple terms, risk governance is a systematic approach to risk decision-making (Tinkle 2014).

The International Risk Governance Council (2008) believes risk always accompanies change, and in Jasanoff' s (2016) view risk assessment begins with the tacit presumption in favour of that change. This can be translated as a strategic willingness and capacity to accept risks, because they are crucial for achieving the development of new technologies, innovative products and economic advancement. The fundamental challenge for effective risk governance lies here, which is to enable societies to benefit from change while minimising the negative consequences. As Bowman and Hodges (2008.p484) point out, the principal governmental risk governance approach to achieve this aim is by enacting relevant regulation. Yet they argue that nano-specific state regulation is likely to play only a small part in an evolving governance web for an emerging technology with indeterminant futures. Thus, when considering NM, with their risk uncertainties, technological complexities and scientific ambiguities, it is not surprising that there continues to be calls for nano-specific EU regulation (Centre for International Environmental Law 2017). There seems to be no EU political appetite to replace REACH, as the principal chemical safety framework for nano regulatory decisions, particularly with its institutional and industry endorsements (OECD 2013; Nanotechnology Industry Association 2013; NANOFORCE 2012; European Chemical Industry Association 2011). Instead, there has been substantial EU research investment in developing supporting concepts such as 'Safety by Design' (SbD) processes and, the more recent, 'Regulatory Preparedness' and 'Sustainable innovation Assessments' initiatives (Katalagariniakis 2018). The purpose of these initiatives is to provide predictive tools for anticipating future problems and eliminating them at the discovery/early innovation stages. I discuss the prospects for these concepts to be incorporated within an adaptive and integrative framework for nano risk governance in later Chapters (Stone *et al.* 2018; Linkov *et al.* 2018).

I have discussed briefly, in Chapter 1, that there are critical flaws in applying REACH to NM, in its underpinning regulatory sciences, which I will discuss in more detail later in this Chapter. I shall also discuss the recent policy/regulatory initiatives still under development and their implications. But, before I do so, I must briefly mention a fundamental unresolved additional problem in relation to EU nano risk governance. This is the continuing dissonance between the EC, nanoscientists, regulators and industry regarding an acceptable definition of what actually constitutes a NP; for if a NP cannot be legally defined, it becomes impossible to govern or regulate.

2.3.2 EU Nanoparticle definition- Why is it still contentious?

It is the exploitation of the unique NP functionalities which occur mainly within the 1-100nm metrical range that offer significant socio-economic-environmental benefits beyond those currently existing (German Action Plan for Nanotechnology 2020, 2016; USA National Nanotechnology Initiative 2016,2014; Maynard 2014, NERC 2014). Nevertheless, there are within EU governance institutions (ECHA and EFSA), distinctive scientific differences of opinion as to how a NP should be defined and measured. Therefore, this is not just an abstract governance and jurisprudence problem but has significant impacts for other key stakeholders such as the nano industry.

The EC decided that the only way to differentiate between NPs and other homologous chemicals, at a macro level, was by adopting the nanoscale of 1-100nm. It published its recommendation on the definition of NPs on 18th October 2011 (2011/696/EU). The definition is based on size alone and is designed to be neutral in that it does not related to potential hazard or risk in anyway. This definition is as follows:

European Definition of Nanoparticles, 18th October 2011

'A natural, incidental or manufactured material containing particles, in an unbounded state, or as an aggregate or as an agglomerate and where, for 50% or more of the particles in number and size distribution, one or more external dimensions is in the size range 1-100nm. In specific cases and where warranted by the concerns for environment, health, safety or competiveness the number and size of the distribution threshold of 50% may be replaced by a threshold between 1-50%'.

This definition remains contested due to its lack of measurability and the narrowness of its size range (Krug and Wick 2011). The Arcadis Report (2011) argued that there should be a broader size scale as quantum effects can be exhibited by larger particle sizes i.e. > 100nm scale. Surprisingly, there is continued dissent from the European Food Safety Authority (EFSA) for this EC draft definition. For example, when it received approval from the European Parliament for the EU *Food Information for Consumers (FIC) Regulations 2011 [(EU) No 1169/2011],* it contained its own NP definition variant without the EC minimum particle counts. At the behest of EFSA, the European Parliament more recently amended the Novel *Foods Regulation[(EU) No 2015/2283]*, which provides for a further variation on that draft EC definition. In contrast, the European Chemicals Agency (ECHA) explicitly refers to the definition in EC Recommendation [2011/696/EU] above, in its guidance for the registration dossiers for NM for REACH purposes (ECHA 2016).

Hence, the dissonance as to the exact definition for a NP continues to be unresolved within the EU governing institutions, legislative assemblies, enforcement agencies, and statutory risk governance instruments. This is no small matter, with differing definitions within different regulations, leading to a confusion for research scientists and industry technologists. An example is when a NP may have multiple commercial uses in differing

industry contexts subject to separate regulatory regimes and enforcement agencies e.g. titanium dioxide for food colouring, sunscreens or household paints. Though much researched (NanoDEFINE http://www.nanodefine.eu/), there is as yet no formal adopted standardized scientific methods to differentiate NP threshold values/particle counts to comply with these differing statutory definitions (Stone *et al.* 2017). The EC Joint Research Centre (JRC) has repeatedly defended the EC 2011 definition in three subsequent reports (JRC 2013, 2014, 2015). Consequently, because of this robust defence, there appears little likelihood of a drastic EC revision of the draft definition. Yet this fundamental scientific and legal issue remains unresolved, with the EC proposing a further public consultation which may take place in 2019 (EUR 27240 EN) but with no confirmed timetable as yet.

In conclusion, this critical governance issue for an authoritative scientific descriptor for a NP has still not been settled. Consequently, there are important implications both for nanoscientists, technologists, safety testing methods, industry submissions of REACH registration dossiers, and regulatory decisions and their enforcement. I will discuss next the regulatory framework (REACH) for controlling NM within the EU. In particular, the benefits and disbenefits of this adopted approach that have emerged in its application for that purpose.

2.3.3 REACH and Nanomaterials – The critical issues

As previously mentioned, the EC's continued reluctance to implement a nano specific risk governance framework is still being criticized by civil society groups within the EU (Centre for International Environmental Law 2017). They urged the need for a harmonized framework of legislation supported by a basket of mandatory public information requirements. These include NP identification and particle characterisation, hazard exposure, risk characterization and management measures, and specific market data for

consumer information. Despite such proposals, the EU principal statutory horizontal chemical safety framework for the EU remains REACH [Regulation (EC) No 1907/2006]. It is regarded as the most comprehensive chemical safety regulation in the world with other national models being based upon it e.g. South Korea (AsiaHub newsletter 30.10.2016). Its fundamental goal is to 'protect human health and the environment' by applying the Precautionary Principle [Article 1(3)]. The key mode of action is found in Article 5: **'No Data, No Market'** (Article 5, Chapter 1, Regulation (EC) No 1907/2006).

If a registration dossier providing the required data is not submitted to ECHA, then this fundamental sanction is applied. Compliance with the registration requirement is a powerful incentive for industry compliance with REACH by those wanting to manufacture or trade within the EU single market. Thus, REACH also captures chemical substances manufactured outside of the EU but traded within its boundaries. The key task of REACH is to act as a single portal for the safety testing of chemicals within the EU single market. A Registration dossier must be submitted to ECHA for any chemical substance, with an annual production greater than 1 tonne, with details of its intrinsic physico-chemical properties and their potential to impact on EHS e.g. carcinogenic, mutagenic, reprotoxic (CMR). In addition, there must be included an assessment of EHS exposure and risk levels [REACH Article 14(1)].

In respect of NM, the criticism for REACH is its lack of a separate particle chemistry distinction within its regulations or chemical safety testing procedures i.e. separately identifying the nanoform(nf) from its macro versions. So, REACH allows different forms of the same substance (both macro and nanoforms) to be incorporated within a single registration proposal for authorisation by ECHA (Vaughan 2015). There are no discrete scientific fields for separating out the nanoform of a chemical substance from its bulk or macro form within the registration process. For example, the macro version of gold is

virtually inert, yet its nano version can be a highly reactive catalyst (e.g.@30nm) for drug delivery in the pharmaceutical sector (Mahapatra 2016). However, the EC (2013a) believes that, overall, the harmonisation of the chemical safety testing within a single set of regulations (REACH) has contributed significantly to EU innovation and competiveness [COM (2013) 49 Final]. Yet, in contrast to the EC First Regulatory Review conclusions [COM (2008) 0366], the *Second Regulatory Review of Nanomaterials* published in 2012 [COM (2012)572)], accepted that REACH testing protocols were inadequate for some forms of NM and promised revisions. These conclusions followed reports received from its Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR 2009; 2007). Yet, the EC's continued dilatory response to these recommendations has been much criticized by some Member States (Vienna Declaration 2017), and the nano specific testing protocols revisions will not now be enacted within the REACH Annexes until 1st January 2020 (EC DO/ 56122/02).

This meant that at the expiration of the REACH registration dossiers deadline (31st May 2018), NM were only represented in 29 of the 88,318 dossiers submitted (ECHA 2019) i.e. 0.035% of the total. These numbers for NM seem exceptionally low, and a possible unexpected explanation for this will emerge from the industry respondents interviews in later Chapters. These figures must be considered in the context of the adoption of the EC strategy for nanotechnologies back in 2004, and now questions whether the decision to retrofit existing legislation (i.e. EC Objective 1) to NM was the right one. These concerns have contributed to the development of the first Proposition for this study, which is to test respondents opinions as to whether REACH has achieved the high levels of public and environmental health safety required by EU legislation. The situation has provoked debate

and comment as to whether REACH should be the focus for nano regulation, and this will be a focus in the questionnaire.

In conclusion it is easy to understand the criticism from the European Parliament and NGOs for the EC continued insistence in using REACH for nano regulatory decision-making. Questions continue to be posed as to just how effective REACH has been in guaranteeing safe use of nanoproducts for the publics. It cannot be said with confidence that REACH has yet delivered on the normative target of a 'high levels of human and environmental protection' required by the EU Maastricht Treaty 1992, (Articles 152, 153, 174), the Treaty on the Functioning of the EU 2012, [Article 191(2)], and Article 3(3) of The Treaty of the European Community (2002). This is the legislative requirement that has generated the EU adoption of the Precautionary Principle (COM 2000) within REACH [Article 1(3)]. I will now discuss the role and application of PP within the EU as it has important implications for this study.

2.3.4 The Precautionary Principle and its role in nano-safety.

The Precautionary Principle (PP) is a 'First Order' principle central to EHS policy, protection and regulation within the EU. Its importance is emphasised within the three EU Member States Treaties above, all of which require high levels of EHS protection. In essence, PP is activated when a chemical, process or activity raises a threat of harm to human health or the environment. It triggers the need for precautionary measures to be taken even if some of the cause and effect relationships are not fully established scientifically (UN Environment Protection Assembly 1982, UN Environment Protection Conference 'Rio Declaration' 1992). The specific EU guidance from the EC is found in the *EC Communication on the Precautionary Principle* (COM 2000), which requires that there must be, at minimum, a preliminary scientific evaluation that demonstrates there are '*reasonable grounds for concern*' (COM

2000 p.3). The EU Maastricht Treaty 1992 (Article 174) also links PP to the 'Polluter Pays principle', when requiring that a high level of protection shall be based on the precautionary principle, and that any environmental damage should as a priority be rectified at source, and at the polluters cost.

The EC Communication (COM 2000) does not provide a working definition for PP, but there are several academic definitions for the Precautionary Principle which include the formulation adopted at the Wingspread Conference (Hileman 1998):

> *'When an activity raises threats to the environment or human health ,precautionary measures should be taken, even if some cause and effect relationships are not fully established scientifically '*

With Per Sandin (1999) providing a succinct version :

'If there is a threat which is uncertain them some kind of action is mandatory '

However, for the purposes of this study into EU precautionary policy, I provide the policy definition offered by von Schomberg (2006 p. 47):

> ' *Where, following an assessment of available scientific information, there are reasonable grounds for concern for the possibility of adverse effects but scientific uncertainty persists, provisional risk management measures based on a broad cost/benefit analysis whereby priority will be given to human health and the environment, necessary to ensure the chosen high level of protection in the Community and proportionate to this level of protection, may be adopted, pending further scientific information for a more comprehensive risk assessment, without having to wait until the reality and seriousness of those adverse effects become fully apparent'.*

EC Communication (COM2000.p15) and the above definition identify that the necessity for any action triggering the PP must be based on scientific risk- based evidence (rather than

vague non-probability hazard assessments). Stirling (2016b) implies that PP requires a more scientifically rigorous attention to the implications of our incomplete scientific understanding than might be found within routine regulatory risk assessments. Less prominent is the PP requirement to include 'deliberative' consultation with relevant stakeholders in identifying options for problem resolution (COM 2000 p.21). Von Schomberg (2006 p.33) describes PP as a 'deliberative principle' in that its application involves the deliberation on a range of normative dimensions, which need to be taken into account when making the principle operational in both a policy and regulatory context.

Yet, as Stirling (2016b) points out, few issues of EU technology governance are more vexed than PP, with continually evolving debates within the literatures(cf. Sandin 1999, Sandin *et al* 2002; Von Schomberg 2006,2013, 2014; Tosun 2013; Britt -Holbrook and Briggle 2014; Spruit 2016; Reber 2018; Sandin and Peterson 2019). There continues to be criticisms, from a wide range of commentators, regarding current misuse/misapplication of PP. This is because of its application in a broad (sometimes indeterminate) hazard- based approach (in contravention of EC guidance), and not applied for evidence -based risk management (Boyd 2015; Hansen 2015; European Risk Forum 2015; De Mauley 2013; Lofstedt 2013; Willetts 2012). Yet its virtues are the avoidance of technocratic capture by narrow sectoral interests and enabling more democratic engagement and choices through its deliberative action (Stirling 2016b; Von Schomberg 2006).

The prevailing critical perspective for PP in some sectoral groups implies that the way it is being applied in practice is a constraint on nano innovation. Though civil society groups do dispute the view that the application of PP impacts negatively on EU competiveness and job creation (Centre for International Environmental Law 2017). Nevertheless, the precautionary approach, when hazard scenarios are developed but their probability of

occurrence is unknown, continues to be a typical response to current scientific uncertainty (van de Poel 2016). But Ashford (2015) strongly supports the view that regulation driven precaution can be part of the process of driving new innovation and not blocking it by requiring alternative options to be considered or developed. Thus, by utilizing it positively, and as a reason and incentive to open new scientific lines of enquiry, PP can influence the generation of novel alternative R&D trajectories and product creation (Stirling 2016b, von Schomberg 2013).

The role of PP is to identify the reasons for intervening, but not the actual interventions themselves. The fact is that where there is scientific uncertainty, legal uncertainty will follow, with a greater dependency on the application of the PP and precaution-based regulation (David Azoulay quoted in Jantunen *et al.* 2018 p.26). Stirling (2016b) argues that these criticisms are exacerbated by the asymmetrical power tensions of vested interests involved in the innovation and regulatory systems. In that the intrinsic features of this precautionary approach rests on the normative pillars of preventing serious or irreversible harms (United Nations Rio Declaration 1992). Further, Stirling (2016b) contends that it is the values driven by these pillars that should be the basis for setting of regulatory standards for emissions and exposure to NM.

This thinking may have been an influence for some Member States to set up their own separate *National Registers* for NM, echoing REACH with a 'No registration, No market' approach. The first was France (Decret No 2012-232 du fevrier 2012) with 14,000 NM declarations posted between 2012-2016 (Ministère de l'Environnement, de l'Énergie et de la Mer, November 2016). With these 14,000 NM declarations being in marked contrast to the 29 nanoform dossiers submitted for REACH registration between 2008-18 (see Section 1.4, Chapter1). Now this unilateral national state intervention has been followed by Belgium

(2013), Norway (2013), Denmark (2014) and Sweden (2018). It seems to me that these initiatives imply a lack of confidence in the current EU regulatory process for NM (see the Vienna Declaration 2017). The European Commission responded by setting up a European Union Observatory for Nanomaterials (EU-ON), facilitated by ECHA in June 2017, but the national registers have not been withdrawn in response to that policy initiative.

So, with the ongoing, and well-publicized problems identified for REACH in its application for NM, it is unsurprising that national state unilateral action has occurred citing nano-safety a key factor. These factors can be taken as part indicator that the EC strategy objective 1, for the retrofitting of EC legislation to NM, has not yet been successful and flawed in its implementation. Nevertheless, not all the problems for nano-safety relate solely to these deficiencies in EU risk policy and regulatory instruments. Indeed, there are many continuing negative factors relating to the underpinning regulatory sciences, their current development and future status which I want to examine next.

2.4 Evaluating the current and future status of regulatory sciences for nano-safety

2.4.1 The importance of the intrinsic and extrinsic physico-chemical characteristics for nanoparticles.

There is no specific EU risk paradigm for testing existing and emerging engineered NM (SCENIHR 2009). Neither is there an adopted definition of 'acceptable risk' (SCHER 2013), or an EU risk framework for the management of any emerging sciences (Mazri 2017). Within REACH, the current testing protocols may be reliant on incomplete sets of scientific knowledge and assumptions which can conceal other underlying hazards (Stirling 2016a). The complexity and uncertainty regarding the risk assessment of NPs is confounded by the

differing physico-chemical variables that influence the nanoform intrinsic and extrinsic characteristics. These can differ for the same NP if its variable characteristics differ. For example, the solubility of the macro form of a known chemical substance (e.g. titanium dioxide) can be considered an unambiguous characteristic. However, as a well-used NP, it can show a different dissolution factor for each of its nano variants, depending on the intrinsic properties such as size, shape, coating etc (Stone *et al.* 2017). Consequently, their only common characteristic as NPs is their nanosize (Jahnel 2015b). These molecular variables include their chemistry, size, shape, surface properties, crystalline structure, solubility species, dose, exposure, stability, bio-persistence and endpoints

In 2006, the EC Scientific Committee for Emerging and Newly Identified Health Risks (SCENIHR) reported that there were three important problems regarding the risk assessment of NPs (which continue to this day!). First, is that there is insufficient data concerning nanoparticle physico-chemical characterisation. Second, there is a lack of detection and measurement capability for their environmental fate, behaviour and toxicity (with our understandings of bio-persistence, bioaccumulation and (eco) toxicity still being major outstanding problems). Finally, there is a lack of Standardized Operating Procedures (SOP) to generate reproducible experimental data on human and (eco)toxicology. Fadeel *et al.* (2018) recently made the point that these multi-faceted problems for regulatory sciences are still unresolved, and likely remain so in the foreseeable future. The critical question is by what means can science, policy, and regulation provide resolutions for these significant and outstanding problems.

2.4.2 New paradigms for nanomaterial risk analysis

Upward of 200 million euros have been invested by the EC into nano research funding to resolve the critical scientific data gaps for the regulatory sciences supporting REACH

(NanoSafetyCluster2018). With a particular emphasis on progressing from traditional animal based toxicological testing to predictive profiling of nanotoxicity utilizing multi-cellular high throughput screening (HTS) techniques (JRC 2014; Whelan 2014). The purpose of which is to meet the European Union 3Rs policy for replacing animal testing which is to be found in both Directive (2010/63/EC) and endorsed by REACH (Regulation 33). Jahnel (2015b) reports that there are strengthening scientific views that high-dose animal toxicological studies are unrealistic and unjustifiable, with minor-overdosing leading to erroneous conclusions (i.e. false positives/false negatives). Stirling (2016a) believes there is too high a level of incertitude to be found within the current toxicological testing regime for it to remain the long-term practice for regulatory decision-making for complex emerging technologies (e.g. nanotechnologies, nanobiotechnology).

To resolve this situation, there are two possibilities for exploration. On the one hand, further investment could be made in overcoming existing animal based toxicological testing limitations and knowledge gaps; alternatively, design and implement alternative conceptual models to recast the whole process for NM risk management (Jahnel 2015b). The model given in Figure 2.1 below is an example of proposed new paradigms for toxicological testing for NM. Its key feature is that it introduces a tiered based approach for risk analysis, supported by in-vitro mechanistic HTS cellular testing, with in-silico modelling to minimise animal testing. The reason for the prospective adoption of this novel approach (apart from deontological grounds) is the potential for a significant number of variations of engineered NM coming to market in the future. This factor, taken with all their possible toxicological endpoints, means that the current case by case approach for animal-based testing regime would be impossible. It would require a high case by case volume of testing, beyond any

rational level of resources, and an unethical abuse of animal experiments (GRACIOUS https://www.h2020gracious.eu/; Stone *et al.* 2014).

The model in Figure 2.1 below has been selected as it is illustrative of the contemporary thinking for novel conceptual approaches for risk analysis for NM. The foundation for this new predictive approach for toxicology stems from USA National Academy of Sciences seminal report, 'Toxicity Testing in 21st Century' (2007). It proposed that an Integrated Alternative Toxicity System (IATS) could dramatically transform testing protocols. By progressing from traditional animal testing methods, to the utilizing of in-vitro HTS cellular testing methodologies using human or other cell lines (Oomen *et al.* 2014). Based on the identification of key biological processes, called Adverse Outcome Pathways (AOP), that drive negative cellular effects (Stone *et al.* 2017). The science foundation for these proposals are found in the significant advances achieved in toxicogenomics, bioinformatics, systems biology, epigenetics, and computational toxicology (EURL ECVAM 2015). The outputs of the new sciences, with their conceptual models, are currently being developed and published. Their remit is in developing predictive relationships to be identified between the physico-chemical structure of the NP, and its expected biophysicochemical activity in the presence of a biological entity. These are known as (Quantitative) Structured Activity Relationships (Q)SAR) [OECD (Q)SAR Toolbox 2019;ECHA 2017, 2013; Oomen *et al.*2015; Nel *et al.*2009, 2013a; 2013b; Nel 2014]. The OECD (2019) published an updated QSAR Toolbox (version 4.3) for regulators and industry on 18th February 2019. Its purpose is to encourage the regulatory acceptance of (Q)SAR by making the technology more transparent, accessible and less resource intensive.

This model introduces a tiered approach to risk decision-making, with the first tier (tier 1) a desk-top type evaluation based on curated nanoinformatics (Robinson *et al.*2016; Hendren

*et al.*2015; Klaessig 2014). The data from the curated NM libraries may be sufficient to confirm that there is no prospective risk from the NP, and further testing is unnecessary. If that reassurance is not forthcoming , then the model moves to tier 2 testing which utilizes a process of dosing multiple cells lines with differing NP concentrations using HTS techniques to produce large data sets (Colin *et al.*2016). These raw data sets are then processed *in-silico*, incorporating Grouping (into specific chemical categories) and READ across techniques, for detailed analysis by the computational modelling to identify (Q)SARs. (OECD2019;GRACIOUS https://www.h2020gracious.eu/). The results from tier 2 can be used for hazard ranking i.e. high-medium -low. If the hazard ranking indicates a need for further in- vitro testing at tier 3 level, then lower level invertebrate sentinel species such as Daphnia or Zebra fish can be studied first. Finally, tier 4 in-vivo testing will only be contemplated if the tier 3 test results indicate such a necessity. So, vertebrate/mammalian testing will become that last option to be studied for NM regulatory risk assessments rather than currently, the first option.

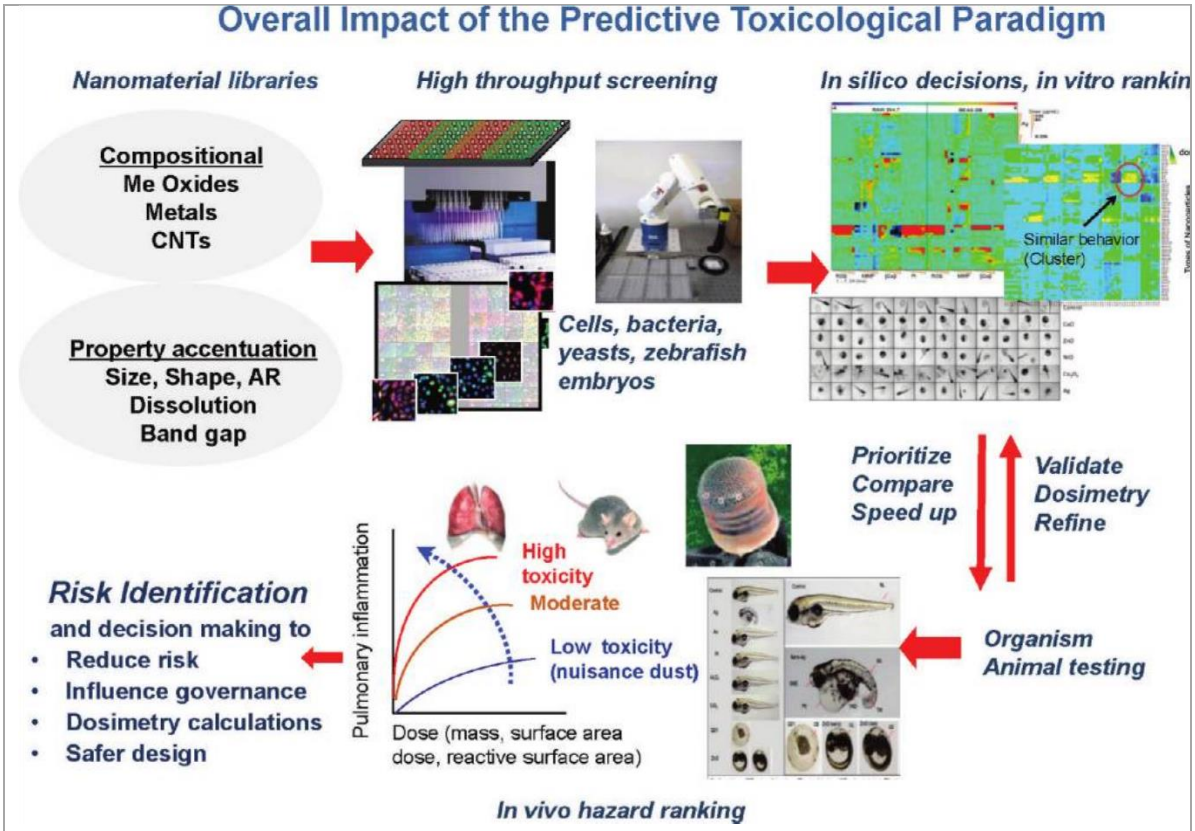


Figure 2.1: Implementation of toxicological profiling using a tiered approach for risk identification and characterization (Source: Nel *et al*. 2013)

These processes can eventually lead to an accurate and efficient estimation of the biological responses to differing nano exposures (Stone *et al.*2017). This is to be achieved by undertaking many thousands of cellular micro-assays which can detect cellular perturbations and identify AOPs. By reaching and interacting with a biological target, the toxicant precipitates a cascade of events leading to identifiable AOPs which may lead to measurable antagonistic outcomes at the cellular, organism and up to population level (OECD 2013, JRC 2014). The ambition is to identify the MoA of the chemical perturbation within the cellular pathways. The MoA can then be intimately linked to the perturbations due to the physico-chemical characteristics of the NP. Consequently, the MoA identifies and describes key cytological and biochemical events which are observable and measurable (JRC 2014; WHO 2009). The ambition here is to then develop the scientific capability to extrapolate the data to determine EHS risks (Rovida *et al.*2014; SCHER 2013). These scientific

developments are not only aimed at the laboratory but for future practical application within nano industry and regulatory settings. The intention is to move from the perceived slow and expensive current case by case animal-based testing, with its doubtful single probalistic results, to a 'weight of evidence' approach (Jahnel 2015a&b; NIA 2013, SEURAT 2013; SCENHIR 2012). 'Weight of evidence' is defined by Gottardo *et al.*(2017 p.40) as '*when evidence from several independent sources lead to a certain conclusion on a property for a nanomaterial*'. As can be seen from Figure 2.1, there may be multiple sources of data on which researchers, technologists and regulators can make safety decisions.

The multi-national regulatory focused EU FP7 funded NanoReG2 and ProSAFE projects (NanoReG2 http://www.nanoreg.eu/; ProSAFE http://www.h202-prosafe.eu/) support this scientific approach to reduce toxicity testing time whilst increasing the amount of data capture. These REACH focused research projects have produced a toolbox for industry and regulators, with scientific instruments for particle characterisation, risk assessment, toxicity testing and exposure measurements of NM. This toolbox also incorporates a *Safety by Design* conceptual approach for underpinning regulatory (REACH) decision-making (Gottardo *et al.*2017). This is an important conceptual approach for this study, which I discuss briefly in the next section.

2.4.3 Safety by Design to facilitate upstream design modification to nanoparticles.

Safety by Design (SbD) is a long-standing engineering process extensively applied across disparate technological platforms such as pharmaceuticals, computers, and aerospace industries (Kraegeloh *et al.*2018). Its purpose is to safely develop new products from discovery to market launch (Gottardo *et al*.2017). In the EU regulatory context, SbD is already established as an important concept, within high profile EU funded nanotechnology

research projects, to promote 'regulatory preparedness'. This is when regulators are given early awareness/foresight by industry of forthcoming nano innovations, and the opportunity to check whether present legislation serves the safety aspects or may need revisions (JRC 2018; Katalgariniakis 2018; NanoReG2 http://www.nanoreg.eu/; ProSAFE http://www.h202-prosafe.eu/; GRACIOUS https://www.h2020gracious.eu/). The purpose of which is to contribute to a 'Safe Innovation Approach' by the nano industry (Katalagariniakis 2018; NanoReG2 http://www.nanoreg.eu/). However, SbD is to be applied in a limited manner, by its use for analytical risk assessment, as a new pillar for supporting REACH, by its focus for NP functionality and potential toxicity (Gottardo *et al.* 2017). In this context, Gottardo *et al.*(2017p.102) define SbD as '*a process that considers and incorporates safety considerations into product design and development, by addressing the functionality of a material and its toxicity in an integrated way'.*

In summary, these important new conceptual and scientific advances discussed above, have the possibilities of re-designing the futures for NP characterization, toxicological testing, and risk characterization for the key actors involved with nano innovation (e.g. government, researchers, industry and regulators). By these means, a more anticipatory approach can evolve from traditional precautionary measures to identify, mitigate or eliminate potential risks from NM and their products. There is still the important stage of proof of concept to be achieved, and the barriers to regulatory acceptance must not be under-estimated (ECHA 2017; Hjorth *et al.*2016). They must achieve demonstrably inherent reliability and validity for specific nano risk assessments tests (ECHA 2017; ECHA 2012). If they do, then they offer a promise as future anticipatory applications with underpinning from a more efficient mechanistic approach to regulatory decision-making (Whelan 2014). These are important and central issues , which are tested within Proposition 2 in Chapter 5, which asks how much

confidence can be placed in these new tools for future nano-safety decision-making. Yet, in respect of the EC Objective 2, it cannot be said its expectations have yet been fulfilled following the above discussions.

The EC Objectives 1&2 can be regarded as focused on the technocratic 'safe' innovation of NM. This leaves EC Objective 3, with its more deliberative intentions to incorporate socio-ethical considerations into nano innovation. The aim is the social alignment of nano innovation by promoting the other limb of the EC *NanoStrategy* for responsible development. I will discuss these issues in detail in Chapter 3.

2.5 Conclusions

This Chapter foregrounds discussions on the potential risks from NM and the attendant EU risk policy. It has critically examined past, present and future EU regulatory policy and controls. In addition, it examines the epistemic underpinning for regulatory sciences, and importance of the emerging novel risk paradigms with their ground-breaking conceptual approaches.

There is an absence of proven risks from NM, with no known human pathologies due solely to exposures to NM (Nel *et al.*2015; Nel 2014). Notwithstanding that lack of evidence, there remains considerable uncertainty in predicting the possibility of future risks from the long term EHS exposure to NM. In particular, risks from 2^{nd} ,3^{rd} and 4^{th} generation NM , many of which are still in the theoretical or experimental stage. The EC policy to retro-fitted REACH to nano-safety has come in for considerable criticisms for its lack of nano-specific tests. Originally rejected, these criticisms are now acknowledged formally by the EC as identifying a fundamental flaw for NM safety testing [COM (2012) 572 Final]. Notwithstanding that acceptance, and further Member States public criticisms, the EC response can only be

described as dilatory. With their solutions not to be enacted within the REACH Annexes before 1st January 2020 (EC DO 56122/02). A further regulatory deficiency has been that the EU draft definition for a NP [COM (2011)275] continues to be contested institutionally and scientifically. This is awaiting a further updated public consultation process promised for some time in 2019. So, the future outcomes for resolving both these regulatory and enforcement deficiencies adds to current uncertainties. Consequently, it has not been possible to quantify with any accuracy just how effective REACH has been for evaluating NM in the market. This is further complicated by the minimal number of REACH registration dossiers submitted during the 2008-2018 period (only 29 registration dossiers).

New paradigms to replace traditional animal-based testing are rapidly being developed and tested. Though awaiting proof of concept, there is an optimism for their future application for industry and regulatory decision-making, and they are in receipt of important EU institutional support from the Joint Research Centre (Gottardo *et al.*2017), European Chemical Agency (2017), and the European Food Safety Agency (2018). Nevertheless, these deficiencies in scientific rigour for regulatory control have left worrying gaps in EU risk governance of NM, and the exercise of its institutional responsibility for public health and safety.

These deficiencies and concerns, which have no immediate solutions to hand, have led to debates by sectoral stakeholders as to the future format for EU nano risk governance. In particular, should it now be re-framed by conceptual approaches which promote a more anticipatory governance approach within EU policy. These issues will be discussed in more detail in the next Chapter.

Chapter 3: Literature Review

3.1 Introduction

The previous Chapter reviewed the grey policy literatures on EU nanotechnology to provide a background for the study's legislative and regulatory framework. In this Chapter, I discuss the theoretical and conceptual underpinnings for the empirical research, which I derive from academic literatures. Framing my work are two theoretical strands, which I believe set out different but complimentary governance perspectives. These I use to develop my analytical approach to examine NM innovation activities, and the potential for new deliberative processes to improve NM regulation efficacy.This approach provides the foundation for the study's data collection (principally through prioritising stakeholder identification and sampling strategies), the critical analysis of empirical materials derived from my field research, and my derivation of the study's conclusions.

The two theoretical literatures are as follows. Firstly, risk governance within which I include the conceptual framings of the Taxonomy of Regulation (Centre for European Policy Studies 2014), Analytical-Deliberative approaches (Rosa and Renn 1999) with related work on integrative risk governance (Klinke and Renn 2012), and work on Safety by Design (Gottardo *et al.*2017; NanoReG2 http://www.nanoreg.eu/; ProSAFE http://www.h202-prosafe.eu/). This is complemented by a second strand of work in the social sciences on the closely related topic of anticipatory governance. It is under this heading I examine work on the Precautionary Principle (COM 2000), Midstream Modulation (Fisher *et al.* 2006) and Responsible Research and Innovation (Horizon 2020; Rome Declaration 2014).

As I seek to show, the conceptual framings of both strands of literatures are highly pertinent in informing the need for and the configuration of new approaches to the regulation of NM.

In particular, I argue the insights offered by these literatures can advance discussions on the development of new EU policy regulation, scientific and technological practices to support delivery of the three EC *NanoStrategy* risk governance objectives. Consequently, here I discuss the scope and purpose of these objectives, including their limitations, and how these limitations might be resolved. This theoretical discussion provides the basis for design of an 'ideal-type' illustrating the conceptual intersections for the empirical examination of the governance for the safe and responsible development of NM which is conducted in subsequent Chapters.

3.2 Risk Governance

The literature on risk governance has grown enormously over the last three decades. Much of this work shares a common goal in seeking to account for the handling of risk and uncertainty under conditions of collective decision-making and decision-taking increasingly found in "risk society" (Beck 1992; Jasanoff 2004,2006; Renn 2005,2008; Klinke and Renn 2012;Bennet 2016). In essence, 'Risk governance looks at the complex web of actors, rules, conventions, processes and mechanisms concerned with how relevant risk information is collected, analysed and communicated, and how management decisions are taken' (Renn 2008 p36). More recently, work in this area has sought to distil core principles of governance that can be used to inform risk-related policy making. From this perspective, risk governance goes beyond the three established components of risk assessment, risk management and risk communication to address how political, institutional, and commercial responsibilities and accountabilities play a crucial role in shaping collective decisions (Rosa *et al.* 2013). Thus, the International Risk Governance Council (2005) describes risk governance as sitting at the confluence of all analyses and actions related to the development of new science and

technologies. A crucial element here is ensuring that stakeholders and publics engage with these new technologies at an early stage, as individuals and societies perceive technological risks in disparate ways (Douglas 1992; Adams 1988). Moreover, in developing these technologies, researchers have argued that risk governance principles should be applied in a systematic manner throughout all aspects (formulation, development and implementation) of the new product innovation decision-making process (Tinkle 2014).

Applied to nanotechnologies, work from a risk governance perspective has highlighted the multiple novel biophysicochemical characteristics that NM can exhibit. Consequently, there is a necessity for new nano-risk metrics and procedures for nano-risk evaluation, if regulators are to keep pace with the rapid trajectories of nanotechnological developments. Marchant *et al.* (2011b.p23) label this the 'pacing' problem in which regulatory controls constantly lag behind innovation at the frontiers of science, as do ethics (Jasanoff 2016).

However, compliance with criminal-based safety regulation such as REACH is not the only legal responsibility that NM innovators and product manufacturers have to exercise within the EU. A further EU governance policy response for achieving safe NM is their civil legal obligation to ensure safe products under the requirements of the EU Product Liability Directive (85/374/EEC). This imposes on all nano producers a duty of care/ legal liability, in respect of their consumers, for any defects or harms from the finished product, component part or any raw material supplied by them. To establish liability under Directive 85/374/EEC, the injured person must prove the existence of the defect, clear evidence of the damage/harms, and that there exists a causal link between the two (Article 2). The aggrieved consumer may then pursue a Product Liability Tort (i.e. civil action for compensation) through the Courts to obtain appropriate financial compensation for any harm by means of awarded damages (Freeman *et al*. 2018). At the heart of this civil redress is the concept of defect. If

the defective product does not provide the level of safety that a person is entitled to expect, taking all the circumstances into account, then the producer is at fault (Article 6(1)). These protective rights run in parallel with formal 'black law' regulations such as REACH in an EU governance policy endeavour to secure product safety within the EU.

Now in respect of such potential risk of harms from NM, these currently arise from so-called passive nanostructures associated with existing NM on the market, as well as the likelihood of active nano-manufacturing systems being developed in the near future. As Renn and Roco (2006.p153) reflect therefore, "Active nanoscale structures and nano-systems have the potential to affect not only human health and the environment but also aspects of social lifestyle, human identity and cultural values". Consequently, I discuss in detail below key concepts within the risk governance literature that apply to NM policy, design and implementation. First, however, I consider how risk governance fits in with the wider palette of hard and soft law within the *Taxonomy of Regulation* to provide clarity on the range of measures available to regulators in handling risks arising from novel technologies.

3.2.1 Risk Governance and the 'Taxonomy of Regulation'

Regulation is the usual method to control commercial activities by the state (Bowman 2017; Calster and Bowman 2002), with evidence-based regulation used to establish the scope of legitimate, socially accountable innovation processes in manufacturing (Macnagthen *et al.* 2016). This use of formal regulatory controls features in the 'Taxonomy of Regulation' (CEPS 2014, Figure 3.1) as one element in a broad portfolio of public policy tools that extends far beyond the remit of established 'black letter' law and other 'command and control' approaches (CEPS 2014). The Taxonomy enables consideration of how more nuanced hybrid constructions of hard and soft law might be achieved that blend regulatory with forms of self-regulatory activity and moral suasion (Vaughan 2015). Such a portfolio approach is essential

in addressing risk governance of the complex challenges posed by regulating, controlling and using new technologies, and provides a lens through which existing EU regulation of NM can be viewed and analysed (Arnaldi 2017). Stone *et al.*(2018) for example, consider that risk-based decisions on NM have to be taken within the context of this portfolio approach of hard and soft law, arguing that all policy tools are needed to support current EU risk governance of NM. This necessity is due to the ongoing scientific and regulatory uncertainty, complexity and ambiguity surrounding their development, manufacture and sale. It is, therefore, unsurprising that the use of REACH, to regulate risks associated with the production and marketing of NM, has been a continuing source of political, scientific and legal debate within the EU (cf. Bowman 2017; Reichow 2016; Vaughan 2014; Stokes and Bowman 2012; Stokes 2012; Som *et al.* 2010). Some have argued that by using REACH to manage NM, the EU has defaulted to tried and tested regulatory procedures. This is despite the criticism of its inadequacy in meeting current challenges posed by novel NM, and the possible future nanotechnology delivery systems (Stokes and Bowman 2012). I use the taxonomy here to identify the different risk governance tools that are being used for the regulatory controls for NM. Specifically, I test whether REACH, as currently implemented, offers the necessary hybrid hard/soft law approach required to regulate the manufacture of NM to ensure acceptable levels of environmental and public health risks (Vaughan 2014; Stokes and Bowman 2012, Stokes 2012; Som *et al.* 2010).

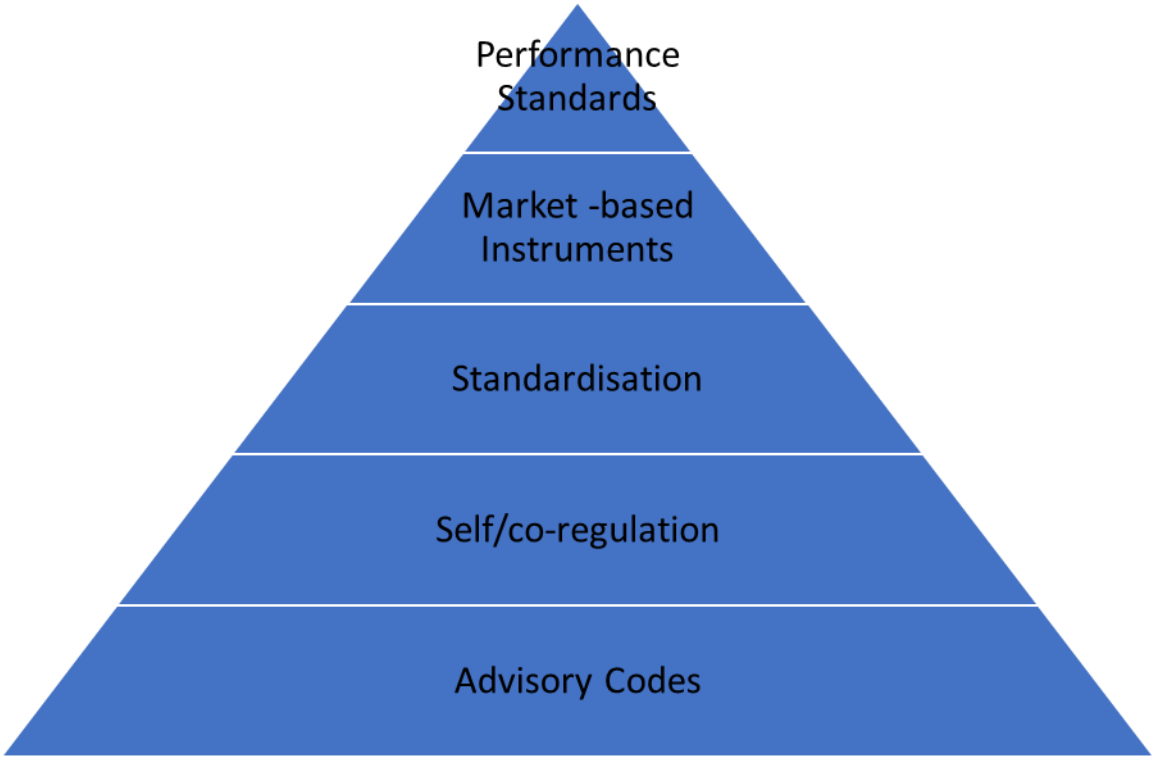


Figure 3.1: Taxonomy of Regulation (source: Centre for European Policy Studies 2014)

The base of the taxonomy comprises 'soft' law, exemplified by industry advisory codes to promote self-regulatory 'safe' approaches to nano-manufacturing. An example is the EC *NanoCode* (European Commission 2008c) which aims to encourage a culture of self-regulation in the nano industry; but so far it has been difficult to judge whether this has been successful. The next step in the taxonomy is the essential scientific and technology standardization of new methods and tools for accurate NP characterization, exposure assessment, and determination of EHS risks. However, these activities need substantive advances in NM metrology if they are to be effective. In particular, the development of scientific and industry SOPs are essential elements in fulfilling Objective 2 of the EC's *NanoStrategy*, yet both are problematical and unresolved (Fadeel *et al.*2018). Next upwards in the taxonomy is the application of market-based instruments to steer the course of the innovation processes. These can include government funding for risk research and industry innovation grants. Again, very little research exists on this topic and consequently it is difficult to judge whether

such measures are making a telling contribution to delivering the *NanoStrategy*. Finally, at the apex of the taxonomy are statutory Environmental, and Public Health and Safety compliance standards approved by the European Parliament (e.g. statutory emission or exposure levels). These are essential in setting the markers for regulatory controls of NM and the enforcement of any infractions.

The Taxonomy provides a useful heuristic with which to consider the roles of complementary 'hard' and 'soft' regulatory approaches to address the needs of nanomaterial product development and authorisation. I now consider specific risk governance approaches that have been applied to nanotechnologies and examine their utility in relation to the current study.

3.2.2 An analytical-deliberative approach to risk governance for nanomaterials

Rosa, McCright and Renn (2013) make a strong case that emerging technologies in the 21st century need a different set of risk governance decision tools due to their inherent technological complexity, scientific uncertainties and socio-political ambiguities. They advance the analytical-deliberative model (see also Klinke and Renn 2012; Renn 1999; Stern and Finsberg 1996) as a useful starting point in addressing risk arising from these technologies, including NM. This model emphasises the need to integrate regulatory frameworks within a properly democratised governance of risks. To undertake these actions requires synthesising the systemic knowledge underpinning evidence-based risk management (*analytical*), with the creation of a culture of innovation responsibility which is deliberative by being participative and inclusive of multiple stakeholders (*deliberative*). Here I adopt Dryzek's (2000.p1) definition of "deliberative" as "the social process where deliberators (stakeholders) are amenable to changing their judgements, preferences and views during the course of their interactions, which involved persuasion and not coercion,

manipulation or deception". According to Habermas (1984), optimal policy outcomes are those that achieve consensus amongst all parties, based on improved and enhanced arguments delivered through a deliberative process. Though Carralho and Nunes (2018) believe that, realistically, workable agreements are more likely in most circumstances. The analytical-deliberative model, therefore, potentially provides a fruitful way of thinking through how the expanded risk management paradigm foreseen in the EC *NanoStrategy* document [COM (2004) 338] might be achieved. For example, this could be by incorporating regulatory, risk assessment and socio-ethical components into its decision-making processes. Using this approach, I identify in Table 3.1 below how this might apply to the *NanoStrategy's* three Risk Governance Objectives.

Table 3-1: The EC NanoStrategy objectives from an Analytical-Deliberative perspective

EC *NanoStrategy* Risk Governance Objectives	**Analytical-deliberative framing of objectives**
EC Objective 1 proposes that maximum use would be made of existing regulation though adjustments may be necessary.	Analytical
EC Objective 2 which recognises that existing parameters for EHS chemical safety testing may not be appropriate for the unique properties of nanoparticles, requiring new methods and tools for risk assessment, and refinement of nano-scale metrology and standardisation activities.	Analytical
EC Objective 3 proposes that the Risk Management paradigm to be expanded to incorporate Socio-ethical considerations into the R&D process with the creation of a culture of responsibility which is participatory and inclusive.	Deliberative

Rosa *et al.* (2013) note that the *analytical* framing requires reproducible scientific knowledge to be applied within a regulatory decision-making framework; whilst the *deliberative* must rely on a mutual exchange of arguments and reflections by stakeholders, with the aim of a consensus to mobilize legitimate actions and social acceptability. Clearly, however,

developing a model based on the possibilities implicit in the relationships in Table 3.1 requires much greater attention to the structures, mechanisms and configuration of governance. With the need to address the three risk characteristics relevant to NM production, namely its technological complexity, scientific uncertainty, and socio-political ambiguity currently inherent in nanotechnologies. This requires turning to other risk governance tools, specifically the adaptive and integrative risk governance framework specifically designed for NM.

3.2.3 Adaptive and integrative risk governance for nanotechnologies

Klinke and Renn (2012. p278) define adaptive and integrative risk governance as "the ability of politics and society to collectively design and implement a systematic approach to organizational and policy learning in institutional settings that are conducive to resolve cognitive, evaluative and normative problems, and conflicts of risks". According to these authors, the advantage of this risk governance approach is that it can address public policy challenges that result from insufficient and/or competing knowledge concerning the three risk characteristics of technological complexity, scientific uncertainty, and socio-political ambiguity described above. This accords with Stone *et al.* (2018) assertion that any viable risk-based approach for nanotechnologies must go beyond 'black letter' legislative controls to directly involve key stakeholders, including civil society, in risk decision-making processes, through the facilitation of interactive networks of relations. Stone *et al.* (2018) provide some guidance as to how this might be achieved, by proposing three elements for effective adaptive and integrative risk governance framing specifically for NM (see Table 3.2). Linkov *et al.* (2018) are supportive of these views in emphasising the need for multi-stakeholder involvement in situations where quantitative risk assessment remains uncertain or incomplete – exactly the situation currently pertaining to NM development and production. In these circumstances,

multiple data sources, including reviews of various EHS endpoints and technological outcomes, must be drawn upon and evaluated in risk decision-making and decision-taking processes. Based on these observations, Table 3.2 below outlines how Stone and Linkov's findings might be used to inform my research design and empirical analysis in two main ways. Firstly, to provide for an analytical benchmark of the effectiveness of REACH to the current operation of the three EC Objectives. Secondly, to inform the possible development of new hybrid (formal and informal) governance approaches to enhance the effectiveness of adaptive and integrative risk framings for NM futures.

Table 3.2:Comparison of EC NanoStrategy objectives against selected published criteria for adaptive and integrative risk governance of nanomaterials.

Domain	**EC NanoStrategy (2004)**	**Stone *et al.* 2018.**	**Linkov *et al.* 2018**
Regulatory compliance (Analytical)	*EC Objective 1* 'Maximum use would be made of existing regulation though adjustments may be necessary'	Legal and other (nano-specific and general) regulatory requirements are necessary to ensure compliance and to stimulate proactive approaches to safety	A broad evidence base is necessary for regulatory considerations in cataloguing potential risk outcomes
Nanoparticle characterization and risk analysis (Analytical)	*EC Objective 2* 'Recognises that existing parameters for EHS chemical safety testing may not be appropriate for the unique properties of nanoparticles, requiring new methods and tools for risk assessment, and refinement of nano-scale metrology and standardisation activities'	Identifies the continuing need for dynamic, advanced scientific tools and strategies for nano-risk assessment, mitigation and transfer	Promotes the continued development of risk analytical tools to resolve incomplete answers or outcomes and to comprehensively catalogue risks from NM
Social appraisal of nano-innovation (Deliberative)	*EC Objective 3* 'The Risk Management paradigm to be expanded to incorporate socio-ethical considerations into the R&D process with the creation of a culture of responsibility which is participatory and inclusive'	Promotes the fostering of dialogue with civil society by behavioural insights to determine societal concerns for nano-innovation risks, mitigation, and transfer.	Identifies that multi-stakeholder insights are necessary to bridge gaps in experimental risk assessment data and outcomes.

As can be seen in Table 3.2, Stone et al.'s (2018) and Linkov et al.'s (2018) findings on NM map neatly onto the intentions of the three EC *NanoStrategy* objectives and, I argue, provides for an insightful means of evaluating their current effectiveness and efficiency. Additionally,

they are being strongly suggestive of identifying potential pathways for improving their future design and implementation. In doing so, the findings from both studies provide a schema for the research design for this study, by informing, respectively, current and anticipated future risks arising from NM development and production. I consider anticipated future risks arising from NM later in the Chapter. But, before that, I examine some of the practical issues that arise from the discussion so far, namely how can the multiple stakeholder groups, foreseen by Stone and Linkov, be involved in oversight of risk governance for NM production and development? To do so, I turn to debates in risk governance on a second highly relevant concept: *Safety by Design*.

3.2.4 Safety by Design – risk governance to oversee 'safe' nano-innovation?

In Chapter 2, I showed how the established system of EU regulation is being rapidly outpaced by nanotechnological developments, resulting in this sector 'overflowing' its current regulatory boundaries (Bowman 2017; Stokes and Bowman 2012). Marchant *et al.*(2011b. p23) call this the 'pacing problem', whereby a growing gap is developing between this emerging technology and its legal-ethical oversight. Marchant *et al.* believe that governments are more static that dynamic in these situations, and the potential for a traditional regulatory approach to catch up is not promising. Therefore, researchers are increasingly advocating the need for new perspectives to steer the transition from nano-safety being simply about regulatory controls, to embracing its socio-ethical dimensions within a new taxonomy for the safe and responsible development of nano-innovation (see for example Gottardo *et al.* 2017). One potentially viable approach of addressing this challenge is Safety by Design (SbD). SbD emerged in process engineering but is now applied across disparate technological platforms including pharmaceuticals, computers, and aerospace industries (Kraegeloh *et al.*2018). It

seeks to provide an operational map for directing new products from the discovery stage to commercialization as efficiently and effectively as possible (Cooper 2001). In its stage-gating form, it fits well with the modern manufacturing value chain pathway where, at each stage, progress is tested against selected parameters such as occupational and consumer risks/safety, economic viability, product quality parameters, operational feasibility, and product marketability (Cooper 2018). If any of these tests fail, then the prospective product may be deemed unsuccessful and a decision taken to discontinue development.

Importantly, SbD is already established as an important concept within EU funded research projects to achieve 'regulatory preparedness' for nano-innovation (JRC 2018; NanoReG2 http://www.nanoreg.eu/; GRACIOUS https://www.h2020gracious.eu/ ProSAFE http://www.h202-prosafe.eu/), and 'Safe Innovation Approach' (Noorlander 2019). SbD is acting in an analytical risk assessment capacity, as a proposed new pillar for REACH NM regulatory control (Gottardo *et al.* 2017). In this role, SbD addresses the temporal discrepancy described by Owen *et al.* (2009), as the difference between market readiness and full understanding of all potential risks. In doing so, kits application contributes to the 'early warnings' for adverse EHS impacts that the European Environment Agency has identified as necessary for all novel technologies (EEA 2013). In this context, Gottardo *et al.* (2017. p102) defines SbD as "a process that considers and incorporates safety considerations into product design and development, by addressing the functionality of a material and its toxicity in an integrated way".

However, applying SbD this way is I argue a wasted opportunity, in that its effect is simply reflecting the demands regulators place on applied science, to provide quantitative probabilistic data on novel NM for decision-making under REACH. In doing so, it perpetuates the narrow normative definition of 'safety' that is central to established regulation. Crucially,

there is no intention that this decision-making takes a broader deliberative approach which could incorporate multiple normative values (e.g. societal concerns and values) into the decision-making process. Instead, the European Commission foresees decision-making and decision-taking on NM approvals being conducted within the traditional Expert Groupings (NANoREG2 D6.03 http://www.nanoreg.eu/). I argue that an opportunity is being missed here to use SbD in a more creative and far-reaching way. Namely, to redesign and refocus the current narrow regulatory approach so that it is participative and inclusive of non-experts including civil society as foreseen in EC Strategy Objective 3. This is supported by Ribeiro *et al.*(2018) who consider that aligning technical programmes with societal goals will allow a shaping of the innovation process, lessening the chances of technology 'lock-ins' and pathway dependencies. Similarly, Nordmann (2018.p335) notes the importance of societal alignment in technological development, leading to "more horizontal relationships with a constant negotiation over the needs and concerns of diverse actors". I develop this deliberative application of SbD at length in Chapter 6 as a new concept: Safety by Social Design (SbSD).

Risk governance, therefore, provides a range of theoretical concepts that can be used to interrogate REACH's NM approvals process and to consider the effectiveness of implementation of the three *NanoStrategy* objectives. However, in foreseeing future risks associated with the development of entirely new NM, another theoretical approach is required to identify how these can be addressed as part of R&D practices: namely anticipatory governance. I consider this next.

3.3 Anticipatory Governance of Nanomaterials

This study seeks to answer whether EU risk governance can be progressed from its current traditional risk management methodology (chiefly a precautionary mode) to one of

anticipatory risk prevention, where safer alternatives are considered at an early, upstream stage in the innovation process (Malloy *et al.* 2016). Jasanoff (2016) argues that a contributory factor in failing to identify unintended future consequences from novel technologies is that design and R&D processes are rarely if ever exposed to public scrutiny. Jahnel (2015*b*) similarly contends that adopting socio-ethical approaches to scrutinizing technological development would confer a democratic quality on risk management decision-making, and a procedural legitimacy to any new technologies that are forthcoming. Both authors foreground the need for foresighting in the policy process, which is the focus of a second strand of governance inquiry, namely anticipatory governance. This can be defined as "a broad-based capacity extended through society that can act on a variety of inputs to manage emerging knowledge -based technologies while such management is still possible" (Guston 2014. p204).

Genus and Stirling (2018.p62) characterise "anticipatory" as: *a pragmatic means of exploring value-laden positions of society to reduce the indeterminacy of future unintended consequences and impacts*. This implies that being anticipatory is not a substitute for accurate forecasting of predicted consequences and outcomes, but instead recognises our limited capacity to shape innovation for plausible futures (Guston 2013b). Despite this limitation, the aim of Objective 3 of the EC *NanoStrategy* is to incorporate socio-ethical considerations into nano-risk management. Grumwald (2011) notes that to achieve this requires developing appropriate tools and methodologies which can be incorporated within R&D processes to shape the innovation process, rather than the technology itself. Such anticipatory approaches have their origins in EU environmental law, such as the Precautionary Principle (PP) which is both precautionary and deliberative in its actions (COM 2000), and which I shall discuss next.

3.3.1 The Precautionary Principle and Anticipation

From the discussion in Chapter 2, it could be concluded that PP is generally used solely for risk minimisation, i.e. in a precautionary mode. In fact, Gottardo *et al.* (2017. p100) appear to confirm this conclusion by their explicit description of the role of SbD within the NanoREG 2 project as: 'it forms an exemplary platform for the early stage application of the **precautionary principle** in R&D projects…. Including precautionary measures and tools…..' However, this narrow interpretation of the utility of PP is in contrast to the fact that it was also designed to have an explicit anticipatory purpose which is deliberative and future facing, on which I want to briefly comment.

The EC Communication on the Precautionary Principle (COMM 2000.p6) is explicit not only that it requires the scientific evaluation of risk, but ' all interested parties should be involved to the fullest extent possible in the study of various risk management options that may be envisaged once the results of the scientific evaluation and/or risk assessment are available and the procedure be as transparent as possible.'

With this in mind, Von Schomberg (2006) sees the PP as deliberative as well as precautionary in scope across a range of normative dimensions. Here the term normative refers "*to all the prescriptive statements and/ or value judgements in contrast to factual scientific statements"* (Von Schomberg 2006.p33). Von Schomberg's inference is that the PP can provide a platform for technology mediated normative interactions by stakeholders, allowing for their participation in decision-making and problem solving. Building on von Schomberg (2006), Reber (2018), Genus and Iskandarova (2018) and Von Schomberg (2014) offer contemporary interpretations of PP that are both anticipatory as well as precautionary in their operation. By virtue of its anticipatory characteristics, they argue that PP is in fact a precursor of Responsible Research and Innovation (RRI), as both practices are future facing, safety is the

fundamental concern, they act in both precautionary and anticipatory modes, and are adaptable to multi-level stakeholder participation.

3.3.2 The role of Responsible Research and Innovation in Anticipatory Governance

The roots of RRI lie in seminal publications in science and society (Jasanoff 2004; Latour 1993) and following on from the work on Constructive Technology Assessment (Schot and Rip 1997), and Real-Time Technology Assessment (Guston and Sarewitz 2002) that connects science and technology studies with social science and policy issues. However, RRI has a broader scope than either of the concepts above, as it comprises socio-ethical as well as wider governance issues (Burget *et al.* 2017). Its policy importance is reflected in its appearance in the EU 6th and 7th Research Frameworks of *Horizon 2020,* with the purpose of progressing risk debates, beyond limiting techno-scientific and economic considerations (e.g. cost-benefit analysis), towards a more broadly-based deliberatively driven innovation policy (Felt 2014; Levidow and Neubauer 2014; Stahl 2013). Academic debate on the RRI concept has been led by Owen *et al.* (2013) and Stilgoe *et al.* (2013), providing focussed and concise definitions and understandings of Responsible Innovation.

Nonetheless, separate policy debates on RRI emerged in the EU Rome Declaration (21st November 2014). This Declaration defines RRI as how "societal actors work together during the whole research and innovation process in order to better align both the process and its outcomes with the values, needs and expectations of European Society" (Rome Declaration 2014 .p1). This definition takes 'responsible' to have a meaning beyond that of obligations for minimum statutory compliance, or simply a tacit understanding of the need to act 'responsibly' (Solbu 2015).

Yet beyond these policy circles the RRI concept is barely known, and certainly lacks traction with NM and nano-industry practice (van de Poel *et al.* 2017; Auer and Jamia 2017). Roig (2018) suggest that currently there are two drawbacks in promoting industry recognition and adoption. First is that RRI is used on an *ad hoc* basis as it is without any statutory formality. Secondly, and closely related to the first point, there is no accepted template for the implementation of RRI in innovation contexts. This is problematic as a key aim for RRI under the Rome Declaration (2014) is to contribute to delivering smart, sustainable, inclusive solutions to our societal challenges. Moreover, RRI lacks the practical framework that would allow its implementation in a variety of research and industry settings (Goujon 2016; Antelo 2016; Wickson and Carew 2014), while its process steps are highly problematic (Burget *et al.* 2017; Blok and Lemmens 2015).

If RRI is to move from being an engaging but impractical idea to practical implementation, then a risk governance framework must be devised in which it can have a practical application. This needs to be in the form of a framework for implementation that is readily understandable by academia and industry (Winickoff 2016). In my own experience at RRI conferences and workshops, it is this lack of an authoritative and accepted operational framework or roadmap which is understood to be its single biggest deficit (in fact, this was a significant discussion point at an RRI conference I attended at the European Parliament in January 2016).

The lack of industry engagement continues to be a problem for RRI. Shelly-Egan (2016) believes that RRI has traction at the macro scale (International & National Governments) and meso scale (International Organisations e.g. OECD, and research funders such as EPSRC) but has made little progress at the micro scale (Research labs, SMEs). Though Valdivia and Guston (2015) believe RRI is compatible with the role of markets, they also acknowledge that social interaction costs must be factored into the overall cost base for nano-innovation and must be

an additional cost overhead for cash strapped enterprises. In particular, SMEs struggle to implement 'soft law' initiatives due to corporate pressures, limited finances, and their distrust of the reliability, measurability, and business value of the RRI outcomes (Roig 2018; van de Poel and Robaey 2017). Thus, the imposition of extra innovation costs is thus likely to create further barriers in attracting business investment partners to the nano industry projects (Friedrichs 2014, European Risk Forum 2014).

On a more optimistic note, van de Poel *et al.* (2017) believe that industries are committing to more socially orientated outlooks, with a gradual movement to social alignment included in Corporate Social Responsibility (CSR) policies and business plans (e.g. sustainable products). So, this groundswell towards more socially aligned business activities may provide opportunities to identify missing links in industry contemporary thinking and best practice in respect of RRI. With the purpose to illustrate that it can have the potential for mutually beneficial outcomes to both the business and consumer**.**

I draw five conclusions from this debate. First is that RRI has been adopted formally within critical EU policy documents (*Horizon* 2010; Rome Declaration 2014) as a central policy driver for societal alignment of innovation. Secondly, RRI currently lacks an accepted operational framework appropriate for various R&D settings. Thirdly, it recognises that nano innovation is not the work of single individuals but is shared collectively among multiple actors for socio-ethical outcomes (scientists, technologists, investors, manufacturers, marketers, retailers, consumer groups). Fourthly, there is a lack of engagement with industry particularly SMEs, with RRI being either invisible, misunderstood, or simply ignored because of more pressing temporal, financial, technological and market-based pressures. Finally, to offset the predicted additional social interaction costs, there may be a need for incentives, governmental or others, to encourage active R&D engagement and adoption of RRI.

Having considered the potential role of RRI in anticipatory governance, I now conclude by considering where and how RRI might be implemented in the NM production process.

3.3.3 Midstream modulation – the upstream management of risk

The Collingridge Dilemma (1980.p11) states that if policy interventions occur too early, they potentially deter development of promising new technologies; if too late, then technology lock-in or path dependencies can occur. By 'path dependencies' I mean "*decisions dependent on past knowledge trajectories and that are limited by current competencies"* (Nordmann 2018. p334). Consequently, the timing of the testing is important, yet it is in the early stages of innovation that there is the greatest opportunity for control. The delicate balance to be achieved is not to be too risk averse at this point in the product development (Jasanoff 2016; Owen *et al.* 2013), to late and it contributes to the pacing problem previously discussed above (Thier 2018). By applying a 'mid-stream modulation' approach, where societal concerns are brought into contact with innovation processes upstream of regulatory controls and market selection, therefore, offers the best opportunity to pragmatically influence the safe development of NM (Flipse and van de Loo 2018; Lukovics and Fisher 2017; Flipse *et al.* 2013; Fisher, Mahajan and Mitcham 2006, Schot and Rip 1997).

The identification of the 'right' moment for RRI intervention is not easily determined. Nordmann (2018) suggests that this may need to be a graduated process over separate stages of the innovation process. Whatever the point of intervention, midstream modulation aims to enhance responsive capacity, by asking interdisciplinary stakeholders to reflect on the social and ethical aspects of the proposed nanotechnological development (Boer *et al.* 2018). Fisher, Mahajan and Mitcham (2006) define the role of 'midstream' as providing a focus on R&D governance in a societal context rather than simply on technoscientific considerations. They consider that upstream must be carefully calibrated to avoid too early interventions, or

too late when the downstream focus and activity becomes engulfed in passing regulatory hurdles and market selection. 'Modulation' refers to consequent reflexive actions to modify the direction of the innovation pathways (Flipse and van de Loo 2017; Fisher, Mahajan, and Mitcham 2006).

Consequently, mid-stream modulation not only supports improved risk governance by allowing flexibility for decision-making in innovation, it also responds pragmatically to the risk versus benefit challenges of the commercial context (Von Schonburg 2014). It is both reflexive and deliberative, encourages risk governance from within the innovation process, and gives rise to goal directed modulation (Fisher *et al.* 2006). However, the barriers to effective RRI engagement must not be under-estimated (e.g. poor communication strategies; limited knowledge of complex science). These can foster an undermining of trust amongst actors involved (Kuzma and Roberts 2018), particularly as innovation trajectories are rarely linear, and often messy activities (Krabbenborg and Mulder 2015).

Nonetheless a crucial question is whether NM industries will respond positively to what will be an extra temporal and financial burden, without a clear business advantage? The industry-based European Industrial Research Management Association (2015), believes that business can respond positively to RRI, but will need to develop new organisational and communication competencies. These could include building business orientated models incorporating RRI with their stakeholder network(s), focused on social-ethical growth, innovation and sustainability as new corporate goals**.**

3.4 Conclusions

I have reviewed two strands of governance literature to provide the conceptual underpinning for the empirical analysis in subsequent Chapters of this thesis. I have shown, first, how the

Taxonomy of Regulation identifies a wealth of policy tools available to regulators, offering multiple ways of bringing together hierarchical, market-based and networked policy tools and regulatory controls for NM. I then proceeded to outline how risk governance (analytical-deliberative and integrated risk governance) concepts can be coupled with insights from anticipatory governance (three concepts identified were the Precautionary Principle (PP), Safety by Design (SbD), and Responsible Research and Innovation (RRI)). Importantly, I have identified from the literature that these concepts are closely related theoretically, and, therefore, have high complementarity in public policy terms. The important link here is the Precautionary Principle, which Reber (2018), Genus and Iskandarova (2018) and Von Schomberg (2014) all claim is a precursor to RRI. Similarly, Gottardo *et al.* (2017), Kraegeloh *et al.* (2018) and Suarez-Marino *et al.* (2017) all note the Precautionary Principle is an essential driver of the Safety by Design concept.

Consequently, in Figure 3.2 below, I outline an 'ideal type model' schematic which illustrates the linkages between three concepts previously discussed, which I propose will have leading roles in this thesis for empirical examination of the governance of the safe and responsible development of NM.

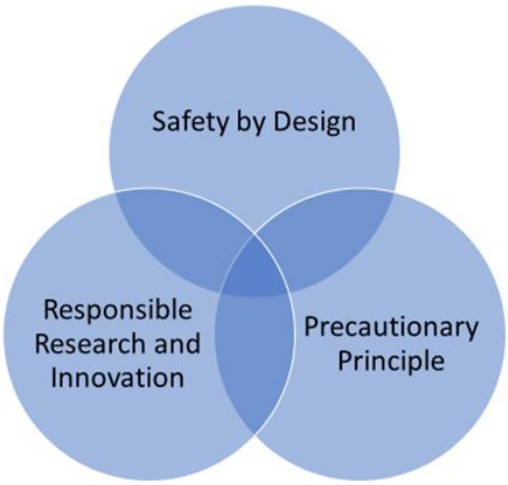


Figure 3.2: Schematic of the 'ideal type model' conceptual intersections for the governance of the safe and responsible development of Nanomaterials

The schematic provides conceptual pointers to an iterative process of EU policy progression to achieve its aim for the safe and responsible development of NM. The Precautionary Principle can be viewed as a proto-typical aspect of anticipatory governance whose highly developed precautionary features have tended to disguise its equally significant, if much less well-known, deliberative intentions (COM2000). The importance of Safety by Design in NM regulation is gathering momentum, with its role in developing 'regulatory preparedness' for nano-safety now foregrounded by the EU (JRC 2018; NanoReG2 http://www.nanoreg.eu/; ProSAFE http://www.h202-prosafe.eu/; GRACIOUS https://www.h2020gracious.eu/). The influence of the PP within SbD offers the prospect of a meso-level approach to anticipatory governance. However, by bringing RRI into play as a third element, there is the prospect for the anticipatory governance of NM by integrating public perceptions in the nano innovation process. I argue that, if these three elements can be harnessed effectively and implemented efficiently by industry, NM development could be viewed by publics as proceeding in a socially

acceptable, ethical and legitimate manner (RIVM Report 2014; Renn and Grobje 2010). Clearly this is an important component of this research and is discussed in detail in later Chapters.

Chapter 4: Methodology

4.1 Introduction

In this Chapter, I identify my research theoretical framing, the research design, its implementation methods and my own positionality. Central to the research is the primary empirical data that I have collected from selected expert actors actively engaged with nanotechnologies. But, firstly, I identify the theoretical framing within which I have conducted my research.

4.2 Theoretical Framing for my research design

I have primarily adopted an Inductive approach based on Grounded Theory i.e. theory development 'grounded' in the data collected (Glaser and Strauss 1967). This approach allows me the opportunity to progress inductively from observations to theory generation (Robson and McCartan 2016), and to offer novel perspectives resulting from my own systematic data analysis (Saunders *et al.* 2012). This study is exploratory in its methodology, in seeking to inductively fill existing knowledge gaps identified from the literatures and the respondents (Kumar 2014; Saunders *et al.* 2012; Gallagher 2010; Churchill 1999). It is an appropriate methodology for developing an anticipatory approach for nano risk governance, which is acknowledged to be multi-dimensional in its practice (Guston 2014; Von Schomberg 2013; Stilgoe *et al.* 2013;Owen *et al.* 2013). The reason is that it requires the adaptation and integration of EU policy, regulation, and its underpinning science with deliberative actions. This is in response to the multiplicity of diverse factors that can impact on the safeguarding of nano products. Consequently, this research is qualitative in design, using softer instruments for data gathering such as observations and interviews (Gallagher 2010;

McDaniel and Gates 2006; Churchill and Iacobucci 2005). I have summarised this framing in Figure 4.1 below.

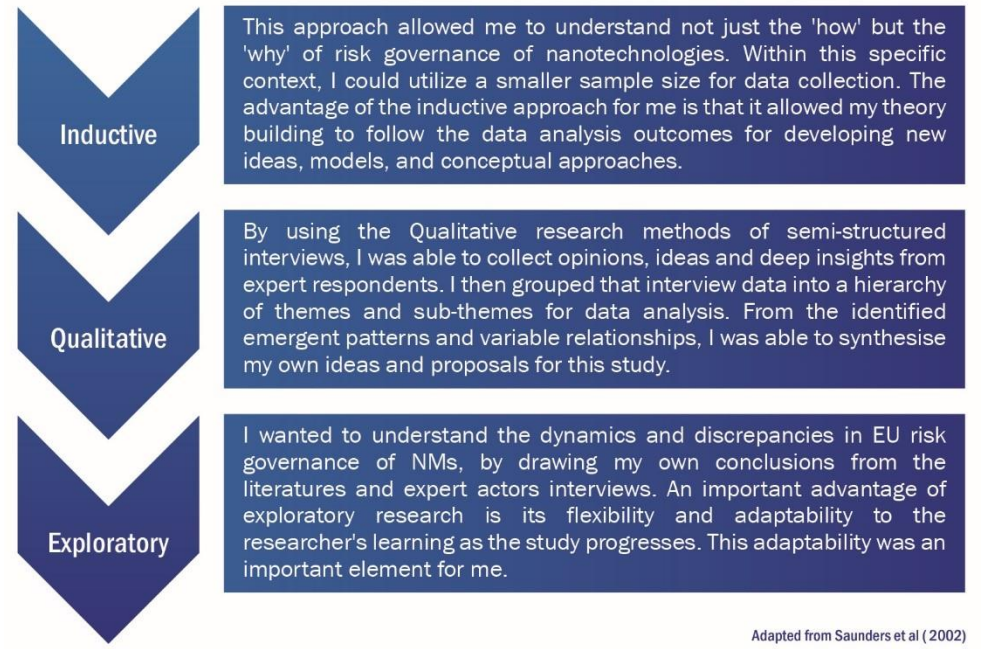


Figure 4.1: Primary theoretical Framing for Research Design

In conclusion, this type of design framework allows research flexibility and adaptability, in responding to changes identified from new, pertinent insights that emerged from the research process (Saunders *et al.* 2016, 2012). The adoption of this qualitative research approach has allowed flexibility and adaptability in the methodology in response to the evolving nature of the study (Mahapatra 2016), with the disaggregation of the raw interview data into meaningful groupings for comprehensive analysis, linkages, relationships and emergent patterns (Patton 2015; Kumar 2014; Saunders *et al.* 2012; Hsieh and Shannon 2005). With my own learning from the emergent themes, patterns and relationships, then allowing me to make appropriate adjustments for future data collection (Mach *et al*.2005; Saunders *et al.* 2002).

Notwithstanding the above, because Induction exploration involves inference as to the best possible explanation i.e. conclusions based on the available evidence to support the subsequent reasoning (Robson and McCartan 2016), these explanations can be contested by contradictory cases (SAGE Encyclopaedia of Qualitative Research 2008 p.429). Consequently, to mitigate this possibility, Patton (2015) and the SAGE Encyclopaedia (2008) recommend a mixed methods methodology, whereby the Inductive reasoning is supported by the secondary approach of Deductive evaluation from other information sources to test and support the study conclusions. Therefore, the validity of the reasoning can be tested by recourse to triangulation and evaluation of the study findings against existing published research, briefing papers, professional/industry guidance and practices, and other relevant data sources (Patton 2015; SAGE Encyclopaedia 2008). This deductive approach will be applied, in later chapters, in tandem with the inductive evaluation of the empirical findings, with both approaches contributing to the final study conclusions.

In the next section, I follow on from this explanation of the theoretical framing to discuss the detail of my research design. Specifically, the processes for the data collection and data analysis.

4.3 Research Design

4.3.1 Introduction

The forming theories for this study are risk governance and anticipatory governance, and I needed to develop a research design that allowed me to test their dynamics and discrepancies as identified in Chapters 2 and 3. In this section, I identify the methods and procedures which I used to collect and analyse the data from respondents (Kumar 2014). The research framework, in Figure 4.2 below , provides an overview of the plan for data collection,

its analysis and interpretation to address my research objectives (Hair *et al.* 2003). It provides a hierarchy of relationships between the research theory, design, implementation with the methods selected.

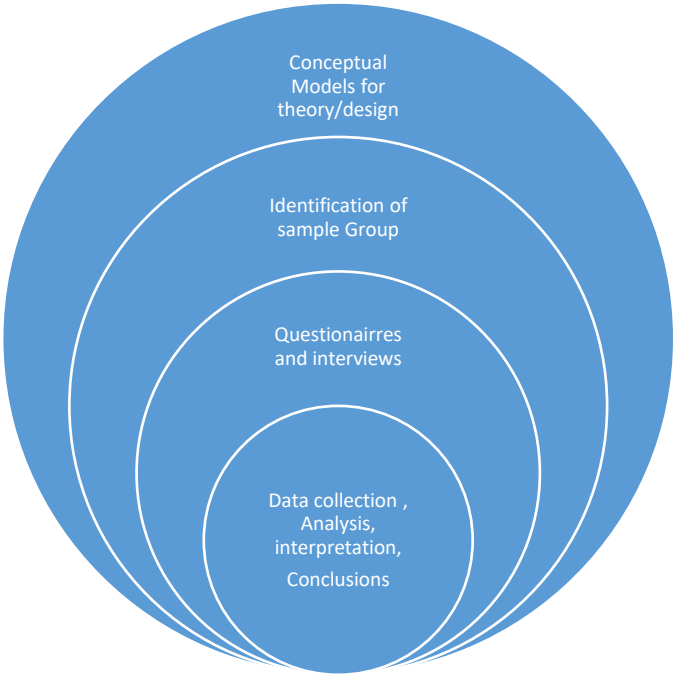


Figure 4.2. Research Framework :adapted from Saunders *et al*. (2012)

Figure 4.2 illustrates that within this framework hierarchy, each step influences the step that follows. Once the theoretical framing for the research design and its methods have been selected, then follows the task of the implementation of that design plan. This is of a critical importance as, ultimately, the quality of the data collected is dependent on developing the appropriate design and implementing it correctly.

4.3.2 Semi-structured Interviews

When reviewing the possible methods for gathering empirical data for this study, I considered the options for data gathering. These included the self- administered survey questionnaire circulated to as many prospective respondents as could be identified, either in hard copy or online. But this has a low response rate, offers little options for supplementary questions, and interesting and insightful responses are difficult to pursue in any depth (Saunders *et al.* 2012).

Consequently, I selected the semi-structured interview as offering the opportunity to ask questions on the key themes/concepts, develop new lines of enquiry, and delve deeper into idiosyncratic responses during the interview process itself (Kumar 2014; Saunders *et al.* 2012). This approach offered to me the flexibility and adaptability to apply discretion to amend questions, depending on the sectoral interest of the interviewee, redirect the flow of the conversation, and probe new insights as they arose (Jankowicz 2005; Sekaran 2003). Reflecting back on my experience of this process, this flexibility was essential as each interview proved to be slightly different. The face to face interviews offered a rich source of information, explanations, with new and unexpected insights. They also allowed me to project my own enthusiasm and commitment for my research, establish my credibility, and develop a good rapport. (Sekaran 2003).

4.3.3 Development of the Questionnaire

The semi-structured interview method allowed me the opportunity to develop my own research schedule of questions. It allows for consistency in approach, but with flexibility in response to divergent expert knowledge, individual experiences and opinions (Savath *et al.* 2013). My starting point was the development of a draft questionnaire reflecting the critical issues identified from the literatures in Chapters 2 and 3. Then I considered customizing the questionnaires for the different sectoral interests, but this proved to lack applicability due to the diversity of interests even within the individual groupings e.g. academia. A further option was to provide a separate set of individualized questions for each interviewee e.g. by reading up on their published papers, but this proved to be logistically impractical.

Instead, I developed an 'adaptable approach' (Mach *et al.* 2005) for a common framework of questions (see Appendix A). This became more of an abridged 'menu' from which the interviewees could select the key topic areas in which they felt competent to make responses.

For example, social scientists could discuss in depth the concept of Responsible Research and Innovation, but not multi-cellular assay techniques. This questionnaire was shared in advance and acted as the base point for all discussions. I provided additional information or documents, as appropriate, to the interviewee on their expert subject area. For example, a key reference document in this study is the novel Toxicological Paradigm (see Figure 2.1, Chapter 2) which was a helpful heuristic in discussions with environmental nanoscientists, toxicologists, government policy makers, regulators, and industry. But, of little value, when interviewing social scientists other than demonstrating deontological alternatives exist to traditional animal based regulatory testing. I would also make the point that whilst the 'menu' simplified the interview process, I undertook considerable advance research for each interviewee on their organisation, policies, briefings and published papers. The purpose was a familiarization process to establish an easier personal rapport, to show respect for their positions, and to smooth the interview process. In the next section I will discuss the process for my framing and construction of those interview questions provide in the abridged questionnaire.

4.3.4 Constructing the Interview Questions

The framing for the questions needed to reflect the research objectives for this study, identify any policy and regulatory lacuna, and current gaps in science and technology knowledge and practice. (see Appendix A for the Research Schedule of Questions). A first example is Research Objective 1 (RO1) which is '*to critically review whether the current EU chemical safety regulations (REACH) provide acceptable public environmental health assurances for nano-safety'.*

The term 'acceptable' is defined by the Oxford English Dictionary as 'tolerable or allowable within prescribed parameters 'e.g. cost-benefit analysis (OED online https://www.oed.com/).

Without specific parameters, it can be ambiguous in its interpretation, but it is a common descriptor in policy, legal and many risk- based situations. For example, it is found in the REACH Annexes XI para 1.1.1(1) and Annex XIV para 3(1) in respect of reducing risks to 'acceptable' levels. Three key EC Scientific Committees (SCHER, SCENHIR and SCCS), in their 2013 joint report into 'new challenges for risk assessment', identified that there continues to be no adopted definition of 'acceptable' risk by the EU. This report concluded that individual understanding of 'acceptable' may be based subjectively on conservative and non-scientifically derived factors, that are not easily avoidable, as well as validated risk assessment data. Consequently, with 55 respondents interviewed from six sectoral groups and their sub-groups, I recognised that their responses/opinions would be subjectively framed, but within the parameters of their own experience due to their differing backgrounds, education and experiential learning. The three RO1 questions in the Schedule of Questions do not specifically use this term but, in the interview responses, this term is regularly used by respondents. Consequently, I have interpreted its meaning for the respondents data in accordance with the above OED definition above i.e. 'tolerable or allowable' when synthesising my conclusions.

Relevant questions have been developed relating to RO1 for inclusion in the questionnaire that have arisen from the literatures. For example, the EC definition of a NP, proposed in 2011, is still not formally approved, with no given date for the next public consultation (EUR 27240 EN). As I pointed out in Chapter 2, if you cannot scientifically identify a NP with accuracy, then you cannot enforce relevant legislation. Secondly, I was able to establish there are significant criticisms of REACH for its lack of nano specificity in its testing protocols. This is an issue of critical importance as it must undermine the efficacy of REACH for assuring public environmental health safety. Thirdly, there are cross -sectoral criticisms regarding the over- application of the precautionary principle (PP) for hazard rather than evidence- based

risk situations. The treaty bounded PP is central to the EU policy goal of achieving a high level of human and environmental health safety. It is important to test whether an over-application of hazard-based approaches, instead of evidence -based risk, are a response to the inadequacy of current regulatory controls.

Research Objective 2 (RO2), aims ' to determine to what extent can existing and emerging scientific methods, tools and models provide for future competent risk analysis of nanomaterials'. In Chapter 2, I discuss that traditional toxicological animal testing is criticised for potentially flawed single probalistic tests (false positives/negatives). The questionnaire examines the prospects for their replacement with novel alternative scientific tools and toxicological paradigms to generate a 'weight of evidence approach'. As well as their potential to contribute to activate the implementation of the Safety by Design conceptual approach within nano R&D practices.

Finally, Research Objective 3 (RO3) aims 'to consider the development of a deliberative model to facilitate socio-ethical considerations for safe design into nano risk management'. The role of RRI is foregrounded in Chapter 3 as the principal EU policy mechanism to facilitate this change. In that Chapter, I discuss the EU intention for RRI to play a de facto policy role in the co-regulation of techno-scientific innovations for both safe and responsible innovation. But, there continuous to be an important policy omission, in that there is no accepted template proposed for the implementation of RRI into innovation practices. So, discussing the role that RRI might play, as a bridging mechanism for normative values to facilitate the safe design of NM, is a key part of the interview.

So, in conclusion, I have provided the framings for the interview questions which have been identified from the literature reviews. The detailed questions are provided in Appendix A for

this Chapter. In the next sections I will discuss the issues regarding the sample selection, its composition and its size.

4.3.5 Sample Selection.

In Chapter 1, I foregrounded Funtowicz and Ravetz (1993) proposal for a *post-normal* scientific approach when traditional methodologies are ineffective for governance of emerging technologies as very relevant to this thesis. In such circumstances, this novel conception for the management of complex techno-scientific-related problems, recommends that the quality assurance of scientific inputs to the policy process requires an 'extended peer community' consisting of all those with a stake in the dialogue (Funtowicz and Ravetz 1993.p739). Ideally, *post-normal* science offered me a new research pathway to incorporate respondents beyond the traditional triple helix of government, industry and academia (Wiek *et al.* 2016) with the other identified nanotechnologies stakeholders.

Now the selection of the right actors to interview is critical to the success of this research project (Kumar 2014; Saunders *et al.* 2012). From the literatures, I identified key sectoral groups that have important influences and interests in the EU risk governance of nanotechnologies. I also identified the key sectoral groups from a series of publications by the OECD which related to issues on good governance, policy and practice for regulation and regulators (OECD 2013a, 2013c, 2014a, 2014b, 2015a, 2015c, 2015d). These documents identified that key experts would come from government, regulators, academic communities, nano industry and their representatives, jurisprudence, and non-governmental organisations (NGOs). Here, I define experts as individuals who are recognised as specialists in their field of study, are professionally established and well-recognised in their professional networks(Mahapatra 2016). But, as argued by Wynne (1998) and others e.g. Stilgoe (2006), people with science education or education in a particular discipline need not be the only experts who are

invited contributors. In that respect, the final group needed to achieve the recommended 'extended peer community', was to be inclusive of non-expert lay members. However, this opportunity was not available to me.

The reason is that at that time of finalising the research strategy (2013-14) the nanotechnologies community was still nascent, divided into discrete sectoral groups, without established cross community networks, or trusted environments where lay members could engage in collaborative discussions. In 2010, in the EC Special Eurobarometer Science and Technology Report on public opinion within EU member states, determined that less than 11% of citizens considered they had an understanding of the emerging science and technology innovations. The FP7 NanOpinion project (https://nanopinion-edu.eu/) launched in 2012 reported on its public engagement programme in 11 EU countries and, *inter alia*, concluded that there was little public understanding or engagement with nanotechnologies by the EU lay community. It also concluded that networks/trusted environments for better public understanding and collaborative actions were not visible.

So, without the necessary logistical resources to develop such a lay community network, my alternative response was to look to non-governmental organisations(NGOs), with a particular interest in nanotechnologies, to act as proxy representatives for lay opinions. Whilst this approach has gone some way to mitigate the absence of lay opinions, I have to accept there are limitations in applying this research in a *post-normal* context when lay stakeholders are not directly involved with the debates.

In respect of the other sectoral groups, my expectation was that each sectoral group would provide differing perspectives as to the current and future efficacy of EU risk governance instruments. My aspiration was that conversations with selected respondents, with their deep understanding of their own sector, would provide me with the fresh insights to inspire

novel ideas and solutions to reshape the current frameworks. But risk governance for nanotechnologies is a multifaceted topic, involving policy and regulation, interwoven with complex science and technology, across international boundaries, with continuing contested and conflicting interests. No single sectoral group, with their own vested interests, would be able to provide the detailed insights needed for a fully rounded perspective of the current efficacy of EU risk governance for NM.

From the OECD publications, I identified that respondents would need to be from a range of relevant contributory backgrounds, with the appropriate educational/professional backgrounds, and overlaid with relevant specialist experience in the nano world. By utilizing the findings from the OECD literatures, I aimed to interview 'expert' actors from the following sectors:

- Policy makers (Government and Legislators)
- Jurisprudence (Academic and Practicing Lawyers)
- Regulated entities (Industry)
- Regulatory agencies (ECHA, EFSA,HSE)
- Academia (Universities)
- Non-Governmental Organisations (NGOs)

So, my first sieve of the stakeholders was their separation into these distinct sectoral groups. Though there will be inevitable intersectoral overlaps in their interests (e.g. environmental lawyers advising nano industry clients). These overlaps may be collaborative at times, and in other times they may be conflicting (e.g. regulators advising or enforcing on industry). However, their sectoral viewpoints will have collectively shaped the current EU risk governance framework as it is today, and their voices will also influence its future shape and practices (Mabey and Salaman 1997).

It quickly became clear to me that within each sectoral group there are a sub-sets of different actors which would have to be teased out. A good example is the Industry group which differentiated from multi-national companies to small and medium companies (SME). In addition, the perspectives provided by national and international chemical trade organisations proved important. The reason is that they develop and promote policy viewpoints on behalf of significant numbers of member companies and represent them at EU governmental levels e.g. Nanotechnology Industry Association (NIA), European Chemical Industry Council (Cefic).

From my study of the grey literatures for Chapter 2, I concluded that, whilst being treaty-bounded to follow the same overarching EU policy and adopted regulation, the UK government and the EC had differences in policy weightings for hazard and risk for NM. Consequently, I decided to conduct separate interviews within relevant UK Government Departments (Dept of Business, Innovation and Skills and the Department of Environment, Food and Rural Affairs) and within key EC Directorate- Generals (Environment, Health and Food Safety-Santé, GROW, Joint Research Centre, and Research and Innovation).

I also needed to determine whether those differences of policy opinion at governmental level were reflected within the EU and UK regulatory agencies. At a European level, the European Chemicals Agency (ECHA) and the European Food Standards Agency (EFSA) are the principal enforcement agencies for nano related regulations. Within the UK, I needed to approach the Health and Safety Executive (HSE) and the Environment Agency (EA) are the designated Competent Authorities for REACH regulations.

As for the others sectoral groups, Savath and Brainard (2013) correctly predicted that the sub-sets within the academics grouping would be diversified. These included materials scientists, environmental nanoscientists, toxicologists, omics scientists, social scientists and

social philosophers. For the legal practitioners, I have labelled them as Jurisprudence as the discussions related more to the theory and construction of the EU legal framework rather than its detailed practice and enforcement. The sub-sets for this group were law academics and practicing environmental lawyers. The final stakeholder group is the Non-Governmental Organisations (NGOs), with few in number with specific interests in NM.

The one common issue I needed to take into account for all these groups is the question of Bias in their responses. The SAGE Encyclopaedia (2008.p60) refers to bia*s* as a predisposition or partiality, and Glaser (2002) believes that bias can be a threat to the validity of the study i.e. the factual soundness of the data, its interpretation and concluding findings. However, it is important not to confuse bias with error(Roulston and Shelton 2015), if the respondents subjectivity refers genuinely to their individuals experiences, feelings, opinions and preferences. The SAGE Encyclopaedia (2008) suggests these subjective responses can allow the individual to properly situate an objective problem and coherently apply the analysis to a real-world situations. This is the outcome I hoped to achieve from my interviews, but with necessary caveats. By this I mean, weighing differing sectoral viewpoints against each other when drawing my conclusions, by highlighting where they agree or disagree , explaining why and then justifying my own conclusions.

4.3.6 Sample Size

The application of qualitative research techniques generally allows for a relatively small number of interviews, with the nature and content of the interview being more important than the number of respondents (Zigmund *et al.* 2010; Jankowicz 2005). However, for the research to be authorative in its outcomes, the interviews needed to be in-depth, rich in data, and highly informative (Saunders *et al.* 2012, Creswell 2012). The logical relationship between

the sample selection technique and research focus is important. The sample size is dependent on a number of factors:

(a) What data is needed to answer the research questions?

(b) Will the participants provide credibility to the research outcomes?

(c) What can be achieved within the resources available?

Patton (2002)

These criteria are particularly relevant when collecting qualitative data using structured or semi-structured interviews (Saunders *et al.* 2012). Also, the validity of the results will be functions of the research design, the data collected and analytical process rather than the sample size (Patton 2002). Nevertheless, the literatures are not helpful on the important matter as to how many respondents should be interviewed. For example, for a general study at PhD level, Creswell (2009) suggests that 25-30 interviews may suffice, whilst Gerson and Horowitz (2002) suggest a minimum of 60 interviews. Saunders *et al.* (2012) suggest that where comparisons are to be made between heterogeneous groups, who will each be treated as a separate homogenous population, it will need to be of a significant size. Though no helpful metrics are offered for assistance to the researcher.

With no definite guidelines for non-probabilistic purposive sampling sizes, I adopted the suggestion that the researcher continues to interview until there is a sense of "data saturation" being reached (Bryman 2012, Saunders *et al.* 2012). That is, when the new data is simply confirming themes and conclusions already expressed and does not suggest new insights or theoretical categories. Though conceptually helpful, this idea provides little practical guidance as to the estimation of the sample size, and it finally came down to my discretion to make that judgement (Brannen *et al.* 2012, Saunders *et al.* 2012; Guest *et al.* 2006). The total respondents interviewed was 55 from the 72 approached.

Table 4-1: Breakdown of Respondents by Sector

Sector	Interviewed
UK/EU Government	12
Academic	20
UK/EU Regulators	3
NGO	3
Industry	14
Jurisprudence	3
Totals	55

Ideally, I would have preferred a more equal spread of numbers amongst the sectoral groups but there were difficulties in accessing some groupings which will be discussed later. The respondents included senior academics in philosophy, environmental nanoscience, nanotoxicology and jurisprudence (UK/EU/USA); senior governmental scientists and policy makers (UK/EU); industry included directors, chief executives and departmental heads in multi-national companies, SMEs and national/international chemical organisations (UK/EU); senior UK regulators; jurisprudence academic and environmental lawyers (UK/USA), and NGOs(UK/EU). The listing of the interviewees is giving in the Appendices for this Chapter.

In conclusion, the key sectoral groups for this research project were identified, in sufficient numbers, and were interviewed to provide a rich source of data for this study. In the next sections I will discuss the process of converting that raw data into useful formats for data analysis.

4.4 Data Analysis

4.4.1 Research Objectives, Propositions and supporting Conceptual models

The starting point for my analysis is how that data can be investigated so that I can achieve the research objectives for this study (Kumar 2014). These objectives are the explicit statements of what I need to know to be able to generate new insights on the forming theories for this study and their application to NM (Bryman 2012; Saunders *et al.* 2012; Jankowicz 2005). By generating and then utilizing my Research Objectives, I have been able to operationalize my enquiries into the effectiveness of the individual EC strategy risk governance objectives 1, 2, & 3 (Saunders *et al.* 2012; Jankowicz 2005). In Table 4-2 below, I have set out a progressing rationale for their framing within their testable propositions, and the supporting concepts from Chapter 3 to provide an analytical structure for data analysis. The propositions-based methods adopted here, provide testing mechanisms for empirical analysis in a structured manner to facilitate inductive reasoning from the primary data (Hoddy 2018).

Table 4-2: Research Objectives, Propositions and supporting Conceptual models

EC Objective	**Research Objectives**	**Propositions**	**Conceptual models**
EC Objective 1 Maximum use would be made of existing regulation though adjustments may be necessary	*Research Objective 1* To critically review whether the current EU chemical safety regulations (REACH) provide acceptable public environmental health assurances for nano-safety	*Proposition 1* 'Current EU chemical safety regulation does provide sufficient public environmental health protection from potential risks associated with nanomaterials.'	*Conceptual Frameworks* a).Taxonomy of Regulation (CEPS 2014) b).Analytical-Deliberative model (Rosa, McCright and Renn 2013) c)Precautionary Principle **(**COM 2000)

EC Objective	Research Objectives	Propositions	Conceptual models
EC Objective 2 Recognises that existing parameters for EHS chemical safety testing may not be appropriate for the unique properties of nanoparticles, requiring new methods and tools for risk assessment, and refinement of nano scale metrology and standardisation activities	*Research Objective 2* To determine to what extent can existing and emerging scientific methods, tools and models provide for future competent risk analysis of nanomaterials	*Proposition 2* 'That novel scientific tools and predictive paradigm(s) can provide future confidence for industry and regulators in nano-safety decision-making'	a).Analytical-Deliberative (Rosa, McCright and Renn 2013) b).Alternative Toxicological paradigm model (Nel *et al.* 2012)
EC Objective 3 The Risk Management paradigm to be expanded to incorporate socio-ethical considerations into the R&D process with the creation of a culture of responsibility which is participatory and inclusive	*Research Objective 3* To consider the development of a deliberative model to facilitate socio-ethical considerations for safe design into nano risk management	*Proposition 3* 'RRI can act as an anticipatory governance mechanism for embedding socio-ethical values for safe design within nano-innovation'	(a).Analytical-Deliberative (Rosa, McCright and Renn 2013*)* (b).Responsible Research and *Innovation.*(Rome Declaration 2014) (c) Safety by Design. (Gottardo *et al.* 2017) (d).Mid-stream Modulation (Fisher *et al.* 2006**)**

The testable propositions are informed by the literature analysis and findings from Chapters 2 and 3. These are arguments whose purpose is to test the veracity of those findings against the opinions and insights gained from the interview data. For example, Proposition 1 is addressing the fundamental criticism that REACH is currently unsuitable to be applied for

nano-safety due to its lack of nano specificity. For Proposition 2, current traditional animal testing protocols for regulatory purposes , with their single probalistic testing procedures, are challenged as being flawed and unethical. There is significant EU funding being invested in the discovery and development of novel replacement scientific techniques and toxicological paradigms. By applying Proposition 2 to the data, I am testing whether these new techniques and models can be judged to provide for future competent risk analysis. Finally, from Chapter 3, we learn that the RRI concept is regarded as the EU *de facto* policy mechanism for promoting the social alignment of nano innovation. This to be driven by an inclusive and participative process that can incorporate the socio-ethical concerns of non-expert and civil actors into an anticipatory approach for safe design. The purpose of Proposition 3 is to examine whether RRI can act as that bridging mechanism for anticipatory governance and, in doing so, influence their safe design.

In Figure 4.3 below, I illustrate the interdependence of the research objectives and the propositions in determining the overall efficacy of the current EU risk governance framework for achieving the key aim for the safe and responsible development of NM .

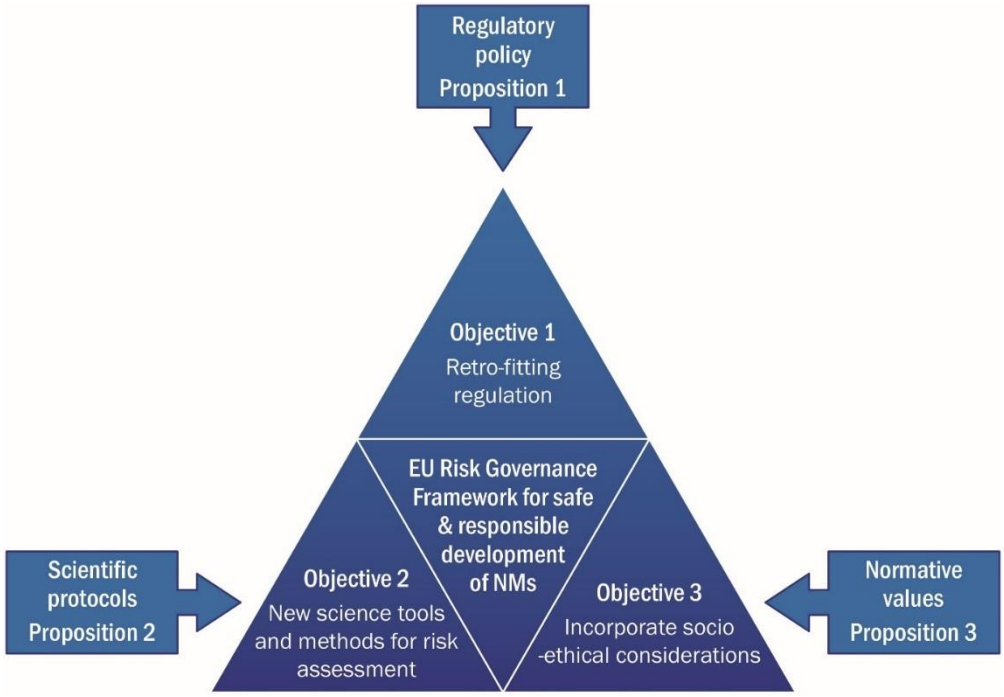


Figure 4.3. The interdependence of the Research Objectives and Propositions for determining the efficacy of the EU Risk Governance framework

In respect of the conceptual models, their purpose is to provide framings in which the data can be analyzed. They help to identify patterns and relationships to enable reasoning and learning that facilitate logical outcomes. As mentioned in Chapter 3, though not lineal in application, they do provide for a progressive evaluation for the data analysis. They allowed me to infer the implications from the study findings as to relevant current and novel theory and practice (Gallagher 2010). In addition, they have challenged me to develop a new, refined conceptual framework for EU risk governance of NM from the gathered empirical data (Grix 2010).

In the next sections, I will explain how I undertook the data management, coding and analysis of the raw data. I will illustrate how the structure for this research has been applied to provide answers to the questions posed by the research objectives and propositions.

4.4.2 Empirical Data Management and Coding

From experience, I learnt the benefits of early transcription and analysis of the individual interviews, while their freshness, subtleties and insights were still in my mind. Once gathered, the raw data then needed a process of management and analysis to support the inductive development of any theoretical explanations identified within the contexts for this research (Saunders *et al.* 2012). For this study, I utilized the *Nvivo* Data Management System for the systematic process of storing , coding, annotation and memoing of data. I identified 27 codes which I used for the separation, storage and organisation of the raw data collected.

The first step is the allocation of data for its categorization by dissecting it into component themes, sub-themes, open and axial codes. Then to endeavour to identify patterns and relationships between variables to support the generation of new or adapted theory (Bryman 2012; Saunders *et al.* 2012; Zikmund *et al.* 2010; Jankowicz 2005; Glaser and Straus 1967). To assist in this process, I developed a bespoke database using the *NVivo* Data Management System. Its purpose was for the storing, coding and manipulating of the primary empirical data, with a modifiable template of open coding for data organisation and analysis (see Appendix C to this Chapter). I followed a stepwise approach recommended by Taylor *et al.* (2013), by which I mean I used distinct steps to use the coding narrative as descriptors of the data characteristics and interactions given by the sectoral actors.

The process of identifying and selection of the themes and codes was a mixed approach. Braun and Clarke (2006) suggest that in an Inductive approach the themes should emerge from the data itself. I considered that the forming theories of Risk Governance and Anticipatory Governance are so prominent for this study that they should be pre- selected as the two key themes. Gray (2014) suggests that the nature of themes is to capture important meanings from the data that address the research questions being asked in the study. Both

these themes proved their case, from the amount of relevant data captured, that this was the correct decision. What did emerge from the data was the need for a major sub-theme for risk management (under the Risk Governance theme), due to the quantity of data emerging on that topic.

In respect of the coding, Straus and Corbin (1998.p62) define Open Coding as ' the naming and categorizing of phenomena through the examination of the data'. This is the process for the disaggregation, examination, comparison and categorizing the raw data (Gray 2014). Examples of open codes used are for *Current Regulation* and *Safety by Design* which are foregrounded in the interview data. In terms of Axial Coding, their purpose is to identify categories that make connections between different strands of data. Gray (2014) suggests this approach requires to be able to identify the context for those linkages, the actions and interactions and possible consequences. Examples that I used are *Fate, Behaviour, Exposure and Environmental Effects of NM* ; and *RRI and Safety by Design* .

In conclusion, I have designed within the *Nvivo* data management system the architecture for collating and categorizing the raw data into appropriate themes and codes. However, *Nvivo* does not provide the analytics for the exploration and critical evaluation of the categorized data. This has to be undertaken by myself applying specific techniques which I shall discuss next.

4.4.3 Directed Content Analysis of Data

The exploration of the gathered data was undertaken by applying *Directed Content Analysis* (DCA) (Hsieh and Shannon 2005). As mentioned in the literature review, there are already existing alternative paradigms available to apply to nanotechnologies, but which need proof of concept testing (e.g. Figure 2.1.- Toxicological profiling using a tiered approach for risk). So, what is required is an approach that will be a test bed for those available theories, which have

limited current application, due to uncertainties for their broad acceptance (Hsieh and Shannon 2005). In this case, Directed Content Analysis is defined by Hsieh and Shannon (2005. p1281) as 'a *research method for the subjective interpretation of the content of text data through the systematic classification process of coding and identifying themes and patterns'.* The goal for the researcher is by using this method to be able to validate or extend our understanding of current theory or theoretical framings.

DCA gave me the opportunity to validate existing theory, concepts and models or extend them conceptually. In essence, it involves making interpretations of the data by its systematic and objective induction into the thematic and coding categories (Gray 2014). The process commences with the identification from the literatures of key concepts or variables as initial theme or coding categories (e.g. Risk Governance, Anticipatory Governance). Then the identification of sub themes and/or open codes which emerged from both the literatures and respondents data (e.g. Current regulation, RRI). This coding approach promoted the development of a representative range of insights, interactions and explanatory concepts referred to by respondents.

My getting to know and understand the implications, explanations, and identifying further lines of enquiry from the data, is critical in the analytical process. I make the point above, that early personal transcription and review of the data provided the opportunity to closely scrutinize it whilst the discussions were still fresh in my mind. For me, this proved invaluable in developing my understanding and for the critical evaluation of the data. So, this thematic/coding approach was applied to ensure that a representative range of insights, interactions and explanatory concepts referred to by interviewees were captured. The final stage of the analysis involved the mapping, interpretation and synthesis of answers to the key research questions and propositions posed in this study. Whilst I made every effort to ensure

that the results truly reflected the attitudes, beliefs, and values of the participants (Srivastava & Thomson 2009).

I want to raise a final point regarding this type of research design, before I move on to the research implementation section. This is made by Creswell (2009), who views this type of qualitative research as more orientated towards credibility, authenticity and transparency rather than validity. Though agreeing with Creswell, Saunders *et al. (*2012) point out that such weakness can be offset by the strength in its inherent flexibility to new interview insights and then to explore complex issues in-depth. This I found to be an important outcome stemming from this research design.

4.5 Research Implementation

4.5.1 Selection of respondents and negotiating access

As I discussed in 4.2.4 above, I identified then differentiated the relevant sectoral groups for this study. The second stage was to identify and approach directly the potential participants. To be of real value to the study, they needed to be able to provide an information rich interview to allow me to gain theoretical as well as practical insights (Saunders *et al.* 2012). Flick (2009) suggests the need for relevant specialist background, knowledge, experience and skills to be able to do this. I did not wish to apply a randomized approach as I wished to select the most suitable candidates for interview (Patton 2002). Therefore, the selection was by non-probability sampling which relied on my identification or personal recommendation from others. As my research approach is to investigate within heterogeneous groupings, Jankowicz (2005) advises that this necessitates the application of common generic criteria in the selection process. I have set out in Figure 4.4 below , the common selection criteria that was applied in each case.

Figure 4.4. Criteria for Common Selection Characteristics for Respondents: Source: Jankowicz 2005

It is accepted that these criteria are broadly framed and, therefore, requires a greater reliance on my judgement in the selection process. In identifying suitable respondents, the major deficit was my lack of an active personal/professional network in the nanoscience and technology sectors. This proved to be a constant and difficult hurdle to overcome. Whilst my supervisors suggested suitable interviewees within their academic specialism, it was much more difficult to identify suitable candidates in UK / EU Governments, Regulators, Industry, Jurisprudence and NGOs sectors. This was eventually achieved by various means:

- Identifying key commentators from the literature reviews
- Attendance at nanotechnology conferences/seminars and workshops and identifying appropriate candidates to approach directly
- Respondents providing personal introductions or recommendations for other potential participants in their sector
- Webinars speakers on nanoscience and technology related subjects

Consequently, the method that I adopted was to combine two research approaches. Firstly, I followed the methodology example of Macnaghten and Chilvers (2014) and Savath and Brainard (2013) by selecting a Purposive sampling approach for examining heterogenous

groups. This allowed me to use my judgement on who to approach to provide information rich interviews (Gray 2014). Secondly, I applied Snowball sampling, in which colleagues and respondents shared their informal networks with me to recommend further potential candidates (Kumar 2014). This sampling technique is applied when it is difficult to identify members of a desired population, though it is not statistically representative of that total population (Saunders *et al.* 2012;Zigmund *et al.* 2010). For a nascent community, as is to be found in nanotechnologies, this proved to be the most appropriate and productive method to adopt.

Overall, the selection of respondents proved to be a difficult, protracted and frustrating task. Not all of those contacted were prepared to consent to interview, or often proved elusive in keeping pre-arranged appointments. In some cases, the delay was months in making before the interview was finally achieved. The personal learning for me is that snowball respondents require considerable effort to track down, then to pin down for interview dates (Kervin 1992). One very helpful commonality amongst those interviewed is that 95% had achieved doctoral status. This meant that once they had engaged with me, there was an often an empathy which was an important and positive element for obtaining a high-quality, in depth interview.

With much personal effort, and some timely introductions, I was able to undertake 55 interviews (schedule of interviews in Appendix B for the Chapter). But, despite the best efforts of myself and sympathetic others, it proved impossible to obtain a European regulatory perspective for NM directly from the European Chemicals Agency (ECHA) and the European Food Standards Agency (EFSA). Both declined repeated invitations to participate which is the major disappointment to me in this study. Finally, I was advised by an Executive Director of ECHA to approach the EC Joint Research Centre (JRC) with my request for interview on the EU regulatory issues for nano policy, risks, and safety. The JRC is the science portal for the EU

and, by lucky coincidence, I attended a conference where a suitable JRC representative kindly agreed to be interviewed. In addition, the respondents from the EC Directorates-General had close working relationships with ECHA or EFSA and were able to provide proxy insights into their regulatory thinking. So, I was able to triangulate information inductively and deductively for the ECHA and EFSA regulatory viewpoints from these proxy insights, their own websites, and their relevant publications (Saunders *et al.* 2012).

In conclusion, the selection of respondents was of critical importance to the success of this study and it proved to be very demanding process. To ensure that I could maximise the benefits from those interviews I decided to carry out a pilot study to finesse my approach which I discuss next.

4.5.2 Pilot Survey

Kumar (2014) suggests that when a researcher has limited knowledge of their study area that they should undertake a short pilot survey. The purpose of this approach is to develop, refine and test the research design and, in particular, the Schedule of Questions. I approached a small number of interviewees from different scientific disciplines to discuss my research approach and to test my draft questions. As I explained in 4.2.3 above, my initial approach was to provide a separate set of individualized questions for each interviewee, but I found that this would be logistically difficult and impractical because of the amount of time it required. Consequently, I developed an adaptable approach recommended by Mach *et al.* (2005), which by iteration, and the experience from the pilot study, I modified the original draft to a smaller list of common questions (see Appendix A). This abridged schedule became a menu from which the interviewees could select the topic areas in which they felt most competent to discuss. The Schedule of Questions was shared in advance of the interview and acted as the base point for discussions. I provided additional information or documents as

appropriate to the interviewee and their subject area. For example, a key reference document in this study is the novel '*Toxicological profiling using a Tiered approach for risk identification and characterization*' (see Figure 2.1, Chapter 2) which was relevant, and very helpful in discussions with some environmental nanoscientists, toxicologists, government policy makers, regulators, and industry. But of little value when interviewing social scientists, other than to demonstrate that alternatives exist to traditional animal based regulatory testing. In the next section, I will discuss the process I undertook to conduct interviews to obtain answers to those questions.

4.5.3 Conducting the Interview Process

Data gathering from an interview format has become a standard technique in qualitatively researching subjects of complexity (Denzin and Lincoln 2018). My standard approach was with open-ended questions to encourage respondents to offer their perspectives on the issues raised, with variations on the questions asked in accordance with the flow of the conversation (Denzin and Lincoln 2018; Easterby –Smith *et al.* 2008; Jankowicz 2005). This method also allows the interviewee to raise their own questions and objections within the interview process (Latour 2000). I was able to present relevant questions, observe, listen, interpret and respond to their answers, and to gain understanding for the reasoning behind the respondents attitudes and opinions (Saunders *et al.* 2012; Zigmund *et al.* 2010). I chose this interview approach as it most suited my research questions and my personal communication style (Jankowicz 2005).

However, as I progressed in my programme of interviews, I faced significant barriers to its completion. An important Confounding Factor is that this research has been conducted part time and incorporated within the confines of a busy business and family schedule. These extra-curricular demands provided constraints for time scheduling of the interviews. In

addition, some respondents were located in different countries, continents and time zones. So, to interview internationally based respondents in Europe or in the USA, face to face, ranged from the financially difficult to the impossible. Thankfully, modern technology provided the remedy in terms of Skype video or telephone calls. The interviews occurred across a spectrum of intercontinental time zones according to the convenience of the interviewee.

Table 4-3. Breakdown of the interview format

Face to Face	Skype Telephone	Skype Video
23	21	11

Table 4-3. provides a breakdown of numbers for each type of interview format. Every respondent was formally promised anonymity and that they would not be quoted publicly without their prior consent. This contributed to their being open and honest in their answers subject to any organisational constraints. For example, one interviewee, from an international aerospace company had an adjudicator present online to intercept any commercial confidentiality issues. In another instance, a regulator would not allow the taping of the interview, due to organisation rules, so hand notes had to be taken instead. I think the fact that so many interviewees had doctoral qualifications provided a spur to their generous co-operation with me. With their permission, each interview was audio recorded and then transcribed by me. The transcriptions required 225-250 hours of my time and were more problematic when the Skype signal was weak, or if English was a second language.

This labour was offset by my learning in terms of new, sometimes idiosyncratic insights. Almost without exception, I found the interviewing process to be a rewarding and valuable learning experience, and well worth the preceding effort. From many respondents, I felt I

benefited from a high level one to one tutorial from a subject expert in that field. This made up for the many frustrations that occurred in making those individual arrangements, by being a satisfying personal experiences in itself. However, I understand that those personal experiences, to a certain extent, are reflective of own positionality in relation to this research which I discuss next.

4.6 Positionality of the Researcher

Whilst I believe I have made every effort to accurately reflect the data collected from my respondents, no research investigation is neutral (Jankowicz 2005). My role as researcher was to capture the reality of the data and then interpret and accurately represent it (Holloway and Francis 2011). Chiseri- Slater (1996) believe that all researchers are shaped by their subjective–contextual factors such as their life history and experiences. They are positioned by their age, gender, race, class, nationality, personal circumstances and intellectual pre-disposition. Consequently, my Positionality must be regarded as an influencing factor on this research and it needs to be known, explained and understood by others.

My first degree was a BSc (Hons) in Environmental Health Sciences which took me into a practitioner career in local government, where I specialized in environmental risk management and environmental protection. This required a detailed understanding of risk management theory and strategy, relevant UK/EU legal frameworks, regulations, and compliance and enforcement processes and procedures. This included attending the law courts as an expert witness in prosecutions. At a later date, I supported the development of my managerial career with a Master's in Business Administration (MBA). This gave me a better insight into the business/ commercial sectors, and their responses to a variety of regulatory challenges. In 2003, I joined the University of Birmingham as Head of Teaching in

Environmental Health. At this time, the School was developing its research interest and capability in environmental nanoscience. This was a novel subject which caught my interest and, initially, I studied it more for personal than academic interest. Eventually, I gained sufficient understanding to be asked to lead knowledge transfer workshops and seminars for industry professionals and environmental health practitioners. It seemed a logical step for me to develop my academic interest into a PhD proposal. In 2013, I left the university to set up my own environmental health sciences consultancy which included clients with nanotechnology interests. This experience provided a deeper insight into the pressures and problems in organising and operating a privately-run profit -making business.

So, my professional background and experiences have fitted me with a number of positive attributes to make this study a success. Firstly, I am comfortable with the language of government, regulation and academia. I understand the politico-economic, policy, legal, and organisational structures in which they have to operate. The cross- linkages between the differing sectoral groups, and the strengths and weakness in their communication and collaborative processes. My own communication skills have been honed over my professional life in response to many external influences. They have proven to be an essential asset in the recruitment and interviewing of respondents.

In respect of this study, I realised I needed to develop my theoretical sensitivity which Glaser *et al.* (2004) say is essential for grounded theory studies. This requires the development of the ability to evaluate data by relating it to normal models of theory, and then synthesising it for novel emergent theory and conceptual approaches. This sensitivity is developed by a deep understanding of the relevant literatures for that subject area (Glaser 1978).

So, responding to this advice, I have accessed many differing sources of knowledge, information and published research from peer-reviewed academic writings and grey

literatures. As my own ideas have developed, during the timeline of this research project, I felt confident to contributed to the ongoing debates in this dynamic and contested research area. I have presented elements of my research findings at six international conferences during the period 2014-2018 (see Appendix D for full listing). I also attended as a delegate an influential two-day conference on Responsible Research and Innovation hosted in the European Parliament in 14th-15th January 2016 in Brussels. It offered renowned speakers presenting at plenary sessions or chairing workshops such as Arie Rip, Jeroen van de Hoven, Richard Owen and Philip Macnagthen. This event provided for me a richness of insights into the emerging and dominant themes for Science and Technology in Society (STS). Specifically, insights into EU RRI policy and its potential for facilitating safe and responsible innovation. But also evident were the conference frustrations regarding the urgent and unresolved need for an RRI operational template for industry, with the provision of a deliberative mechanism for responsible innovation.

The development of my theoretical sensitivity had an impact on my philosophical outlook, which had been forged by the critical examination of my personal and professional experiences. My longstanding approach had been one of direct personal observations, with careful evaluation of facts, as my way of verifying phenomenon and establishing the truth as I see it. This could be categorised as being 'positivistic' in my outlook (accepting only that which can be personally or scientifically verified). However, the hybridity of this study has necessarily taken me to the previously unknown world of social sciences. When matters have become less certain, more fluid and subjective in their interpretations. With a research approach that requires a more fundamental understanding of the meaning of experiences rather than simply their measurement and management. I would now interpret my philosophical stance as more representative of *Critical Realism* (Bashkar 1979, 1975). This

philosophy requires an acceptance that knowledge becomes meaningful by its relationship to some worldly entity. The critical realist questions what we are learning about in the world itself that makes knowledge possible, and what causal explanations can account for them. With that knowledge and causal explanations being open to revision by empirical research (Hoddy 2018).

In conclusion, this research project has caused a shifting in my own positionality in response to what I have learnt. Whilst I have consciously avoided any overt bias, there may be some element of unconscious bias in the conduct and conclusions to be found in this study. One of the objectives of applying for research ethical approval is to minimise such an effect which I shall briefly discuss next.

4.7 Ethics

Research needs to be undertaken within the ethical boundaries of the research organisation. The University of Birmingham sets out clear guidelines for the standards of behaviour for the researcher conduct in respect of its integrity, non-maleficence and voluntary nature. Ethical approval for this study was given by the University Ethics Committee.

An important condition for that approval is that the Informed Consent of individual participants must be obtained. For this study, anonymity was given without any conditions proffered, as was respecting wishes for prior consent before personal quotation in the thesis or future papers (this has not been necessary to date). Every respondent was briefed as to the purpose of the interview and a written Informed Consent pro-forma sent with other relevant information (see Appendix E). The very high proportion of respondents with a doctoral qualification meant little induction was necessary prior to the interviews themselves. The voluntary nature of the proceedings were emphasised, confidentiality and anonymity

assured, with the offer of a written copy of the transcript to be sent (which was only requested once). No issues of ethical significance emerged during the interview process.

4.8 Conclusions

The inductive/qualitative/exploratory approach has proven to be suitable, relevant and an adaptive component of my research methodology. The semi-structured interviews of carefully selected expert respondents has delivered the richness of data that I hoped for. The design and construction of the *Nvivo* data management system proved very time consuming but, ultimately worthwhile, in being able interrogate data held within easily accessible codes. The Directed Content Analysis demonstrated its suitability as a basis for constructing a novel conceptualized framework for the operationalization of RRI within the nano innovation process. It also influenced me to see this project as a treasure trove of data to be mined carefully and efficiently. I believe that this has been important and innovative learning to be taken from this research. In addition, there has been an evolution in my own personal philosophy, which was unexpected, but has contributed to the personal growth I have achieved during this project.

Chapter 5: Evaluating the efficacy of the EU risk governance of nanomaterials : The Strategy for Nanotechnologies from 2004

5.1 Introduction

In this first empirical Chapter, I evaluate the efficacy of the EU risk governance approach to promote the safe and responsible development of NM [COM(2004)338]. A critical assessment of the extent to which risk governance mechanisms are delivering on the *NanoStrategy's* three key objectives is presented, through semi-structured interviews, with experts drawn from the key stakeholder group sample outlined in Chapter 4. The risk governance instruments I discussed with these experts included relevant EU policies, regulations, and scientific research targeting the specific properties of and the safety concerns for NM.

I examine here the state of progress towards achieving the EC *Strategy's* Objectives 1 and 2 respectively. Using Rosa, McCright and Renn (2013) *Analytical-Deliberative* model, I classify these objectives as *analytically-oriented* (Table 3-2). Consequently, I have derived for each EC policy Objective a corresponding research proposition with which to test the primary data from respondents. My intention is to establish the inter-relations between the aspirational normative standards set out in the *NanoStrategy*, and the current on-the-ground empirical reality of risk governance of NM as perceived by leading industry, academic, regulatory and other stakeholders. To do so, I compare the stated objectives of the two research propositions with interview responses, enabling the two EC strategy objectives to be examined empirically (Saunders *et al.* 2016; Vaus 2002). The two propositions are as follows:

Proposition 1 [derived from EC Objective 1] : Current EU chemical safety regulation does provide sufficient public environmental health protection from potential risks associated with NM.

Proposition 2 [derived from EC Objective 2]: That novel scientific tools and predictive paradigm(s) can provide future confidence for industry and regulators in nano-safety decision-making

I examine the two propositions here in turn to provide in-depth consideration of the emerging risk governance of NM in the EU. The propositions-based approach I have adopted provides for empirical analysis in a structured manner, facilitating inductive reasoning to develop conclusions from the primary interview data.

The Chapter identifies three broad findings from the empirical research. First is that, in overview, nanotechnologies offer the prospect of important future benefits, and that concerns for nano-safety may be overstated. However, there continue to be unresolved risk uncertainties regarding their potential acute and chronic environmental health and safety (EHS) effects (Hemphill 2017; Gottardo *et al.* 2017). Secondly, interviewees were in broad agreement that there are significant deficiencies in the risk governance mechanisms of the *NanoStrategy* to realise 'safe use' of NM; in particular, REACH lacks a sufficiently robust evidence base to provide regulatory and public confidence over acceptable 'safe' levels for NM. This is due to the absence of nano-specific risk assessment testing protocols within REACH, even though it remains the de *facto* nano-safety framework for the EU. Respondents commented how some EU Member State governments, who were dissatisfied with this situation, had pressured the EC to bring forward proposals (published in September 2017) for nano-specific testing protocols to be included in revised REACH Annexes. Subject to EU Council and Member Sates approval, these will be effective from 1

January 2020 (EC DO 56122/02). This is an example of a policy preceding the ability to implement its aspirations, with its possible resolution 16 years later from publication. With this policy change for REACH testifying to the political salience and timeliness of my research.

Thirdly, and following from this second finding, respondents expressed the view that current EU chemical safety regulations still do not provide sufficient EHS protection from potential risks associated with NM. With the evidence I will demonstrate later, I conclude, therefore, that proposition 1 is not fulfilled. In turn, this invites consideration of whether novel risk analysis paradigms can be developed that can address the current flawed approach to EU NM governance – the contention addressed by Proposition 2. Here, interviewees expressed optimism that cutting-edge risk analysis approaches (emerging in disciplines such as Systems Biology and (nano)informatics) could provide new frameworks for NM safety testing. Though, currently, these lack proof of concept as to how such data could be incorporated into regulatory risk assessment , as well as lacking validation of their predictive power for *in-vivo* outcomes. Consequently, interviewees noted that, at present, there continues to be a heavy reliance on the criticised traditional single probabilistic testing of animals in the laboratory (indeed, this is a mainstay of the revised REACH Annexes which indicate that major changes are unlikely in the near future).

From the testing of both Propositions 1 and 2, I conclude that current EU risk governance instruments – and their regulatory and scientific procedures – do not yet provide an effective or efficient EU-wide safety and responsibilisation system for NM. However, I do show the potential for a novel approach for developing a new risk governance system, capable of delivering the key objectives for the *NanoStrategy* into the 21st century. How a revised and updated nano-governance framework might be taken forward is the focus of

analysis in Chapter 6. In the meantime, I will now set out how I have undertaken the testing and evaluation of the primary data relevant to this Chapter.

5.2 Evaluating EC Nano Objectives using the two research propositions

The process for the derivation of the two research propositions from the *NanoStrategy* risk governance Objectives 1&2 is discussed in Chapters 3 and 4. Testing propositions in terms of their efficacy requires the recognition of the underlying patterns and relationships between these propositions and the qualitative data sets, utilizing the qualitative coding (Bryman 2012; Srivastava and Thomson, 2009; Jankowicz 2005; Taylor-Powell and Renner 2003). Using Direct Content Analysis, I identified risk governance and anticipatory governance as the key themes with risk management the major sub-theme. Additionally, I identified concepts and variables to provide 27 coding categories for *inter alia* current regulation, RRI, and risk policy (the themes and codes are given in the Appendix C). I then allocated qualitative data, relevant to each code, as a basis for developing explanations to confirm or deny the contentions made in each proposition, through exhaustive analysis of the primary data set. As I show, my findings seek not only to explore the emerging governance of NM , set out in the EC *NanoStrategy*, but to also to advance debates in the literatures on risk governance and adaptive and integrated systems (see Chapter 3).

As explained in Chapter 4, I applied an inductive approach to my qualitative data set which comprised semi-structured interviews with 55 experts in nanoscience, policy/regulation, and industry; supplemented deductive evaluations of other triangulated information.

A first step in my evaluation is to establish clearly the purpose of the EC strategic objectives 1, 2 and 3. According to the *NanoStrategy*, this is to provide a policy and regulatory risk

governance framework to promote the safe and responsible development of NM; to be achieved by introducing an integrated, coherent EU-wide approach [COM(2004)338]. I formalised the EU's aim diagrammatically as an integrated risk governance model in Chapter 4 (Figure 4.3). This Figure illustrates the critical interdependence of the three strategy objectives with their interlinking in order to deliver the strategic goal of safe and responsible development of NM. Importantly, I would argue, that this model enables the identification of the fundamental requirements for any successful *NanoStrategy*, or indeed of governance of any new technology. To take this forward, in this Chapter, I have evaluated the empirical data with a view to establishing the extent to which progress has been made towards fulfilling *NanoStrategy* objectives 1 and 2.

5.3 Evaluating EC Objective 1

EC Objective 1 seeks to minimise the need for new nano-specific legislation. When the *NanoStrategy* was introduced in 2004, the draft REACH regulations were close to achieving final EU Parliamentary ratification (approved 2006, enacted in 2007). Consequently, the effect of this Objective meant that, rather than implement new nano-specific regulation, NM were included under this generic chemical safety legislation [SEC (2008) 2036]/ [COM (2008) 0366 final]. But, as previously mentioned, without nano-specific provisions or testing protocols (Bowman 2017), and with regulation proceeding at a faster pace than the supporting safety test guideline development and validation. By applying research proposition 1, I seek answers as to the effectiveness of this approach in delivering the EU nano- safety policy. Drawing on the primary data derived from the 55 interviews, this first proposition is evaluated below in three stages. Firstly, I report interviewee's perceptions of the intrinsic hazards and risks posed by NM. This leads to discussion of one of the

fundamental guiding principles of EU environmental law, the Precautionary Principle, and its application to NM. The third section then considers whether REACH is appropriate for regulating NM development safely and responsibly, now and into the future. I then summarise findings from the analysis of the data for proposition 1 before moving on to consider Proposition 2.

5.3.1 Intrinsic hazards and risks from Nanomaterials

As discussed in Chapter 2, there is no experimental evidence supporting the view that NM are intrinsically hazardous *per se*, though, of course, this does not mean that individual NM are not toxic if they exceed threshold exposure levels of vulnerable targets. Nevertheless, the lack of nano-specific acute toxicity evidence (Nel *et al.* 2013a) lends credence to Proposition 1 that current regulation is effective for nano-safety (although epidemiological evidence for chronic, multi-generational effects are little explored). Indeed, as one nanotoxicologist pointed out in interview:

> "Until you have gone through everything, and are then willing to set a value, you must assume that there is no harm at all [from NM] (Academic interview. 6th December 2013).

This viewpoint (which, interestingly, contradicts the EU precautionary principle approach to safety - see 5.3.2 below), was supported by academic respondents (including other nanotoxicologists), who asserted that the potential risks from NM were consistently overstated. Other sectoral respondents took a less sanguine view, with many emphasising that the biggest problem for government, regulators and industry was the continuing scientific uncertainty surrounding the safe long-term use of NM and their products. The overall consensus amongst interviewees was that continued caution was needed in policy, regulatory and scientific terms when regulating NM. This is not surprising bearing in mind

the potential unpredictable quantum properties of NM, which do not conform with the traditional knowledge frameworks for classical physics and chemistry. As previously mentioned, (Chapter 1), Maynard (2007) describes NM development as taking society into a new *post-chemistry* world. This is partly because there is no definitive understanding of emerging risks from NM that enables regulators to manage them effectively (Mazri 2017); as, indeed, they essentially span all chemistries in the periodic table as well as their potential for infinite variations in sizes, shapes, coatings and multi-component materials. Clearly, there is a need to determine acceptable EHS risk standards (e.g. emission/exposure levels) for various categories of NM, whilst not under-estimating the challenges in this task. As a nano manufacturer pointed out to me:

> "We can make three different types of the same NM in a morning and they will have different functionalities. So, what is safe? Am I worried about the safety of NM? No, I am not" (Interview 35. 16th August 2014)

However, others argued that this technology must achieve a greater level of maturity before such judgements are made. What is clear from the above quote (interview 35) is the need to understand that changing one or more intrinsic physico-chemical parameters (size, shape, electrical charge etc.) on the same NM composition (e.g. metals, metal oxides) may potentially impact positively or negatively on its toxicity. This poses the question whether there have been exaggerated concerns regarding nano-safety when there are no authoritative indicators of long-term risks, which may take many years to emerge, if at all (European Risk Forum 2015; Boyd 2015; Hansen 2015; Willetts 2012; De Mauley 2013; Lofstedt 2013). This led an EC administrator respondent to observe:

> "I think we have a good understanding of the hazards posed by NM , but we are still lacking an understanding of the drivers of toxicity – especially nano-specific

> toxicity – and whether the argument on bio –accumulation holds, or it doesn't" (Interview 23. 1st April 2014).

From this respondent's perspective, therefore, it seems that whilst significant nano-safety issues are unresolved, there is no clear evidence of exceptional or specific toxicity from NM and their products. This supports the criticism against alleged nano-specific toxicity highlighted in the literature (Donaldson and Poland 2013), as the toxicity response may be identical to its macro version i.e. indistinguishable, except to possibly magnify the negative phenotypic (biological) responses. Nonetheless, there are systemic knowledge gaps that can be costly for industry who regard the defining of regulatory acceptable risk levels for NM as crucial to their business performance. By this they mean the referencing of approved prescriptive standards (e.g. emission/exposures levels) as a necessity for achieving essential pre-marketing legal compliance. Such companies want to be in a position where they can achieve chemical safety compliance against validated and acceptable legal standards, without the concerns that they will retain the long-term responsibility for future liabilities for their products. This puts EU regulators in a difficult position as they endeavour to manage the current complexity, uncertainty and ambiguity associated with nano-safety over the entire product lifecycle. Prevailing political considerations emphasise the socio-economic benefits of nanoscience and technology; yet as the respondents above emphasise, this downplays the considerable uncertainties of determining acceptable levels of risk (Jasanoff 2016; Bennet 2014; Maynard 2014). An environmental lawyer stated the industry position to me very succinctly:

> "What industry says it needs is an agreed, reliable, widely recognised evaluation system which provides a high degree of assurance regarding the safety of NM and their commercialized products" (Interview 18. 20th February 2014)

This statement highlights that this industry aspiration has not been achieved, casting doubt on the validity of EC Objective 1 and consequently on Proposition 1. However, these comments also suggest that expert opinion does not believe NM pose any greater hazards than other chemical substances (German Action Plan for Nanotechnology 2020; NanoReG2 http://www.nanoreg.eu/; COM (2012) 572 Final). Moreover, there are other important factors that must be considered before such a definitive conclusion can be drawn. These include interviewees perspectives on how EU risk policy for NM interleaves with EU environmental policy principles, more generally, and their views of the efficacy of the current regulatory instruments for chemical safety – namely REACH – in handling NM. I consider these points next.

5.3.2 Nanomaterials-an over-reliance on the Precautionary Principle?

Beck (1992) asserts that in our contemporary "risk society", science and innovation co-produce risks. Likewise, Jasanoff (2016) notes growing recognition that contemporary approaches to risk management require social-technical, as much as techno-scientific understandings. For example, there is no universal definition of risks from emerging technologies that can inform policy makers and regulators in responding to new and evolving risks and their management (Mazri 2017). This is particularly true of nanotechnology, where the evaluation of risks is riven by uncertainty, complexity and ambiguity, to an extent that NM are considered to spill over conventional regulatory boundaries (Vaughan 2014; Stokes 2012; Stokes and Bowman 2012, Som *et al.* 2010). Bowman (2017) asserts that the rapid trajectories of nano innovation that are outpacing nano-specific regulation is, as a consequence, likely to play only a small part in evolving patterns of its governance. That is, nanotechnology does not fit easily into existing political-

administrative responsibilities, because it is a fluid technology with applications spread across diverse socio-technological regimes from the supra-national to the local scale (see Figure 1.1, Chapter 1). An EC Administrator summarised the current situation for me as follows:

> 'Traditionally, it is the public authorities who take responsibility for evaluating the risk. This cannot continue with the emerging technologies' (Interview 53. 8th March 2016)

This comment highlights a critical issue for consideration, namely, what will be the future division of labour between industry, government, regulators, academia and society for articulating an acceptable level of 'risk' from NM? The starting point here is that there is no generally adopted definition of acceptable risk by the EU (SCHER 2013). Neither is there an EU specific risk paradigm to test risk levels for natural and novel engineered NM (SCENIHR 2009). The EC has indicated that it expects solutions to come from the scientific community with its enormous policy commitment and financial investment by the EU in nano-safety funded research projects > €200m to date (NanoSafetyCluster https://www.nano-safetycluster.eu/)

The EU's default position has been to rely on the Precautionary Principle (PP) as its main tool for controlling incertitude for risks from chemicals to human health and the environment (EHS). The purpose of the PP is to be actionable to promote proportionate measures to resolve threats to prevent significant or irreversible EHS damage (Reber 2018). However, an EC briefing to the EU Parliament Environment, Public Health and Food Safety Committee, in September 2018, describes the PP as encouraging conservatism with an over-emphasis on intrinsic *hazard* rather than evidence-based *risk*; and that the PP needs to be applied sensibly, rationally and wisely (Committee Briefing on Plant Protection

Products 18th September 2018). According to the Maastricht Treaty (1992), the PP is meant to be applied where preliminary objective scientific evaluation indicates there are *reasonable grounds for concern* that potentially dangerous effects on the environment, human, animal or plant health may arise that are inconsistent with the *high level of environmental protection* required under Community law [TEU 1992]. This provides the rationale for applying the PP, given it is deployed in a proportionate manner (von Schomberg 2006).

The development and international governmental acceptance of the PP approach has had a high-profile international genesis (e.g. Rio Declaration 1992). It seeks to build a common understanding of how to assess, appraise, manage and communicate risks that science is not yet able to evaluate fully (EC Communication on the Precautionary Principle, COM 2000). The importance of this principle is emphasised by the fact it is highlighted within three EU treaties (as detailed in Chapter 3). All of them stress its importance in delivering a *high level of human health and environmental protection* within the European Community. PP is normatively defined, in that it applies the *Analytical-Deliberative* framework in its balance of evidence decision-making, by combining scientific evidence with deliberative consultation outcomes (von Schomberg 2006; COM2000). Its purpose is to identify provisional precautionary measures until further technoscientific, and cost-benefit analysis has been conducted (Holbrook and Briggle 2014; Von Schomberg 2012, 2006). Crucially, it is also enshrined within REACH (Article 3), which places a legal obligation on chemical manufacturers and importers not to adversely affect human health or the environment, with this provision expressly underpinned by requiring the application of the PP.

Nonetheless, there has been much academic and public debate on the PP's inappropriate application of the PP as a broad *hazard*- based approach, rather than the scientific, evidence -based risk management basis specified in the EC Communication on PP (see for example European Risk Forum 2015; Boyd 2015; Hansen 2015; De Mauley 2013; Lofstedt 2013; Willetts 2012; EC Communication on the Precautionary Principle 2000). Certainly, this viewpoint has support amongst nano-industry respondents and interviewees from among the chemical industry associations. These respondents believe that the overemphasis on 'precaution' is detrimental to the EU innovation trajectories for nanoscience and technology. Thus, one interviewee from an international chemical industry association complained:

> "You are pushing [nano] technology backwards if the concerns are not fully understood in terms of their [NM] development. There is too much emphasis on the uncertainty and the application of the precautionary approach" (Interview 40. 13th November 2014)

This alleged overemphasis on precaution within the EU (see Chapter 2) is shared by other sectoral actors as well. This was summarised by industry respondents as an incorrect application of the PP, with too much importance attached to speculative hazards (lacking a scientific basis), rather than being applied with a scientific evidence base to specifically identified endpoints of risk e.g. carcinogenic, mutagenic, reprotoxic (Maynard 2014; COM 2000). Exemplary of this was one nano manufacturer's comment that:

> "the main limitation of the PP is that it acts in a merely defensive manner and is not capable of providing us with a model of anticipation" (Interview 2. 13th February 2013).

Another industry respondent vented their annoyance to me as follows:

> "You are pushing technology backwards in terms of development if there is too much uncertainty and the application of the PP [is followed unreflectively]" (Interview 14. 2nd October 2013)

These comments offer important insights into the frustration of industry respondents over how the PP is interpreted and applied within the EU. The perception is that it is utilized as a 'stopping' mechanism, rather than its original purpose which was to establish a 'holding' position within the continuum of innovation, pending problem resolution (Stirling 2016a; Defra Chief Scientific Adviser 2015; UK Chief Scientific Advisor 2014; Pollard and Rocks 2014). Critics thus allege that hazard avoidance becomes the main concern for the EU, rather than the normative qualifier of evidence-based risk concerns (Defra Chief Scientific Officer 2015).

Hemphill (2017) asserts that the PP should not be a stand-alone model; instead, it should adopt an 'anticipatory' role. The *Oxford English Dictionary* defines 'precautionary' using such terms as 'preventative, protective, safety', but for 'anticipation' there is a different inference of 'expectation, prediction, and forecasting'. So, is there a potential for 'precaution' to be modelled more on the lines of 'anticipation'? I examine the prospects for this in Chapters 6 and 7, where I challenge the perceived shortcomings of the current policy which focuses on hazard-based applications of PP, by developing a more anticipatory governance approach, which accommodates its deliberative role. Such an approach might underpin EC Objective 1 more effectively than current arrangements.

So far, the discussion identifies significant shortcomings and industry frustrations in the manner of the current application of PP within the EU (Interviews 2, 14, and 40). It identifies a need for progression from precaution to anticipation in its application, which is considered further in subsequent Chapters. But there remains an important preliminary

issue that needs examination first. That is, if there is a recognition of a negative over-application of PP, this may be in response to and symptomatic of a poorly functioning EU risk governance and regulatory system for NM. Consequently, this requires the evaluation of the current EU regulations in respect of their role and efficacy in providing assurances for nano-safety. This demands examination of the role of REACH as the principal EU chemical regulatory framework. The key question to be addressed is whether REACH is currently structured to provide assurance in NM safety decision-making as required by Proposition 1.

5.3.3 Nanomaterials and REACH

Applying regulatory-based limitations of one sort or another is the traditional means for legislative states to control/restrict innovation practices and minimise risks (Calster and Bowman 2002). EC Strategy Objective 1 aims to retro-fit generic chemical safety regulation to NM via REACH (COM (2004) 338). However, given that it was not designed to accommodate their unique biophysicochemical properties (Vaughan 2014; Stokes 2012; Stokes and Bowman 2012, Som *et al.* 2010), a key question arises as to whether NM exceed the boundaries of the REACH regulatory regime? Certainly, there are contentious issues with this policy, with the EC Definition of NM a primary example. The current EU definition for NM confines their size within the 1-100nm range (2011/696/EU). In their interview, one academic explained that the definition is contested due to cellular inability to differentiate between minute variations in nanoscale, which undermines current regulatory efficacy.

> "Can biological systems distinguish between 100nmn and 101nm? No! Industry will move its particle size if it can get the same functionality from 100nm to 101nm" (Interview 18, Academic. 5th May 2014).

The techno-scientific capability to modify the NM size and size distribution was confirmed by one nano manufacturer (interview 35 above), who confided to me that it is technologically easy to produce different size variations of the same NM. This means that technically manufacturers can deliberately produce particles that evade categorisation as NM. To the outsider, this may seem to be a minor matter, but it is important to policy makers, researchers, regulators and industry seeking legal clarity and policy coherence. The reason is that the manufacturer is the formal REACH registrant who, by experimental or other means, determines the physico-chemical properties that are identified in any chemical safety dossier submitted for REACH compliance (REACH, Article 14). Consequently, it will be the REACH registrant who determines, in advance, whether the chemical substance meets or exceeds the EU definition criteria (e.g. whether it is 100nm or 101nm in size). In interview an EC administrator noted that:

> "The biggest issue for us as regulators is that it is enforceable. We need something that is authoritative for the courts" (Interview 27. 10th April 2014)

The EC science portal, the Joint Research Centre (JRC), recognises that this metrical measurement deficiency needed to be overcome (NanoDefine 2017; JRC 2015). However, the latest word on this comes from a recent paper in *Nature Nanotechnology* (Vol 14 March 2019) which provides another strong criticism of the current situation. It finds that '*the current EU definitions for NM are ill-defined… and pose major and unsolved analytical challenges that make it nearly impossible to classify NM according to EU regulatory requirements'* (Miernicki *et al.* 2019.p1)

However, important as this outstanding problem is, there is another more contentious issue raised by interviewees, namely REACH's lack of nano-specific toxicological tests for risk assessment. Without doubt, this was the most significant hindrance raised by

interviewees in assuring for public environmental health and safety required to enable EC Objective 1. In fact, this singular deficit has been publicly recognised by the EC (COM (2012) 572 Final), with further strong criticism driven by the European Parliament that NM safety issues are not being fully addressed within the REACH dossiers (COM (2013) 49). Surprisingly, considering the time lapse since REACH enactment in 2007, only in October 2017 were new draft guidelines for scientific testing protocols adapted for NM published, even those will not be enacted until 1st January 2020 (EC DO 56122/02).

This revision of REACH, coming 10 years after it was enacted, could thus be described as dilatory, especially given the strong steers to the EC from public authorities in Germany, Austria, Switzerland, Liechtenstein and Luxembourg (Vienna Declaration March 2017). In March 2018, the EC made a further announcement on NM, in its latest review of REACH that:

> "While REACH is able to address emerging issues such as the risks from nanoforms of substances, the lack of specific information about nanoforms covered by REACH registration dossiers remains an issue……..some scientific gaps remain as to the suitability of test methods for nanoforms of substances and these are addressed in the OECD test guidelines programme" (Commission Staff working document accompanying {COM(2018) 116 final} 5th March 2018. p42)

One might think this further formal acknowledgement of the continuing inadequacies of REACH to address NM safety would have led to calls for new nano-specific regulation from interviewees. However, my research revealed the opposite. Despite these shortcomings, previously recognised by the EC in its 'Second Regulatory Review of Nanomaterials '[COM (2012) 572 Final], all the interviewees were unanimous in indicating that none wanted new

nano-specific regulation enacted to supersede REACH. An environmental lawyer explained the legal and scientific deficits relating to current NM risk analysis:

> 'So, I am anti-new regulation where an existing general framework is capable of managing the chemical assessments. There are also problems in that there is no gold standard for the reproducibility of the NM, there is a lack of accepted ecotoxicological data, lack of professional expertise to advise companies and regulators of the possible safety issues from the NM (Interview 17. 11th February 2014)

An EC Administrator also underlined for me the responsibility of and difficulty for industry, as REACH registrants, in identifying NM from other macro variants of the same chemical substance:

> 'It is very difficult for companies to say which [particles] are nano and which are not NM. So, at the moment, conventional methodologies apply. This leaves a very large grey area when the registrant wants to say whether it is nano or not. So, there have not been very many companies registering for nano substances' (Interview 32. 25th July 2014)

In fact, only 29 nanoform dossiers were submitted for REACH registration in the period 2008-18 (Nanotechnology Industry Association 2018). The "very large grey area" the respondent mentions here refers to concerns that nano manufacturers may be deliberately classifying their chemical form as non-nano so as to avoid the extra resource demands it might entail if they declare an NM. An NGO respondent also provides an opinion on this matter:

> "The number of NM that have been registered [for REACH] is low, and the quality of the information on those nanoforms is poor" (Interview 55. 7th April 2017)

What emerged from these interviews with industry respondents was anecdotal evidence of a tacit approach by some small to medium size enterprises (SME) nano manufacturers to evade the legal requirements set out in REACH. This is achieved by keeping annual production at levels below the legally defined REACH trigger levels for compulsory registration (e.g. 1 tonne per annum), so as to avoid invoking this legislative responsibility, and also by the possibility of manipulating NM size. This attitude has not been reported in other studies in the literature, and it should be noted that this finding is based on a relatively small sample size. Nevertheless, such an approach by industry would have a clear commercial purpose: namely, to avoid the significant overhead testing costs and delays that can result from REACH compulsory testing prior to getting products to market (the importance of this issue will be illustrated in Chapter 6). Indicative of this issue are the remarks of a SME manufacturer of NPs:

> 'I have kept production levels below the REACH trigger levels so that we are not obliged to access REACH. It is complicated and expensive for SMEs. Strangely, the prize for growing your company is that it will have to comply with REACH' (Interview 35. 16th August 2014).

The concomitant advantage for industry is that if they follow the REACH testing procedures then they are fully compliant with their legal obligation requirement for trading in the EU Single Market. However, if their production levels are less than 1 tonne per annum, the business and its nanoproducts are exempt from the REACH provisions, but still able to trade without hindrance, unless it is a substance of very high concern (REACH, regulation 58). Both the Centre for European Policy Studies (2012) and Scruggs *et al*. (2014) have highlighted the disproportionate financial and technical demands on SMEs to achieve REACH registration compared to that for larger industrial concerns. In respect of this study,

none of the five SME nano manufacturers interviewed had an annual production level that exceeded one tonne per annum. Consequently, none had to bear the expense of submitting a REACH registration dossier.

A related question is whether the unique biophysicochemical characteristics displayed by some NM can currently be adequately analysed using REACH protocols. The publication of EC draft amendments to the REACH Annexes (September 2017), for nano-specific testing, confirms my findings from interviewees' expressed concerns regarding the lack of efficacy of REACH in respect of NM (EC DO 56122/02). As mentioned above, further confirmation of this finding is given in the Commission Staff Working document attached to the EC General Report on the Operation of REACH (COM(2018) 116 final), in March 2018, for the European Parliament and European Council. ECHA has provided new guidance which argues that the REACH Annexe amendments will enable sectoral actors to better understand the risk characteristics of NM, how they are used, handled safely, and the potential risks to EHS and their management and control (ECHA /NR/18/23).

Nonetheless, even with the release of new nano-specific guidelines, the fast-pace trajectories of nano innovation may result in these new measures not providing timely regulatory assurance of nano-safety as required by Proposition 1 i.e. the 'pacing ' problem discussed in Chapter 3 (Marchant *et al.* 2011b). In this context, Jasanoff (2016) poses a critical question: how does regulation keep up at the expanding frontiers of science? Stirling (2016b) argues that, in these circumstances, any decision-making regarding risk levels can only be probabilistic due to the incertitude of current scientific knowledge. This was echoed by one EC administrator in interview as follows:

> "The first part is dealing with the uncertainties on the hazard side, such as [NM risk] characterization and toxicity testing, then in-vivo and in-vitro[testing], which is part

> of the risk equation. The second part is exposure, over a long time. The third part is to multiply these two, and you obtain the probabilistic risk, then the uncertainties can become high" (Interview 19. 21st February 2014)

Certainly, the inadequacies in REACH had not gone unnoticed in EU Member States. Also, the lack of meaningful responses by industry to the EC Nanocode (2008) for a voluntary register of NM highlighted a gap. Prior to the Vienna Declaration (2017), unilateral action was taken by some member states to implement an alternative solution to fill the 'hard law' gaps with National Registers for NM (discussed in detail in Chapter 2). Asked in interview about the reasons behind unilateral action of this sort, an EC administrator observed:

> "I think it is a combination of the fact that the regulatory process is so slow … and the French scheme resulted from them being annoyed that they saw nothing happening in Europe… so the Registers have been seen as a way to collect all sorts of information without opening the REACH discussions. Nobody wants to open the debate on REACH!" (Interview 22. 25th March 2014)

Not surprisingly, the view among industry respondents was different. All my industry interviewees condemned unilateral action by EU member states as expensive for companies from a compliance perspective, and laborious and repetitive in terms of data collection. In addition, the EC have rejected setting up an EU wide nano register due to its high costs (projected at EUR 2.5 billion annually; CASG-Nano Meeting 16th March 2016). Instead it has now established an EU Observatory for NM facilitated by ECHA (EU-ON 7.12.2016), and operative from 14th June 2017 (ECHA/PR/17/11). The EU Observatory offers a web-based portal to curate scientific information on NM which will be an open

access platform. However, in interview one NGO respondent expressed doubts to me as to its real value:

> "I am not saying it is completely useless, but it is a compilation of existing information. The premise is that the what, how much, and where, do not exist and are not available. So, the Observatory will not answer any of these questions, nor ask any new questions". (Interview 55. 7th April 2017)

The implication here is that the EC's policy response is chiefly about meeting the political frustrations of its Member States, rather than enhancing regulatory efficacy. Amongst Members States there is disagreement over whether to introduce further national registers or support the EU Observatory. This has had an undermining effect and provides evidence of continuing member state disarray on this subject. This disharmony also evinces a distinct lack of confidence in the current EU risk governance instruments and processes for NM safety. It certainly undermines Proposition 1 that those instruments provide a necessary assurance of nano-safety. Yet given the trajectories of nano innovation the question remains as to how the EU will address risk issues arising from the predicted 2nd, 3rd and 4th generation NM (Roco 2005), which will be essential components in the convergence and fusion of new technologies predicted for the 4th Industrial revolution (World Economic Council 2015) e.g. nanobiotechnology. The policy view within the EC is that REACH will still be appropriate (excepting for specialist regimes such as pharma and pesticides), provided that the underpinning science supporting the REACH regulation is agreed upon. On this point, an EC administrator respondent commented in interview that:

> "Instinctively, I would think REACH would cover those issues. The reason I say that is that whatever the technologies are REACH is technology neutral. The reason is that REACH is looking at the products of various technologies. This is always a

> [biophysicochemical] property-based approach, so when we ask about properties of new materials then the features in REACH, the principles of legal obligations, the legal process, they apply whatsoever" (Interview 32. 27th May 2014)

This could be taken as an overconfident – even complacent – statement, given the many criticisms of REACH to date; with the continuing technical and scientific uncertainties in respect of the biophysicochemical composition and functional properties of future engineered NM.

Summarising the first part of this Chapter in relation to proposition 1, a number of important findings emerge from this analysis of the current NM regulatory landscape. The first point is a fundamental issue of regulatory classification: what is/is not a NM under REACH? Although this critical outstanding legal issue is subject to significant research investment (e.g. FP7 project NanoDefinehttp://www.nanodefine.eu/), there continues to be a lack of applicable metrology and quantifiable metrics for sizing and defining NM essential for scientific standardization and regulatory enforcement (Miernicki *et al.* 2019). This metrical difficulty may be a contributory factor for the criticisms regarding the low number of classified NM within REACH registrations (interview 55). However, I have found anecdotal evidence of deliberate REACH avoidance by some nano manufacturers (interview 35 an example). Clearly both these factors undermine the basis of Proposition 1, and the fulfilment of EC Objective 1. Secondly, to some extent, this is compounded by the 'delayed capture' of NM within REACH provisions. The regulations have neither captured NM efficiently i.e. all NM in use within the EU ambit, or effectively i.e. evinced validated nano risk assessment results for regulatory decision-making (interview 19).

Yet, it is important to point out here that, with little exception, the respondents were opposed to replacing REACH with new nano-specific regulation. Their dispute is not with

the principle of nano capture within a single overarching EU chemical safety regime *per se*; rather, it is centred on their lack of confidence in the current application of REACH to be able to provide the necessary assurances for EHS safety. This is an important policy and regulatory issue in respect of the 'rightness' of drafting EC Objective 1 to require the retrofitting of legislation to NM. This viewpoint again undermines Proposition 1.

Thirdly, there is the potential for some NM to be vetted by vertical regulations (regulations for food and feed, cosmetics, biocides, pharma etc.) rather than being covered by the REACH umbrella. If there is active REACH avoidance by nano-manufacturers (interview 35), then within the Taxonomy of Regulation, the higher levels of hard law compliance are also undermined, weakening overall prescriptive performance standards (e.g. limiting emissions/toxicological exposure levels). Consequently, it is reasonable to conclude that there has been an unwitting reliance on the PP and the soft law components of the Taxonomy (e.g. self -regulation) to achieve the acceptable risk standards for safe use.

I conclude from this analysis that, in this *post-normal* era (Funtowicz and Ravetz 1993), risk governance for NM safety will need to look beyond traditional 'black letter' regulatory measures to ensure effective long-term solutions for nano-safety. This entails further exploration of 'soft law' approaches (including responsible innovation) as a means of addressing the fast trajectories of nano-innovation. In turn, this signposts a move away from reliance on traditional top down 'command and control' to hybrid forms of 'hard and soft law' governance (Bowman 2017; Hemphill 2017; Vaughan 2015) as foreseen in the Taxonomy of Regulation (Chapter 3,Figure 3.1). This supports Bowman and Hodges (2008. p484) contention whereby they argue 'that nano-specific state regulation is likely to play only a small part in risk governance for NM (this is subject to further detailed discussions

in Chapter 6). Collectively, I submit that these findings confirm that Proposition 1 cannot be efficacious at this time.

If Proposition 1 cannot be supported, then this demands consideration of the potential role to be played by EC Objective 2 for the safe and responsible development of NM. To do so, I shall utilize Proposition 2 in the next section to analyse interviewees' viewpoints on whether Objective 2 of *the* EC *Nano Strategy* has been fulfilled: namely that "*existing parameters for EHS chemical safety testing may not be appropriate for the unique properties of NM, requiring new methods and tools for risk assessment, and refinement of nano scale metrology and standardisation activities"*.

5.4 Evaluating EC Objective 2

5.4.1 New regulatory spaces: novel nanogovernance to support future industry and regulatory safety decision-making

EC Objective 2 recognises the necessity for new science for EHS chemical safety testing for NM due to their unique quantum properties. Thus, Fadeel *et al.* (2018) clarify the continuing major environmental nanoscience challenges relating to the laborious process of generating dose-response data for multiple toxicity end-points. Difficulties also arise in correlating these results to actual exposure levels within manifold settings e.g. occupational, consumer and ecological exposures. This requires investment in the experimental development of new risk assessment testing protocols and other methodological tools (COMM (2004)338). Substantial scientific financial investment has been made by the EC since 2004 into nano safety research projects, but the development of these new tools, for measurement and modelling, is still incomplete (NanoSafetyCluster Winter Newsletter 2018). The intention is that these novel models for predictive toxicological and exposure-based decision-making can provide solutions to the on-going

debate as to how 'acceptable risk' from NM can be scientifically articulated and evaluated. In addition, the new testing methods could provide for early warnings, requested by the European Environment Agency (EEA 2013), which are faster, more economical and ethically sounder than current traditional animal testing (e.g. OECD (2018c) Test 413: sub-chronic toxicity: 90-day inhalation mammalian testing).

Currently, there is no EU definition of risk from NM (SCHER 2013). As significant, there is no specific risk paradigm to test natural and emerging engineered NM (SCENIHR 2009). Consequently, the default approach used across the EU is to consider each nano risk profile separately, and to design bespoke scientifically complex toxicological testing scenarios. This is costly in time and resources e.g. OECD (2018c) Test 413 and relies on the ethically doubtful traditional animal testing. As one SME nano manufacturer commented to me:

> 'Current toxicological testing is not fit for purpose. [It is just] too time consuming and expensive' (Interview 24. 16th August 2014)

Among my interviewees, there was a cross-sectoral consensus that a new approach to toxicological testing is now essential. Not only because of excessive resource and time costs, but for the ethical benefit of reducing vertebrates testing in accordance with REACH (Regulation 33), and the EU '3Rs' policy (Directive 2010/63/EC). However, providing new scientific based Integrated Alternative Testing Strategies (IATS), that address the industry frustrations articulated above (interview 24), requires a robust analytical framework that can evaluate evidence-based risk to determine EHS threats (Rodricks and Levy 2013). Additionally, all new tests must undergo an extensive process under the auspices of EU Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM https://ec.europa.eu/jrc/en/eurl/ecvam). The parameters for this framework must

incorporate the context of the risk, the inherent risk characteristics of the toxicant, and the exposure levels to that vulnerable agent (OECD 2003).

The extant literature also identifies that any new approach must address substantive, procedural and interpretive aspects of risk analysis. Only then can the 'weight of evidence' be provided to strengthen the results-based legitimacy for risk management of NM (Gottardo *et al.* 2017; Jahnel 2015b; Hristozov *et al.* 2014; SCENIHR 2012). Crucially, this would address the fundamental test set by Jasanoff (2016) that any aggregation of harms must remain within socially tolerable boundaries.

Taking these issues together provided the basis for the second Proposition examined in this Chapter which is that "Novel risk analysis paradigm(s) can provide high levels of public confidence in nano-safety for industry, regulators and civil society, now and into the future'.

I draw upon interviews to assess the prospects for the development and application of these prospective novel solutions, to replace the existing testing regimes, in the following sections.

5.4.2 The prospect for novel risk assessment paradigms to replace traditional regulatory decision-making tools

In interviews, respondents acknowledged that there is a lack of confidence in the current format for traditional toxicological testing for NM and were receptive to the idea of finding viable alternative options. This was evident in the consensus across sectoral groups that future nano risk assessment lies within novel paradigms for toxicological testing derived from new life science discoveries (e.g. Systems Biology, Omics). The aim behind these approaches is that traditional laboratory observational testing on vertebrates and lower level organisms can be minimized or eliminated. The IATS procedures could replace animal

testing with predictive profiling of cellular nanotoxicity using high throughput mechanised testing of NM inoculated cell lines (JRC 2014; Oomen *et al.* 2014; Whelan 2014). If successful, this process would enable identification of disruptive cellular metabolic Adverse Outcome Pathways (AOP), with their causal observable and measurable Mode(s) of Action (MoD) (Stone *et al.* 2017; JRC 2014; OECD 2013; WHO 2009). The goal of using these new procedures would be to extrapolate the measured outcomes to determine risks to human and environmental health (Rovida *et al.* 2014; SCHER 2013). Hence, AOPs offer a new methodology for describing toxicological hazards, based on mechanistic profiling, rather than an association with traditional pathological endpoints (e.g. carcinogenic, mutagenic, reprotoxic). Additionally, it relies on nanoinformatics and modelling approaches whereby the toxicity profile of an unknown NM can be predicted from the existing data on other NM, via, for example, quantitative structured activity relationships (Q)SARS) or artificial intelligence approaches.

Interviewees provided a variety of responses, on whether such an approach might provide enhanced predictive accuracy for nano risk decision-making and contribute to the fulfilment of Proposition 2. To frame my discussion with selective respondents, I chose an exemplar toxicological paradigm (Figure 5.1 below), previously seen and discussed in detail in Chapter 2, which proved to be a successful prompt for our discussions. My purpose was to canvas expert views on its future value as a tiered sequencing predictive tool, with a view to replacing traditional animal based observational toxicology utilizing current OECD risk assessment protocols. In summary, the purpose of this novel toxicological model is to provide a systematic and measured approach for the tiering of potential hazard levels (low-medium-high).

I will briefly recap that the starting point is curated nano safety and nanoinformatics tools which leverage these datasets, and which assist in the design of mechanistic cellular testing of different concentrations of NM. This would enable detection of potential AOPs, and their causal MoDs due to toxicant effects from NM. The data sets would then be analysed *in-silico* for decision-making as to predictive hazard levels(low-medium-high). Models and tools of this nature are currently under development in a number of H2020 projects including:

NanoDefinehttp://www.nanodefine.eu/,SmartNanoToxhttp://www.smartnanotox.eu/),NanoGenToolshttp://www3.ubu.es/nanogentools/),NanoCommons(https://www.nanocommons.eu/). Similar predictive models on release and exposure are currently under development e.g. FP7 projects GUIDEnano http://www.guidenano.eu/, and H2020 projects CaliBRATE http://www.nanocalibrate.eu/home, and NanoFASE http://nanofase.eu/.

Further decisions can then be made and actioned as to whether lower level sentinel organisms or even vertebrate testing becomes necessary, leading to the initiation of a higher tier testing of the NM.

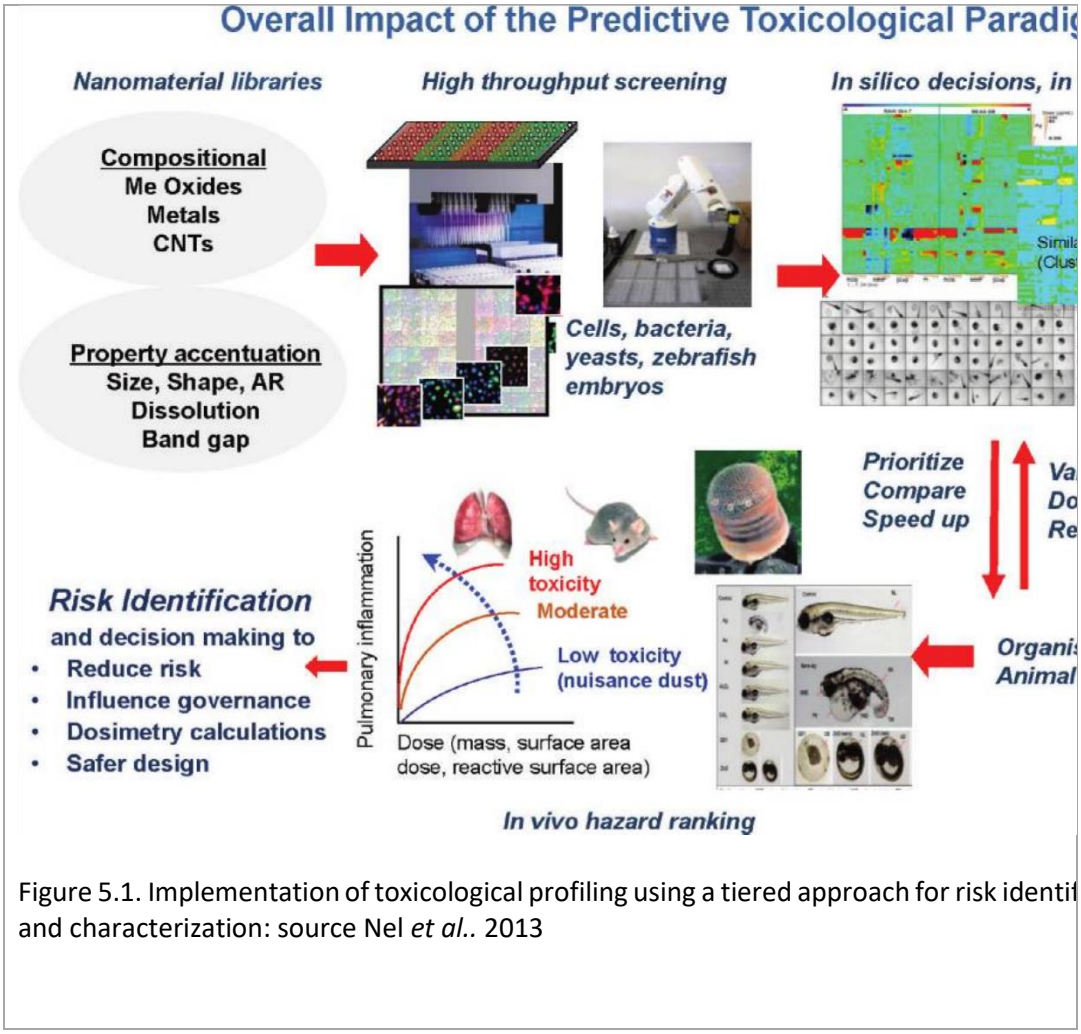


Figure 5.1. Implementation of toxicological profiling using a tiered approach for risk identif and characterization: source Nel *et al.*. 2013

The scientific issues for this model have been discussed in detail earlier (see Chapter 2). Importantly, the regulatory groundwork for the incorporation of such integrated alternative toxicological testing protocols into EU legislation is already in place within the REACH regulations; whereby the offer for alternative testing protocols to be submitted for approval is mentioned in a number of occasions within the regulations including REACH Articles 1 & 13. However, to date a full consideration of this approach has not yet been made by a cross-section of industry, regulatory and academic stakeholders, which is what I undertake in the following section.

5.4.3 Policy, regulatory and industry attitudes to novel risk assessment paradigms for nano-safety

Article 13 (1) of REACH states that any scientific information generated for human toxicity should be generated, whenever possible, by means *other* than vertebrate animal tests - for example, using *in vitro* methods or qualitative or computer generated Quantitative Structured Activity Relationships (QSAR models). An interviewee from a national chemicals industry organisation voiced support for this approach as follows:

> 'We support the 3Rs work, which you may be familiar with. Very much so. We must reduce the number of animals tested and reduce animal testing. We need to use animals sparingly and not just when we need to obtain [regulatory] testing. They apply the "Crack-it" approach to set a hypothesis and then solve the problem without animal testing strategies. A lot of it is about validation testing. Even with high throughput screening there is a need for much validation still to be done' (Interview 12. 2nd October 2013)

The group testing of chemicals, with similar biophysicochemical properties/ structures shows promising possibilities for NM, which could result in improved financial and temporal economy for risk decision-making and moving away from animal testing as proposed by interviewee 12). The NM need to display a common system of biophysicochemical characteristics, such as shape, size surface charge (intrinsic factors), and/or solubility, agglomeration/aggregation (extrinsic factors); a common set of exposure scenarios, or applications within a specific type of consumer product e.g. cosmetics. (ECHA 2017; Stone *et al.* 2017; Jahnel 2015a, 2015b; Oomen 2013; Stone *et al.* 2013). Such an approach is supported within the EC and the JRC; thus, a senior EC Administrator explained their position:

> ‘So, we are now moving towards an artificial grouping of NM. This is a response to problems which have not yet appeared. We are trying to find a reply to a problem which we have not yet seen‘ (Interview 19. 21st February 2014)

However, it was evident that other Commission interviewees had reservations concerning reliance on these novel experimental techniques to inform regulatory practice:

> **‘**We don’t have problem with Grouping or Categorization of materials or Read-Across. What we do have a problem with is if you jump too fast ahead, with some of these approaches when you do not have the evidence base, then we have a concern. As you might simply be paying lip service to the safety issues of the NM. That industry will use any data that they have and claim it. We do not believe that industry have taken all the opportunities that they might have done so. We believe that they could have put more effort into gathering evidence which would give much more comfort regarding [Grouping] and READ Across’. (Interview 22. 25th March 2014)

Interestingly, this caution is evident in the guidance published by ECHA (2017), which restricts the Grouping approach to nanoform variants of the same chemical substance (e.g. copper, titanium, or zinc nano variants). ECHA does not yet support applying this concept to such a mixture of these different substances for chemical safety testing utilizing the QSAR, Grouping and Read-across methodologies (ECHA/NA/17/12). Nevertheless, REACH aspires to avoid animal testing, with vertebrate testing as the last , not the first, resort (Article 25(1). It already has a European Parliamentary approved regulatory mechanism within which new risk analysis paradigms can be adopted and implemented (REACH Article 1(1) and Article 13(1)). But there is still the crucial caveat that policy, scientific and regulatory barriers still need to be overcome in terms of ‘proof of concept’ for regulatory acceptance, legal compliance and industry adoption.

I found that there was strong support for this new paradigm of predictive toxicology from all interviewees in the environmental nanoscience sphere. For example, one environmental nanoscientist noted that:

> "There is currently a drive to optimise nanotoxicity testing methodologies, to avoid poor practices, such as overdosing in animal experiments. Furthermore, novel approaches that enable, for example, fast, parallel, in vitro- testing high throughput screening are becoming widely used" (Interview 43. 21st November 2014).

However, without exception, those most familiar with the new techniques opined that the new assays and models need proofing by further scientific experimentation, assessment of predictive capability relative to *in-vivo* studies, and validation via inter-laboratory comparison before it can be said to be able to provide authoritative and, critically, reproducible answers for industry and regulators. The most important deficit is the lack of validated data sets to provide the required confidence for regulatory certainty in risk assessment (Lynch 2017). This new toxicological model is predicated on being able to identify the AOPs for specific NM and their causal MoA which contributes to the biochemical failure of cells (JRC 2014; Vinken *et al.* 2014; OECD 2013, 2012c). Scientific confidence needs to become much higher to be accepted by ECHA. Thus, an industry respondent, whose global chemicals company had spent 3 million euros on alternative testing to animal studies, explained to me the important issues of predictive accuracy, and the conservatism of ECHA towards them:

> "We consider that *in-vivo* studies are 90% accurate for human prediction effect. We see that *in-vitro* [assays] are as least as good in respect of predictivity, but it is not that good for looking at the data and seeing that it is clear cut. Perhaps no better than 80%, at its very best……. The regulators, in the end, such as ECHA, if

> they take the results of the animal study, they are covered. If they take something new, then they take all risks" (Interview 47, 3rd December 2014).

This statement neatly summarises the dilemma currently facing EU regulators. This novel but not fully proven paradigm has exciting predictive potential. Yet, civil society expects that ECHA must have confidence beyond reasonable doubt (criminal evidential test) before they would accept and then approve new chemical safety testing protocols for incorporation into the REACH process. In respect of Proposition 2, it can be concluded that regulatory confidence for enhanced predictive capacity does not yet exist. Interviewee 47 above makes this critical point that if EHS harms emerge due to inadequately accurate testing protocols, then the regulators will have to take their share of blame too. Not surprisingly, their stance is one of conservatism until substantive proof of concept and validation through the standard processes is available to them.

In conclusion, this highly significant new scientific model has ***the potential*** for a paradigm shift in toxicological testing for NM. It has the potential to address directly the pragmatic issues raised under EC Objective 2 in a novel manner which has a prospective future for, as yet, unheralded techno-scientific advances in nanoscience and technology. As I have shown, it has the potential to trigger a cognitive transition from concerns of vague unspecified potential hazards to more specific EHS risk scenarios and/or endpoints i.e. to move from vague speculative risks to specific plausible risks (Sutcliffe 2015, Maynard 2014). There continues to be substantial EC investment in necessary scientific experimentation to underpin these novel approaches, with substantive advances in underpinning systemic knowledge for these new methodologies for nano risk assessment (NanoSafetyCluster Winter Newsletter 2018 https://www.nano-safetycluster.eu/).

Nonetheless, I detected a palpable sense of anticipation, amongst industry actors, that these emergent scientific techniques can better inform future nano risk and regulatory decisions. This is intended to be achieved by offering to industry enhanced regulatory flexibility, agility and greater predictive certainty than the existing REACH protocols. For example, the experimental development of mechanised cellular testing techniques has the potential to provide more responsive, accurate and cost-effective answers both for industry and their regulators. This could provide much earlier warnings of product failure before technological lock-in occurs. There is also the added deontic benefit of reducing animal testing as promoted within EU policy and regulation [EC Directive 2010/63/EC; REACH Articles 13(1) & 25(1)].

Nonetheless, the challenges for these new techniques, which are still scientifically and temporally distant, is how the high throughput datasets can be integrated into routine risk assessment and regulation. Consequently, the conclusion I draw is that Proposition 2 is not fulfilled, and that the intent of EC Objective 2, for new validated risk assessment methods and tools, has not yet been achieved. This is despite the significant research investment and scientific progress made recently, which does, however, promise much for the future. On this last point, I offer a final comment from a nano manufacturer:

> 'They are looking at a different paradigm which is far more logical and will lead to a result which we can use; rather, than the response that we must use the traditional methods and it will be £5m and 5 years to complete. Anything that has a faster throughput process, faster screening process, and allows me, as a NM producer, to assess 43 different choices, and allows me to identify the best choice to focus my attention is the right way forward' (interview 35. 16th August 2014).

5.5 Conclusions

In this Chapter, based on exhaustive discussions with interviewees, particularly from industry, regulatory and academic backgrounds, I have sought to develop plausible means for moving regulation, and its supportive sciences, forward to resolve the critical issues identified in relation to current and future public environmental health risk management for NM. My analysis has resulted in a number of key findings.

First is the general dissatisfaction with the current structure and application of REACH in respect of ensuring nano-safety, with its questionable ability for accurate exposure-driven risk analysis. Symptomatic of the current dissatisfaction, is the criticism of a compensatory over-application of the PP, as a 'stopping' rather than 'holding' mechanism in nano innovation, in response to this regulatory deficit. An industry respondent (interview 2) claims that it acts in a merely defensive manner and is not capable of providing us with a model of anticipation. In response, I argue that there is a possibility for a movement along the 'precaution to anticipation' spectrum which I develop further in Chapter 6. This proposal can address the current criticism of PP and would allow it to revert to its original purpose as an analytical-deliberative driven 'holding' mechanism when risk uncertainly is detected.

The second important finding is paradoxical in that it seems to contradict this first finding. Thus, interviewees from all backgrounds were unanimous that there should not be any new nano-specific regulations to resolve the current dissonance concerning REACH and NM. This finding is explained by an environmental lawyer (interview 17) who summarised opposition to new nano regulation on the grounds that the existing general EU chemical safety framework should more adaptive and integrative in its capability for nano risk

assessment. This key research finding is now reflected in the policy amendments proposed by the EC publication in its draft revised REACH Annexes for nano-testing (EC DO 56122/02). Even more recently, the EC General Report on the Operation of REACH (March 2018) concluded that there are some scientific gaps remain as to the suitability of test methods for nanoforms of substances, and these are being addressed in the OECD test guidelines programme.

An EC interviewee clarified this position (see interview 32 above), noting that the EC believes that REACH is technologically neutral and can be adapted to any future relevant biophysicochemical developments in science and technology. The effect intended by the amended REACH Annexes is that REACH will be structured to more accurately assess potential risks from NM and, by doing so, will meet the requirements of Proposition 1 at some time in the near future.

A third important policy issue presented in this Chapter is that there is cross -sectoral consensus from respondents that current traditional animal based observational toxicological testing regimes are no longer appropriate and need to be phased out. This position is not only in response to long standing ethical issues, as found in the EU 3Rs policy, but due to emerging scientific doubts that the single probabilistic test results may be flawed in predicting long term nano risks and nano-enabled products, due to incorrect scientific assumptions and epistemic gaps (Stirling 2016a, Jahnel 2015b). So, what is proposed to address anticipated nanoforms emerging to future markets, is the development of novel predictive risk analysis regimes. These IATS predictive methods replace traditional single probabilistic testing regimes by utilizing multiple data sources (Linkov 2007) and provide a 'weight of evidence' for decision-making (EFSA 2018; Gottardo *et al.* 2017; Jahnel 2015b; Hristozov *et al.* 2014; SCENIHR 2012). This new approach was endorsed by one

environmental nanoscientist (interview 43), who predicts that future risk assessments will be by fast, in-parallel, *in-vitro* testing utilizing high throughput cellular screening, rather than traditional *in-vivo* testing. This will also have the additional deontic benefit that higher order vertebrate testing becomes a last resort and not the first (European Chemicals Agency 2017; Rauscher *et al.* 2017; Oomen *et al.* 2015; Valsami-Jones and Lynch 2015; JRC 2014). This chimes with the aspirations incorporated within the REACH regulations (Articles 13(1) and 25(1)) and confirms that there are no legislative barriers to prevent progress towards integration of these initiatives into current regulations.

These prospective paradigm(s) changes (see Figure 5.1) promise a future of faster, flexible and more economic risk assessment tools and techniques. This is founded on the 'weight of evidence approach', which will be accessible to researchers, industry and regulators. In addition, it will allow the new scientific techniques of 'Grouping' and 'Read-across' with *in-silico* decision-making to be applied to NM. This will be subject to specific criteria, as a supplementary methodology, to hasten the risk assessment process and aid the acceleration from discovery to market. This promise of 'Grouping' NM together for risk analysis, is recognised by an Industry respondent (interview 12) and supported by EC policy makers (interview 19 & 22). Though, as yet, with a restricted application by ECHA to variants of single nanoforms rather than mixtures of NM (ECHA/NA/17/12).

These new approaches with their 'low cost risk-analysis' advocated by Maynard (2015. p200), can also have the effect of encouraging new investment in novel NM and their applications with the promotion of nano-entrepreneurship. This can further assist in avoiding the Collingridge dilemma (1980) of implementing policy controls which stifles investment with the potential loss of genuine techno-societal benefits. I also believe that the predictive potential of this new paradigm provides an opportunity to offer a more

anticipatory approach in future proofing nano-safety than is currently reflected in the current EU precautionary culture. Consequently, these new paradigm(s) can be viewed as positive steps in supporting both Propositions 1 and 2. But it has to be remembered that this is disruptive and ground -breaking regulatory science sitting at the edge of the frontiers of nanoscience and technology knowledge and understanding. So, such approaches may have their frailties in achieving proof of concept in ensuring that regulation is keeping pace with rapid nanotechnology trajectories. The consequence of a lack of validated alternative testing approaches was pointed out by an industry respondent (interview 47), who expressed the view that ECHA will, therefore, continue to rely on animal studies until this further proving is achieved. The same respondent explains that this is due to the fact that this long-established ECHA *modus operandi* provides the least organisational exposure for them to public censor of their regulatory decision-making.

So, the reliance on the single probabilistic testing methodologies is likely to continue for the time being, even with the doubts as to whether such tests realistically provide safety assurance for the whole of the (un)anticipated NM product lifecycle. Consequently, based on the discussion in this Chapter, I present in Figure 5.2 below, an outline schematic for a tiered novel predictive risk analysis methodology, which has emerged from the discussions above, showing how it might be incorporated within regulatory decision-making.

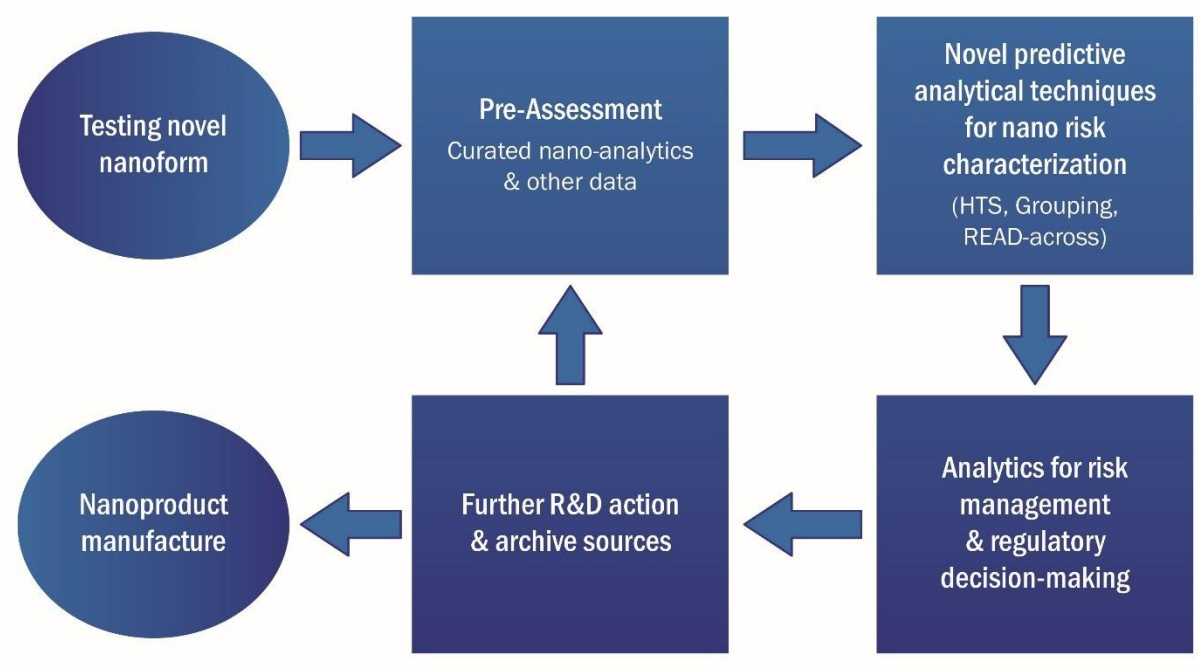


Figure 5.2. A potential approach for applying novel predictive sciences for industry hazard and exposure risk analysis and regulatory decision-making

In essence, Figure 5.2 summarises visually the findings from this Chapter, as derived from the empirical data extracted from my cross-sectoral expert interviews. It illustrates the sequential approach for nano safety testing that is being proposed in the new toxicological paradigm. The first step is the evaluation of current scientific and safety-related knowledge by accessing curated nanoinformatics and, at this stage, it may be possible to eliminate any potential threats from the NM. If not, then the sequence of testing described in Figure 5.1 above is undertaken. At each stage, an evaluation is undertaken as to whether safety questions have been answered satisfactorily, or further testing is needed or justified with animal subjects. The consequent risk analytics from the testing will provide datasets on which industry risk management and EU regulatory decision-making can be based. This may require further R&D responses by the manufacturer and/or action by regulator, or the information is archived for future referencing.

The analysis in this Chapter has thus covered the ground relating to the current EU risk governance framework for NM, its shortfall in addressing EHS gaps, and potential novel scientific analytical solutions for a faster and more robust determination of the risk and regulatory decision-making. I have demonstrated that the criticisms of REACH, and its PP underpinning, indicate that it does not yet satisfy Proposition 1 in providing assurances for nano-safety though there are now EC proposals tabled for its fulfilment from 1st January 2020 (with scientific efforts to ensure the availability of validated test guidelines and guidance currently underway e.g. Malta Project https://www.nano-safetycluster.eu/news/324/15/The-Malta-Initiative.html). I have also discussed the criticism that the PP is used too defensively within the EU and is not deployed in an anticipatory role. Following this conclusion, I suggest that there is the potential to progress 'precaution' approaches along the spectrum towards 'anticipatory' actions, which I will develop further in Chapter 6.

I have discussed in detail the novel toxicological paradigm for NM predictive risk analysis and concluding that there is a genuine potential to replace single probabilistic animal toxicological testing with a 'weight of evidence' approach. This indicates that Proposition 2 is currently unfulfilled as the novel paradigm(s) must provide high levels of public confidence in nano-safety for industry, regulators and civil society, now and into the future. This is not yet forthcoming but, nevertheless, I believe a paradigm shift in the *modus operandi* for NM regulatory sciences, based on these novel tools and techniques, is the future. Once achieved, it will provide impetus for REACH to progress to meet the industry aspiration (interview 18) for an agreed, reliable, widely recognised evaluation system with a high degree of assurance for nano-safety.

In the meantime, there will continue to be a reliance on industry acting in a voluntary responsible manner towards nano-innovation i.e. at the lowest level in the hierarchy of the Taxonomy of Regulation. In the next Chapter, I discuss how this reliance could be transformed into a more formal industry commitment to regulators and civil society by promoting Responsible Research and Innovation (RRI) within a Safety by Design (SbD) style process, and their integration into the product development process and regulatory framework.

Chapter 6: Taking forward the anticipatory governance approaches for nanomaterial innovation

6.1 Introduction

Building on from Chapter 5, here I examine how the governance gaps identified in the preceding analysis of EU nano risk policy might be bridged. This Chapter's starting point is that whilst there was widespread consensus amongst stakeholders on the need for *safe* innovation of NM, that pose no or tolerable risk to public health and the environment, innovating *responsibly* is likely to be much more controversial because of its socially constructed nature. Consequently, here I undertake an examination of the possibilities for decision-making on nano innovation changing from reliance on traditional risk calculations made by experts, to additionally incorporating the risk perceptions of publics in the final decision-taking (Rozell 2018).

I do so first by presenting empirical evidence from the cross-sectoral interview sample on obstacles and barriers to realising EC Objective 3 of the EC *NanoStrategy*. Importantly, these interviews covered not only how the PP might be augmented, to address the need for high levels of public health protection, but also discussed how the ethical dimensions of the innovation and development of NM could be tackled. Based on interviewee responses, I then seek to develop a policy approach capable of addressing EHS concerns and embedding socio-ethical values within EU NM innovation and development. The intention is to align these processes more closely with the values, needs and expectations of civil society (cf. Rome Declaration 2014).

Consequently, I identify the Responsible Research and Innovation (RRI) concept as a cornerstone for elaborating my proposed approach to EU risk governance. The growing importance of RRI was confirmed by its formal adoption by the EU first in Horizon 2020 and then in the Rome Declaration (2014). Whilst there are a number of policy, academic and industry definitions of RRI extant in the literature (e.g. Owen *et al.* 2013; Stilgoe *et al.* 2013; Von Schomberg 2013; European Industrial Research Management Association 2015), here I adopt the Rome Declaration (2014.p1) definition as :

> "Societal actors work together during the whole research and innovation process in order to better align both the process and its outcomes with the values, needs and expectations of European Society" (cf. European Commission 2012*b*).

Mertens (2018) sets out three reasons why RRI can be an effective tool for intervening in product innovation. First is that it can address radical novelty and unpredictability which requires early assessment; secondly, this early assessment can influence and amend innovation trajectories; and, finally, anticipation of unknowns prepares for unpredictable futures. Reber (2018) describes RRI as being driven by technology mediated interactions with stakeholders. Notwithstanding these possibilities, the main barrier to applying RRI in an industry setting is that it does not have a recognised policy mechanism for implementation (Burget *et al.* 2017; Goujon 2016, Antelo 2016; Blok and Lemmens 2015; Wickson and Carew 2014). Consequently, this Chapter seeks to develop a practical mechanism to implement RRI within a holistic Analytical-Deliberative model for NM development (see Figure 6.6). I do this in steps in this Chapter by synthesising insights from RRI with other decision-making models.

The PP plays an important role in developing the Chapter's argument as it underpinned RRI's origins and emergence (cf. Reber 2018, Genus and Iskandarova 2018, Von Schomberg 2013),

as both PP and RRI are designed to be both precautionary and anticipatory. As I show later, both are also suited to inclusive multi-level stakeholder participation. Related work by Gottardo *et al.* (2017), Kraegeloh *et al.* (2018) and Suarez-Marino *et al.* (2017) also identifies the PP as a precursor to the closely related 'Safety by Design' (SbD) concept that seeks to eliminate (and if not eliminate to control) EHS risks at the design stage of products. Importantly, these authors assert that SbD provides an exemplary platform for the timely identification of nano-innovation uncertainties and risks (Jantunen *et al.* 2018).

In developing this conceptual model from work set out in the previous Chapter, I argue that as PP is the critical EU treaty bounded principle for preventative health and environmental protection, and is closely related to the evolution of both RRI and SbD concepts, it offers a powerful high-profile policy instrument for harnessing RRI and SbD in tandem to address the stated goals of the EC *NanoStrategy*. Therefore, in this Chapter, I propose an implementation model that combines these conceptual approaches to enhance anticipatory action to modulate EU NM innovation and development (Fisher *et al.* 2006), but with more clearly defined democratic processes (Kraegeloh *et al.* 2018; Flipse *et al.* 2018). By doing so, it sets out the foundations for a co-sharing of responsibility for nano innovation (van de Poel and Robaey 2017). It further reinforces that responsibility role by ensuring that all reasonable means are applied to gain knowledge on potential risks before the technology is introduced to market (van de Poel 2016).

As discussed in Chapter 4, I derived from each EC policy objective a corresponding research proposition, which I use here to establish the inter-relations between the aspirational normative standards for EU nano policy as set out in the Strategy, and the current on-the-ground empirical reality of risk governance of NM as perceived by leading stakeholders. Here

I compare and contrast EC Objective 3, and its corresponding research proposition, with interview responses to enable my empirical analysis. The third proposition is as follows:

Proposition 3 [derived from EC Objective 3]- 'RRI can act as an anticipatory governance mechanism for embedding socio-ethical values for safe design within nano-innovation'.

I examine the practical implications of this third proposition on NM development through in-depth consideration of interviewee responses drawn from the cross-sectoral survey to provide rich empirical analysis in a structured manner. The primary data shows that the application of RRI and SbD within nano innovation receives strong cross-sectoral support, though industry representatives were less enthusiastic. I identify reasons for this industry attitude, noting that these probably originate in the day-to-day technoscientific, financial and market driven pressures on SME nanomanufacturing businesses. The Chapter also highlights the contrasting socio-cultural norms over what is meant by acting 'responsibly' in the innovation context and considers the role of financial and other incentives as a policy response.

I argue that a solution to this impasse may lie in recasting SbD as a policy mechanism to inculcate RRI into everyday business practice. Thus, rather than having a single normative 'safety' function within NM product development (van de Poel and Robaey 2017), I propose the pragmatic deployment of SbD to engineer change in business management, reorient product development, and to encourage wider social learning among industry and regulatory actors. I contend that this novel approach would also be assisted by introducing a systematic linear stage-gating process to help mitigate the traditionally 'messy' business process for nano-innovation (Gottardo *et al.* 2017; NanoReG2 http://www.nanoreg.eu/; Cooper 2001). While EU funded research projects present SbD as an undifferentiated procedure based solely on regulatory 'safety' (NanoReG2 http://www.nanoreg.eu/;ProSAFE

http://www.h202-prosafe.eu/), I argue that this misunderstands the potential opportunity for harnessing RRI and SbD in tandem to develop a normatively driven 'design' profile for NM , co-produced with civil society, and conterminously with a more traditional 'safety' profile. This approach would be driven practically by PP, RRI and SbD acting in combination. I designate the novel outcome of this synthesis of approaches as 'Safety by Social Design' (SbSD).

In the latter part of the Chapter, I argue SbSD would offer an adaptive and integrated multi-modal approach, combining quantitative experimental risk analysis data with qualitative data derived from deliberative processes. It foregrounds RRI's role in industry, by taking it from a position of being relatively invisible to operationalizing it within the SbSD process. In turn, this provides a foundation for fulfilling the expectations for RRI to shape 'design strategy' for nano-innovation, as envisioned by von Schomberg (2013). SbSD could thus facilitate meaningful engagement of socio-ethical values for 'safe design' into nano-innovation as a means of fulfilling EC Objective 3. The starting point for this new conceptual and practical approach is the empirical analysis of cross-sectoral interview data, and the framework for this is described in the next section.

6.2 Proposition and conceptual basis for analysing the empirical data

As in Chapter 5, here I examine qualitative interview materials drawing on the relevant literature and conceptual models identified in Chapters 2, 3 and 4. To do so, the patterns and relationships between the secondary data and my study goals have been formulated into **Proposition 3.** In review, this states '*RRI can act as an anticipatory governance mechanism for embedding socio-ethical values for safe design within nano-innovation.* I

define anticipatory governance as 'a broad-based capacity extended through society that can act on a variety of inputs to manage emerging knowledge-based technologies while such management is still possible' (Guston 2014. p225). This process includes ideas in anticipatory ethics, future-oriented responsibility, upstream public engagement and deliberation (Hester *et al.* 2015).

The Rome Declaration(2014) notes RRI is a procedure that could potentially play an important role in EU policymaking on innovation in cutting-edge technologies such as NM. The Declaration proposes the encouragement of societal actors to share responsibility in the co-production of the processes and outcomes of innovation R&D. Thus, in my cross-sectoral interviews, I explored with respondents what role RRI might play in inculcating normative values into the nano-innovation process for safe design outcomes. On the basis of their responses, I then explore potential policy mechanisms for enacting RRI for that safe design. By examining Proposition 3, I also seek to critically examine the capability of RRI to instil a more anticipatory approach to EU nano risk governance than is currently offered in the manner in which PP is utilized. Specifically, this would focus upon co-produced evaluations of the social value and utility of the outputs of nano-innovation. By this means, the Chapter investigates whether current EU regulatory-driven risk governance, when modified by an RRI component, can achieve the fulfilment of EC Objective 3.

I begin this Chapter's analysis by examining the underlining tensions and barriers experienced by industry actors engaged in the nano- innovation process. Initially, I underestimated the depth of feeling amongst them of these daily tensions, and the relational influences and pressures caused by the pursuit of divergent business objectives (Reichow 2016). These tensions were most definitely on display as I conducted the industry

respondent interviews, particularly those arising from the financial, technical, marketing activities and social engagement of SME nano manufacturers.

6.3 Obstacles and barriers shaping nano-innovation at the business level

Policy statements published by international and national chemical industry organisations, such as the International Council of Chemical Associations (ICCA https://www.icca-chem.org/) and the European Chemicals Industry Council (Cefic https://cefic.org/), foreground their support for the concept of 'responsible care' within the industries they represent. This industry commitment seems strongest among multi-national chemical manufacturers, with less evidence of adoption amongst SMEs (van de Poel *et al.* 2017). However, multi-nationals may focus on Corporate Social Responsibility (CSR) policy and brand image rather more than the principles for RRI (Hemphill 2017; van de Poel *et al.* 2017; Owen *et al.* 2012). In fact, van de Poel *et al.* (2017) identifies that few companies have developed and adopted explicit RRI strategies within their corporate plans. In interviews I sought to gauge the scale of industry 'buy-in' for the responsible research and innovation concept for nano SMEs. Importantly, this issue was regarded by industry respondents as often opaque, with its implementation depending on corporate culture (e.g. business values, norms, attitudes and behaviours) that defines the identity and mode of operation of firms (Herzog 2011; Schien 2009,2006). Industry interviewees acknowledged that innovation cannot occur in isolation, and that this organic process always required interaction with other organisations and actors (Ruggui 2015, UK Government Chief Scientific Adviser 2014; European Science Foundation 2013; Von Schomberg 2013; Rip 2012; Deuten and Rip 1997),

but RRI did not appear within their list of business priorities as a means to engage outside the traditional group of innovation actors.

Despite, interview 53, noting that multiple actors are involved in NM production, manufacture and marketing. To this matrix of influences, we can add investors, insurers, government funders and regulatory agencies. On top of this can be layered the potential for a high likelihood of product failure, product functional under-performance, problematic manufacturing in product scaling-up, decreasing technological relevance and lack of market appeal (Christensen 1997). One academic respondent emphasised that NM innovation is a multifaceted progression, requiring businesses to manage both techno-scientific complexity and the diversity of actors within the structure of the innovation process itself:

> '[Innovation] complexity tells us that there are lots of interactions and feedback loops. The eventual outcomes in terms of its shape and its success are not dependent on any single actor for its success, but in the series to be found in the whole chain and its lateral connections' (Interview 48. 12th December 2014).

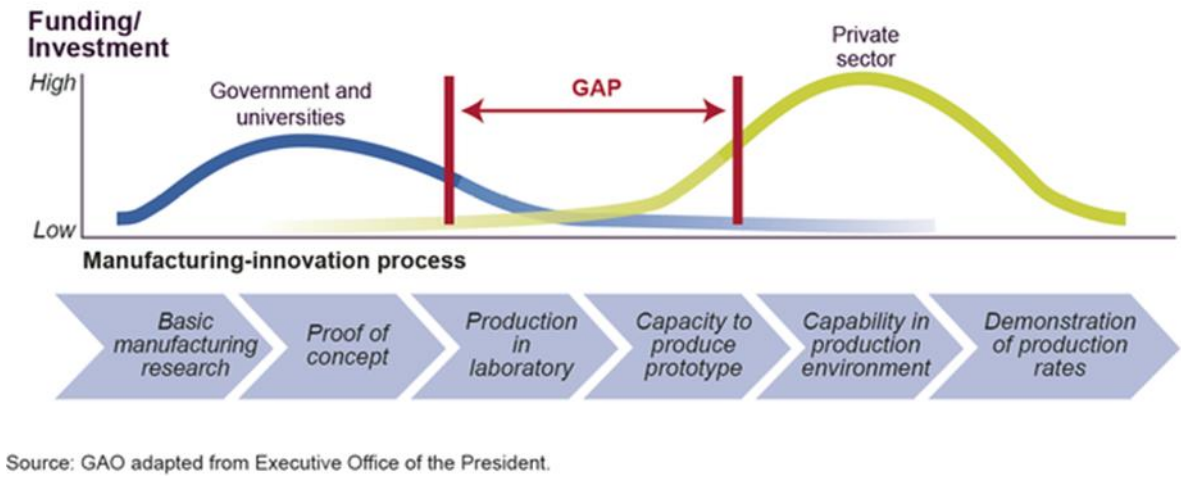
This complexity was explained to me by a leading nano manufacturer in their description of the EU market for NM as follows (see Case Example).

Case Example: Nano entrepreneur describing the complexity found in nano-manufacturing.

> 'There are four different applications of nanomaterials. First is as a replacement technology - I use micron today, but I will now use nano tomorrow. Secondly, as a little drop of nano does you good - nano used to enhance an existing product, for example to strengthen a coating (I call it pixie dust!). Thirdly, is to use nano as a carrier for a different functionality; one example would be as a drug carrier. Finally, as a brand-new application from a new discovery – whether this is to develop a new market or into an existing market does not really matter. If it is to replace a micron material with a nanomaterial, then it is difficult to enter the

micron market unless you make the right connections. In fact, this is the dominant thread. It is about making the link between your capabilities and what their application requirements are…. In my experience, it takes about seven years from discovery of a new [nano] material to the time it is being used. It is very difficult to keep yourself [financially] alive during this period and you need a good product that will keep the funders investing' (Interview 35.16th August 2014).

This brief case example illustrates the complexities of identifying the correct application for the NM, and the demanding nature of business survival. Industry managers require an astute understanding of market conditions, a capability to seize new market opportunities, and a determination to maintain business stability in trying market conditions while new products are marketed. The final crucial point in interview 35 is the need to keep the business "alive" during product development and marketing. This is known colloquially as traversing the 'Valley of Death'. It is illustrated in Figure 6.1 below as the 'GAP' above the innovation value chain



Source: GAO adapted from Executive Office of the President.

Figure 6.1. Bridging the capital investment funding gap in the Nanomanufacturing Innovation Value Chain. Source: USA Government Accountability Office (2014)

Significant numbers of SMEs fail to successfully traverse this 'gap' before their product gets to market (D/G Research and Innovation 2017; USA Government Accountability Office 2014). Another important point made in the case example is the difficulty of technology transition. This was supported by a global aerospace respondent who offered their experience of the difficulties and barriers to overcome when innovating new products:

> 'A key aspect in … [named company]….is the technology transition. The company set up a group to look at all the lab scale technologies and then identify the path from transition to manufacture or high-volume scaling. The key challenge is with the marketplace. There is a cost to production of the materials (for example foundry capital costs, or growth chambers for carbon nanotubes). So, this costs a lot of money. Then to upscale to the implementation to full scale production. It may not be marketable in a relatively small-scale marketplace which may only have a volume of thousands of units instead of the millions needed to make it financially viable' (Interview 13. 13th October 2013).

These failures often arise because of the inability to make the transition of high - performance NM from the lab bench to profitable industrial scale processes. In fact, this is where a significant number of nano innovations fail (Directorate-General Research and Innovation 2017; USA Government Accountability Office 2014). This is a well-recognised phenomenon that often contributes to investor risk aversion to disruptive technology projects, including nanotechnology. Rip (2012) makes the point that this is a substantial challenge even for large well-founded companies, which often prefer these early risks to be taken by SMEs. An NGO respondent concurs with Rip's observation:

> "They [multi-nationals] say to me that innovation works best at the smallest level and to let them [SMEs] do the dirty work and [they] only pick up the product once it is in a more marketable form" (Interview 49. 5th May 2015).

This apparent risk aversion was supported by an interviewee from another global aerospace manufacturer:

> 'The biggest problem is identifying funding streams (within our company). If we are lucky 1 in 10 or even 1 in 20 will spark further interest to take it further. It is often down to the enthusiasm of the staff member' (interview 14. 12th November 2014).

While larger financially-sound manufacturers are reluctant to invest in novel technology, the difficulties faced by SMEs in the innovation of nanoproducts was explained to me by a representative from a UK government sponsored technology hub:

> "We give SMEs the opportunity to takes risks. ….. If they fail, they can pick up the pieces quietly and start over again. …. but having [already] been through the process of product maturation where we have been incubating companies through the Valley of Death… for investors, the problem is one of technical risk aversion where if you back the wrong technology it can break your company…. I have seen good companies slowly lose their investors and go under as they simply did not understand what is needed to be done to make their company successful" (Interview 25. 7th April 2014).

A SME nano-manufacturer provided a further insight into the continuous demands placed on businesses from his own personal experience:

> 'What happens is that technology that you could integrate your materials into disappears as the landscape changes year on year … we knew enough about developing the new technology, but we did not know enough about commercializing it.' (Interview 8. 22nd August 2014).

The key finding from these interviews is that innovation is a highly unpredictable set of processes that can unleash changes that threaten company survival. Thus, industry

interviewees persistently returned to the financial, technology and marketing pressures facing SMEs. These include the need for constant technological fixes, upscaling production to match market volumes, and commercializing their products in crowded marketplaces. Crucially, these business challenges are often overlooked in the literatures on the business application of RRI. This oversight has led, in my view, to an unbalanced view of the commercial perspective of the nano-innovation process. There is also a lack of awareness of the parlous financial state for many SMEs as illustrated above. I think it is reasonable to conclude from the above interviews that constant techno-economic pressures side-line the adoption of RRI by SMEs. Indeed, it is quite possible that SMEs consider that they have no other choice but to offload that responsibility and product liability to an unknown future (cf. Gee 2015; Owen 2015*a*; Beck 1995).

Packaging responsible innovation as a value-adding driver for business and economic success is a daunting challenge in these competitive business environments. The framing of RRI as contributing to product competitive advantage, generating market share, or enhancing shareholder value, may be one answer. But this overlooks the implicit goal of many industry respondents which was to 'aim low' to secure business survival via minimum legal compliance. Moreover, an academic with regulatory experience underlines how little regulation supports commercialization:

> 'In no way does the regulatory framework help the passage through the 'Valley of Death'. There are a number of factors including how the product is designed, and a number of other issues to do with the economy and commercialization of that product which regulation does not influence at all' (Interview 36. 16th September 2014)

In summary, the commercial nano innovation space appears fraught with potentially fatal business pitfalls irrespective of company size, but particularly so for SMEs. In turn, this poses challenges for framing the introduction of more regulation as a positive influence on NM innovation and commercialization. Macnagthen *et al* (2016) believe that the current pragmatic or consequentialist risk-based approach for EU regulation has limited impact on shaping the outcomes of the R&D process. A general impression that I gained from nano-manufacturer respondents is that regulatory compliance (REACH) is just another obstacle to progressing novel NM to market, and one to be avoided if at all possible (see Chapter 5). If their prime motivation is to develop then sell their nano innovation to a larger company, they want to achieve that before they have to invest in expensive testing regimes. This prompts the question of whether and how EU regulation and RRI could be harnessed together to positively influence nano innovation outcomes to address EC Objective 3. If so, then they must both move from being regarded as obstacles to innovation to being crucial contributors in enhancing business survival and profitability. I now discuss how the empowerment of RRI as a deliberative process within nano R&D might achieve this.

6.4 Responsible Research and Innovation and nanomaterial product development: a way forward?

As discussed in Chapter 5, recent EC policy pronouncements on REACH confirm that NM will be further regulated following adoption of the revised testing Annexes from 1st January 2020 (EC DO 56122/02). Nevertheless, the yawning gap between rapid nano techno-scientific advances and their ethical and regulatory oversight through legal and public policy means is growing – what is described as a 'pacing' problem for regulators (Bowman 2017; Reichow 2016; Marchant *et al* 2011; Owen *et al* 2009). With no new EC policy solutions to the pacing

problem emerging, Hemphill (2017) argues that a new form of 'hybrid' public-private governance framework should be implemented to fill this gap. Hemphill uses the term 'public governance' to refer to EC public policy, regulation, and EHS standards for risk management that together underpin public research, manufacturing and consumer safety controls (cf. Hemphill 2017; Hemphill 1992). 'Private governance' is self-regulation by actors that comprises a mix of actions for responsible innovation, risk management and voluntary industry standards (cf. Hemphill 2017). The proposition does not go so far as to suggest that this is the perfect solution for mitigating EHS nano risks, but that it may be the best option at this time given the continuing uncertainty surrounding nano-safety. In this context, I take 'hybrid governance' to mean 'possible combinations of hard and soft law elements that complement each other, influencing day-to-day activities in the same sector to support the same end-goals' (Vaughan 2015. p3). This hybrid governance can be viewed as a further iteration of the Taxonomy of Regulation (CEPS 2014) previously discussed. In this way, formal and informal norms may be 'yoked' together to provide an alternative policy solution to EC top-down hierarchical governance. There will, of course, be doubters on both sides of this argument. Those who suggest that the emphasis on private governance will undermine the role of public governance and provide loopholes for the less scrupulous; whilst others may argue that public consultation is too costly in time and resources with little value adding benefit.

While I agree with Hemphill (2017) that key components of private governance are responsible innovation, risk management, and voluntary industry codes, as the preceding analysis shows, I would argue the contextual industry sector circumstances are of equal importance. In particular, that NM applications will necessarily influence the actual selection of the policy and regulatory tools that are necessary for application to specific nano- enabled

products. The test for this hybrid governance model, if it is to be of value, is that it must emphasise foresight with both precaution and anticipation within adaptive systems (Wiek et al 2016). [Note: This mirrors the discussion in Chapter 5 regarding the correct application of the PP]. Both the public and private governance frameworks will need to be complementary and acting in synchronicity if they are to influence the relentless dynamic of nano- innovation. Feitshans (2013) suggests that for governance models to be truly effective they need to be continuously adaptive to their contextual dynamics. This theme of governance 'adaptivity' is a constant in the literatures from Klinke and Renn (2012) and others. Following the preceding discussion, if Proposition 3 is to be fulfilled, then the hybrid governance model must also be responsive to normative values and associated socio-ethical issues.

This is where RRI (Rome Declaration 2014) can have a specific role to play as explained to me by an NGO representative:

> 'RRI definitely is a valuable approach. But the one thing that I find very interesting in that approach is that it provides something of a systemic change in the R&D process to provide safer, more socially beneficial products**.** The other side of the coin, in that discussion, is that all systemic changes must meet systemic obstacles…… [Named companies] are operating in an economy and within a regulatory system which does not reward this approach'. (Interview 55. 7th April 2017).

The lack of regulatory incentives or tangible support for companies to incorporate RRI into its business processes is a critical issue raised by this respondent, which I will discuss later in this Chapter. But for now, having discussed the business section meters for implementing a viable RRI approach, I will now examine the specific benefits and constraints raised by

interviewees regarding the utility of RRI to meet the requirements of Proposition 3 i.e. as an *anticipatory governance mechanism to embed socio-ethical values into the EU nano-innovation process*.

6.5 Aligning RRI with nanomaterial innovation and development

As previously mention in Section 6.1 , Mertens (2018) offers three reasons why RRI can act effectively in NM product innovation. These are its ability to promote early assessment of radical novelty and unpredictability; secondly, this early assessment influences the amendment innovation trajectories; and finally, it assists in the anticipation of unknowns and prepares for unpredictable futures. All three capabilities can then be applied for RRI in its technology mediated interactions with stakeholders (Reber 2018). Notwithstanding these possibilities, Stilgoe *et al* (2013) comment there are major limitations in applying RRI if it does not develop the capacity for adaptive foresight. Nordmann (2014) summarises this position succinctly by stating that anticipation is the cornerstone of responsible innovation. However, Torgersen and Fuchs (2017) argue anticipation requires upstream debates that avoid assumptions that emerging technologies, such as nanotechnology, are simply derivatives of established parent chemicals and technologies. This important point was illustrated by comments made in an interview I conducted with a science philosopher:

> 'We should avoid that the RRI model becomes only a new way to merely confirm the existing arrangements' (Interview 52. 22nd February 2016)

To avoid such a scenario, Jahnel (2015*b*) suggests that RRI must become a central component of EU nano risk governance policy. There are two strong arguments in support of this. First Reber (2018) and others argue that RRI is an inheritor of the mantle of PP, as

they are both designed to be safety concerned, yet futures facing by incorporating deliberative action. Consequently, this highlights the 'precaution' element in its formal application. Secondly, Macnaghten and Chilvers (2014) propose that responsible innovation is essentially 'anticipatory' in nature. In that, it takes the debate on risk governance beyond the current narrow consequentialist framing of EHS, to emphasise upstream questions such as why NM products are being developed, and what societal aspirations these novel products might meet. This blend of precaution and anticipation provides the necessary downstream knowledge for decisions on the hard and soft impacts of innovation (Mahapatra 2016).

Nevertheless, persuading industry actors that RRI is more than a 'moral notion' (e.g. aspiring to a rightness of behaviour), and has a practical and beneficial purpose is a challenging EU policy hurdle. RRI will require careful elaboration, in a manner sensitive to the complexities of nano-innovation, if it is to become a focus of meaningful co-design and decision-making (Grunwald 2017; Gianni 2016; Pelle 2016, Greenbaum and Groves 2013; Bessant 2013, Sykes and Macnaghten 2013). Torgersen and Fuchs's (2017) study of upstream participation shows how expert practices can be shaped by specific socio-ethical contexts, thereby aligning R&D outcomes more closely with societal values. However, I argue the case also needs to be made to businesses that incorporating socio-ethical considerations within nano-innovation is more than a moral imperative and has a capability to enhance business value and outcomes too. This viewpoint is extensively supported within EU and national governmental policy publications which directly address the purpose and outcomes for beneficial commercial nano exploitation (cf.EC NanoCode 2008, UK Nanotechnology Strategy 2010, USA National Nanotechnology Initiative 2014, 2016 & 2019; German Nanotechnology Strategy 2020, EU Horizon 2020).

Foley *et al* (2016) believe that by this means the nano-innovation regulatory process could move beyond its current largely negative perception that 'precaution' is applied as a 'brake' to innovation and the development of novel NM. As discussed in the previous section, this has resulted in SMEs not engaging with RRI as it is thought that it stifles innovation practices or lacks business relevance. Indeed, Macnagthen and Chilvers (2014) consider that short term commercial pressures are trumping longer term societal and ethical concerns. On this issue one NGO respondent stated to me that:

> 'I am genuinely interested in any ideas as to how we can include [RRI] within the governance framework section (for business) which reflect opinions and issues relating to the socio-economic environment. The problem is, that no-one is coming forward with any views on how we might do this'. (Interview 49. 5th May 2015).

Whilst an academic interviewee suggested that:

> '[RRI] must be broken down, clearly defined and context specific – otherwise it means nothing more than something we regard as 'nice' (Interview 31. 25th May 2014)

This statement acknowledges widespread criticism of RRI for, variously, lacking implementation guidelines and state backing (Macnaghten *et al*.2016), having no clear boundaries (van Outheusenden 2014), and instigating an open-ended process (Delvenne 2017; Wickson and Carew 2014). As interviewee 31 comments identify, that addressing these challenges means developing an RRI model that offers individual interpretive flexibility to match specific business contexts. To me, this interpretive flexibility and contextual specificity are crucial issues, if RRI is to have any real relevance whatsoever within the nano innovation process. Van de Poel *et al* (2017) make the point that little attention is given to

the business context such as the resources available and the type of market the company operates within. Therefore, the crucial question then becomes: how can RRI be implemented in a way to stimulate a cultural change among businesses, by effectively incorporating socio-ethical issues into NM innovation and development, yet be reflective of contextual issues? I focus on this question next.

6.6 'Strong' RRI: driving social learning to change business culture

Coenen and Grunwald (2017) describe the traditional innovation consultative arrangement in business as follows. An 'expert' group assesses the technology in a predominantly elite manner, posing questions that are to be answered by themselves or another expert body. These authors characterise this as a 'weak' RRI activity. On the basis of the preceding analysis, I argue what is now needed to strengthen RRI is formal participatory civil engagement to identify societal benefits and disbenefits arising from the innovation process. This reflects the intentions of Proposition 3 and EC Objective 3, by being inclusive of a wider range of civil society opinions. Coenen and Grunwald (2017) and Grunwald (2016) identify this 'strong' model for inclusive participation beyond the simple one-way communication of knowledge transfer. Applied to NM development, this implies active co-participation by civil society in nano product design and specification. This would not apply simply to a specific NM, but more generally across the sector to build trust in nanotechnology futures incrementally (cf. Deeker *et al* 2017, Reichow 2016). One academic interviewee describes the setting needed for this to be achieved:

> 'Adaptive Governance is to do with an ongoing social learning process … we should not take the future and its technological implications as a kind of given

> which we are trying to manage before they even exist! So, we need to work in real time, with social learning within the experimental mode.' (Interview 50. 21st June 2015)

To achieve the aspirations of this interviewee, 'strong' RRI will need to be incorporated within an adaptive model of continuous collaborative social learning that includes multiple actors in the decision-making process (Murashov and Howard 2016; Rijke *et al* 2012). In its simplest form, social learning is learning by direct experience or from the experiences of others (Bandura and Walters 1977). Clark (2010) proposes that social learning in a technoscientific environment, as referred to in interview 50 above, is strengthened between individuals and organisations, by connecting the actors from different expert networking communities, and increasingly entwining government and civil society through these procedural arrangements. Potentially, this approach could be extended to the adoption of the proposal from Van Wezel *et al* (2018) that business incubators (the high-performance technology hubs discussed in interview 25 above) are supplemented by 'societal incubators'. The existing technology hubs could provide the spaces for such civil and technologist interactions. This is a proposal to implant scientific and normative outcomes, from experimentation and collective learning, early into the upstream process for developing nano-commercial products. Though to build industry confidence in this process will need careful planning for issues such as protecting commercial confidentiality.

Another way forward is suggested by Van Wezel *et al* (2018) who propose that a cornerstone for embedding wider societal norms and values within experimental research and technology projects, is to imbue this philosophy within higher education programmes for scientists and technologists. In my interviews with academics, one respondent made this point:

> 'We believe that education and training is the most significant way to change cultures, and that is why RRI is a key priority for the EPSRC and is include in the curriculum for the Centres for Doctoral Training' (Interview 42. 21st November 2014)

'Strong' RRI thus requires broad societal engagement and also the means of enabling an adaptive social-learning process to encourage and cement longer-term productive relationships. Lee and Petts (2013) emphasise that to achieve productive and influential outcomes of this kind, means developing industry competencies and public engagement skills not readily available to SMEs. In addition, Flipse and van de Loo (2018) note that non-expert stakeholders may need to develop interactional capacity and greater technoscientific knowledge to engage meaningfully in their critically productive manner. By this means, such actors can become more trusted and valued by industry, not just for critical capacities but also for unexpected creative insights and perspectives (Fisher *et al.*2006). Such competencies will have to be acquired by all parties if well-informed and timely opinions are to be incorporated within the nano innovation decision-making.

Notwithstanding the need to resolve this issue, I believe RRI can be beneficial in its anticipatory bridging role as posited in Proposition 3. I discussed this point at length with an EC Administrator who flagged the frailties of current nano policy as follows:

> 'One failure of (EU) governance is that classically we have looked too much to the technological potential of that particular innovation, but we do not address it in the innovation context. So, the shift is in their development from responsible technology to responsible innovation that defines and incorporates socio-ethical values…. The essence is to move from a technological exploitation point of view to the innovation point of view but with social objectives. But this lesson is not well appreciated yet' (Interview 53. 8th March 2016).

This statement is a good summation of the preceding discussion, and also of the views held by the EC administrative respondents. In EU terms, there is a lack of incentive operating within its political economy and current regulatory system to recognise the value of incorporating legitimate socio-ethical concerns into nano innovation. I believe that the lack of researcher and industry engagement with this adaptive and integrative approach would benefit from forms of industry incentivization. These incentives could raise nano-innovation practices beyond lowest common denominator issues, such as minimal legal compliance, to aim higher to incorporate wider societal aspiration and obligations. The relevance of this proposal and the forms it might take are discussed next.

6.7 Incentivizing business uptake of RRI

The dilemma for EU policy makers since RRI was first proposed in *Science and Society* (EU *Horizon 2020*) is to find the triggers for its adoption and implementation by businesses. As interviews with industry respondents confirm, there is strong evidence of the daily difficulties they face in the nano innovation space, and the absence of government initiatives to facilitate these. An NGO respondent emphasised this point:

> '(Company name) … (Company name) ... and SMEs and others are operating in an economy and within a regulatory system which does not reward this approach**.** Without addressing those issues, there is very little chance that these approaches can multiply and gain real traction at the appropriate scale, because the economic and legal incentives are going in exactly the opposite direction' (Interview 55. 7th April 2017).

However, whilst proposals for incentivization have an immediate attraction, we need to be mindful of Maynard's (2015.p200) warning that responsible innovation needs to be integrated into business practices in a manner that does not "exacerbate the dilemmas

entrepreneurs face*".* Notwithstanding that cautious note, the lack of regulatory recognition for responsible innovatory approaches (Kraegeloh *et al* 2018) puts the onus on voluntary industry responses. Forms of incentivization that could encourage voluntary responses include financial incentives (e.g. encouraging/attracting new investors, reduction in insurance premiums) passporting through regulatory regimes (by demonstrating that key criteria have been met); reduction of potential risk of future liabilities (in relation to the EU Product Liability Directive); industry certification/accreditation; and a distinguishing '*Responsible innovation*' Charter-Mark and/or trade-mark for customer recognition in market branding (Kraegeloh *et al* 2018; Stone *et al* 2017; van de Poel *et al* 2017; Suarez-Merino 2017). In interview an EC administrator also commented on the importance of supporting incentives with other complimentary approaches:

> '…. growing awareness of companies and their attitudes that if they are bound within certain [regulatory] ecosystems, they may be helped directly by funding local authorities or other incentives' (Interview 53. 8th March 2016).

Bush (2010) notes the use of these types of incentives constitute a form of hybrid governance in itself. Von Schomberg (2013) acknowledges that such a form of hybrid governance, correctly designed, can cover deficits in public governance with a market equivalent. He believes that the predicted volume of new nano processes/products to market are no longer manageable by government(regulatory) agencies alone. Thus, such incentives could become valued self-governing elements within the context of private governance discussed above. This conceptual approach can be developed as a meaningful, even powerful, contribution for embedding RRI which certainly deserves further exploration. Interviews with EC administrators, industry and academic representatives thus generated interesting and potentially valuable ideas with which to progress an integrative and adaptive

social learning model for nano-innovation. As interviewees comments make clear, the basis of such a social learning model lies in its having interpretive flexibility appropriate to contextual socio-cultural and business settings. I recognise that this could be both a strength and a weakness, as it may generate competing or even contested choices in individual adoptive practice. These must inevitably run up against the pragmatic commercial drivers and alternative choices found in nano-manufacturing. This dilemma was highlighted for me by one SME nano manufacturer:

> 'The last thing I want to do is to develop a toxic material. My preference is for benign, but I may use a material with some toxic effects to achieve functionality… if we think they have toxic potential, then we use them responsibly'. (Interview 24. 16th August 2014).

This statement takes us to the heart of the matter, which is the socio-cultural differences amongst cross-sectoral actors as to how 'responsibility' is framed. For industry, NM functionality for product utility may be paramount for driving product profitability, meaning responsibility is about 'acceptable/tolerable risk' rather than 'social desirability'. However, RRI, in its focused sense, is fundamentally concerned with anticipating problems within wider socio-cultural and ethical contexts, rather than restricted to risk/safety issues. Maynard (2014) makes the point that a major influence of RRI is in creating adaptable systems that respond to unexpected consequences, but, importantly, they must be based on plausible futures. If such outcomes are achieved, then it can be said to fit with Proposition 3, with its capability to transform innovation discussions into a public dialogue (Stilgoe 2011). Yet interviewee 24 above implies that 'responsibility' is narrowly defined around levels of toxicity potential rather than a value-led approach to nano innovation. Therein lies the major challenge for RRI, how to motivate a SME to move from unstructured and

internalized self-regulation to embedding a more formalized RRI procedure within its manufacturing process. An EC Administrator respondent summarised these barriers very neatly:

> 'SMEs struggle to incorporate RRI into their corporate space due to competing demands on technoscience progression, financial survival and investor resistance' (Interview 53. 8th March 2016).

Moreover, Solbu (2015) emphasises that any credible RRI model needs to go beyond a research/industry tacit understanding for what it means to act 'responsibly'. However, finding a shared notion from amongst all the interviewees as to how this framework might work proved challenging. The fact is that for RRI to be implementable and effective it must be adaptable in dissimilar research and industry settings within differing R&D contexts. How RRI may be incorporated into business practice is currently being research by EU funded projects such as PRISMA (http://www.rri-prisma.eu/) which is examining how responsible innovation can be better integrated into different industry innovation practices; COMPASS (https://innovation-compass.eu/) which is researching a RRI self-check tool for SMEs, and SMART MAP (https://cordis.europa.eu/project/rcn/203167/factsheet/en) which developed open and collaborative dialogues between industry and societal actors (Industrial Dialogues).

Interviewee 53 addressed this point regarding the importance of recognising differing industry sector contexts for RRI by commenting:

> 'RRI can be different in different forms in different industrial settings. Very often topics need a case specific approach, but with general principles applying' (Interview 53. 8th March 2016).

There are both strength and a weakness in resolving this conundrum. The strength is that it would apply across the range of differing industry settings; the weakness that it may bring inefficiencies due to different interpretations and applications of its principles. Nevertheless, I think this is a risk worth taking. After all, embedding other relatively new principles into business practice, such as 'Environmental Management Systems' and 'Sustainability' have taken time for their value to be recognised in the commercial world. With this in mind, the temptation might be to make RRI a means to an end – just one more set of standardized procedures. As the same EC administrator considered the pitfalls of doing so:

> 'There is a risk it becomes instrumentalized and set within boundaries, and consequently loses its flexibility and currency'. (Interview 53. 8th June 2016)

Stirling *et al* (2018. p15) describe 'instrumentalization ' as the engineering in of our pre-existing aims and by doing so constraining/limiting potential outcomes'. Nevertheless, by reminding ourselves of the previous criticisms of the 'looseness' of policy guidance for RRI implementation, the instrumentalization of RRI, into a more formalized anticipatory governance process, may simply be needed at this stage to kickstart the process of industry adoption. Without such a mechanism, RRI may continue to be a vague moral notion with no practical purpose or long-term influence. Consequently, in the following sections I consider the potential for utilizing the Safety by Design (SbD) concept as a mechanism for the practical application of RRI within the nano innovation space.

6.8 Synthesising anticipatory decision-making approaches: the Precautionary Principle, Responsible Research and Innovation, and Safety by Design

SbD is an engineering process currently applied across disparate technological platforms such as construction, pharmaceuticals, computers, and aerospace industries (Kraegeloh *et al* 2018; Gottardo *et al* 2017). Its purpose is to provide an operational map for directing new nanoproduct projects from discovery/idea(s) to market launch as efficiently and effectively as possible. In its stage-gating form, it fits well with the modern manufacturing value chain pathway where, at each stage, progress is tested against selected parameters viz. occupational and consumer risks/safety; economic viability; product quality parameters, operational feasibility, and product marketability (Cooper 2001,2008). If any of these tests are failed, then the product may be deemed as a failure and a decision taken to discontinue development.

The purpose of SbD is to identify risks in the early stages of technology development , and to identify solutions to mitigate or eliminate them (van de Poel and Robaey 2017). As previously mentioned, SbD is an engineering process now practised within a number of industries (Suarez-Marino *et al*. 2017; Gottardo *et al*. 2017). In the EU policy/regulatory context, SbD is now established as an important concept within EU funded research projects to achieve 'Regulatory Preparedness' and 'Sustainable Innovation Assessment'(Katalagariniakis 2018; Gottardo *et al*. 2017). Previously discussed in Chapter 2, this is when the EU regulators are given early warning by industry of forthcoming nano innovations, the timeliness of which allows the checking that current legislation serves the safety aspects or may need revisions (JRC 2018; NanoReG2 http://www.nanoreg.eu/; GRACIOUS

https://www.h2020gracious.eu/). This is in an analytical risk assessment role for SbD to act as a new pillar for REACH NM regulatory control (Gottardo *et al.* 2017). In this context, Gottardo *et al* (2017.p100) describes the role of SbD as a process that considers and incorporates safety considerations into product design and development, by addressing the functionality of a material and its toxicity in an integrated manner. The application of SbD is this format is principally driven by regulatory sciences and can be described as built on the single narrow normative value of 'safety' only (van de Poel and Robaey 2017). There is a lack of evidence from the EC that this new decision-making process will be inclusive of a broader deliberative engagement outside of nominated expert actors. Notwithstanding this current policy position, I suggest that now SbD is being foregrounded by the EC for full engagement within the NM regulatory compliance process, it provides an opportunity to address that deliberative deficit by acting as the mechanism to incorporate RRI into nano innovation processes for the following reasons. First is the strong cross-sectoral support by interviewees for the perceived benefits of incorporating a Safety by Design approach within nano-innovation. This is demonstrated by a précis of cross-sectoral interview comments:

> 'I believe 80% of the risk factors can be dealt with at the design stage' (EC Administrator. Interview 23. 1st March 2014)
>
> 'Applying Safety by Design is good business' (Academic. Interview 43. 21st November 2014)
>
> '(For defence) Safety by Design needs to be right at the beginning' (Environmental Lawyer. Interview 17. 11th November 2014)
>
> 'Absolutely…. the checking of the materials in terms of their safety and their functionality would up the sense of development' (EC Administrator. Interview 32. 27th May 2014)
>
> 'Safety by Design makes sense' (UK regulator. Interview 30. 20th May 2014)

These positive comments are representative of the broad-based cross-sectoral support for SbD, though industry respondents were more muted in their support. The lack of enthusiasm was not restricted just to SMEs, as might be expected, but shared by a respondent from an EU based major chemicals manufacturer. This is a global company with a public policy commitment to the International Council of Chemical Associations initiative for 'responsible care' (see section 6.3). Yet the company interviewee was quite clear on their negative stance to SbD:

> 'All products undergo risk assessments before they are marketed, and we publish all our results on the risk assessment…we are trying to do this is a transparent way. This is a huge shift in the [company name] attitude. We do not specifically do safety by design. We do not use this for what we are doing' (Interview 47. 3rd December 2014)

This response provides a window into the thinking of this international nano manufacturer on the subject of SbD. This viewpoint is held despite public virtue signalling for their own transparency through the process of scientific publications. The implication here is that the nano industry does not see adopting SbD as priority within their manufacturing process.

What this mindset does imply is that adopting SbD for NM development is a strategic issue for the nano industry and not for one-off technology exercises, so that SbD is required to fit within its corporate business plans, product portfolios and marketing strategies or not at all. Such corporate positioning would allow it to have its greatest influence on innovation outcomes and be the right way to deploy SbD to achieve strategic impacts.

Notwithstanding this somewhat contrarian view from industry respondents, I believe that the strong cross-sectoral support evidenced above for SbD within nano innovation encourages the exploration of new possibilities as to how it might be utilized outside of the

current narrow regulatory framing. So, as my second reason, I offer a conceptual argument for believing that RRI and SbD can be combined in a practical manner to deliver both analytical and deliberative outcomes. The foundation for this viewpoint is that RRI (Reber 2018; Genus and Iskandarova 2018; Von Schomberg 2014) and SbD (Kraegeloh *et al.* 2018; Gottardo et al 207; Suarez-Marino et al 2017) are both posited as contemporary inheritors of the PP. In that for all three conceptual approaches safety is the fundamental concern, but they do have a future-facing capability which can be founded on a deliberative mechanism. Thus, collectively, they have the potential to act in both precautionary and anticipatory modes and can be the focus for multi-level stakeholder deliberative participation. It is my proposal that PP, as identified as a precursor to SbD and RRI, acts as the sponsoring concept for linking both together (see Figure 6.2) and, in doing so, provides the conceptual foundations for enabling Proposition 3.

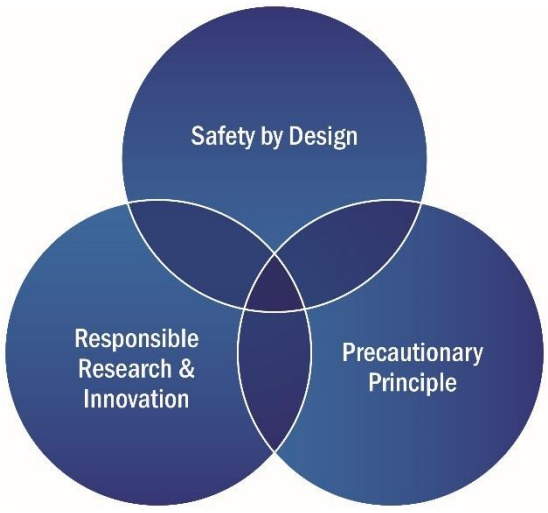


Figure 6.2. The Precautionary Principle as sponsor for combining Safety by Design and Responsible Research and Innovation.

As discussed in detail in Chapters 2 & 3, PP plays a critical policy and regulatory role for promoting high levels of public health environmental protection within the EU. PP is paramount within EU treaties and risk policies by its explicit responsibility for delivering on EU health and environmental protection obligations. It is also foregrounded within REACH

as a fundamental component in the application of those chemical safety regulations [REACH Article 1 (3)]. As a consequence, its tenets, as set out in [COM2000], are central to EU risk policy making and regulatory action for protecting its communities. Its tenets design it to be applied proportionally in both a precautionary and deliberative manner (COM2000). Consequently, as an identified precursor of both SbD and RRI (see literatures above), PP provides both justification and legitimacy for bringing together RRI and SbD into a new policy configuration (see Figure 6.3 below). By harnessing these concepts, it provides for a precautionary and anticipatory hybrid governance framing described earlier in the Chapter by Hemphill (2017). I believe this new conceptual approach offers an enhanced capability to resolve safety and responsible design issues for NM, with its emphasis on the co-production and shared responsibility for nano-enable products. By inviting others to share in the shaping of this emerging technology, they may bring novel contributions that result in a more effective process for achieving safety (van de Poel and Robaey 2017).

The outcome from the blending of the three extant concepts is to generates a novel conceptual approach which I term 'Safety by Social Design' (SbSD) in Figure 6.3 below.

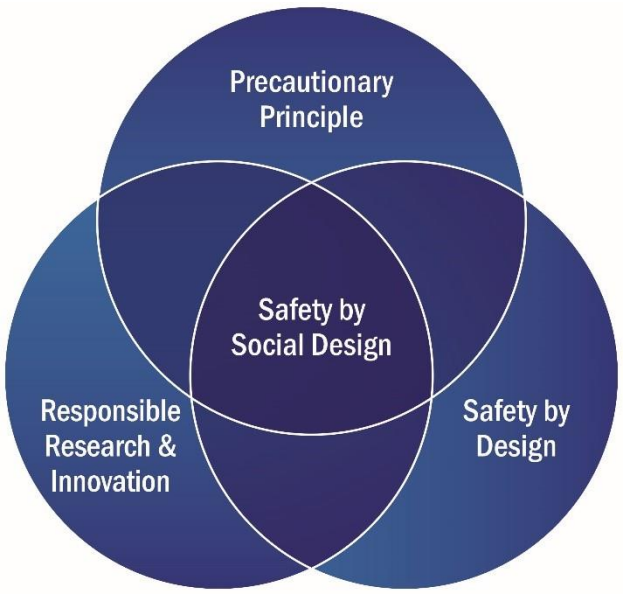


Figure 6.3. Safety by Social Design – a composite of the Precautionary Principle , Safety by Design, and Responsible Research and Innovation concepts

I provide a more detailed justification for this novel approach as follows:

The three policy and regulatory principles being applied here are all approved and adopted by the EU. Of the three, the PP is the most important in its role as a ' First Order' principle as it is the foundational principle within three EU treaties and within REACH [Article 1 (1)] for promoting 'a high level of human and environmental protection'. It is applied when there is 'reasonable grounds for concern' (COM2000.p2). Its policy and regulatory positioning provides for a high level of legitimacy as it sits the politico-economic, technoscientific and socio-ethical intersect. In its guidance document (COM2000), it is meant to be deployed in both a precautionary and anticipatory role, when there is scientific evidence that identifies reasonable grounds for concern for adverse effects from a chemical process, activity or product. As a consequence, it has two limbs, firstly as a 'Precautionary' limb(COM2000.p2) in which it acts as a 'holding' position on the innovation process until further optional

analysis is undertaken; secondly, as an 'Anticipatory' limb (COM 2000.p6) which requires the involvement of relevant stakeholders in a deliberative engagement for shared decision-making in selecting the most appropriate option.

I identified in Chapter 2, that there continues to be significant criticism of the PP for its precautionary limb being applied within a 'hazard-centric' scenarios which make it difficult to make any accurate assessment or measure of the probabilities of risk occurrence(van de Poel and Robaey 2017). With its 'Anticipatory' limb, its role is more likely to be observed in the breach for problem resolution. So that this central policy and regulatory principle is not being correctly applied.

My proposal is to utilize SbD and RRI to activate the Precautionary-Anticipatory limbs of PP for NM within the contemporary construct of SbSD. Firstly, SbD can be applied as both a principle, for upstream modifications (Gottardo *et al* 2017) within a stage-gating engineering process to resolve complex techno-scientific risks (Cooper 2001). Currently, SbD is adopted by the EC for application within regulatory sciences as a new pillar for REACH (Gottardo *et al* 2017; NanoREG 2) but with networking confined within expert groupings. So, SbD I propose that the role of SbD can be to activate the expert driven techno-scientific component for the precautionary limb.

Secondly, I am proposing that RRI be the bridging mechanism to activate the Anticipatory limb of PP, thereby facilitating the deliberative engagement of non-expert /civil actors in a manner to influence the outcomes of the nano innovation. This democratic engagement will then provide a platform for a further list of socio-technical feasible options to be tabled as solutions to the identified problems.

Collectively, the interlinking and interaction of the three principles provides for the new construct of SbSD. Within this construct, the precautionary and anticipatory debates are

hardwired together for shared decision-making and outcomes on a range of issues including potential risks, regulatory compliance , social utility.

I will explain in the next section why I believe that SbSD can enhance the current EU risk governance framework and, in doing so, enable the fulfilment of EC Objective 3.

6.9 Evaluating the benefits of Safety by Social Design

'Democratization' of the current risk governance framework requires its adaptation to facilitate debates with the potential for multiple value-led outcomes (van de Poel and Robaey 2017). To achieve this goal means amending this framework so that it is deliberatively as well as analytically constructed. To do so, my proposal is that SbD is conceptually linked with RRI and PP to promote a culture of co-creation/shared responsibility for the safe and responsible outcomes for novel innovation products (EC Horizon 2020 .16. EC2016). This new construct I have identified as SbSD.

Kahneman (2003) highlights a drawback in standard innovation practices in that technical actors can be constrained by bounded rationality, and seldom grasp the socio-ethical considerations within their complex projects. RRI is judged to have the capability for deliberative intervention into innovation processes (Von Schomberg 2013; Stilgoe *et al* 2013; Owen *et al* 2013), and offers opportunities for incorporating civil actors norms, values and concerns into R&D processes. In other words, the technical actors (scientists, technologists) can interact responsively and reflexively with non-expert and civil actors to modulate nano innovation trajectories (Flipse and van de Loo 2018; Lukovics and Fisher 2017; Flipse *et al* 2013; Fisher *et al* 2006). A jurisprudence academic outlines why this form of governance is favoured above the current criticized single probabilistic regulatory testing regimes:

> 'That is why I (would) use governance more that regulation as more solutions may be found there. What I mean by governance is the producers building in some sort of foresight into what they do and led by soft law… that the soft law supplement is the way forward until we resolve the regulatory issues for NM'. (Interview 39. 5th November 2014).

In contrast to conventional risk management, the new risk governance methodologies will run alongside traditional comparative assessment methods. Thus, quantitative multi-criteria evaluations can be used to identify alternative options in respect of EHS, techno-economic costs, product viability and social utility (Linkov *et al* 2018; Malloy *et al* 2016), and then incorporated into deliberative discussion with civil actors. Nevertheless, Nordmann (2018) highlights a critical issue with regard to implementing deliberation: when is it the right moment for those interventions? Too early, and the intervention could stifle or lose all the anticipated benefits; but too late, and the late recognition of technology driven problems can meet the resistance of technological lock-in and pathway dependency (Owen *et al* 2009). Nordmann (2018) suggests that the 'right' moment lies on a continuous innovation scale which triggers action when societal concerns are identified or arise in advance of technological lock-in occurring.

Whilst helpful this advice is somewhat vague and, as such, may be this concern points towards adopting a more resource and process efficient stage-gating approach (Cooper 2001), based on a commonly accepted modular engineering process which will integrate easily within existing nano R&D practices. It provides for a step by step methodology for multiple stakeholder engagement at pre-determined stages in the innovation process (e.g. pre-manufacture). Flipse and van de Loo (2018) believe that, by such experiences, critical outsiders can bring unexpected insights, whilst developing technological and interactional

expertise for future RRI collaborations. Ribeiro et al (2018) suggests that this can be in the form of a graduated process of 'societal alignment' of innovation with societal needs and values. Nordmann (2018.p335) contrasts that 'societal alignment' does not mean 'societal control'. Instead proposing that '**control** suggests that science, technology and innovation can be steered via top down mechanisms based on technical rationality; whilst **alignment** moves the focus to more horizontal relationships and constant negotiation over the needs and concerns of diverse actors. This means less controlling and more of an influencing action. An academic respondent provides examples of potential contributions from civil actors:

> '…they could (learn to) reframe the questions that they ask, such as can I make it more biocompatible, or more recyclable? Is there a place for a cleaner, more renewable way of doing this? There is always a possibility that someone will use the NP for some use for which it was not intended' (interview 29. 5th May 2014).

In conclusion, my proposal for the re-configuration of SbD and RRI together offers the prospect for enhanced democratization of the nano innovation process, and the incorporation of a process for multi-value led outcomes. This is achieved by operationalizing RRI within the modified SbD process, which I identify as SbSD, and which offers the prospect of fulfilling Proposition 3. In Figure 6.4 below, I provide a schematic for RRI acting as the democratic bridging mechanism for socio-ethical considerations into the SbSD process and acting as a social learning model.

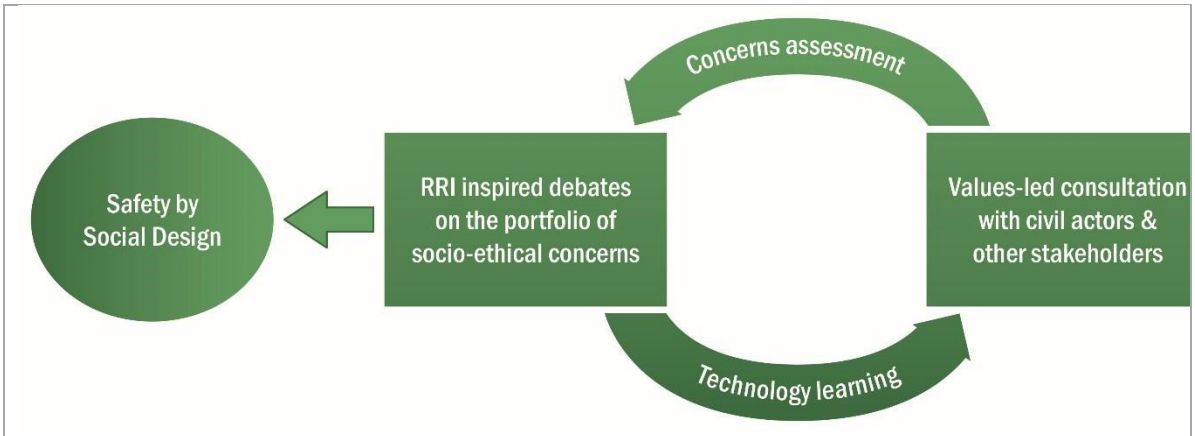


Figure 6.4. Responsible Research and Innovation concept acting as a bridge for socio-ethical considerations into the Safety by Social Design process as a social learning model

I contend that utilizing RRI as a bridge for socio-ethical criteria into the SbSD process meets Genus and Stirling's (2018.p62) definition of 'anticipatory' i.e. 'in the sense of exploring possibilities (not making predictions) and analysing intended and potentially unintended impacts that might arise'**.** It offers a practical means of exploring the socio-ethical values-led positions of stakeholders which can then influence the innovation trajectory. It also can assist in addressing an important issue, highlighted by van de Poel and Robaey (2017), of reducing the indeterminacy of future unintended consequences and impacts by this shared responsibility for safe design. RRI's 'deliberative' values-led consultations can be described as participative and inclusive to wider societal perspectives, with the expectation that expert actors respond reflexively and positively to these deliberative interventions.

Appropriately implemented, this proposal for deliberative value-led interventions amounts to a significant change to the proposed EC *modus operandi* for SbD. By this I mean, SbD would no longer focus only on analytical-led 'regulatory preparedness' but transforming its role into a dual conceptual approach that is simultaneously analytical and deliberative. This construct is founded on both the practical development and adoption of 'Risk' and 'Design' profiles for the NM (see Figure 6.5 below).

The inputs for the 'Safety 'Profile are derived from the tiered quantitative and qualitative analytical risk assessment processes for NM identified in Chapter 5. Hansson (2009.p1069) advocates safety as the inverse of risk, that is when the risk is high then safety is low with the converse to be true. So that within the processes of the 'Risk' Profile, when probabilities for harm are identified risk management actions are devised to mitigate them. The testing of the risk assessment data against approved scientific/legal standards, allows the identification of essential risk management implications, and the actions necessary to determine risk tolerability, risk management actions and to achieve regulatory compliance.

The 'Design' Profile is a more broadly-based matrix accommodating diverse information and product utility scenarios that can influence the shaping of the nano-enabled product. Examples are given in Figure 6.5 below, including industry sectoral applications (food, computers etc), industry best practices (approved codes of practice), techno-economics (cost-benefits of scaling up for manufacture) mixed with the civil actor value-led concerns. This matrix can then produce design parameters for the NM or its product to achieve.

These can be both eclectic and narrowly product dependent, and inclusive of the range of value-led concerns expressed in the civil consultation process. Possible examples of concerns could include not misusing rare natural resources, avoiding adverse manufacturing practices and emissions, and evaluating the product social utility. Collectively, the Safety and Design Profiles provide for the critical inputs to the SbSD decision-making. With the two profiles then simultaneously available for debate and decision by business actors and their relevant stakeholders in trusted consultation fora.

The participants in this consultative forum need not be restricted only to those involved in the data collection and developing the profile presentations. The debates will weigh the

relative merits/deficiencies of the constituent data and decisions within the 'Risk' and 'Design' profiles.

Figure 6.5. Safety by Social Design model – With 'Safety and Design' profiles provide for the analytical and deliberative inputs and outputs

These profiles will influence co-decisions regarding nanoproduct safety, feasibility, marketability and social utility. Taking all these above factors into account, I define Safety by Social Design as "the *process that assesses safe product design and social utility by evaluating its functionality, potential (eco)toxicity, predicted consumer applications and its societal alignment in an adaptive and integrative manner'*.

These SbSD outputs will influence both regulatory readiness and nano-enabled product development, manufacturing and marketing. In this novel format, I believe that SbSD will enable the fulfilment of Proposition 3 which states that *RRI can act as an anticipatory governance mechanism for embedding socio-ethical values for safe design within nano-innovation'*. The strategic consequence is that by this mechanism EC objective 3 could be fully enabled.

However, my research is founded on the prospects for the enablement all three EC nano strategy objectives within the ambition of a single holistic model. I discussed in Chapter 3 the prospects for an adaptive and integrative risk governance model (Klinke and Renn 2012) encompassed within an analytical -deliberative framing (Rosa, McCright and Renn 2013) to enable this ambition. Van de Poel *et al* (2017) suggest that adaptive risk management can be a useful tool for realising the benefits of RRI within a social learning process as to the risks and their future management. What I am proposing next is that such a model is possible and can be developed within an adaptive and integrative risk governance framework. This will be a whole system approach which addresses the critical discussions in Chapters 5 & 6. I discuss these possibilities in the next section.

6.10 Safety by Social Design as a facilitating mechanism for an adaptive and integrative EU Risk Governance Framework for Nanomaterials

The intentions of the model in Figure 6.6 below is to provide an adaptive and integrative risk governance approach that goes beyond basic legal compliance responsibilities, with the societal alignment of the nano innovation process as a critical outcome. The model has a modular framework that combines the processes for risk characterization with socio-ethical

concerns. Firstly, the model is based on the discussions in Chapter 5 regarding the novel scientific tools and risk assessment paradigms. The analytical data would be sourced from curated nanoinformatics libraries to inform the tiered design approach for any necessary experimental risk assessments discussed in Chapter 5. These multiple data sources provide the essential 'weight of evidence' for risk management and regulatory preparedness decision-making (see Figure 5.2, Chapter 5). Secondly, I foreground the role of RRI as the democratizing influence for the participatory involvement of non-experts/civil actors in the nano innovation processes. Their purpose is generating any relevant socio-ethical concerns, arising from the proposed nano innovation trajectory, to facilitate its societal alignment (see figures 6.4& 6.5 above). By capturing Figure 5.2 ,Chapter 5, within Figure 6.5 above, I propose in Figure 6.6 below, an Analytical -Deliberative model that is both precautionary and anticipatory in its actions, and with the prospect for enabling and fulfilling the three EU *NanoStrategy* Objectives.

Critically, this model needs to work in 'real time' within a reciprocating social learning environment in order to secure greatest impact (interview 50). By this I mean that there will be a continuous updating of current science ,technology and societal attitudes into the system essential for the open-ended character of responsible innovation (Genus and Stirling 2018). The updating mechanisms will incorporate information/data/protocols from many different sources. Examples will include curated informatics held in scientific observatories, libraries, online databases etc, published experimental science and technology protocols, new regulatory guidance and updated approved industry codes of practices. All these sources can update and inform each of the activities occurring in the different modular components, which are inclusive of the reflexivity learning by those involved in the processes.

By harnessing both the analytical and deliberative processes, foresight can be built into the innovation process (interview 39), helping facilitate a cognitive shift from narrow technological exploitation to societal alignment of nano innovation (interview 53). This approach can be considered 'strong' RRI (Coenen and Grunwald 2017), because its participation is broader that an 'expert' grouping and more representative of civil society participation.

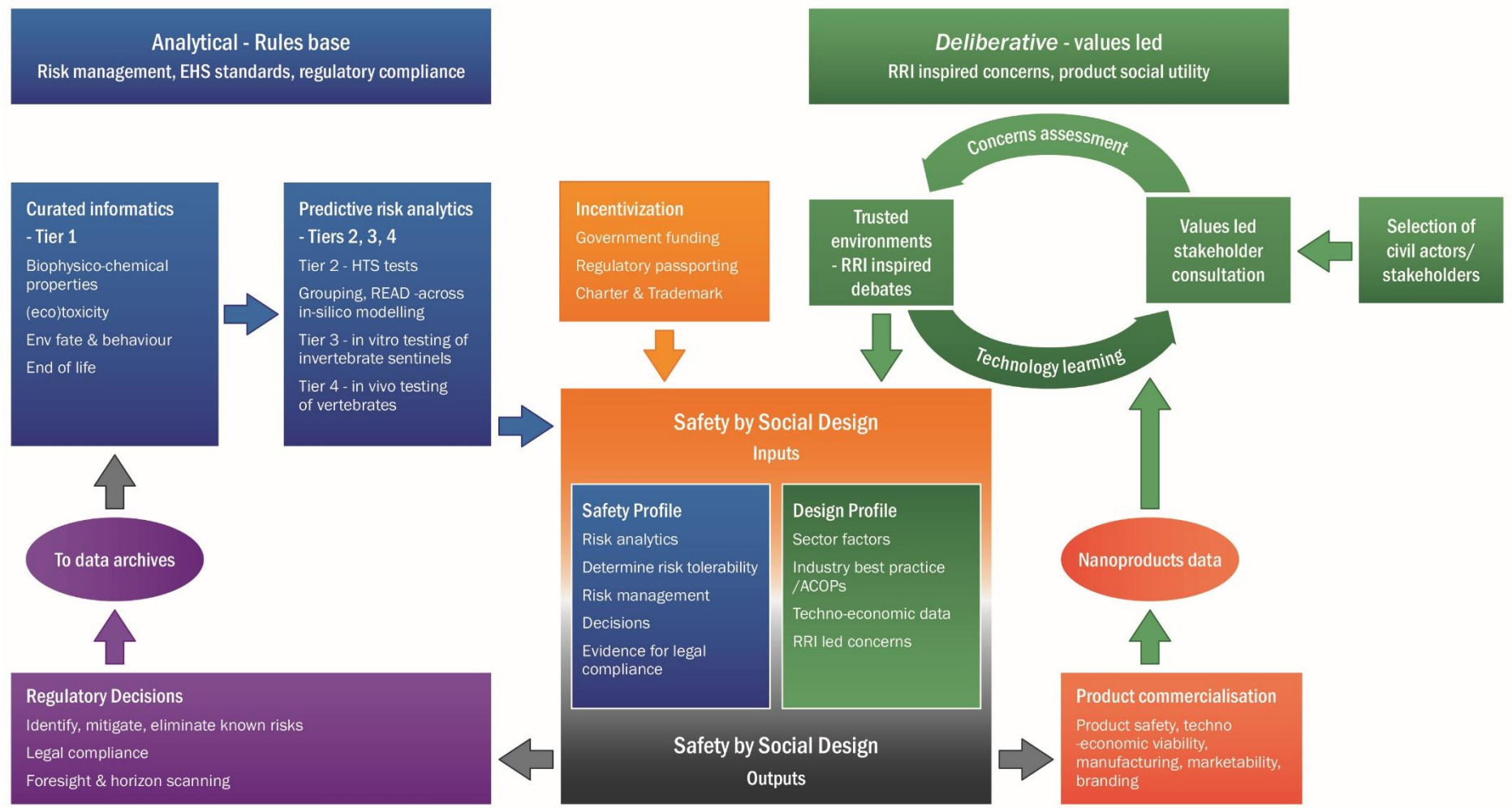


Figure 6.6. An adaptive and integrative EU risk governance framework for NM facilitated by Safety by Social Design

Note: The colour sections identify separate processes and/or sub-systems within the model

Yet, whilst this proposal is progressive, I recognise several limitations at this time. First is the fact that it is Hazard-centric rather than Exposure-centric, as the novel methodologies and tools discussed in Chapter 5 do not yet have the capability to confirm exposure assessments and their toxicological impacts. These are predicted to come online in due course

Secondly, it is still lacking the full identification of practical and beneficial outcomes for business engagement that might seize the imaginations of SME managers (see interview 31). The principal factors are that the persistent daily pressures that business, particularly SMEs face (interview 53). I, therefore, propose the answer lies *inter alia* with governments offering financial funding and advisory incentives with basic payments (or tax breaks) to help fund the additional costs of the civil consultations. There would not necessarily be a need for new regime, but it could be incorporated into existing innovation grant funding mechanism as appropriate. By this means, I believe it would attract the interest of the nano industry and their investors to utilize SbSD process, with higher payments and advisory top-ups to companies that are willing to take RRI beyond a minimum requirement. Von Schomberg (2013) and Bush (2010) believe that such state initiatives could enhance industry self-regulation and motivation. In addition, I propose the development of a portfolio of other incentives for adopting SbSD/RRI (previously discussed in section 6.7 above). These included a 'Responsible Innovation' product charter mark/trademark, as a bold statement of company commitment and a visible branding badge to encourage others to be involved. Such actions would contribute to more effective industry self-regulation identified in the Taxonomy of Regulation (CEPS 2014) and the proposed private governance approach by Hemphill(2017).

Reviewing Figure 6.6 conceptually, I argue that it offers a plausible means of enabling Proposition 3 and fulfilling EC Objective 3. It does so by achieving the criteria for incorporating responsible innovation and risk management within the same framing, and thus provides

shape and form for public- private risk governance. A critical output from this model is that RRI acts as a bridging mechanism to incorporate socio-ethical concerns in a structured manner into the nano-innovation process. This may be criticized as instrumentalizing this concept (interview 53), with Genus and Stirling (2018) also expressing their doubts regarding the over-attenuation of RRI. But I believe current circumstances dictate the need to make a start, and to overcome the current stalled progress, by providing a pragmatic opportunity to implement an opaquely perceived concept. By this means, it not only enables the production of safe NM, but allows an early risk assessment, NM modulation and product modification to influence their marketability and social utility prior to manufacture.

Finally, I examine this proposition against the recently published criteria for adaptive and integrative risk governance for NM previously discussed in table 3.2, Chapter 3. In review, I selected key recent publications that have addressed in detail the critical research areas for this thesis. The domains are regulatory compliance requirements, scientific tools for risk analysis and characterization, and the social appraisal of nano innovation. This analysis is given in Table 6-1 below.

Table 6-1. Comparative analysis of published criteria for adaptive and integrative risk governance

Domain	EC Nano Strategy 2004.*[COM (2004) 338]*	Linkov et al 2018 *Environment Systems and Decisions 38.*	Stone et al 2018 *Risk Analysis.* 38. 7	Adaptive and Integrative model *(*Figure 6.6*)*
Regulatory compliance requirements	EC Objective 1 The strategy proposed the retro fitting of safety legislation for NM which is found not to provide the necessary assurances for nano-safety	A broad evidence base is necessary for regulatory considerations in cataloguing potential risk outcomes	Legal and other (nano-specific and general) regulatory requirements are necessary to ensure compliance and to stimulate	Identifies that updated nano specific legislation with a broad evidence base is necessary for accurate risk assessment to achieve safety levels and

Domain	EC Nano Strategy 2004.*[COM (2004) 338]*	Linkov et al 2018 *Environment Systems and Decisions 38.*	Stone et al 2018 *Risk Analysis.* 38. 7	Adaptive and Integrative model *(*Figure 6.6*)*
			proactive approaches to safety	regulatory compliance.
Scientific Risk Analysis and characterization for NM	EC Objective 2 Requires the designing and adoption of new experimental tools and protocols for nano risk analysis and characterization	The new risk analytical tools continue to give incomplete answers or outcomes to comprehensively catalogued risks from NM	Identifies the continuing need for dynamic, advanced scientific tools and strategies for nano risk assessment, mitigation and transfer	Incorporates the novel scientific and toxicological paradigms for faster, more economic methods, tools, and protocols for risk analysis and characterization.
Social Appraisal of nano innovation	EC Objective 3 Proposes an expanded risk management paradigm to include socio-ethical considerations	Acknowledges the need for multi-stakeholder insights to bridge gaps in experimental risk assessment data and outcomes	Promotes the fostering of dialogue with civil society to determine societal concerns for nano innovation risks, their mitigation, and transfer	Proposes a methodology based on RRI principles for civil actor consultation and incorporation of their value- led concerns into the SbSD process for safety and product development decision making

From the above analysis, I believe that the modular framework I propose for an adaptive and integrative model in Figure 6.6 above, demonstrates its capability to meet the expectations of all three EC *NanoStrategy* Objectives. In practical terms, I suggest that this novel approach

has the potential to facilitate more reliable and conformable R&D outcomes. It could do this by encouraging the devising of new scientific risk analysis tools, alternative integrated safety testing strategies, and inspiring the exploration of new product ideas, when imagining different plausible futures for the nano applications.

A final note is that the significance of the above findings are reflected in three recently funded EU H2020 projects (all commencing 1st January 2019) which seek to address issues raised above. Their objectives include the development of a new policy framework for NM, to support a modular risk governance decision-making framework, addressing different aspects of NM governance, to be overseen by a new EU Risk Governance Council comprising of EU Member States, public authorities, scientific experts, civil society and industry representatives. (RiskGone: https://riskgone.wp.nilu.no/home-riskgone-project/about-us/ ; NanoRigo:https://cordis.europa.eu/project/rcn/220129/factsheet/en;Gov4Nano: https://www.gov4nano.eu/)

6.11 Conclusions

In Chapter 5, I focused primarily on the 'hard' law options and identified gaps in the EU regulatory control (REACH) of NM, the inadequacies of current regulatory nano sciences and their emerging alternatives, and a perceived over-reliance on the PP in its preventative rather than its deliberative mode. In response, I have examined in detail in this Chapter the potential for 'soft law' options to fill the risk governance gaps (interview 39). My focus has been on the analysis and evaluation of the respondents data sources in respect of the 'soft law 'options (Hemphill 2017; Petratos 2015; Lee and Petts 2013; Owen *et al* 2013; Bowman and Hodges 2008). Specifically, the Chapter addresses the *deliberative* component of the *analytical-deliberative* model (Rosa, McCright and Renn 2013) for an evaluative pragmatic application

for RRI, and the prospect of developing a deliberative mechanism for activating RRI within the SbD process. I examined the entwining of the PP with RRI and SbD conceptual approaches to provide the justification and legitimacy for the genesis of a novel approach I label SbSD. I also propose that a further benefit is a contemporary application PP to progress it from its current perceived precautionary mode (as discussed in Chapter 5)towards a more anticipatory mode.

I found significant cross-sectoral support for both RRI and SbD from respondents, with the exception of industry representatives. Those interviewees offered idiosyncratic opinions of what it means to innovate 'responsibly', lacked buy-in for the RRI concept, and were lukewarm towards SbD. There are, however, some mitigating circumstances for these behaviours by SMEs (though not for international companies), due to the complexity of the financial, scientific, technological and market forces that innovating SMEs must work within (interviews 35, 13, 25, 8). There is a possible explanation in that these demands result in 'responsible' innovation being purposively interpreted as narrowly addressing EHS for their nano-enabled products (i.e. minimum legal compliance only). Nonetheless, this situation does not relegate the desirability for more overt mechanisms for socio-ethical considerations to be incorporated within their innovation processes. Current EU funded research projects such as COMPASS and PRISMA (see Section 6.7 above) will contribute to a further understanding of these matters

What this Chapter has sought to do is to identify an offering for industry that demonstrates that there can be a positive business value in engaging with RRI as promoted by the EU (Rome Declaration 2014). I consider that SbSD has that potential to add tangible value to business in respect of risk management, regulatory compliance, public product viability/ marketability, and social utility. To stimulate greater business engagement (especially SMEs), I propose

state-led and other business-related incentives as further motivation for RRI engagement. I believe that these proposals offer 'soft law' solutions with which to fill the current 'hard law' gaps in EU nano risk governance. In doing so, it enables the terms of Proposition 3 to be fulfilled and EC Objective 3 to be enabled.

Finally, I finished this Chapter by bringing together all the critical findings from Chapter 5 & 6 from this study and merging them into a single holistic model which is adaptive and integrative for nano risk governance (Figure 6.6). This modular design provides for sub-systems, pathways and processes for the responsible innovation of NM which incorporates all of the aspirations of the EC *Nano Strategy*. It can also contribute into current policy discussions and, in some instances exceed them, if based on the expectations of recently published criteria for a framework for adaptive and integrative risk governance for NM (Table 6-1). In addition, it can make a contribution to EU intentions for the development of a new policy framework for NM, to support a modular risk governance decision-making framework addressing different aspects of NM governance, which will be overseen by a newly established EU Risk Governance Council.

It is my proposition that this model (Figure 6.6) provides an option for a comprehensive risk governance framework that could address the policy options for NM now being researched by the EU research projects. Through its social learning characteristics, it is receptive to legislative amendments; adaptive to new technological advances in nano innovation and so contributing to minimizing the 'pacing' problem; responsive to new scientific thinking and practices for risk analysis and characterization; with a mechanism for the incorporation of timely socio-ethical concerns within the nano innovation processes. I suggest that, by this means, the EC vision for the safe and responsible innovation of NM may be achieved.

Chapter 7: Conclusions and Recommendations

7.1 Introduction

This Chapter offers conclusions from this study on the regulatory effectiveness of policies promoting the safe and responsible development of NM. It does this by drawing together the findings from the evaluation of primary and secondary data, in the previous two Chapters, to assess progress towards achieving the EC *NanoStrategy* aim and objectives for this sector [COM (2004) 338]. The adoption of the *NanoStrategy* effectively created a new regulatory space and policy discourse for nanotechnologies, at national and international scales. The progression towards the realisation of the three key risk governance objectives from it have been the focus of my research.

In brief, the thesis's key findings are fourfold. Firstly, there continue to be EU legislative deficiencies due to: (a) the critical flaws in the REACH regulations due to its lack of specificity for NM safety testing, and (b) the scientifically contested EC definition for NM. Both of which fundamentally undermine legal authority for enforcing regulatory compliance. Secondly, there are critical scientific gaps that prevent comprehensive nano-risk analysis of the EHS implications of NM production and nano-enabled products. Thirdly, there are clear indications that the nano industry is seeking to avoid engaging with either product regulation (REACH) or social-ethical appraisal of NM production. Finally, to compound these deficiencies, the *NanoStrategy* does not provide a bespoke overarching EU risk governance framework to scrutinise either the EHS effects or the wider social implications of current and future nano-innovation pathways. I argue these policy shortcomings are aggravated by EU regulatory under-performance in failing to address what the EC has itself recognised as manifest

shortcomings in regulating NM via REACH, compromising further the effectiveness of the *NanoStrategy*. I discuss these findings in more detail below.

7.2 Summary of the main findings

Perhaps the most surprising finding from the primary data analysis was evidence in Chapters 5&6 of industry avoidance in engaging with REACH, Safety by Design(SbD) and Responsible Research and Innovation (RRI). It is a particular concern that respondents commented on legal loopholes in the REACH registration being exploited by NM companies through their manipulation of annual manufacturing outputs, so they fell below the REACH trigger tonnage levels (Chapter 5). The fact that only 29 nanoform dossiers were submitted for REACH registration in the period 2008-18 may be telling in that respect (Nanotechnology Industry Association 2018). This gives some credence to NGO respondents claims that there are NM within the consumer market currently that have not been through the REACH safety testing regime. In response, industry respondents cited the daily financial, technical and market-driven barriers to their financial survival especially for SMEs involved in NM manufacture – with the prospect of having to comply with a burdensome regulatory regime (REACH) if they successfully grow their business. Chapters 5 and 6 offer a more complete understanding of the commercial factors driving this resistance to regulatory standards and reluctance to participate in deliberative engagement.

Building on these findings, I proposed novel policy measures that might address these regulatory and deliberative shortcomings. On the deliberative side, I offered a novel way of implementing RRI by linking it with the existing industry design approach, Safety by Design (SbD). SbD has now a strong presence in some industries (as discussed in para 6.5) and has been adopted by the EC as both a policy concept and engineering process for achieving the

safe development of NM(Gottardo *et al.*2017). I now propose to utilize it to also act as a platform for implementing RRI in manufacturing settings. By co-joining PP/SbD/RRI approaches together in one platform, I argue that SbD and RRI could facilitate new expert and civil society dialogues along the nano-innovation value chain, enabling NM innovation processes to be made more transparent and accountable to consumers. In doing so, I suggest that they also provide a contemporary setting for the Precautionary Principle that enables it to meet both its precautionary and deliberative objectives for which it was originally devised(COM2000). I recommended the introduction of a new package of incentives to be made available to industry (Chapter 6) to help companies move away from the closed and opaque R&D practices that currently typify NM production. The resulting 'Safety by Social Design' conceptual approach and the mechanisms for its implementation, discussed in Chapter 6, are key outcomes from this study (see Figure 7.1 below).

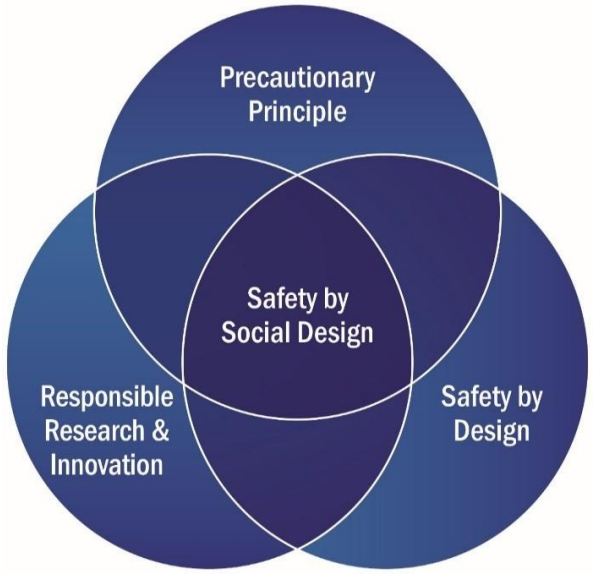


Figure 7.1. Safety by Social Design model – synthesising the Precautionary Principle, Safety by Design, and Responsible Research and Innovation concepts

Conceptually, this study provides a novel construct in SbSD, by the synthesis of PP with SbD and RRI. In doing so, it thereby extends the current reach of each of these existing approaches For example, it allows the two limbs of PP to be activated in both their precautionary and anticipatory forms in response to identified uncertainties(Per Sandin 2002, von Schomberg 2006, Stirling 2016 etc). It promotes SbD beyond the single normative value of 'safety' to a position whereby it may have multiple normative values(van de Poel *et al.*2017,Gottardo *et al.*2017). Finally, it activates RRI in an industry context, so that deliberative action can be taken in resolving socio-ethical problems relevant to NM innovation(Owen *et al*.2013, Stilgoe *et al*.2013. etc) . The aim is the greater alignment of nano innovation with societal norms, values, needs and aspirations (Ribeiro *et al*.2018, Nordmann 2018).

The SbSD conceptual approach then facilitates the proposed development of a novel adaptive and Integrative Risk Governance model for NM which does not currently exist. This proposes a holistic model of risk governance to fill that current the gap. In doing so, my intention that the Safety by Social Design (SbSD) concept offers an alternative for solutions to the regulatory and deliberative shortcomings identified in implementing the EC *NanoStrategy,* in that it may be a means of fulfilling its three risk governance objectives. In recap, these are summarised as:

EC Objective 1-Maximum use would be made of existing regulation though adjustments may be necessary.

EC Objective 2 - Existing parameters for EHS chemical safety testing may not be appropriate for the unique properties of NPs, requiring new methods and tools for risk assessment, and refinement of nano scale metrology and standardisation activities.

EC Objective 3- The Risk Management paradigm to be expanded to incorporate socio-ethical considerations into the R&D process with the creation of a culture of responsibility which is participatory and inclusive.

The model is structured to compliment mandatory EU regulatory compliance outcomes with deliberatively framed socio-ethical alternatives. The main aim is societal alignment of the nano-innovation process more closely with society norms, needs and values as aspired to in the EU Rome Declaration (2014). The model is adaptive as it is driven by continuous social learning with opportunities for multiple expert and non-expert actor engagement. It is integrative by incorporating all the elements identified in Chapters 5 and 6 as essential contemporary and future facing factors for nano risk governance decisions. By this I mean that the framework acknowledges and incorporates not only evolving scientific risk analysis knowledge, techniques and protocols, but foregrounds Responsible Research and Innovation (RRI) within the SbSD process as the facilitating concept for an inclusive and participatory engagement of relevant expert and civil actors.

I argue that the real value of this new SbSD approach is that it can address not only the EHS issues of 'safety' attached to NM, but also opens up new avenues for deliberative engagement with key stakeholders (van de Poel and Robaey 2017). Importantly, business engagement with socio-ethical issues of NM would be actively encouraged by adopting the principles of RRI (Reber 2018; Genus and Iskandarova 2018; Von Schomberg 2014; Owen *et al* 2013; Stilgoe *et al* 2013; Von Schomberg 2013). Civil society value-led concerns could then begin to inform industry and regulatory safety and design decision-making, at early product development stages, rather than arising in marketing focus groups at the end of the NM development process and/or release onto the market. Overall, I believe that SbSD could thus provide a new mechanism for instilling new dialogues and co-ordinating new collaborative activities among

stakeholders in a timely way. I believe that is approach will help avoid technological lock-in, build consumer trust and acceptance of nano-enabled products, as well as in the regulatory process itself.

However, I recognise that this model in itself is not a panacea, and that there are barriers that need to be resolve. Here I address the significant underlying structural problems that need addressing through future EU policy action. Firstly, the need for adopting nano-specific regulatory processes, such as validated Test Guidelines and Guidance documents tailored for NM, in order to provide authorative and reproducible datasets needed for industry and regulatory safety decision-making. Secondly, there is the need for proof of concept for the new scientific concepts and tools that will support the new toxicological paradigms to be utilized within the model. Fadeel *et al.(*2018) makes the point that solutions to this problem are still temporally someway off. Thirdly, the absence of policy mechanisms for meaningful industry engagement in respect of RRI and SbD is proving particularly problematic. I suggest possible solutions in terms of industry incentives in respect of future research and technology funding, taxation breaks, regulatory passporting, and charter marks. There will also be a need for new structures(possibly within technology hubs) to place and develop the Trusted Environments where these industry and civil collaborations can take place.

Notwithstanding the above, all of which could be resolved in time, I propose that SbSD could become the central processing component for both risk analytical (quantitative) and social-ethical (qualitative) data (see Figure 7.2 below). These data sets would feed into separate 'Risk' or 'Design' profiles for evaluation by expert-civil society panels. These discussion outcomes would provide the foundation for a broad range of decisions in respect of nanoproduct risk management, regulatory compliance, product viability, marketability and its social utility. I define 'Safety by Social Design' as "*the process that assesses safe product design and social*

utility by evaluating its functionality, potential (eco)toxicity, predicted consumer applications and societal alignment in an adaptive and integrated manner'.

Having briefly outlined my main findings, I now turn to answering the three questions posed in the introduction to this thesis based on my analysis of the primary qualitative data.

7.3 Analysing the research propositions

In Chapter 4, I describe how the three research propositions that underpin the research in this thesis were derived from the three EC *NanoStrategy* risk governance objectives [COM (2004) 338] to provide the fundamental analytical framing for this study. The structure for the thematic analytical framework to address these questions is discussed and set out in Table 4-2 of that Chapter. As set out in Chapters 5 and 6, each proposition was validated through analysis of qualitative interview responses from the cross-sectoral sample of 55 respondents in this study.

However, an important point for research set in a *post-normal* context must be highlighted. It is that there were no lay members amongst the 55 respondents interviewed for the reasons discussed in para 4.3.5 above. Instead, I proposed that the NGO respondents could act as their proxies, and I believe that to an acceptable level that has occurred. Nevertheless, I do need to emphasise that the absence of lay members in the debates needs to be recognised as an important factor for this study and its subsequent findings. Though I do not consider it significant enough to skew the findings sufficiently to invalidate the study outcomes.

Below I address each proposition and summarise the outcomes of the Chapter analysis.

7.3.1 ***Research proposition 1****: 'Current EU regulation (REACH) does provide assurances for public environmental health safety*

Proposition1 reflects on the question whether the EC *NanoStrategy* risk governance objective for the retro- fitting of existing legislation to include and cover NM has been effectively implemented. My analysis endorses that there is a basic definitional problem at the heart of the EU *NanoStrategy* – namely that there is no scientific consensus currently as to what constitutes a NP. It follows that, without an accepted measurable scientific metrical definition, with legal authority to clarify what differentiates a NP from any other chemical substance, enforcement action under REACH is problematic and challengeable. A draft EC definition of NM was proposed in 2011 (2011/696/EU), but interviewees noted there was scientific disagreement over the validity of this draft leading to the EC's Joint Research Centre (JRC) conducting further scientific reviews (JRC 2013, 2014,2015). Whilst supportive of the proposed EC definition, these reports have not yet brought this issue to an agreed conclusion, resulting in the EC proposing a further public consultation which may take place later in 2019 (EUR 27240 EN). With Miernicki *et al* (2019) recently concluding that this situation means that nano innovation may be facing a pathway full of legal uncertainties. Without a legally authorative definition, enforcement of NM regulation via REACH becomes extremely problematic, undermining regulatory assurances for nano-safety. Notwithstanding the efforts of the EC in funding the EU FP7 NanoDEFINE project (http://www.nanodefine.eu/) to find a scientific solution to this critical issue.

This problem is further complicated by the identification of the cross-sectoral disillusionment of respondents with the inadequate nano-specific provisions within REACH for addressing nano-safety. The original REACH regulations are silent on NM and treating them like any other chemical substance (Bowman 2017). However, advances in scientific understanding has

identified that their unique properties require nano specificity in the published REACH risk assessment protocols. This disillusionment is further exacerbated by a deep frustration caused by the perceived dilatory EC response to requests for policy action to resolve this critical safety issue. Thus, there are strongly expressed complaints from industry and other respondents that this regulatory deficit has resulted in an over-reliance on the application of the Precautionary Principle (PP) based on policy intention rather than evidence-based risk assessment (COM 2000). These frustrations may have been the trigger for some EU Member States to set up their own National Registers for NM and nano-enabled products e.g. France (2012), Belgium (2013), Denmark (2013), Norway (2014) and Sweden (2018).

Notwithstanding the strength of these complaints there was, counter-intuitively, no demand from any respondents for new nano-specific EU safety regulations to supplant REACH. This is a surprising and unexpected finding, bearing in mind the strength of feeling expressed about the current legal loopholes in NM definition and REACH regulations. So, interviewees are not averse to REACH *per se* as the principal EU chemical safety regime. Instead, their preferences is for a revision of the REACH annexes to incorporate nano-specific testing protocols. Since I drew these conclusions from the empirics, the EC have announced a REACH upgrade of exactly this sort, with the aim of providing nano-specific testing protocols from 1st January 2020 (EC DO 56122/02). Amending REACH in this way offers the prospect of meeting EC Objective 1, and it is highly likely that a metrical solution will be found for the current scientifically contested EU nano definition in due course (EUR 27240 EN).

However, these policy proposals offer no solution to nano manufacturers exploiting existing loopholes in REACH, so that they do not need to submit chemical registration dossiers for regulatory approval prior to bringing new NM to market (Jantunen *et al* 2018). Closing these loopholes, by significantly reducing annual manufacturing tonnage trigger levels for NM for

example, is unlikely in the foreseeable future as recent history has demonstrated laggard response by the EC in NM matters. Consequently, I believe this unsatisfactory situation flags up an urgent need for different perspectives to be incorporated into how the EU policy can achieve nano-safety outcomes. One approach suggested by interviewees is greater emphasis on industry self-regulation. Though not ideal this proposal does suggest a foundation for a more formalised approach that could draw upon aspects of a self-regulative approach based around principles of responsible innovation. This matter will be discussed in more detail in section 7.3.2.

Thus, Proposition 1 cannot be accepted as REACH manifestly does not provide acceptable public assurances for nano-safety at this time, though it is recognised that efforts have been made in this direction (ECHA 2017(a),(b),(c)). The explanation lies partly in the flawed EU policy to retrospectively apply REACH without nano-specific amendments. It is compounded by the dilatory (ten-year) lag in the EC approving new nano-specific REACH amendments, and the still unresolved nano definition issue. This EC laxity may have contributed to resistant behaviours by NM companies, with evasion of REACH registration protocols meaning products may be on the market containing untested NM. This is particularly important when the NM is included in a product because it exhibits a very specific functionality which may influence its reactivity and thus its untested potential toxicity. So, any evasion tactics reflect poorly on both the nano industry and the EC policymakers, who have not yet signalled that they are aware of this issue and have not attempted to close that loophole.

Notwithstanding these regulatory gaps, there also continue to be sizeable knowledge deficits in epistemic nanoscience, risk assessment testing protocols, risk characterization, and accurately derived EHS safety standards which also undermine the capability for regulatory

action. I discuss opportunities to provide new solutions to these long-standing dilemmas in the next section.

7.3.2 ***Research proposition 2****: 'That novel scientific tools and predictive paradigm(s) can provide future confidence for industry and regulators in nano-safety decision-making'*

The second research proposition addresses the current lack of scientific knowledge underpinning the enforcement of REACH and other EU nano regulation. It is derived from the EC *NanoStrategy* second objective that '*Recognises that existing parameters for EHS chemical safety testing may not be appropriate for the unique properties of NPs, requiring new methods and tools for risk assessment, and refinement of nano scale metrology and standardisation activities'*.

Testimony to this lack of nano-specific scientific protocols was an industry interviewee who summarized for me the widely-held opinion that the current toxicological testing methods for NM were "not fit for purpose" (Interview 24, Chapter 5). There is increasingly compelling evidence that current single probabilistic toxicological tests, that use vertebrates and other organisms for regulatory evaluation, provide flawed results e.g. false positives/false negatives (Stirling 2016a, Jahnel 2015b). I therefore canvassed opinions among interviewees on the novel toxicological techniques that are now emerging for NM evaluation, which utilize multi-cellular testing assays rather than animal tests, and which employ multiple primary and secondary data sources (cf. ECHA 2017; Stone *et al* 2017; Hjorth *et al* 2016; Jahnel 2015a, 2015b; Oomen 2013; Stone *et al* 2013; Nel *et al* 2013). Importantly, these techniques derived from emerging Systems Biology work offer the prospect of moving from single probabilistic testing to a 'weight of evidence' approach for nano-risk characterization (Gottardo *et al* 2017; Jahnel 2015b; Hristozov *et al* 2014; SCHENIR 2012). Research projects are now being

extensively funded by the EC for the development of future predictive toxicological profiling for tiered hazard and risk-ranking of NM (NanoSafetyClusterhttps://www.nano-safetycluster.eu/).

Analysis in Chapter 5 concluded that these novel cellular based methodologies have the potential to lead to faster, flexible and more economic risk analysis as demanded by industry and could offer them a number of important potential benefits. These include accelerating nano risk characterization processes, reducing regulatory compliance timescales, hastening nanoproduct discovery to market, and the deontic effect of minimizing animal testing. With other economic outcomes such as reducing nano entrepreneurial costs, earlier payback on investments, and promoting investor interest. However, much experimental work needs to be conducted to develop the necessary scientific methods, tools and protocols for these techniques (Fadeel *et al*. 2018), and to ensure they are predictive of *in-vivo* outcomes to protect general public health and that of consumers. Proof of concept is still outstanding and until there is, current animal testing for regulatory purposes will continue. These outstanding issues suggest a regulatory approach based around multi-cellular testing and Systems Biology still lie some way off (Hjorth *et al.* 2016). Consequently, I have to conclude that whilst these innovative scientific solutions hold much promise and are greeted with optimism amongst all respondent groups they cannot, as yet, provide the assurances for nano safety decision-making that allows Proposition 2 to be accepted with confidence.

Reflecting on the uncertain timescales for implementing these new solutions, I conclude that current and proposed scientific methods for risk assessment do not yet provide for a competent risk analysis for NM. This conclusion, combined with current deficits for NM in the REACH regulations (section 7.3.1), identified for me that novel approaches to EHS risk analysis and socio-ethical challenges deserve their opportunity to be critically evaluated as

mechanisms to fully realise the risk governance objectives in the EC *NanoStrategy* 2004[COM (2004) 338]. I discuss these possibilities next.

7.3.3 ***Research Proposition 3*** *- RRI can act as an anticipatory governance mechanism for embedding socio-ethical values for safe design within nano-innovation*

This third research proposition asks whether RRI can be the mechanism to enable the intention of EC Objective 3 which is 'the risk management paradigm to be expanded to incorporate socio-ethical considerations into the R&D process with the creation of a culture of responsibility which is participatory and inclusive' [COMM(2004)338].

Reflecting on the substance and tenor of industry respondent interviews, it is clear that many believe they already have a culture of responsibility within their manufacturing and design processes. Within their narrow framing this may be true, in that none believed they manufactured nano enabled products that were not safe or fit for the purpose for which they are designed. Perhaps this partly explains interviewees conservatism for engaging with formalised structures for responsible innovation outside of minimum legal compliance requirements. Whilst this reflects their minimum ethical stance of not doing any 'harm', it does not necessarily imply a position of progressively doing societal 'good' (van de Poel *et al* 2017). Certainly, the daily technical, financial and market pressures, discussed in detail in Chapter 6, also provided perceived and real barriers to industry participation with EU responsible innovation policy. In their quest for business survival, RRI and other policy initiatives seem of little concern to most industry respondents or were simply ignored.

In stark contrast, other respondents including EC administrators, nanoscientists, social scientists and NGOs support and promote the principle of RRI application to nano innovation. However, the absence of any regulatory recognition ,or formal mechanism to insert RRI into

NM production, nor incentives for its adoption, have clearly undermined its implementation. Crucially, none of the respondents in this study offered a delivery platform which could achieve this goal. It is widely recognised the absence of such a platform is a critical barrier for nano industry adoption and implementation of RRI (Burget *et al.* 2017; Goujon 2016, Antelo 2016; Blok and Lemmens 2015; Wickson and Carew 2014). As discussed in Chapter 6, it is important to note here that the significance of the above findings are reflected by the fact that there are three further recently funded EU H2020 projects (all commencing 1st January 2018) which seek to address the issues raised above. Their objectives include the development of a new policy framework for NM, to support a modular risk governance decision-making framework addressing different aspects of NM governance, and to be overseen by the establishment of an EU Risk Governance Council comprising of EU Member States, public authorities, scientific experts, civil society and industry representatives.

RiskGone: https://riskgone.wp.nilu.no/home-riskgone-project/about-us/

NanoRigo: https://cordis.europa.eu/project/rcn/220129/factsheet/en

Gov4Nano: https://www.gov4nano.eu/

I argue in Chapter 6, for repurposing SbD to act as the platform for inserting RRI into the nano-innovation process. I outlined recent work justifying RRI (Reber 2018; Genus and Iskandarova 2018; Von Schomberg 2014) and SbD (Kraegeloh *et al* 2018; Gottardo *et al* 2017; Suarez-Marino *et al* 2017) as directly compatible with the EU's longstanding Precautionary Principle. On this basis, I propose that the hybrid combination of PP, SbD, and RRI offers a novel approach that I label as 'Safety by Social Design' (Figure 7.1 above). Through this mechanism, expert and civil actors could participate in a pre-planned manner, in trusted environments, in debates over both 'risk' and 'design' elements to shape NM decision-making. By foregrounding SbSD in this way, I suggest that it can offer the potential for a prospective

deliberative model to meet the intentions of EC Objective 3. Nevertheless, I acknowledge the current resistance to this approach amongst industry representatives, which I would hope to counter by proposing financial and other initiatives to be introduced as a portfolio of new business incentives. These might include government funding, charter marking, regulatory passporting, and branding recognition (Stone *et al.* 2017; Wiek *et al.* 2016).

In summary, my analysis and evaluation of research Proposition 3 shows an RRI driven deliberative model could be constructed and pragmatically implemented for nano innovation with SbSD at its heart (see Figure 7.2 below). However, its successful implementation will require a pro-active governmental strategy to promote its benefits, with financial and other incentives to motivate the nano industry to overcome their innate prejudices.

Though I do not underestimate the difficulties in terms of the barriers to be overcome and possible limitations of my proposals themselves. These can be separated into five distinct areas. Firstly, the EU policy approval still needed for the adoption of the new toxicological paradigms for scientific and regulatory testing of NM. Secondly, the continuing need for EU funding of NM related research, for epistemic advances to provide the scientific underpinning for these new paradigms and provide the essential proof of concept before they will be accepted for regulatory purposes. The third issue is of a socio-cultural nature with some evidence that industry is undertaking avoidance tactics to NM registration under REACH. Neither does industry fully accept that need to engage with either SbD or RRI as they believe they already develop their products safely and responsibly and can see little value in these new approaches. Fourthly, there is the lack of an active 'infrastructure' where industry can engage collaboratively with stakeholders within in trusted environments. Finally, there will be a need for further policy action supported by financial investment to provide the proposed

incentives for industry engagement which is currently absent. So, these barriers / limitations are not insignificant will need resolution before all my proposals can be fully activated.

As a consequence, my overall reflection on the three research propositions is that currently none can be upheld, because none of the corresponding EC nano risk governance objectives have been implemented successfully (despite being extant since 2004). However, my analysis indicates that there are a range of policy, regulatory, scientific structures and other EU funded initiatives that are beginning to emerge that could have important roles to play in enabling these objectives in the short-medium future (5-10 years). As identified in Chapter 4, the three EC risk governance objectives are interdependent in their actions and their outputs (see Chapter 4. figure 4.3). This requires them to be collectively attained, by synchronizing their relevant mechanisms for implementation, if they are to achieve the overall EC goal for the safe and responsible innovation of NM. Consequently, in the next section I synthesize my conclusions and reflections from this study to offer a future perspective for EU nano risk governance that may deliver on the EC *NanoStrategy*'s key aim.

7.4 Adaptive and Integrative EU Risk Governance Framework for NM

Jahnel (2015b) postulates substantive risk governance gaps due to uncertainties and variabilities in current science and technological practice when evaluating risks from NM. As a consequence, Jahnel suggests that a new paradigm for NM risk policy is necessary which is exposure driven, as opposed to the current hazard- based approach. It will require a flexible tiered methodology that is continually informed by technoscientific advances in our biophysicochemical understandings of the NM release, fate, bio-behaviours and (eco)toxicity. In figure 7.2 below, I propose a novel adaptive and integrative social learning framework for

EU risk governance that I argue could meet this criteria. However, in this figure I go further than Jahnel through incorporating the novel conceptual approach of SbSD with the intention of capturing within the nano innovation process the values-led contributions from non-expert and civil actors. The purpose is to allow these contributions the opportunity to influence NM commercial applications and manufacturing decisions. The SbSD mechanisms provide sequential inputs and outputs to and from the 'Risk 'and 'Design' profiles, that produce options and answers to questions relating to risk management, regulatory compliance, product feasibility, viability & marketability, and its overall social utility. By doing so, I argue the proposed model would provide a means of tackling the full range of goals contained in the three EC risk governance strategy objectives. Here I outline briefly how the model would work in practice.

7.4.1 Development of 'Risk' profiles for Safety by Social Design decisions

The Tier testing approach has been discussed in detail in Chapter 5, but I summarise the reasoning for its incorporation into this model as follows. The nanoinformatics libraries are the first line of the testing regime. (i.e. Tier 1). The libraries are continuously updating curated repositories where current technoscientific knowledge and practice can be sourced for specific NM. This in itself may provide sufficient curated scientific evidence for confirmation of a lack of concerning risk related issues (e.g. within the nano production process, use phase, pathways for environmental release, end of life releases, and any hazards relating from NM consumer useage and /or environmental releases). Such scientific confirmation will then avoid the need for further safety testing. If that information/data is incomplete, then a systematic process of hazard, exposure and risk assessment occurs in Tiers 2,3, & 4.

The nanoinformatic tools will assist in the design of that risk assessment testing strategy for the characterisation of potential risk(s). This risk characterization may trigger further precautionary technoscientific measures to modify NM biophysicochemical properties, functionality or even require chemical substitution. Any redesign may necessitate further re-testing. This characterization will include testing the data against approved scientific /legal standards, risk tolerability, the identification of essential risk management steps, and the actions needed to achieve regulatory compliance. At this stage, it establishes a 'Risk 'Profile for the NM detailing biophysicochemical properties, its functionality, (eco)toxicology implications, related risk factors, and their collective influences on the projected nanoproduct application(s), manufacture, and safe use. This 'Risk' profile is then incorporated within the SbSD matrix with recommendations for a 'go/no go' decision based on the expected purpose for which the NM is to be used. Remembering that some known NM currently have multiple uses e.g. titanium dioxide is widely and diversely used in sunscreens, paints ,food colourants for example.

7.4.2 Development of 'Design' profiles for Safety by Social Design decisions

In parallel, I am proposing there is the dynamic process for the development of the NM 'Design 'parameters. With RRI as the conceptual bridging mechanism, the design parameters are informed *inter alia* by value-led concerns from invited non-expert and civil actors. Within trusted environments, this normative data can be collected honestly and timely with the purpose of informing the nano innovators on a portfolio of community driven concerns. These could include misuse of natural resources, adverse manufacturing practices/emissions, EHS impacts, product social utility and consumer marketability. How these novel collaborative

mechanisms might look in practice is currently being explored by EU funded research projects such as:

COMPASS (https://innovation-compass.eu/)

PRISMA (http://www.rri-prisma.eu/).

These collaborative discussions can be wide ranging and include detailed consideration of the industry sector (e.g. food, computers, environmental remediation), current relevant approved industry codes of practice (ACOP), techno-scientific data relating to production design, costs and controls, and the value-led concerns that might have been generated by previous consultations. All this data will be relevant to and incorporated within the 'Design' profile for the NM and its nano-enabled products.

The 'Risk' and the 'Design' profiles can be made simultaneously available for debate and decision by business actors and their civil stakeholders in consultation fora. Participation need not be restricted only to those involved in the prior data collection and profile preparation, with new actors invited at this time. The debates will weigh the relative merits/deficiencies of the constituent data and any proposed recommendations/decisions offered within the 'Risk' and 'Design' profiles. These profiles will influence co-decisions regarding risk management, regulatory compliance, product feasibility, marketability, social utility and societal alignment.

7.4.3 Benefits arising from the Adaptive and Integrative EU Risk Governance Framework

The new framework I have outlined here has clear benefits for policymakers, scientists, regulators, societal interests and business over existing approaches. First is that it provides a whole system model from NM discovery, to manufacture, through to product marketability. Secondly, with its analytical and deliberative structure, it recognises that innovation does not

occur in isolation, that it is not independent of society, but is instead a dynamic multi-staged process that is fundamentally dependent on companies interacting with business partners, regulatory organisations, and civil communities (Ruggui 2015, UK Government Chief Scientific Adviser 2014; European Science Foundation 2013; von Schomberg 2013; Rip 2012; Deuten and Rip 1997). For policy makers and scientists, the framework prioritises the need for evidenced and reproduceable scientific knowledge to underpin novel developments in NM risk governance strategy and its design; in doing so it offers guidance on modes for effective interaction of science and risk decision-making (Jahnel 2015b). I would argue that the framework could encourage NM businesses to interact early with regulators to develop mutual awareness, as is the aspiration for the evolving EC policy for a new era of industry /regulator relationships to develop 'Regulatory Preparedness' and 'Sustainable Innovation Assessment' (Katalagariniakis 2018). This novel framework can identify and address upstream, early issues of concern, promote mid-stream modulation, and minimise foreseeable delays which may help ease the passage for industry in achieving nanoproduct regulatory compliance. For regulators, it emphasises and assists in their need for technology foresight, including constant horizon scanning and trend watching, to maintain their regulatory preparedness in an ever-changing innovation space. This helps mitigate known risks and encourages the engineering-out of poorly quantified risks, for new nano products coming to market, and supports the other emerging EC policy for a 'Sustainable Innovation Approach' for NM (Katalagariniakis 2018).

This integrative framework foregrounds the need for open dialogues between NM businesses and civil actors. Such early dialogues with prospective consumers may yield unexpected insights for industry which enhance nano product utility, branding and its marketability. Finally, for societal interests it is an opportunity for contributing to the development of

nanoproducts which are of value to society. If trust is episodic in nature (Baumann and Le Meunier-Fitzhugh 2014), then over time such a co-creation process can generate a greater trust and confidence in the nanotechnology sector, their enterprises, and the safety and utility of nano products that come to the market.

Finally, as can be seen in section 7.3.3 above, the EU is making a considerable investment in its funding of three recently commenced major research projects that are addressing the topics of a risk governance framework for NM, and the establishment of a new European Risk Governance Council to oversee its operation. I believe that the findings from my research and this proposal for an adaptive and integrative risk governance framework can make a contribution to those debates.

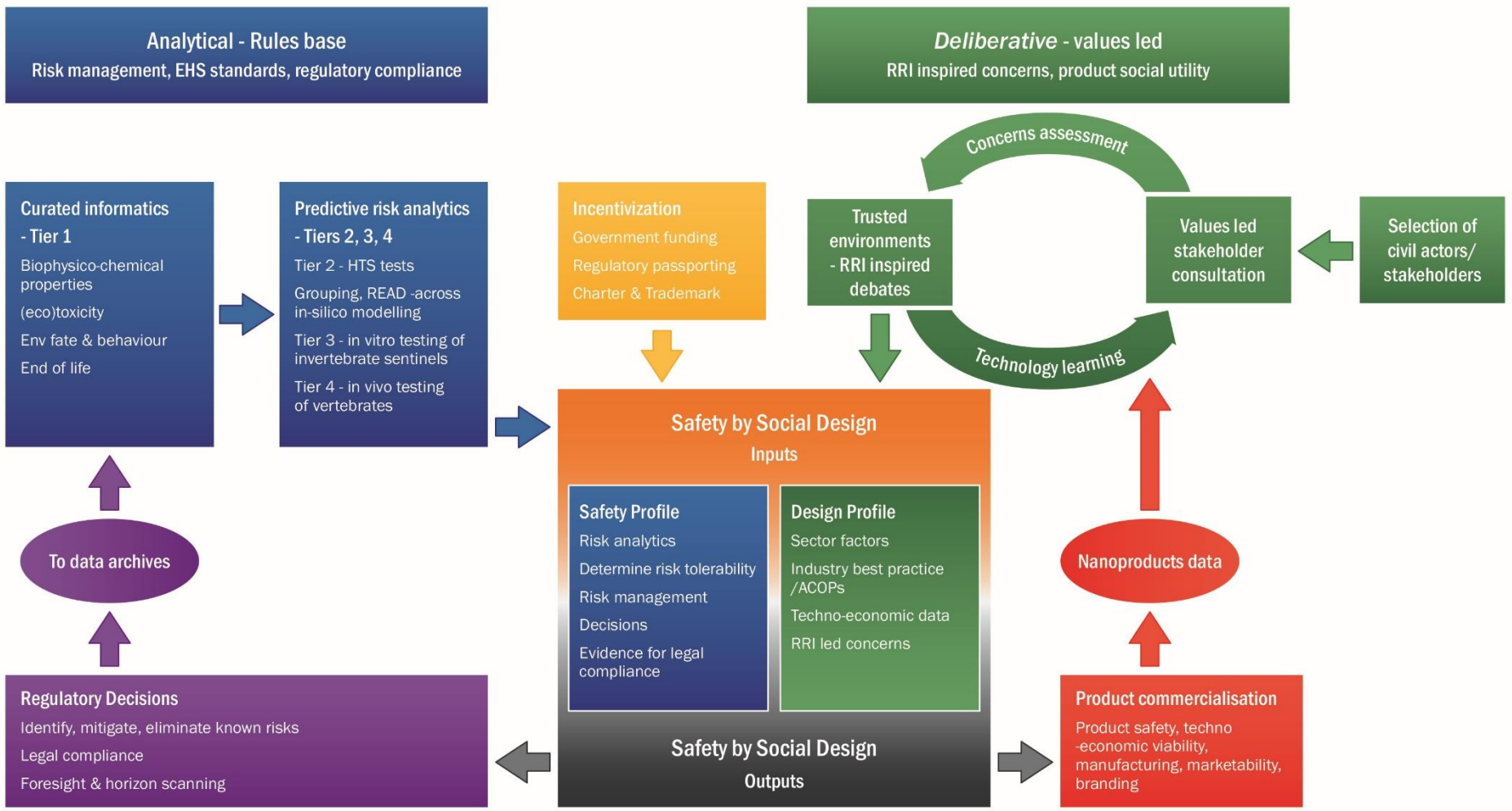


Figure 7.2. An Adaptive and Integrative EU Risk Governance Framework for NM facilitated by Safety by Social Design

Note: The coloured sections represent separate processes and/or sub-systems

My intention is that this novel framework provokes new dialogues between hitherto-siloed actors, triggering social learning processes that not only promote the circulation of information to continuously inform and update stakeholders (see Chapter 6), but also makes these stakeholders more aware of differing attitudes, opinions and interests in relation to NM development and production. I discuss in detail in Chapter 6 (Table 6-1) how this model meets, in some cases exceeds, the tests set for an adaptive and integrative risk governance framework for nanotechnologies recently proposed separately by Linkov *et al* (2018) and Stone *et al* (2018). I also contend that their test criteria fit within the ambit of the three EC strategic risk governance objectives which are the genesis for this study. With the above model (figure 7.2), also illustrating its future facing capability by a continuous iteration of EU risk governance policy, nanoscience risk analysis, regulatory sciences, and socio-ethical engagement with civil actors. In the next section, I will briefly consider how my proposals have addressed limitations in the main conceptual frameworks which I have applied in my empirical analysis for this study.

7.5 Novel conceptual contributions from this study

Based on the analysis of cross-sectoral qualitative data using codes derived from the theoretical literatures (discussed in Chapter 4), I have been able to develop fresh perspectives on the current regulatory landscape for EU NM development and production. I have also been able to offer solutions to some of the more intractable conceptual problems which have so far beset regulatory progress towards ensuring safe NM and acceptable risks they might pose. I summarise these contributions in the Table 7-1 below, with each contribution having been devised for the discussions in Chapters 5 and 6.

Table 7-1. Contributions to existing conceptual limitations identified in this study

Current conceptual limitation	Thesis contribution
In the Taxonomy of Regulation (CEPS 2014) (Chapter 3, figure 3.1), the 'hard and soft' law stages, within the hierarchy of regulation, can and are being applied independently of each other without necessarily referencing to the outcomes of the other stages	This model provides a structured approach that systematically synchronizes hard/soft law elements together in a whole system approach. By doing so, the outcomes from each stage readily informs the risk and design profiles which can be collectively evaluated for SbSD outcomes.
The Analytical-Deliberative model (Rosa, McCright and Renn 2013) does not offer a detail process mapping for its application within nano R&D practices.	Figure 7.2 maps the principal stages that generate and process both analytical and deliberative data for risk, regulatory, social utility and product decision-making
Responsible Research and Innovation (Rome Declaration 2014; Horizon 2020) has been criticized for its lack of an effective implementation platform to engage non-expert/civil actors with the nano industry in a meaningful dialogue for nano innovation.	Anchoring RRI within the established 'Safety by Design' process provides for the conceptual evolution of 'Safety by Social Design 'to foster deliberative engagement by civil participation. Consequently, RRI is activated as an anticipatory bridging mechanism for deliberatively generated concerns to be inculcated within nano innovation .
The current EC application of 'Safety by Design' for regulatory preparedness is predicated on only one normative outcome which is 'safety'.	The evolution of 'Safety by Design' to 'Safety by Social Design' facilitates the potential for multiple normative outcomes within the innovation process. The purpose then is not only to provide safer NM, but socially relevant, marketable and ultimately less contested nanoproducts.
Precautionary Principle (COM2000) has been designed to be both precautionary and deliberative in action. Yet it has been much criticized for being applied within the EU in a solely preventative manner.	The compatibility of RRI and SbD with PP legitimizes their linkage to formulate SbSD. Within this contemporary setting, the precautionary and deliberative roles for which PP was originally designed can now be properly exercised.

This table illustrates that the risk governance framework proposed here are, primarily, offering an extension of current boundaries for the main conceptual framings in terms of current policy debates. There are also contributions from this study in terms of extending our

understanding of academic literatures with chief amongst these is the new concept I label 'Safety by Social Design'. It offers a novel conceptual approach for the societal alignment of NM innovation within its analytical-deliberative framing which foregrounds the co-creation and shared responsibility for safe and responsible nano innovation. It is a construct built from the combined features from established concepts .i.e. PP/SbD/RRI, that provides for both precautionary and future facing anticipatory responses. By exploring current and future possibilities (Genus and Stirling 2018), it has the potential to contribute to meeting the challenge set by Guston (2014.p225), ' for a broad-based capacity extended through society that can act on a variety of inputs to manage emerging knowledge-based technologies while such management is still possible'. It has the possibilities as a conceptual hub for managing and interpreting those analytical and deliberative inputs within the proposed adaptive and integrative model in figure 7.2. By doing so, it may facilitate a holistic approach to risk determination, nano safety decision making, and product evaluation for social utility.

In respect of its trio of forming concepts, SbSD could extend their conceptual reach within the innovation process. It activates RRI for purposeful anticipatory exploration of future facing socio-ethical positions (Guston 2014 and others), provides for 'strong' RRI by broad-based stakeholder engagement (Coenen and Grunwald 2016), emphasises the need for continuous social learning (Murashov and Howard 2014) and promotes the democratization of the innovation process as a key feature for social alignment (van de Poel *et al* 2017). Within the proposed model in figure 7.2, there is an understandable framework for activating RRI within a broadly-based holistic framework for nanosafety (Winickoff 2016), and an outline of the proposed process steps that are needed (Burget *et al*. 2017; Blok and Lemmens 2015). Finally, the lack of industry traction for RRI (van de Poel *et al*.2017; Auer and Jamia 2017) is

considered with the proposals for a portfolio of incentives to attract the nano industry attention to RRI and encourage its adoption.

There are continually evolving debates within the literatures of the role, value, purposes and application of PP (cf. Sandin 1999 and others). In particular, the criticism on the over emphasis on its hazard -centric precautionary role and its lack of deliberative application. However, von Schomberg (2012.p147) is explicit in describing PP as a 'deliberative principle….that involves deliberation on a range of normative dimensions'. SbSD provides for a novel contemporary setting in which this deliberative feature can be foregrounded, so that both the PP precautionary and anticipatory limbs are more equitably balanced in their contributions to the risk problem-solving process (COM2000; Per Sandin 2002, von Schomberg 2006, Stirling 2016).

Finally, SbSD provides the conceptual setting for SbD to progress beyond its single normative feature of evaluating 'safety' (van de Poel and Robaey 2017; Gottardo *et al*. 2017; NANoREG2 D6.03 http://www.nanoreg.eu/). By adopting a 'mid-stream modulation' approach (Fisher *et al*. 2006), societal concerns can be connected with the innovation processes upstream of regulatory controls and market selection. Therefore, it offers the opportunities to pragmatically influence the safety -related decisions upstream in the innovation process (Flipse and van de Loo 2018 and others) by minimising the potential for pathway dependency (Nordmann 2018) and technological lock-in(Owen *et al*. 2009). With the prospect of reducing future indeterminacy of innovation socio-politico-economic-environmental impacts as proposed by van de Poel and Robaey (2017).

Collectively, these three core principles are embedded together in forming SbSD, which is at the heart of the novel bespoke adaptive and integrative risk governance framework proposed by this study(figure 7.2). Such an overarching risk governance framework does not currently

exist to provide governance of nanotechnologies, scrutinise their EHS effects, identify their potential socio-environmental implications for future nano-innovation pathways, and possible contributions to sustainable futures. Klinke and Renn (2012) and others believe that integrating analytic reasoning with stakeholder deliberation provides for a more valid co-interpretation of risks and safety issues that can enhance the competence of risk decision-making and assign a fairer share of that responsibility for their management. Stone *et al* (2018) and Linkov *et al* (2018) regard such an adaptive and integrative framework as critical for the safe and responsible development of NMs now and into the future. I propose that the framework in figure 7.2 can make a prospective contribution to meeting these aspirations.

Now that I have reviewed the conceptual contributions of this study, in the next section I reflect on how this research impacts on the future outlooks for nanotechnologies.

7.6 Safety by Social Design and Nanotechnology futures

I have illustrated in Chapters 5 and 6 that my research identifies the broader policy, scientific, regulatory, and societal debates for future risks and benefits that may accrue from NM and nano-enabled products. These debates address unresolved concerns arising from the broad palette of uncertainties relating to nanotechnologies future development, their technology applications, and the safety of consumer products. These uncertainties relate to NM functionality, technological applications, risk assessments, safe use, social utility and marketability.

In terms of functionality and applications, this study identifies that there are continuing critical deficits in scientific knowledge and expertise in identifying and understanding NM environmental fate, behaviour and toxicological effects. Fadeel *et al* (2018) provide clarity that these outstanding problems are significant and are not readily surmountable. These

environmental nanoscience deficiencies underscore a multiplicity of continuing regulatory nanoscience problems which may take decades to resolve. Whilst RRI is promoted as a general policy tool for innovation practices within the EU, the EC has yet to accept that the socio-ethical concerns of European civil society should be incorporated within its 'regulatory preparedness 'policy for NM. Rather, such discussions are still restricted within the confines of expert actor groupings (Gottardo *et al* 2017; NANoREG2 http://www.nanoreg.eu/)

I argue that the proposed risk governance framework in Figure 7.2 offers a novel methodology to collect and collate experimental scientific and normative data from more diverse sources into a single decision framework. It builds on current EC scientific policy, experimental and regulatory foundations and practice but, additionally, offers a conceptual based mechanism for civil society to have a purposeful role within the nano innovation process. By identifying the SbSD concept as the coordinating mechanism of the model, it enables socio-ethical considerations to be firmly grounded into the nano innovation process. There are of course substantive challenges here – for example, successful implementation of the framework will require the development and sustenance of horizontal relationships across networks of diverse expert and civil society actors, and the engendering of trust and reciprocity between them. Nonetheless, the potential benefits could be considerable, not least that my approach could stimulate the transitioning from traditional closed expert driven innovation to a more open and transparent nano innovation culture. It has the potential capability to realise the ambitions articulated in the EC *NanoStrategy* for the safe and responsible development of NM.

Finally, all the major issues debated in this study have wider applicability and transferability. I believe that this model offers instructive guidance on how an international charter for societal alignment with nanotechnologies might be brought about. I also consider that its

broad principles are technology neutral and have the potential to be adaptive to other emerging technologies. It combines the analytical with the deliberative and so is both precautionary and anticipatory in its application and outcomes. It thus has possibilities as the basis for a risk governance roadmap for other emerging technologies.

7.7 Future Research Directions

My research has identified that there continue to be considerable knowledge and conceptual gaps in EU nanoscience and technology knowledge and practice. A critical starting point in addressing these gaps is to resolve outstanding issues over nano definition specifications and metrical measurement tools. Additionally, this research identifies that emerging NM safety techniques for understanding NM biophysicochemical properties, cellular toxicology, and risk characterization still lack essential proof of concept necessary for regulatory acceptance. Moreover, further research is needed into whether lack of compliance by industry with REACH (particularly over compilation of registration dossiers on new NM) is widespread, and whether this practice is putting workers and consumers at any measurable risk. There will need to be a continued powerful policy, financial and research push from EU governments, regulators, academia and industry to resolve these issues.

In terms of nanoscience and technology in society, there is still a need for the development of a detailed roadmap to incorporate RRI and SbSD within industry practices. The engagement with civil actors sounds straightforward but setting up the infrastructure for trusted networks and making them function effectively over long periods for mutual win-win scenarios, is far more difficult in practice. Further research is needed into building and promoting consultative fora so that they become a prominent part not only for innovation, but for business planning, organisational practices, Corporate Social Responsibility strategies, and product branding.

This will require ongoing research funding to develop relevant case studies/scenarios to inform industry implementation practices and the ongoing business benefits that can accrue. To complement these developments, there will be a need for research into new training packages for organisational learning, competencies development, in tandem with new internal/external communication strategies.

Another important issue emerging from this study is the need to undertake further research for a menu of options containing business orientated incentives, to encourage and fund industry practical engagement with RRI and SbSD. It is imperative that the research includes objectives that offer firm evidence of the business benefits for adopting RRI and SbSD into business strategy and practice. That research must examine whether co-produced nanoproducts can add genuine value to the business nanoproduct portfolio and its financial bottom line.

I made the point at the beginning of this Chapter (section7.1), that there is a lack of a bespoke overarching EU risk governance framework to scrutinise either the EHS effects or the wider social implications of current and future nano-innovation pathways. So, the recent EU funding to research this matter and for the proposal for the establishment of an EU Risk Governance Council is applauded and I anticipate important developments and benefits in this technological sector.

My final observation is that the emergent NM industry sector must begin to take more seriously the need for product development to be aligned within socially acceptable boundaries, as espoused by Jasanoff (2016). The design of the model in Figure 7.2 above is readily adaptable to nano future trajectories and is aimed at achieving this aspiration. By doing so, it can support the delivery of the EU strategic goal for the safe and responsible development of NM.

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Appendix A Research schedule of questions

Question Number	Question Topic	Research Objective
1	What are your views on the commercial potential and societal benefits of nanomaterials?	N/A
2	What is your opinion on the current definition for nanomaterials	RO1
3	Do you have any concerns regarding regulatory safety testing of nanomaterials with specific reference to REACH?	RO1
4	With continuing uncertainties for the safe use of NMs, is there an over- emphasis on undefined hazard rather than evidence-based risk	RO1
5	Can emergent scientific risk analysis techniques and novel cellular predictive toxicological models[3] replace current regulatory testing regimes including animal testing	RO2
6	What are the prospects for Safety by Design approaches to significantly influence upstream risk/safety decisions during the nano innovation process?	RO2
7	Can RRI be the EU policy instrument for embedding socio-ethical concerns for safe design into the nano innovation process?	RO3
8	How do you consider RRI can be implemented within the nano innovation processes?	RO3
9	How can the benefits of adopting RRI be promoted to industry	RO3
10	Is the future for EU risk governance for nanotechnologies a combination of statutory and industry self- regulation?	RO3
11	Are there any other relevant issues you wish to raise	N/A

[3] A Diagram is attached to aid discussion –'The Implementation of Toxicological profiling using a Tiered approach for risk identification and characterization' (Nel et al 2013)

Appendix B Date listing of interviews per stakeholder category (n=55)

Stakeholder Category	Date Interviewed (dd.mm.yyyy)	Reference
Regulator	7.3.2013	RG01
Industry	13.6.2013	IND01
Government	18.6.2013	Govt 01
Regulator	10.7.2013	RG02
Academic	11.7.2013	AC01
Academic	12.7.13	AC02
Academic	13.7.2013	AC03
Industry	22.7.2013	IND02
Academic	13.8.2013	AC04
Industry	22.8.2013	IND03
Industry	23.8.2013	IND04
Industry	2.10.2013	IND05
Industry	14.10.2013	IND06
Industry	12.11.2013	IND07
Academic	4.12.2013	AC05
Industry	23.3.2014	IND08
Jurisprudence	11.2.2014	JP01
Jurisprudence	20.2.2014	JP02

Stakeholder Category	Date Interviewed (dd.mm.yyyy)	Reference
Government	21.2.2014	Govt 02
Government	28.2.2014	Govt 03
Government	6.3.2014	Govt 04
Government	25.3.2014	Govt 05
Government	1.4.2014	Govt 06
Industry	3.4.2014	IND09
Industry	7.4.2014	IND10
Industry	8.4.2014	IND11
Government	10.4.2014	Govt 07
Academic	1.5.2014	AC06
Academic	5.5.2014	AC07
Regulator	20.5.2014	RG03
Academic	22.5.2014	AC 08
Government	27.5 2014	Govt 08
Non-Governmental Organisation (NGO)	30.5 .2014	NGO01
Government	1.7.2014	Govt 09
Industry	16.8.2014	IND12
Academic	6.9.2014	AC09
Academic	8.9.2014	AC10
Academic	24.10.2014	AC 11

Stakeholder Category	Date Interviewed (dd.mm.yyyy)	Reference
Jurisprudence	5.11.2014	JP03
Industry	13.11.2014	IND13
Government	14.11.2014	Govt 10
Academic	21.11.2014	AC 12
Academic	21.11.2014	AC13
Academic	24.11.2014	AC14
Government	25.11.2014	Govt 11
Academic	3.12.2014	AC15
Industry	3.12.2014	IND14
Academic	5.12.2014	AC16
NGO	5.5.2015	NGO 02
Academic	21.6.2015	AC17
Academic	25.1.2016	AC18
Academic	22.2.2016	AC19
Government	8.3.2016	Govt 12
Academic	20.5.2016	AC20
NGO	7.4.2017	NGO 03

Coding

Each interviewee was allocated a code for their sector and the interview date sequence

AC- Academic

Govt- Government

IND-Industry

JP-Jurisprudence

NGO-Non-Governmental Organisations

RG- Regulator

Appendix C NVIVO database screen showing the Analytical Themes and Codes

Nodes

Name	Sources	References	Created On	Created By	Modified On	Modified By
Anticipatory Governance	0	0	30/11/2015 14:20	MEA	30/11/2015 14:20	MEA
Communication with stakeholders	33	82	30/11/2015 14:27	MEA	18/05/2017 11:17	MEAB
Environmental Sustainablility	20	45	20/12/2015 11:38	MEA	18/05/2017 11:17	MEAB
Future develoment of NMs	25	53	30/11/2015 14:35	MEA	02/05/2017 12:54	MEAB
Innovation	2	2	15/07/2016 13:43	MEAB	02/05/2017 13:23	MEAB
Innovation Value Chain	36	122	30/11/2015 14:30	MEA	18/05/2017 11:17	MEAB
Political Economy	22	65	20/12/2015 11:36	MEA	18/05/2017 11:17	MEAB
Responsible Research and Innovation	0	0	08/03/2019 14:26	MEA	08/03/2019 14:26	MEA
RRI and Safety by Design	48	180	30/11/2015 14:24	MEA	18/05/2017 11:17	MEAB
Safety by Design	0	0	28/07/2016 11:18	MEAB	28/07/2016 11:18	MEAB
Self Regulation	15	33	30/11/2015 14:31	MEA	18/05/2017 11:17	MEAB
Risk Governance	0	0	30/11/2015 13:42	MEA	30/11/2015 13:42	MEA
Benefits of Nms	13	19	20/12/2015 11:32	MEA	20/05/2016 10:37	MEAB
Current Regulation	45	148	30/11/2015 13:43	MEA	02/05/2017 13:06	MEAB
Ethics	8	33	07/01/2016 11:32	MEA	17/05/2016 11:46	MEAB
Future Regulation	36	82	30/11/2015 13:55	MEA	02/05/2017 13:26	MEAB
International Harmonization	22	53	30/11/2015 13:58	MEA	20/05/2016 10:55	MEAB
Nano Definition	31	54	30/11/2015 13:43	MEA	18/05/2017 11:17	MEAB
National Registers	12	27	30/11/2015 13:54	MEA	18/05/2017 11:17	MEAB
Optimal Governance	8	32	17/02/2016 11:17	MEA	18/05/2017 11:17	MEAB
Risk Policy	39	99	04/01/2016 13:35	MEA	18/05/2017 11:17	MEAB
Strategic Policy and Planning	27	69	30/11/2015 13:59	MEA	20/05/2016 11:34	MEAB
Technology Assessment	20	47	30/11/2015 14:02	MEA	20/05/2016 10:53	MEAB
Risk Management	0	0	30/11/2015 14:08	MEA	30/11/2015 14:08	MEA
Alternative testing options	36	154	30/11/2015 14:11	MEA	18/05/2017 11:17	MEAB
Current Risk Assessment Testing	36	77	30/11/2015 14:09	MEA	18/05/2016 12:24	MEAB
Fate, Behaviour, Exposure and Environ	10	24	30/11/2015 14:15	MEA	20/05/2016 11:37	MEAB
Lifecycle Analysis	31	51	30/11/2015 14:10	MEA	02/03/2017 12:09	MEAB
Nano safety	35	118	04/01/2016 13:11	MEA	18/05/2017 11:17	MEAB
Toxicology and Toxic effects of NMs	27	75	30/11/2015 14:16	MEA	14/07/2016 10:07	MEAB

Appendix D Table of International Conferences at which presentations were given 2014-18

Title of Presentation	Conference	Date
Risk Regulation and Responsible Innovation of Nanomaterials: Developing an Adaptive Risk Governance Framework	9th International Conference of the Society for the Study of New and Emerging Technologies University of Maastricht , Netherlands	26th June 2018
Risk, Regulation and Responsible Innovation of Nanomaterials	Nano-safety in Europe Conference Leibnitz Institute**,** Saarbrucken, Germany	11th October 2017
Risk Governance and the Responsible Innovation of Nanomaterials within the European Union	12th International Conference on the Environmental Exposure of Nanomaterials. University of Birmingham. UK.	6th September 2017
What is the future role of risk governance in the responsible innovation of nanomaterials in the European Union?	7th International Conference of the Society for the Study of New and Emerging Technologies, University of Bergen, Norway	14th October 2016
Risk Governance, Regulation and Responsible Innovation of Nanomaterials	9th International Conference on Environmental Exposure of Nanomaterials, University of South Carolina, Columbia, South Carolina, USA	11th September 2014
Implications of Nanotechnology for Food Safety futures	Joint Conference of the International Federation of Environmental Health and the USA National Environmental Health Association Conference, Las Vegas, USA,	9th July 2014

Appendix E Consent Form

UNIVERSITY OF BIRMINGHAM

Environmental Nanoscience Research Group
School of Geography, Earth and Environmental Sciences
College of Life and Environmental Sciences
University of Birmingham
Birmingham
B15 2TT

Tel: [redacted]

CONSENT FORM

Title of the Research Project: Evaluating Progress for the European Union Nanotechnology Strategies for the Safe Design and Responsible Innovation of Nanomaterials

Name of principal researcher: Maurice Brennan

Please tick or initial the box if you agree with the statement

1. I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my or my organisation's involvement in the project being affected in any way ☐

3. I consent to being interviewed. ☐

I consent to the interview being recorded. ☐

I consent to the interview being transcribed ☐

4. I agree to the use of anonymised quotations from interviews being reported in research reports, journal articles and presentations. ☐

5. I understand that data collected during the study may be looked at by individuals from the University of Birmingham and from regulatory authorities where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

6. I would like to request a copy of the typed transcript when it is available ☐

7. I agree to taking part in this study ☐

Signature: Date:

Maurice Brennan

Researcher Date received:

Please complete a copy of the Consent Form (for your own records)

Return to signed Form to : M.E.Brennan.1@bham.ac.uk