Part E Implications for science and governance

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26 Science for precautionary decision-making

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The goals of academic researchers may differ from those of regulatory agencies responsible for protecting the environment. Thus, research must take into account issues such as feasibility, merit and institutional agendas, which may lead to inflexibility and inertia.

A large proportion of academic research on environmental hazards therefore seems to focus on a small number of well studied environmental chemicals, such as metals. Research on environmental hazards should therefore to a greater extent consider poorly known problems, especially the potential hazards about which new information is in particular need.

Misinterpretation may occur when results published in scientific journals are expressed in hedged language. For example, a study that fails to document with statistical significance the presence of a hazard is often said to be negative, and the results may be misinterpreted as evidence that a hazard is absent. Such erroneous conclusions are inspired by science traditions, which demand meticulous and repeated examination before a hypothesis can be said to be substantiated.

For prioritising needs for action, research should instead focus on identifying the possible magnitude of potential hazards. Research is always affected by uncertainties and many of them can blur a real association between an environmental hazard and its adverse effects, thereby resulting in an underestimated risk. Environmental health research therefore needs to address the following question: are we sufficiently confident that this exposure to a potential hazard leads to adverse effects serious enough to initiate transparent and democratic procedures to decide on appropriate intervention?

The choice of research topics must consider societal needs for information on poorly known and potentially dangerous risks. The research should be complementary and extend current knowledge, rather than being repetitive for verification purposes, as required by the traditional science paradigm. Research findings should be openly available and reported so that they inform judgements concerning the possible magnitude of suspected environmental hazards, thereby facilitating precautionary and timely decision-making.

([1]) The author would like to thank Mette Eriksen for conducting the searches on SciFinder. Helpful contributions on earlier versions were made by John Bailar, Carl Cranor, David Gee and David Kriebel.

26.1 Science and the Precautionary Principle

The case studies in this volume illustrate that science can provide powerful evidence for targeted prevention to protect against hazards to the environment and public health. However, the chapters also shows how science can be insufficient, and it can be misinterpreted or ignored, so that appropriate intervention is deferred or abandoned. This chapter explores the strengths and weaknesses of environmental health research seen from the perspective of the wider needs of society and the use of 'Precautionary Principle' (PP).

At the outset, societal investment in environmental research would seem unwise if it is irrelevant, poor, or difficult to access. Research support should favour studies that stimulate timely decision-making and prudent action to prevent hazards. While not disregarding the need for basic research, I shall focus primarily on the weaknesses of current applied research in the environmental field and the possible avenues for science to become more useful for future environmental health decision-making.

Some researchers have raised the concern that the PP may potentially make further research redundant, given that an intervention has already been decided upon (Goldstein and Carruth, 2004). But any decision on environmental health hazards should be considered tentative and amenable to change, as justified by further research (including intervention studies to determine if the action had the intended effect). The basic problem is that prevention has too often been deferred due in part to the alleged absence of convincing scientific evidence, as illustrated by the case studies in this volume ([2]). The error is recognised only when decisive evidence has finally been gathered, and it is realised that action should have been initiated much earlier on. With time, nearly all exposure limits for hazardous agents have decreased as new evidence documented that harm occurred at lower exposure levels than previously believed. Thus, when scientific evidence is incomplete, environmental standards are more lenient. But can science provide better support for prudent decision-making, so that adequate protection may be decided upon from the beginning?

For research to provide sufficient documentation for potential intervention, it has to be both reliable and pertinent. Thus, the quality of research has two sides — the methodology and the utility. One could also refer to these two aspects as the validity and the relevance. The two are of course related, but even research considered 'poor' from a narrow methodological perspective could nonetheless be highly relevant. Still, a study of limited validity is most likely also to have little impact, especially if the conclusions cannot be trusted. While the researchers should focus on securing a high methodological level, that should not turn them into sceptical ivory-tower nit-pickers preoccupied with methodological precision and technical detail. On the other hand, focusing mainly on environmental implications of the research can lead to inappropriate (or apparent) advocacy for particular policies or precautionary action that may be inspired, though perhaps not justified, by the research.

Environmental health is often considered a field of applied research, usually multidisciplinary. Researchers and their employers are engaged in science not just for purely altruistic reasons. Universities and other research institutions are enterprises that need to fulfil the institution's mandates, satisfy requirements stipulated by funding sources, and avoid going into debt. Within the EU, more than half of the research and development activities carried out are funded by industry, while slightly more than one-third is paid for from public sources (Eurostat, 2011). The EU's new Horizon 2020 research programme is intended to increase the public financing of 'smart investment' in research and innovation while dealing with pressing societal challenges, including climate change and environmental health problems (EC, 2011). Given the substantial public investment in research (van den Hove et al., 2011), one would anticipate that environmental research, especially the part of it that is reported in academic journals, would somehow reflect priorities expressed by regulatory agencies and other public bodies. The next section of this chapter will therefore examine the research coverage of environmental chemicals and whether poorly documented and potential hazards receive appropriate attention. But there is more to it than the coverage of priority topics.

([2]) As the preface to the first volume of *Late lessons from early warnings* (EEA, 2001) pointed out, 'the absence of political will to take action to reduce hazards in the face of conflicting costs and benefits seems to be an even more important factor in these histories than is the availability of trusted information'.

Under PP-based decision-making, scientific proof or a very high degree of certainty are not required. Incomplete, but reliable evidence can be sufficient to justify a precautionary intervention. On the other hand, if extensive evidence is available, then a conventional risk assessment and subsequent prevention are indicated, and there would be little need to invoke the PP. However, traditional risk assessment is sometimes anti-precautionary when it demands convincing evidence and thus ignores emerging insight and incomplete documentation. Due to its focus on scientific justification, risk assessment may inspire continued elaboration of fairly well documented hazards, so that remaining uncertainties can be resolved to allow firm decisions. When decisions are PP-based, less extensive evidence is required, and some uncertainties are accepted as being inevitable or impossible to remove in the time available for preventing plausible harm. The less extensive requirement regarding scientific evidence can have significant implications for the ways that research is planned, performed, analysed, interpreted and reported (Grandjean, 2008b).

We rely on science as evidence to help justify decisions on environmental hazards. But, as the case studies in the present and the first volume of *Late lessons from early warnings* (EEA, 2001) clearly demonstrate, science does not automatically lead to appropriate prevention or precautionary action. Thus, neither the quality nor the relevance of the science as such will necessarily translate into responsible and prudent decisions. Still, the interpretation of incomplete research data, the evaluation of uncertainties and misunderstandings of the findings can obfuscate the discussion on the urgency of possible environmental protection. So the question must therefore be asked: Can science somehow better serve to support better public policy decisions?

I think that the answer is yes, although better quality and relevance in terms of PP-based decision-making may not be easy to achieve. This chapter will focus on four main issues listed below.

Concerns regarding science as evidence for decisions on environmental hazards:

1) Does the research cover the societal needs for supporting information on suspected, poorly documented or potential hazards?

2) Does the research explore new and emerging hazards so that it could serve as an early warning system?

3) Is the reporting of research findings appropriate to serve as evidence for reducing environmental hazards?

4) If the research is available, is it reliable and independent of vested interests?

26.2 Current research focus is on well-known hazards

The most appropriate and feasible way to assess the topics covered by environmental research is to carry out bibliometric analyses using internet-based databases on scientific publications. Environmental journals are usually categorised in the fields of toxicology, environmental sciences and public health (a total of 78 major journals in both Web of Science and the PubMed database). The Web of Science covers scientific literature back to 1899, but searches are limited to chemical names in the titles of journal articles. However, for recent publications, it is possible to use the SciFinder database, where individual environmental chemicals can be identified from their Chemical Abstract Service (CAS) registry numbers. Using these internet resources, information can be retrieved on how often scientific publications have dealt with chemicals of interest from an environmental viewpoint (Grandjean et al., 2011).

As a starting point, we first used Web of Science to examine the coverage of the seven chemical substances from the 14 case studies reviewed in *Late lessons from early warnings* Volume 1 (EEA, 2001). Table 26.1 shows the number of articles published in the relevant journals during the years 2000–2009, i.e. the 10 years right after the completion of the report. One could have expected that these early warning substances would have faded somewhat from the science radar, given that their environmental impact had already been recognised during the 20th century and that some had been banned several decades ago. However, the number of scientific publications on these substances during 2000–2009 corresponded to about 40 % of all articles available since 1899. The relative coverage before and after year 2000 differed somewhat between the substances. Both sulfur dioxide and DES clearly faded during recent years, with only about one quarter of all titles available in environmental and toxicological publications since 1899 being published during 2000–2009. On the other hand, MTBE became more popular, with three-quarters of all papers available since 1899 having been published during the first decade of this century.

Table 26.1 Total numbers of articles published 1899–2009 and during the most recent 10 years (and percent of total) in environmental and toxicology journals listing 'early warnings' substances in the title

Name	Total number of articles 1899–2009	Articles published 2000–2009	
		Number	% of total
Polychlorinated biphenyls (PCBs)	5 809	2 738	47
Asbestos	2 735	809	30
Sulfur dioxide	2 380	548	23
Benzene	2 075	879	42
Tributyltin (TBT)	672	344	51
Diethylstilboestrol (DES)	603	147	24
Methyl-tert-butyl ether (MBTE)*	542	411	76
Total	14 816	5 876	40

Note: *MBTE uses were expanded during the late 20th century, not restricted like the other substances in the table.

Source: Data from the Web of Science (Grandjean et al., 2011).

These numbers suggest that substantial research continued to be published on these substances, long after the recognition of their importance as environmental contaminants. However, the numbers extracted from the Web of Science are incomplete, as a research article might well address a chemical without the substance name appearing in the title. Thus, when extracting data from SciFinder, we obtained a greater number of articles (total of 8 267 during 2000–2009, asbestos not included). With an average of over 10 scientific articles per substance per month, these early warnings chemicals remained a significant focus of research reports published since 2000. PCBs, in particular, remained very much in focus, as I shall discuss shortly.

Given the continued attention paid to these chemicals characterised by 'early warnings', what about environmental chemicals in general? Thousands of potentially toxic chemicals are being released into the environment, and there is a need to determine their persistence, dissemination, biomagnification and toxic effects, especially when only minimal information is available. So how does published research reflect the societal needs to cover a wide range of potential hazards?

Based on CAS number links from the science journals during 2000–2009, the substances can be ranked in accordance with their numbers of publication links (as SciFinder is not limited to environmental chemicals, we had to manually exclude radioactive isotopes, enzymes, metabolites, etc.). All told, 119 636 articles were published by the 78 scientific journals during the first ten years of this millennium. SciFinder listed a total of 760 056 CAS links from these articles (Grandjean et al., 2011). Thus, on average, each of the many scientific articles had six CAS links, thus not only describing a single substance at a time. The total numbers of publications and links are large and reflect an intense publication activity. However, the coverage turned out to be extremely uneven.

We focused on the 100 most frequent environmental chemicals. Each of them was covered in a minimum of 600 articles — and up to 10 000 — during the 10-year period. Thus, each of the top-100 substances would be addressed in about five to 80 articles every month. The total number of links to the top-100 environmental chemicals was 180 822. Thus, the vast majority of the many thousand chemicals listed were far less popular than the top-100. This finding suggests that research on environmental chemicals is and has been for some time fairly narrowly focused on a limited number of substances.

This conclusion becomes very clear when we examine the 20 most commonly studied environmental chemicals. Each had between 2 000 and 10 000 CAS links during the first ten years of the millennium. The sum of article links corresponds to 12 % of all CAS number links. Assuming they also represent 12 % of all published articles, one or more of these substances would be featured in 14 264 publications during the 10 years, or 119 articles per month, on average. To keep up with the literature in the top-20 substances only, one would have to read five or six papers every work day, without holiday breaks.

All of the top-10 substances are metals (including arsenic, which is regarded as a semimetal). Also well covered are several tar chemicals (polyaromatic

hydrocarbons), solvents and the PCBs — already known from *Late lessons from early warnings* Volume 1 (EEA, 2001) and Table 26.1. For the top-20 substances, an average of 51 % of all articles available in 2009 had been published within the most recent 10 years. Some variation was present: arsenic increased in popularity (74 % during the most recent 10 years), while aluminium decreased after the year 2000 (31 %). Also, the tar chemicals often found in air pollution (e.g. benzo[a]pyrene and phenanthrene) tended to appear more often in recent article titles. Overall, these results show that the chemicals most commonly studied in recent years had already been extensively studied during the previous century. Thus, the chemicals that were popular during the previous century remained a focus (Grandjean et al., 2011).

Two of the top-20 chemicals — lead and mercury — are included in the case studies, and Table 26.2 shows the results for the main substances reviewed in this volume. Thus, whether or not the chemicals are persistent in the environment or the human body, some of them have clearly become persistent and highly prominent in the scientific literature. The tens of thousands of articles on lead, mercury, and other well recognised environmental hazards testify to the enormous investments in studying, reporting and publishing on these prominent substances. It would therefore seem that the choice of research topic in the field of environmental health greatly benefits the well-known chemicals.

The next question to consider is whether research addresses societal needs for more poorly known and potentially dangerous risks. Does academic research in environmental chemicals ignore less-well known compounds that need documentation? We conducted additional studies to examine this question.

26.3 Ignoring new potential environmental hazards

We now focus on the other end of the spectrum, as many environmental chemicals have not been adequately tested. When the US National Research Council conducted a study in the 1980s on toxicity testing, 78 % of the industrial chemicals most commonly produced was found without even minimal test data for toxicity (NRC, 1984). Later follow-up showed little improvement (US EPA, 1998). Even today, the European Chemical Agency complains that gaps in safety data remain and that little has been done to mend the problem so far (Gilbert, 2011). Thus, as metals and tar chemicals attract much research attention, are substances of importance to society being neglected by environmental researchers?

To examine this question, we looked at the high-production chemicals considered in particular need of scientific documentation (US EPA, 2009). This high-priority list was first published in 2006 and included thirteen important substances lacking both a robust hazard data set and exposure information. For the time period of 2000–2009, we found that these chemicals had a total of only 352 links to scientific articles, i.e. an average of only three per month for the entire group (Grandjean et al., 2011). Five of the thirteen high-priority substances were not encountered at all in the 78 journals during the ten years. One could excuse the lack of coverage up to 2006, when the EPA published its list, and perhaps 2007. However, when extending the search to 2010 and 2011, the result was pretty much the same — the priority listing had not inspired any increased number of publications in scientific journals. When compared with the staggering numbers for top-20 substances, the

Table 26.2 Numbers of articles published in environmental science journals during 2000–2009 on chemicals covered in the present volume, as determined from SciFinder links to the CAS numbers

Name	CAS no.	Number of links	Rank
Lead	7439-92-1	8 926	2
Mercury	7439-97-6	4 399	9
p,p'-DDT	50-29-3	1 968	21
Bisphenol A	80-05-7	952	62
Perchlorethylene	127-18-4	898	68
Beryllium	7440-41-7	400	235
Vinylchloride	75-01-4	319	276
Dibromochloropropane (DBCP)	96-12-8	41	> 1 000

publication rates for these high-priority substances appear tiny.

Other substances may be considered likely emerging hazards, about which further information would be highly useful. Triclosan is a biocide often used in cosmetics, but releases into the environment have raised concern (Dann and Hontela, 2011). There were 259 articles on this chemical during 2000–2009, much better than the high-priority substances listed by the US EPA, but way below the popularity of toxic metals. Likewise, the perfluorinated compounds have been in use for decades, and concerns about their environmental fate and toxicity have grown (Lindstrom et al., 2011). The most prevalent member of this group, perfluorinated octanoic sulfate was covered in 271 articles, about the same as triclosan. Thus, each of them was addressed only in about two dozen scientific articles in the scientific journals every year. Accordingly, about 35 articles would focus on lead (and close to 20 on mercury) each time a single article would present evidence on one of these emerging hazards. But can we trust these numbers?

Although the bibliometric data do not distinguish between short, descriptive reports and thorough reviews, the overwhelming emphasis on a small minority of environmental chemicals cannot be explained away. Also, the scientific journals may not reflect research activities outside academic institutions, but one would have to imagine huge numbers of reports outside the mainstream journals to make up for the differences. The conclusion therefore seems inevitable that the long-term prominence of substances commonly covered in articles in environmental journals does not match the societal needs or those of regulatory agencies. Substances that were highly popular in research during the previous century remained so during the first ten years of the present millennium, despite the changing needs for evidence on environmental impacts.

26.4 Inertia and its reasons

An important reason for such inertia and continued focus on well-known substances may relate to the traditional science paradigm, where solid conclusions depend on replication and verification. While a single study should not be relied upon as firm evidence, the extent to which replication is needed seems to have been stretched to the extreme, when well-known environmental chemicals inspire almost 1 000 publications per year.

It may well be that academic researchers do not know or contemplate the needs for environmental health documentation. We may question environmental researchers, who keep studying lead toxicity to obtain even more detailed or perfect results ([3]). However, individual researchers and their institutions may have insufficient access to public and private funding that would allow an unrestricted choice of research topics. This limitation would especially refer to young researchers of low academic rank. Further, if students are taught to replicate and extend their mentor's own research, they will later become the seniors with the same type of expertise and narrow focus on well-known environmental hazards. Existing expertise as well as facilities may favour a continued focus on the same hazards, thereby propagating long-term traditions and ignoring society's changing needs for early warning investigations. In more general terms, a tendency to maintain a narrow focus is likely to be counter-productive in regard to scientific discovery and innovation, as there would potentially be much more to learn from studying new hazards than from replicating studies on old ones.

Several factors may contribute to the estrangement of academic research from societal needs for documentation on environmental hazards. Research institutions have an interest in maintaining highly qualified personnel and efficient use of costly infrastructure. All of the most popular chemicals can be inexpensively measured by instruments that became widely available already in the 1970s and 1980s. Analytical methodologies are already established and well documented. These instruments (atomic absorption spectrometers and gas chromatographs) make it possible within a week or so to generate results sufficient to justify a scientific paper on one or more of the top-20 substances. Under these conditions, why would ambitious researchers and their students take on new substances that might require the purchase of expensive equipment and arduous development of new methods?

The loyalty to established methods and research topics is not just a matter of convenience. In

([3]) The author has published numerous articles on lead, mercury, and other top-20 chemicals in scientific journals, thus being part of the inertia. However, as the chapters on lead and mercury show, real or alleged uncertainties were often used to argue against hazard abatement, thereby requiring more research.

academic research, competition is fierce and each researcher must demonstrate his or her qualifications by frequently publishing articles in scholarly journals. By endeavouring to research the unknown, these researchers would face longer time periods between publications, if any. The mere number of publications is a crucial metric for academic prestige and for obtaining a tenured position. By using existing instruments and methods, a researcher can more effectively expand the CV, especially if the reports can be framed into small incremental manuscripts, each of them contributing an entry on the publications list. So-called vanity publications may contaminate the scientific literature, as they contain little new information, but primarily serve to augment the author's credentials. Whether they contribute new insight then becomes a secondary concern. Similarly, the budget in many research departments is tied to the number of scientific publications, thus also favouring quantity over quality. Such a focus on publication numbers may deny the higher societal goals of environmental research while promoting earthly aspects of personal desires and academic reputation.

The pressure to complete a project on time (or even before the deadline) and to publish the findings with minimal delay also invites the use of short-cuts. Convenience and lack of funds may determine that some parameters in a study are not measured in appropriate detail, e.g. by relying on questionnaire responses rather than actual measurements, which may be too expensive. When a study claims to address an environmental hazard using study parameters that are unreliable or perhaps not representative, the results will often be non-informative. Worse, the results may be interpreted as evidence against the hazard causing any risk at all. Such misleading conclusions are sometimes referred to as Type III errors (Schwartz and Carpenter, 1999). I shall return to this problem shortly (see Section 26.5 below).

The inertia and reliance on convenience are not restricted to researchers themselves, or public research institutions, for that matter. It also affects the funding agencies. If a proposed project deals with a known environmental problem, the principal investigator probably has an impressive track record, the protocol is feasible and easy to comprehend and capable reviewers are readily recruited. That may not be the case with poorly studied substances and emerging hazards. The funding agency can feel comfortable about the proposed time schedule and the anticipated outcome of the project, as the exposures and effects rely on established methods. Uncomfortable surprises are unlikely. Hence, it may be safer and more convenient for grant managers to concentrate on the known hazards.

Scientific journals probably also play a role in maintaining a focus on well-known substances. Peer review of submitted manuscripts is rarely a problem with a manuscript on lead exposure. Bias toward publication of the report may occur when the reviewer finds that his or her own research has been cited, thus demonstrating the sound judgment of the authors of the manuscript. Some of the journals that we explored in the bibliometric databases are regarded as prestigious, with high citation rates. The possibility exists that some environmental chemicals may be held in higher esteem than others, thereby adding to their continued prominence, or publication persistence, no matter what the societal needs may be. This means that there may be an element of circular reasoning involved, where a substance is a popular research item simply because it has been widely studied in the past — a self-prophetic bias that maintains a continued prominence of a small number of scientists and their publications.

The science sociologist Robert K. Merton (Merton, 1968) dubbed this phenomenon a 'Matthew' effect, referring to the New Testament ('*For unto every one that hath shall be given, and he shall have abundance: but from him that hath not shall be taken away even that which he hath*'). Popularity among scientists in the past seems to provide justification for the importance or relevance of continued research in a particular field. The opposite strategy would appear more attractive from the point of view of innovation.

However, it must be said that some conventional research into well-known substances have identified novel scientific breakthroughs that are not only relevant to our understanding of these well-characterised substances, such as mercury and lead, but they have also been scientifically valuable, via analogy, to many other substances.

Clearly, academic research has multiple purposes, a number of constraints and some limitations, when viewed from an environmental health angle. Societal needs for evidence on priority substances or emerging risks are apparently not seen as a high priority for academic research in general. But the choice of research topic is not the only problem.

26.5 Research methodologies and assumptions

Jointly with the inertia in the choice of research topics, traditional scientific thinking may also represent

an obstacle. According to the standard paradigm, we need to justify our conclusions by replicating our findings, securing the highest possible data quality and documenting each component of the anticipated causal link. Such high standards will protect science from making mistakes by claiming, e.g. that lead is toxic to the brain, unless extensive documentation is truly available to back this assertion. The links to scientific traditions extend back to the Leonardo da Vinci's and Galileo's writings. In studying environmental health hazards, the prevalent paradigm determines how the problem is usually framed as below:

> 'The traditional scientist will address an environmental research question as follows: Have we reliably documented through meticulous study and replication that this substance is mechanistically and causally linked to an adverse biological change?'

Along with the demand for replication, tradition calls for a narrow focus. Uncertainty is commonly restricted through rigorous control of the study setting. The advantage of a well-defined study is that it addresses only a single factor under specific circumstances and therefore more likely will lead to firm or indisputable conclusions. However, due to its limited scope, the study will at best result only in an incremental increase in knowledge about the overall issue at hand, including multiple or complex exposure scenarios and the significance of individual vulnerability. Thus, the disadvantage is that this approach leads to reductionism and explores only limited or individual aspects of each hazard. Such proximate and simplistic risks poorly represent the true complexity of environmental hazards.

Examination of the chapters on human health hazards in this volume and *Late lessons from early warnings* Volume 1 (EEA, 2001) allows identification of several assumptions that were, at first, considered valid and important, but were later found to be misleading. Table 26.3 shows some of the most crucial — and erroneous — assumptions that were initially made in regard to one or more of the environmental hazards included in this volume. The case studies in this volume show that relying on these assumptions, while seemingly meaningful in terms of the prevailing research paradigm, led to proliferation of environmental hazards due to the substantial delay in their recognition.

Table 26.3 Erroneous assumptions made in initial evaluations of environmental hazards and the subsequent scientific recognition of the true complexity

Initial assumption	Late scientific lesson
1. Presence of environmental chemicals in the body can be tolerated at 'safe' or natural doses	Delayed effects, cumulated or re-mobilised doses, or toxic metabolites may occur at exposures previously thought to be safe
2. Absence of harm in adult male workers (from routine medical data or mortality) means absence of risk to the general public	Sub-populations, such as children and the elderly, may be more vulnerable to the exposure
3. Acute or short-term effects also reflect chronic or long-term effects	Dose-response relationships for acute effects may substantially differ from those for chronic effects
4. Biological effects may not necessarily be adverse and can be considered harmless	Early changes can predict more serious adverse effects which can develop later on
5. Dose-response relationships are consistent (and 'monotonic'), and no risk occurs at doses below apparent thresholds	Some substances show 'low dose' effects that are not readily predictable from responses to high doses
6. Short-term assessment of exposures from a single pathway can generally be considered sensitive and valid	Most methods for exposure assessment are imprecise, and imprecision usually results in underestimation of the toxicity
7. The placenta and the blood-brain barrier amply protect sensitive life-stages and organs from toxic chemicals	The barriers may be bypassed, as they offer limited protection against industrial chemicals
8. Average findings in exposed subjects indicate the potential for harm to the exposed population	Sensitive sub-groups may show effects that are not apparent from the average data
9. Toxicity evidence from animals and wildlife is not relevant to human toxicity	Animal data have reliably predicted most known carcinogens and many other hazards, and humans may be more vulnerable than other species

A crucial assumption was that a biological change may not necessarily reflect an adverse health effect and could therefore be ignored. Within normal variability, it may indicate adaptation or 'hormesis', therefore being innocuous. With proper justification, the assumption may be true, but biological changes should not be disregarded just because they are prevalent (or unwelcome, for some reason). For many years, researchers believed that the inhibition of an enzyme called ALAD due to lead exposure at blood-lead concentrations thought to be low, was a biological change that had no health implications (as described in the Chapter 3). That may be true in a strict sense, as the enzyme in red blood cells has no important function. However, recent research has shown that serious adverse effects do occur at lead exposures that were previously regarded as too low to be harmful.

Also, habitual levels of lead exposure were called 'natural' simply because they were normal or habitual. But prevalent lead exposures were the result of centuries of increasing lead use. Analyses of lead isotopes and of mummified tissues documented that normal lead exposure were far above what could be considered natural.

For efficiency reasons, toxicology studies have aimed at avoiding considerations of the sex, age and strain of the animals used. If focusing on inbred, adult male rats only, important sources of variability were ignored while making the study more efficient and precise. This problem became centre stage when reproductive toxicology and endocrine disruption began to attract attention (see Chapter 13 on ethinyl oestradiol in the acquatic environment and Chapter 10 on BPA, as well as PCBs, DES and TBT in *Late lessons from early warnings* Volume 1 (EEA, 2001, Ch. 6, 8, 13)). Also, it is only a recent discovery that exposures to environmental chemicals may cause much more toxicity if they happen during vulnerable developmental windows (Grandjean et al., 2008). However, prospective studies of birth cohorts take a long time and are extremely costly, and even multi-generation animal assays are often resisted due to economic burdens on industry.

The assumptions in Table 26.3 prevailed for a long time due to the failure of available, though incomplete data to show clear evidence of a risk. If adverse effects were not proven to exist, the erroneous conclusion was drawn that adverse effects must be absent. Perhaps this is the underlying assumption, which represents the greatest error. It survived, as uncertainties were ignored, whether in regard to exposure assessment, sensitivity of outcome measures, individual vulnerability, statistical analysis methodology or statistical power of the study. Overlooking imprecisions and incompleteness will most often result in underestimation and may lead to rejection of the presence of a (true) risk. Also, these uncertainties are not likely to create spurious associations, unless confounding factors are present.

26.6 Vulnerability of research to criticism

The downside of the traditional strategy to provide ample verification is that science becomes vulnerable to a critique that raises concerns about various possible sources of error or bias, particularly in regard to emerging insights and early warnings. The desire to document the truth, preferably the 'full' truth, makes science vulnerable to purported weaknesses. Thus, while careful scientists must pay meticulous attention to the methodological standards and quality assurance, some colleagues primarily exert these skills when judging the work of colleagues. Such critique may be unjust, but the halo earned from emphasis on the quality of scientific methods thrives from the collusion of admiring colleagues and students (e.g. at scientific conferences).

However, harsh critique and exaggerated scepticism may be particularly inappropriate in regard to emerging insights and early warnings which are often innovative and necessarily tentative ([4]). Thus, the case studies illustrate that astute observations by clinicians, factory inspectors, workers, anglers, bee keepers and community members can sometimes provide valid hypotheses on new hazards that are only confirmed by in-depth research much later.

A common strategy is to disregard studies that do not satisfy certain methodological criteria, sometimes abusing 'criteria' for causality. Although such criteria are useful, UK statistician Austin Bradford Hill noted:

> 'All scientific work is incomplete… All scientific work is liable to be upset or modified by

([4]) When Joe Forman first observed the hole in the ozone layer using low technology instruments he could not believe his results as they conflicted with the satellite data. He returned to the Antarctica to observe the hole three times before he — under pressure from his funding sources — felt confident enough to report his findings. See the chapter on Halocarbons in the first volume of *Late lessons from early warnings* (EEA, 2001).

> advancing knowledge. That does not confer upon us the freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at the given time' (Hill, 1965).

Despite Hill's prudent advice, some researchers may mistake the validity of their own conclusions for meticulousness in identifying presumed violations of the causal criteria or other validity requirements committed by their colleagues.

The overly sceptical focus on scientific methodology may lead to bias and narrow-mindedness. Thus, special interest groups have praised what they call 'sound science', which supports conclusions that are considered attractive (but, of course, is no more reliable than other research, and is sometimes actually less). In particular, so-called black-box epidemiology studies of health hazards have received harsh critique (Taubes, 1995). Some of that exaggerated critique is echoed in the chapters of the present volume.

Expert committees that advise national and international bodies are often tempted to express unreasonable critiques of research results and stress the preponderance of uncertainties. Such critiques may be considered appropriate for highly respected experts and is in accordance with their high methodological standards and unrelenting scepticism. However, a narrow focus on scientific methodology may be coupled with blindness to environmental degradation and social injustice. Not surprisingly, the strategy of criticising research methodologies has been vigorously explored by vested interests, often with the purpose of manufacturing doubt (Michaels, 2005; Michaels, 2008; Oreskes and Conway, 2010).

When a call for guidelines on 'Good Epidemiological Practice' was first promoted, it was at first embraced by researchers as a useful tool to stimulate high quality (and sound) science. However, strict interpretation of epidemiological rules could also be applied in order to disregard epidemiological findings that for other reasons were regarded as unwelcome. It turned out that the initiative originated with industry groups in order to disqualify unwelcome 'junk science' (as described in Chapter 7 on tobacco) (Ong and Glantz, 2001).The scientific rigour that had been considered a prerequisite in the traditional science paradigm was now turned around and became an unrealistic requirement for repetitive, controlled studies that could furnish virtual statistical certainty ([5]). Using strict criteria, unwanted results could then be criticised as junk and the uncertainties were then erroneously interpreted as an indication that no hazard was present.

26.7 Statistics and confidence limits

A key issue is the statistical data analysis. When analysing their results, researchers use statistical methods to determine whether the observed data were 'statistically significant', or whether they can be attributed to chance. The probability that their results are significant is usually expressed as *p* values, or probability values. The *p* was originally proposed by the UK statistician Ronald Fisher along with a limit of 5 % thought to be appropriate. This method allowed the researcher to identify findings that deviated significantly — unlikely due to random variation — so that the hypothesis that no difference was present would be rejected.

From its early application to agricultural plant breeding test designs, the 5 % limit has since been applied much more widely and has become almost sacrosanct amongst scientists from many disciplines. Using Fisher's *p* value limit allowed researchers to classify research findings that — when the *p* value was above 5 % — did not reliably support the 'null' hypothesis of no difference or no association, as the results could be due to random variation. Accordingly, the 'null' hypothesis could be rejected only when the *p* value was lower. A few studies and many anecdotes suggest that scientists place greater emphasis on results that have a *p* value of, say, 4.9 % than on results with a *p* value of 5.1 % (Holman et al., 2001). Statistically, there is no meaningful difference between outcomes with such similar *p* values. But if Fisher's proposed limit is applied in a strict sense beyond Fisher's own recommendations, then one set of results with a *p* value of 4.9 % would be interpreted as rejecting the hypothesis (hereby providing evidence of possible causality), whilst the other with a *p* value of 5.1 % would not refute the null hypothesis and would be considered non-informative.

([5]) An additional criterion often used was that only a 2-fold increased risk above background would be believable, e.g. from childhood leukaemia in residences close to power lines or from heart disease from environmental tobacco smoke. Apart from the much greater impact of a 2-fold increase in heart disease, there is no meaningful statistical difference between increases by a factor of 1.9 and 2.1, one of which would satisfy the criterion for a hazard, the other one not.

As commonly applied and interpreted, the *p* value is used mainly to determine the viability of a hypothesis. Although science in principle aims at falsifying hypotheses — since a definite proof cannot be obtained — it seems to make too little use of the data if we are just determining whether or not the *p* value is below 5 %. If the *p* value is high (well above 5 %), the results are rendered useless, as they failed the only criterion for success, namely to refute the hypothesis (although a hypothesis may theoretically be correct, even though the data deviate substantially from prediction). Sometimes, repeated attempts at falsifying a hypothesis fail, but a joint calculation (so-called meta-analysis) could result in an overall *p* value that perhaps finally reaches statistical significance with *p* less than 5 %, or some other specified level.

In most cases, the null hypothesis is that an exposure has no effect. Thus, in environmental research, the *p* value is used to test a null hypothesis that may be unrealistic or obviously wrong. This would seem to be a serious limitation. Would we ever be tempted to conclude that lead is not toxic, just because a small study has resulted in a *p* value that is greater than 5 %? Of course not. But the traditional use of the significance limit means that scientists are very reluctant to draw conclusions if the *p* value is 5.1 %.

The so-called frequentist tradition in statistics considers the data in isolation and evaluates them in regard to a theoretical null hypothesis, which may or may not be appropriate. Combined with a sacrosanct 5 % limit, the research results may not be as useful as they could be, and the conclusions could even be confusing and counterproductive (Goodman, 2008). The point is that we may be testing the wrong hypothesis and not making ample use of all of the available data. Thus, several case studies have shown that early warnings are often initially not statistically significant, such as the first IARC study of passive smoking, but nevertheless turned out to be robust.

Even if a study has reached statistical significance, this could still be due to chance. If we are conducting a large number of comparisons, then in all likelihood a small proportion of them could happen to be unusual and perhaps deviate from expectation at a statistically significant level. But such deviation is accidental and would be associated with a large number of comparisons. A common method is to adjust the *p* values using a procedure named after the Italian mathematician Bonferroni, thereby requiring *p* values to be significant only at lower values, the larger the number of comparisons. However, this technique, too, can also be used erroneously to disregard an unwelcome study (Perneger, 1998).

The use of an alternative approach to frequentist statistics started back in the 18th century, when UK Reverend Thomas Bayes designed a formula that let the study results modify the prior probability of a hypothesis, thereby generating a posterior probability of the hypothesis based on the new evidence obtained (Greenland, 2008). Bayes allowed inclusion of any results, whether few or large-scale, and no matter the *p* value, to help modify our reliance on a hypothesis and to determine its updated plausibility. One could still focus on the null hypothesis, or perhaps rather the overall outcome of all previous studies. This way, each study would still be useful and would be utilised to modify and fine-tune the hypothesis under consideration. Although attractive, Bayesian statistics sometimes results in serious mathematical complications that limit their usefulness. Also, we may not have a good idea about the exact hypothesis under study, and a prior probability of that hypothesis may be impossible to obtain. Bayesian statistics has therefore been criticised for being subjective and overly laborious. Still, empirical use of Bayesian statistics is gaining support (McGrayne, 2011).

Some scientists and some scientific journals now reject the use of *p* values (Lang et al., 1998). But if we are to limit our reliance on *p* values, how can we best extract a robust statistical summary of a complex study? A key parameter will always be the point estimate of the average effect. But instead of calculating whether this estimate is 'significantly' different (*p* less than 5 %) from no effect, many researchers recommend using the confidence interval (Thompson, 1987). It represents the range of values within which 95 % of averages would fall if a large number of similar studies were conducted. In other words, given the point estimate and the calculated variability, the study would be in accordance with any hypothesis that postulated an effect within the confidence interval. If zero is included in the interval, then the results do not deviate significantly from the null hypothesis. However, they also do not deviate from many other hypotheses, some perhaps suggesting a serious effect. The upper confidence limit indicates how large an effect that would be in agreement with the data. In a precautionary setting, the upper limit would often represent a plausible worst case scenario that would serve as a useful basis when considering intervention.

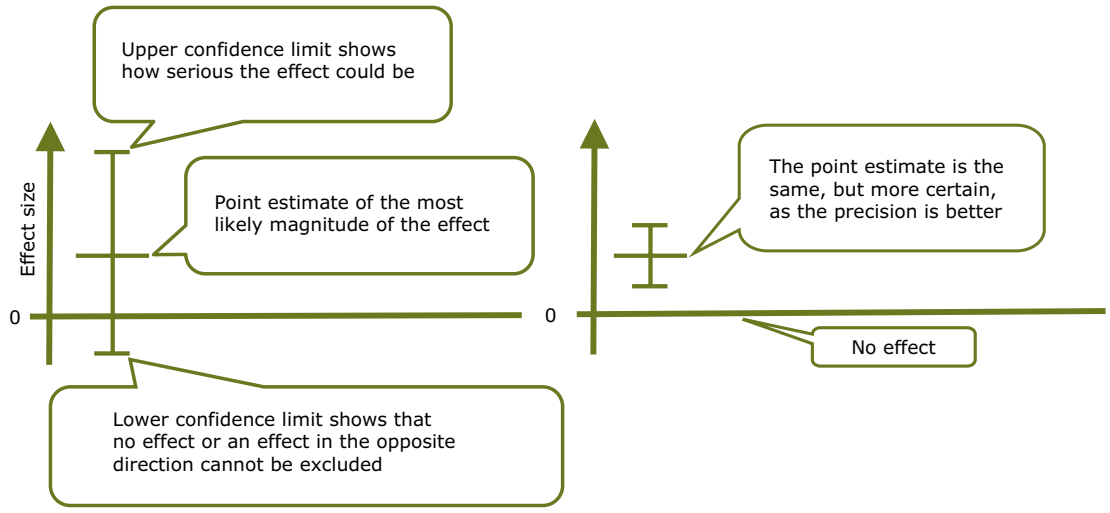
The two studies illustrated in Figure 26.1 show the same average effect, though with different degrees

of certainty. The study on the right shows an effect that is statistically significant, as the no-effect hypothesis (zero effect) can be excluded. The study on the left has less precision, perhaps because it is smaller, and the point estimate does not deviate significantly from no effect (the null hypothesis). However, the upper confidence limit suggests that the study cannot exclude a large effect. In contrast, the significant study on the right would speak against the hazard being very large. Both of these perspectives are relevant, for both studies. A focus on the upper confidence limit would have the additional advantage that it would inspire larger studies with greater precision.

From a precautionary viewpoint, the use of confidence intervals is highly attractive. Instead of concluding that we are not sure that there is an effect at all, we can now also say that the results do not contradict an effect, and that it could possibly be up to a certain magnitude. If a study is large, and when results from two or more studies are combined, the confidence interval will narrow due to the decrease in statistical uncertainty. If a small study (like the one on the left) is in accordance with a potentially large effect, it would call for extended studies to explore whether such a serious hazard is indeed realistic. However, from the 'frequentist' viewpoint, the small study cannot reject the null hypothesis and would therefore not call for any further attention. Hence, the two perspectives differ substantially as to the interpretation of research, the conclusions, and the priorities for further information. Both are useful, and a narrow focus on *p* values should be avoided (Stang et al., 2010).

The choice of statistical analysis is even more important in situations, where we do not have the option of calling for more studies. If a disease is serious but very rare, that number of subjects included will be small, and it may take a long time before enough information has been gathered in order to obtain a p value below 5 %. Perhaps most dramatically, in regard to endangered species, it is simply not possible to sample sufficiently large materials to reach 'significance'. Thus, wildlife biologists some years ago concluded: 'At least part of the blame for the spectacular overexploitation of the great whales can be placed on scientists being unable to agree… In certain circumstances, a population might go extinct before a significant decline could be detected' (Taylor and Gerrodette, 1993). When the researchers examined the frequency and precision of recent monitoring efforts, they concluded that the percentage of precipitous declines that would not be detected as statistically significant would be between 72 % and 90 % for various whale species and 55 % for polar bears. Thus, more than half of the world's polar bears and the great majority of the whales would have to disappear before current studies would be able to conclude that the decrease is 'significant' (based on a one-sided *p* value limit of 5 %) (Taylor et al., 2007). Similarly, to the extent that monitoring and effect studies of environmental hazards are patchy, we are probably overlooking adverse effects, even those

Figure 26.1 The importance of confidence limits



Note: Two studies show the same average effect (horizontal line), but the vertical line suggests that the study on the left has a larger confidence interval and more uncertainty, so that it is both in accordance with no effect (it includes zero and is therefore not statistically significant), but it also cannot exclude a large effect. The study on the right shows the same effect, now statistically significant, but due to the greater precision, this study can exclude the presence of a large effect.

that are serious, simply because the information is uncertain (like the study on the left in Figure 26.1).

To avoid inconclusive results, researchers often carry out power analyses to determine the sensitivity of a proposed study, that is, the likelihood that the proposed study will lead to conclusions on the existence of a hazard of a certain relevant magnitude. If the protocol is not able to ascertain with any confidence the presence of an important risk, then the statistical power is insufficient (as in the monitoring of polar bears). Either the study would be a waste of time and should be disbanded, or the protocol should be expanded to allow sufficient power.

26.8 Bias in research

For the reasons listed above, the research results are often non-informative. Such inconclusive studies are sometimes called 'negative', although this term could suggest that an effect was in the direction opposite to expectation. Worse, such studies have sometimes been thought to represent 'no risk', rather than 'no information'. Such aspects of the traditional science paradigm involve inherent biases toward the null hypothesis. Based on the case studies in the present and the previous volume, Table 26.4 has been revised from previous compilations (Gee, 2009; Grandjean et al., 2004).

Most of the aspects listed in Table 26.4 have to do with the design of the research study and therefore refer to the methodology, rather than the relevance of the research. So, in that respect, greater attention to methodology would be beneficial. However, the main problem is that even though the research results may be less informative than desired, the research may well contain information that is more relevant than the simple claim that the null hypothesis of no effect cannot be excluded. As illustrated in Figure 26.1, we need to ask: How large an effect can the study have overlooked? This question should also take into account the possible existence of vulnerable subgroups, long-term effects, and other issues that may have been ignored.

Two entries in the table refer to the possible existence of publication bias. It is quite likely that some science journals, and more often the mass media, prefer to publish alleged scares rather than to report that there is nothing to worry about (Ioannidis, 2008). But the bias may also be in the opposite direction (Oreskes, 2004). More importantly, our data on publication frequencies (Grandjean et al., 2011) suggest the opposite. The journals publish extensively on well-known chemicals, where new scares are rare, and only occasionally publish on the unknown and emerging environmental hazards which could possibly represent much scarier risks, given that so little attention is paid to them. So the few scares that catch occasional headlines should be interpreted in light of the overwhelming background of environmental hazards that are and have been ignored, some of which could well represent

Table 26.4 Key aspects of research likely to affect the outcome of a study, whether underestimating (false negative) or exaggerating (false positive) the possible existence of an environmental hazard

Methodological features and their main direction of error	
Inadequate statistical power	False negative
Lost cases and inadequate follow-up for long-term effects	
Exposure misclassification	
Insensitive or imprecise outcome measures	
Adjustment for confounders with better precision than the exposure	
Failure to adjust for confounder with effects in the opposite direction	
Disregarding vulnerable subgroups	
5 % probability level to minimize risk of false positives (Type I error)	
20 % probability level to minimize risk of false negatives (Type II error)	
Pressure to avoid false alarm	
Incomplete adjustment for confounders with similar effects	False positive
Post hoc hypothesis	
Publication bias towards positive findings	

serious hazards. Chapter 2 on false positives shows that erroneous alarms are fairly rare.

In summary, the context of justification needs to be balanced with the context of application or, in other words, the quality of the research must be linked with its relevance. So the focus on methodology issues and the preoccupation with verification studies should not happen at the expense of providing evidence on issues of major environmental and social relevance. While polishing the same stone over and over again, we should not ignore all the other shingles and rocks where some scientific gems may yet be hiding.

26.9 The changing research paradigm

Science sociologist Robert K. Merton characterised traditional science by the acronym CUDOS, which stands for Communalism, Universalism, Disinterestedness, Originality and Scepticism. These traits are still valued and are prevalent in many scientific disciplines, but differences occur and the research paradigm within the environmental sciences is changing. All of these attributes for science, whether basic or applied, are needed to secure a meaningful and trustworthy research activity in society. However, the preoccupation with publication, credentials and funding that is common in academia today can lead to social apathy, thereby providing fertile ground for dependence on narrow interests that may include corporate money (Grandjean, 2008b).

Of particular note, Merton characterised ideal science as 'disinterested', but vested interests of whatever origin may make research less neutral and less reliable. Several case chapters in this volume describe how industries have withheld evidence, lambasted whistle-blowers and promoted research that supported the conclusions desired (Kurland, 2003). Especially when cover-up is included in such diversions, the result is that research loses credibility. Transparency in regard to conflicts of interest has been recommended, but complete elimination of financial ties may be the best way to secure trust-worthy research (Krimsky, 2003). Although conflicts of interest undoubtedly occur within academia at large, perhaps an additional problem is that the academic agenda is likely to differ from the priorities of regulatory agencies in environmental health.

Another science culture has developed, as research contracts or privately funded research have grown. They differ in several respects from the CUDOS ideal. The results may not necessarily be published in scholarly journals (and would therefore be missed by our SciFinder searches). When the research is kept secret, it will not inspire further studies at public institutions. A particularly important chemical, bisphenol A (952 publications during 2000–2009), has enjoyed vast industrial popularity and became widely used in food packaging materials and beverage containers (see Chapter 10 on BPA). It was said to be safe at the very low exposures that consumers were likely to receive. However, after several decades of expanding use, independent research eventually uncovered evidence of health risks (Myers et al., 2009). The same pattern was seen with the perfluorinated compounds, where a major US producer for decades claimed that little would escape into the environment, and that essentially no toxicity occurred (Lindstrom et al., 2011). Only recently was it discovered that current exposures may be far from safe (Grandjean et al., 2012), but these chemicals have been disseminated into the global environment and cannot be recalled.

Physics professor John Ziman characterised the 'industrial' (or contracted) research as Proprietary, Local, Authoritarian, Commissioned, and Expert, thereby stressing that this activity builds on local expertise to reach specific goals. The same characteristics may apply to contract research carried out with public funding, but the initiator may not always be apparent. Thus, the Center for Indoor Air Research, the Electric Power Research Institute or the Chlorine Council may sound like charitable donors, rather than industry front groups. But they are in fact organisations funded by corporations with vested interests in the research outcome. However, the reader may be led to erroneously believe that the sponsored research reflects CUDOS values.

The source of funding will also affect the choice of study topics. Accordingly, comparatively little research is devoted to the risks associated with pesticide exposures and the advantages of alternative crop protection methods (Krimsky, 2003). Booster biocides (see Chapter 12), such as Diuron (389 links to articles in 2000–2009 in SciFinder) and Dichlofluanid (39 links), received only a little attention in independent research, some of them much less than the organotin compounds (see tributyltin in Table 26.1) that have been phased out. SciFinder also located only 133 links to Gaucho®, the pesticide that endangered bee populations (see Chapter 16). As there are clear commercial interests in these compounds, the paucity of complementary academic research publications is unfortunate, although perhaps not surprising. Similarly, much less attention is paid to adverse

effects of new technology than to its advantages, although this has recently changed in regard to mobile telephony. Perhaps there is a parallel to physicians collaborating with the pharmaceutical industry in clinical trials of new drugs, which, with patent protection, will be capable of yielding great monetary returns. In contrast, older drugs no longer protected by patent are the subject of far less research, but may be as effective as modern drugs costing far more (Washburn, 2005).

Because evidence is the basis upon which the evaluation of risks must rely, researchers publishing results at odds with certain vested interests have become targets of criticism and intimidation with the aim of suppressing or throwing suspicion on unwelcome information about health risks. Perhaps the best known case involves Herbert Needleman, who supplied the first, weighty documentation of prevalent lead pollution damaging brain development (see Chapter 3 on lead). He was angrily persecuted and harassed with unfounded accusations of dishonesty (Needleman, 2000).

Disagreement usually focuses on the uncertainties and the scientific inference, not the choice of study topic. Harsh critique has sometimes been voiced, as have angry accusations of bias in differing interpretations of evidence (Gori, 1996). Research that has direct implications in regard to considerations of pollution abatement usually receives more wrath than reports on already recognised hazards. Perhaps this is another key as to why researchers favour well-known hazards.

In order to introduce dissent into the literature, possible strategies involve publication in trade magazines disguised as scientific journals. The best examples are Indoor and Built Environment (Tong et al., 2005) and Regulatory Toxicology and Pharmacology (Axelson et al., 2003). These journals tend to publish articles that contain conclusions favourable to the industrial sponsors, no matter their scientific weaknesses. This strategy is counter to the Precautionary Principle, as they argue for 'no risk' when the evidence is uncertain or non-informative. In addition to the tobacco industry, other examples include studies supported by the pharmaceutical industry, which are much more likely to conclude that a drug is safe and efficacious than studies conducted without such support (Jorgensen et al., 2006), but the same seems to happen in toxicology and environmental research (Myers et al., 2009).

As a consequence, public trust is abused by deceit. The purpose of research seeking truth is betrayed, when undisclosed ties taint the research and its conclusions.

Under such contentious conditions, researchers may choose to hedge their conclusions by incessant use of words, such as 'maybe', 'perhaps', 'in theory' and similar terms (Hyland, 1998). By softening the conclusions and avoiding attribution of specific causality, the researchers protect themselves against critique by appearing well-balanced, unassuming and even sceptical toward the implications of one's own findings ([6]). However, this strategy has a downside. To the lay reader, who is not familiar with the traditions of scientific writing, the caveats and reservations may sound like the new results really do not prove anything, and that we are still left with the same uncertainty. To readers with a vested interest, the soft wording can be exploited through selective quotation and by emphasising real or alleged weaknesses (Grandjean, 2008a).

Because of the involvement of research funders, the industrialised (or contracted) science can be better characterized by the PLACE acronym (Ziman, 2000), although often posing like independent, basic research in accordance with CUDOS. If all research today earned CUDOS, no matter its funding, there would be little to worry about. But the weaknesses and biases outlined above suggest that PLACE needs to be supplemented by an additional research, one that better fits with the use of the PP in decision-making.

In this complementary paradigm, environmental research in support of PP-based decision-making would involve stake-holders and therefore become Participatory, rather than Communal or Proprietary as in the other paradigms. It would be Accessible, Transparent, Inventive and Open-minded. Although the various attributes may perhaps not be compared horizontally in Table 26.5, the PATIO characteristics would seem to fit better the research that is needed in a precautionary setting.

A key aspect is that, given the absence of final proof, an integrated evaluation must include uncertainty as a normal condition that needs to be explored and addressed, rather than minimised for the purpose of making research more efficient. An additional feature is the inclusion of the public in exploring how the uncertainty should affect

([6]) Please note how often I use the words 'may' and 'perhaps'. I do so, too, because I do not want to jump to conclusions and therefore present my case with understatement rather than the opposite.

Table 26.5 Main properties of research in three different settings

Academic (normal)	Industrial*	Precautionary
CUDOS ([a])	**PLACE** ([b])	**PATIO**
Communalism	**P**roprietary	**P**articipatory
Universalism	**L**ocal	**A**ccessible
Disinterestedness	**A**uthoritarian	**T**ransparent
Originality	**C**ommissioned	**I**nventive
Skepticism	**E**xpert	**O**pen-minded

Note: * 'Industrial' science is driven by private or other special interest and may violate some of the CUDOS norms in its pursuit of knowledge within fields of commercial or other defined interest, where public interest may be ignored.

Source: ([a]): Merton, 1973; ([b]): Ziman, 2000.

the decision-making. As discussed above, and in agreement with the PATIO paradigm, both study designs and the reporting of research results need to change.

In contrast to the traditional science paradigm, where replication is held as a key to supporting conclusions on causation, the PP does not inspire repetitive verification. If available, replication will be useful, but a hypothesis may well be plausible even in the (temporary) absence of supportive evidence. Given the enormous diversity and complexity of environmental hazards, one implication of the PP is that research is primarily needed to document the extent of uncertainty and, when possible, to narrow this uncertainty to better inform decision-making and eventually to support more precise risk assessments as a basis for interventions that will no longer need to be precautionary. But rather than fine-tuning risk assessments for individual hazards, the vastly incomplete information on most environmental chemicals makes research into uncertainty a very urgent need.

26.10 Precautionary science

As already discussed, the PP does not specifically demand testing of a null hypothesis that an exposure may be without a discernible effect. Rather, information is required whether a hazard could potentially be serious. This point of view should inspire new ways of planning, conducting, and reporting environmental research. So the research question outlined in the beginning of this chapter in accordance with traditional scientific paradigms now needs to be rephrased (Neutra, 2002):

> 'PP-based question on an environmental hazard: Are we sufficiently confident that this exposure to a potential hazard leads to doses of a magnitude that can result in adverse effects that are serious enough to initiate transparent and democratic procedures to decide on appropriate intervention?'

We must pay closer attention to variability and uncertainty when determining their possible magnitude. Unfortunately, standard statistical methods assume that an exposure is measured without imprecision, which is usually not true, although this problem is generally ignored, thus resulting in underestimation of a hazard (Table 26.4). Assessment of the imprecision and its implications is therefore crucial. While uncertainties may be erroneously thought to cause exaggeration of alleged risks, most often the opposite is true (Grandjean, 2008b). The extent of uncertainties can be expressed in terms of confidence limits (Figure 26.1), but the impact may often need to be explored by using sensitivity analyses. One or more worst-case scenarios deserve as careful scrutiny as the null hypothesis: How serious could the effects be; how large an effect can be reasonably ruled out?

The research evidence must be considered in light of both strengths and weaknesses. While a methodological failure may weaken the support for a particular association, the mere occurrence of some scientific weakness does not prove the absence of a risk. Unfortunate and erroneous rejection of warning signals has occurred in the past because of presumed confounding or other biases and uncertainties. As illustrated by the case chapters in this volume, inconsistencies in some methodological aspect have been used to derail conclusions otherwise adopted by the scientific community. Likewise, statistical acceptance of the null hypothesis has sometimes been interpreted as proof of safety. Further, effects within normal variability have been considered irrelevant, although a population-wide shift in the distribution may represent substantial harm. Focus on average effects may also be misleading, as populations at risk

may suffer much greater harm that can be diluted by the results of non-vulnerable groups.

By acknowledging the limitations to the research evidence, a different point of view needs to considered, i.e. what could possibly be known, given the type of evidence available? Studies e.g. with imprecise estimates of the causative exposure and insensitive and nonspecific outcome measures, are likely to detect only the most serious risks and therefore should be interpreted in light of the weight of such evidence. The fact that the null hypothesis could not be rejected with confidence may be irrelevant in such cases.

In general, all conclusions must be accepted as being provisional and temporary. While a study of often-cited publications in major medical journals found that many of the conclusions were subsequently found to be wrong (Ioannidis, 2008), this does not mean that environmental hazards are exaggerated. While accepting that a tentative conclusion based on preliminary evidence may later turn out to be wrong, public health responsibility may still demand that a serious threat be taken seriously, even though a final proof is not at hand. Any actions would then need to be adjusted later on, as more definite evidence emerges. At the same time, we should not ignore that the majority of environmental chemicals are poorly documented (Gilbert, 2011; NRC, 1984; US EPA, 1998), and ignoring such potential risks is likely to involve a very large number of false negative conclusions.

The bibliometric analyses that we conducted assume, as to regulatory agencies, that research results are published. But the science publication industry has undergone substantial change due to the electronic potentials of the internet for low-cost distribution. However, the costs of science publication need to be covered, just like the subscribers paid for the print journals. Thus, the majority of science articles are not accessible to the public on the internet, unless an access toll is paid (although access may be free after an embargo period of 6–12 months). Thus, while a citizen may view the science journal at a public library, the internet favours the academic world despite the stiff subscription charges. Some journals are open access, where the author pays a fee for quality control, processing and maintenance of the website, and the published article is then free for everybody to see. A growing number of journals now use this model. The European Commission recommends that articles arising from EC-funded research must be available after no more than 12 months. Other funding agencies, such as the Welcome Trust, have as a requirement that the results of sponsored research must be published with open access. Groups of universities, e.g. in the Netherlands, have launched a repository, where their research publications can be accessed by anyone. So in regard to the Participatory aspect of the PATIO paradigm, access to information is improving.

Even preliminary data can facilitate PP-based decision-making. While early findings may provide only tentative conclusions, they can later be included in potential meta-analyses or provide a starting point for follow-up studies. This potential assumes that the data from previous studies are available, and that may not be true. Trade secrets may allegedly be involved, and numerous cases have occurred with suppression of information and withholding of evidence (Kurland, 2003). Some public funding agencies now demand that a data-sharing strategy be worked out for major projects, so that other researchers can carry out additional analyses, including meta-analyses. But there is also a risk that such further analyses are not entirely benevolent (Pearce and Smith, 2011). Hostile analyses have occurred, thus making researchers wary with whom they share their raw data.

Given the discussion on coverage of environmental hazards, attention to the needs of regulatory agencies, traditions of science publication and the impact of other players, we can now attempt to answer the four questions posed in the beginning. Stakeholder involvement, innovation, openness and transparency should become new, important assets in environmental research to serve better as documentation and inspiration for PP-based decision-making.

Ways to improve scientific evidence for robust and precautionary decisions on environmental hazards:

1) The choice of research topic should involve stakeholders and consider the societal needs for information on poorly known hazards;

2) The research should be innovative and complementary with the aim of extending current knowledge, rather than repetitive for verification purposes;

3) The findings should be communicated in such a way as to facilitate judgements concerning the possible magnitude of suspected environmental hazards;

4) The research should be openly available and independent of vested interests.

As argued elsewhere in this volume, science does not provide a prescription for the right decisions on environmental hazards. The emphasis on research will be different for those whose first priority is scientific exactitude and those who focus on making policy in the context of environmental protection and public health. When a precautionary perspective mandates action to prevent foreseeable harms, the evidence does not have to meet the most rigorous demands of science. However, world views, political and other preferences, technical and economic feasibility, and alternative options are crucial for decision-making. As illustrated by the case studies in both volumes of *Late lessons from early warnings*, science does not have a good track record for supporting decisions on improving environmental health. This chapter has highlighted some opportunities for environmental research to provide more relevant results, interpretation, and conclusions for prudent and timely decisions on environmental hazards.

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27 More or less precaution?

David Gee

Despite its presence in a growing body of EU and national legislation and case law, the application of the precautionary principle has been strongly opposed by vested interests who perceive short term economic costs from its use. There is also intellectual resistance from scientists who fail to acknowledge that scientific ignorance and uncertainty, are excessively attached to conventional scientific paradigms, and who wait for very high strengths of evidence before accepting causal links between exposure to stressors and harm.

The chapter focuses on some of the key issues that are relevant to a more common understanding of the precautionary principle and to its wider application. These include different and confusing definitions of the precautionary principle and of related concepts such as prevention, risk, uncertainty, variability and ignorance; common myths about the meaning of the precautionary principle; different approaches to the handling of scientific complexity and uncertainty; and the use of different strengths of evidence for different purposes.

The context for applying the precautionary principle also involves considering the 'knowledge to ignorance' ratio for the agent in focus: the precautionary principle is particularly relevant where the ratio of knowledge to ignorance is low, as with emerging technologies.

A working definition of the precautionary principle is presented that aims to overcome some of the difficulties with other definitions, such as their use of triple negatives; a failure to address the context of use of the precautionary principle; no reference to the need for case specific strengths of evidence to justify precaution; and overly narrow interpretations of the pros and cons of action or inaction.

The chapter also points to the need for greater public engagement in the process of framing and decision-making about both upstream innovations and their downstream hazards, including the specification of the 'high level of protection' required by the EU treaty. A precautionary and participatory framework for risk analysis is proposed, along with some 'criteria for action' to complement criteria for causation.

The capacity to foresee and forestall disasters, especially when such action is opposed by powerful economic and political interests, appears to be limited, as the case studies in *Late lessons from early warnings* illustrate. The chapter argues that with more humility in the face of uncertainty, ignorance and complexity, and wider public engagement, societies could heed the lessons of past experience and use the precautionary principle, to anticipate and minimise many future hazards, whilst stimulating innovation. Such an approach would also encourage more participatory risk analysis; more realistic and transparent systems science; and more socially relevant and diverse innovations designed to meet the needs of people and ecosystems.

'The precautionary principle has, within the space of a decade, experienced a meteoric rise' Nicolas de Sadeleer (2010).

27.1 Introduction

Since the publication of Volume 1 of *Late lessons from early warnings* in 2001, the precautionary principle (PP) has received increasing attention and is now included in many laws and constitutions. It has also been the focus of much intense public and scientific debate in the European Union and its Member States, particularly in France where it was enshrined into the national constitution in 2005.

The debate on GMOs in France in the years 1997–2005 (Marris, 2005) is just one example of how debates on the PP can trigger the examination of wider issues, moving from narrow questions of risk and scientific uncertainty to broader questions about the future of agriculture, the direction of scientific research and innovation, and public engagement. Where a political process opens up rather than closes down debates, the result can be 'empowering wider social agency in technology choice' (Stirling, 2008). Debates on future innovation pathways do not necessarily eliminate conflict between stakeholders but often clarify 'what [the] conflict is really about' (de Marchi, 2003).

These realities are reflected in Chapter 19 on genetically modified (GM) crops and agro-ecology, which analyses two contrasting innovation pathways to global food security and sustainable agriculture. It finds that, in addition to some 'top down' genetic engineering, 'bottom up' approaches to agricultural innovation 'are proving capable of getting sustainable, participatory and locally adapted solutions into the hands of those that need them most'.

A catalyst for debate and for timely action

The PP seems to have two roles. First, as a trigger for broad debates on what kind of future we want in a water-, energy- and resource-constrained world and what innovation pathways could lead towards such futures (WBCSD, 2011; WEF, 2012; WBGU, 2012; OECD, 2012; UNEP, 2011; EEA, 2010). And second as a legal and moral justification for more timely actions on early warnings about potential hazards.

The case studies in this volume furnish evidence that contributes to a wider understanding of both roles. While there is much more emphasis on its role in justifying actions on early warnings, the chapters in Parts B and C, on emerging lessons and issues, begin to illustrate the PP's role in facilitating debates around innovation pathways and technological choices. In addition, Chapter 26 on science and Chapter 24 on justice for early warning scientists and late victims, illustrate the PP's role in stimulating discussion about reforms within environmental science, the law and scientific organisations.

The case studies addressing substances or chemicals that are now widely known to be hazardous focus on the combination of early warnings and (usually) late actions. The studies address asbestos, benzene, BSE (mad cow disease), diethylstilboestrol (DES) tributyl tin (TBT) and polychlorinated biphenyls (PCBs) in Volume 1 and DDT, dibromochloropropane (DBCP), vinyl chloride monomer (VCM), lead in petrol, mercury, beryllium, and booster biocides in Volume 2. They primarily illustrate how more precautionary action could be applied to chemical risks emerging now, such as those from Bisphenol A (BPA) and other chemicals, nicotinoid pesticides, and endocrine disrupting substances which are present in some consumer products, including pharmaceuticals, such as ethinyl oestrodiol in the pregnancy pill, discussed in Chapter 13.

The histories of well known technologies, such as X-rays, fishing techniques, fossil fuel power sources and early nuclear plants, can also provide lessons for prudent action on the potential hazards of such emerging technologies as nanotechnology, genetically modified (GM) food, radio-frequency from mobile phones, and the new generation of nuclear plants. The chapters on alien species, floods, and ecosystems, as well as the late actions on climate change, also provide insights into how the management of ecosystems could develop.

Taken together, the examples of late action on known hazards illustrate the high cost of inaction. Globally that cost has been paid in millions of lives and cases of disease and dysfunction, much damage to the environment and species, and very large economic penalties, some of which are described in Chapter 23 on the costs of inaction.

The case studies are not all negative, however. Five of the 34 case studies describe precautionary actions: the European ban on hormones in cattle feed; the regulations and some member state actions on GMOs in Europe; the ban on TBT in France in 1984; the ban on the pesticide Gaucho in France in 1999; and, arguably, the belated but still precautionary European ban on some antibiotics when used as growth promoters in farm animals. These actions,

along with the histories of the 88 claimed false positives analysed in this volume, also illustrate the value of the PP in minimising harm and societal costs.

There are other examples where action was taken quite quickly but only after serious and compelling human evidence became available, sometimes from an observant clinician (in the cases of DES and VCM) or from the victims themselves (DBCP). In these three examples, just four to seven cases of very rare cancers or sperm reduction (DBCP) were sufficient to justify prompt regulatory action.

Barriers to wider use of the PP

One obvious question that emerges from the case studies is 'how can the PP be more widely used, both as a justification for early policy action and as a broad trigger for wider, more upstream debates about innovation pathways?'

Looking across the case studies, there appears to be a number of common barriers to using the PP to justify more timely responses to early warnings. Taken together, these barriers explain much about the decades-long delay between warnings and action. These barriers include:

1 opposition from powerful corporations — supported by some scientists, policymakers and politicians — who fear high economic, intellectual and political costs to themselves from early and sometimes even late actions to reduce risks;

2 key misunderstandings about the PP's definition and meaning;

3 difficulties understanding and dealing with complex biological and ecological systems that are characterised by multi-causality, scientific uncertainty, ignorance and scientific 'surprises';

4 scientific and political tensions between the high strength of evidence needed for scientific causality and the lower strength of evidence needed for timely public policy;

5 inadequate analysis of the costs and benefits of proposed actions and inactions; and unrealistic market prices for hazardous agents that fail to reflect the costs to society of their production, consumption and wastes;

6 political and financial short-termism;

7 a failure in most cases to engage with civil society and the public to help counter the power of the corporate and other stakeholders that may wish to dismiss early warnings.

Barriers 1, 6 and 7 mainly concern political and economic power, whereas barriers 2–5 primarily relate to the more technical process of applying knowledge to policymaking.

There is, of course, no clear-cut separation between these two aspects of regulatory activities or between the roles that scientists play as 'experts' in the process of evaluating the regulatory science used in the policy process. As Jasanoff (1990 and 2011) has pointed out:

> 'Policy relevant science comes into being in a territory of its own that is subject to neither purely scientific nor wholly political rules of the game.'
>
> 'It is not so much scientists (but) experts, who govern the production and evaluation of policy relevant science.'

To help encourage broad and wise use of the PP, this chapter will briefly examine the barriers to its use, focusing initially on the first barrier, relating to corporate power. This is followed by consideration of the more technical barriers 2–5, using the EEA definition of the PP as the framework for the analysis.

Thereafter, Section 27.7 of this chapter briefly addresses political and financial short-termism, before considering wider public engagement as part of the process of creating and managing innovations and their attendant hazards.

27.2 The power of corporations to oppose action

Chapter 11 on DDT notes Rachel Carson's observation that corporations have often focused on 'making a dollar at whatever the costs'. Although this overstates the situation, the case studies provide ample evidence of how corporations responded to early warnings about possible hazards from their products by organising 'product defence' campaigns. Chapter 7 on environmental tobacco smoke describes seven key strategies that the tobacco companies used to defend their products.

The tobacco industry was certainly not alone in using similar tactics, as case studies on lead, VCM, beryllium and climate change illustrate. Indeed it

seems likely that other industries with hazardous products to defend today would employ similar strategies, including trying to control, directly or indirectly, the relevant scientific research.

This was a key objective of the leaded petrol industry, which maintained a virtual monopoly on leaded petrol research from immediately after the 'one day trial' of leaded petrol in 1925, when early warnings emerged from some senior public health scientists, until the 1970s. Without access to independent research the regulatory authorities were vulnerable to corporate influence on the scientific evidence made available to them. This was an issue that Clair Patterson, lead expert and eminent palaeontologist, noted with some vehemence in evidence to the US Congress:

> 'It is not just a mistake for public health agencies to cooperate and collaborate with industries in investigating and deciding whether public health is endangered; it is a direct abrogation and violation of the duties and responsibilities of those public health organisations.' ([1])

Today scientific research agendas are often determined by more independent academics and public sector organisations. However, the way in which technological and hazard problems are framed can result in research that focuses much more on developing products than on the need to find out whether those products are harmful.

For example, over the past two decades public research funding by the EU on nanotechnology, biotechnology and information technology was heavily biased towards product development, with only about 3 % of the EUR 28.5 billion budget spent on investigating their potential hazards. There was a similar imbalance on research into genetic modification in the US, where over the period 1992–2002 the US Department of Agriculture spent USD 1.8 billion on biotechnology research, of which just 1 % went to risk-related research (Mellon, 2003, cited in Chapter 19).

In some areas where research is dominated by issues of intellectual copyright, such as GMOs, there have been problems with access to the organisms in question. There has recently been some opening up of research on GM seeds, however, following a letter of complaint from 26 academics in the US, whose research was inhibited by the lack of access to GM seeds owned by the corporations (Pollack, 2009).

The funding of different innovation pathways is also an issue. For example, the European Commission's Standing Committee on Agricultural Research (SCAR, 2012) has called for increased support for research on the economic and social dimensions of new technologies and farming practices, calling for the highest priority be given to funding low-input high-output systems, which 'integrate historical knowledge and agro-ecological principles that use nature's capacity' (cited in Chapter 19).

There is also a strong bias in the environmental sciences towards research on well known problems rather than on emerging issues (Chapter 26).

Corporations have also realised that the language used in debates about the hazards associated with their products is also important. An example of the use of loaded language was the claim by the leaded petrol industry that 'normal' levels of lead in blood were 'natural' and therefore safe. 'Sound science' was another common term taken over by public relations companies for the tobacco industry to mean science that supports the industry position (Baba et al., 2005). The term has since been used by other industries engaged in product defence who characterise science that does not support the industry position as 'unsound'.

The strategy of 'manufacturing doubt' out of uncertainties in the science was also a key part of product defence in several of the case studies, such as those on tobacco, lead, asbestos, beryllium, benzene and climate change (Michaels, 2008; Oreskes and Conway, 2010).

The long history of corporate misconduct begs the question why corporations adopt strategies of 'product defence' and how such actions could be minimised for the public good. Chapter 6 on beryllium concludes with some reflections on this question by Tee Guidotti, who suggests that corporations quickly lock themselves into product defence because of 'fear, denial and risk of loss'. His conclusion is that if corporations are expected to reverse course as the evidence of harm from their products increases, then 'there must be room for them to turn around'. It seems likely that his suggestions that this may involve 'forgiving past liabilities and reducing punitive damages' will be controversial, whereas his call for more active shareholder engagement on the question of responsible corporate behaviour is likely to be welcomed.

([1]) Senator Muskie Hearings on Air Pollution, 1966, cited in Chapter 3 on leaded petrol.

Chapter 25 addresses the question of why businesses do not react to early warnings with precaution in more depth, looking more closely at the issue of corporate behaviour. It notes that 'blaming business, in particular with hindsight ... may not always be constructive' as it often misses the 'complex or even contradictory set of motives and drivers that businesses face'. The authors, Le Menestrel and Rode, find that corporate decisions are influenced by a mixture of economic, epistemological, regulatory, cultural and psychological factors. Economic motives dominate: 'in virtually all reviewed cases from both volumes of *Late lessons from early warnings*, it was perceived to be profitable for industries to continue using potentially harmful products or operations'.

Corporate short-term interests have dominated over longer-term public interests mainly because the costs of damage to people and environments were, and still are, largely externalised to society as a whole. The external costs of climate change are described by former chief economist to the UK Treasury, Nicholas Stern, as 'the biggest market failure ever' (cited in Chapter 14). This means that corporations bear few of the costs of harm from their activities, except in cases where victims win compensation or ecosystems are restored, where possible. Even here, however, the sums may be largely covered by insurance.

As noted in Chapter 23 on the costs of inaction, external costs need to be internalised into the accounts of corporations via regulations, taxes, charges and permits. Anticipatory assurance bonds would also be helpful, as illustrated by Robert Constanza using the example of *Deepwater Horizon* (Chapter 24).

To deal with some of the non-economic factors influencing corporate responses to early warnings, Le Menestrel and Rode suggest distinguishing between the economic and the 'political' roles of businesses that are given ample opportunity to influence the regulatory process (Scherer and Palazzo, 2011; UCS, 2012). They also call for new institutional arrangements involving rigorous and explicit exposition of the dilemmas and trade-offs involved in reconciling value conflicts, and the organisational pressure to deny the reality of the early warnings. These 'institutional approaches would more realistically complement initiatives based on the idealised principle that being socially responsible is economically profitable'.

Finally, the historical case studies also reveal one or two examples of responsible corporate behaviour, albeit by companies selling hazardous products rather than by their manufacturers. For example, some companies stopped using asbestos in the 1970,; and Johnson & Johnson stopped using CFCs in their aerosols in 1977, eight years before the ozone hole was discovered.

More recent case studies such as on BPA illustrate that some user companies abandoned BPA for some products some years before the European Commission took action on its use in baby toys. The marine and forest stewardship councils encourage responsible environmental actions; and some nanotechnology companies, such as BASF, are working with civil society organisations to agree codes of conduct on the responsible use of nanotechnology in both research and products (EU, 2010). Hewlett Packard has likewise been very active in getting lead and other hazardous compounds out of its electronic goods and Astra Zeneca is working on reducing the envionmental impact of pharmaceutials, by, inter alia, researching the potential for 'green' medicines. There is even some action on the issue of more environmentally realistic accounting, with Puma leading the way.

Meanwhile, as part of the broader debate about innovation pathways from current unsustainable economic activities in an increasingly resource-, energy- and water-constrained world, the World Business Council for Sustainable Development has produced its business vision for the way forward (WBCSD, 2010).

27.3 The precautionary principle — key elements and misunderstandings

Public health decisions about moving from 'evidence to action' are a balancing act between what needs to be known and what ought to be done (Weed, 2004). It took more than 40 years of much scientific endeavour and public debate between the 1940s and the 1980s, before what was known about smoking and lung cancer was applied to protect public health, following sustained opposition from economic and political interests. In this case, the opportunity for **precautionary** action on a **likely hazard** in the 1950s and 1960s was lost. By the 1990s only **prevention of known harm** was possible.

Numerous international treaties and other instruments refer to the PP, as summarised in Box 27.1. Many share common elements but there is also variance in the definitions with respect to: the standard of scientific evidence required to invoke the PP; the extent of the obligation imposed on public bodies to apply the principle; the objectives

Box 27.1 International treaties relevant to the case studies illustrating key elements of the precautionary principle

Rio Declaration on Environment and Development, 1992: 'Where there are threats of serous or irreversible harm, lack of full scientific certainty shall not be used as a reason for postponing costs effective measures to prevent environmental degradation.'

European Union's Treaty on the Functioning of the EU, Article 191(2): 'Union policy on the environment shall aim at a high level of protection taking into account the diversity of situations in the various regions of the Union, it shall be based on the precautionary principle and on the principles that preventive action should be taken, that environmental damage should as a priority be rectified at source, and that the polluter should pay.'

Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), Preamble: 'the need to do more to protect public health and the environment in accordance with the precautionary principle'. In addition, Article 69 provides that: 'To ensure a sufficiently high level of protection for human health, including having regard to relevant human population groups and possibly to certain vulnerable sub-populations, and the environment, substances of very high concern should, in accordance with the precautionary principle, be subject to careful attention.'

UN Framework Convention on Climate Change, 1992: 'The parties should take precautionary measures to anticipate, prevent or minimize the causes of climate change and mitigate its adverse effects. Where there are threats of serious or irreversible damage, lack of full scientific certainty should not be used as a reason for postponing such measures, taking into account that policies and measures to deal with climate change should be cost-effective so as to ensure global benefits at the lowest possible cost. To achieve this, such policies and measures should take into account different socio-economic contexts, be comprehensive, cover all relevant sources, sinks and reservoirs of greenhouse gases and adaptation, and comprise all economic sectors.

EU Directive 2001/18/EC on deliberate release of GMOs, Article 4 (1): 'Member States shall, in accordance with the precautionary principle, ensure that all appropriate measures are taken to avoid adverse effects on human health and the environment which might arise from the deliberate release or the placing on the market of GMOs'.

Cartegena Protocol on Biosafety, 2000, Article 11(10): 'lack of scientific certainty due to insufficient relevant scientific information and knowledge regarding the extent of the potential adverse effects of a living modified organism on the conservation and sustainable use of biological diversity in the Party of import, taking also into account risks to human health, shall not prevent that Party from taking a decision, as appropriate, with regard to the import of that living modified organism intended for direct use as food or feed, or for processing, in order to avoid or minimize such potential adverse effects.'

Regulation (EC) No 178/2002 establishing the European Food Safety Authority and procedures in matters of food safety, Article 7: Precautionary principle: 'In specific circumstances where, following an assessment of available information, the possibility of harmful effects on health is identified but scientific uncertainty persists, provisional risk management measures necessary to ensure the high level of health protection chosen in the Community may be adopted, pending further scientific information for a more comprehensive risk assessment.'

EU Regulation 1107/2009 on plant protection products, Article 1(4): 'The provisions of this Regulation are underpinned by the precautionary principle in order to ensure that active substances or products placed on the market do not adversely affect human or animal health or the environment. In particular, Member States shall not be prevented from applying the precautionary principle where there is scientific uncertainty as to the risks with regard to human or animal health or the environment posed by the plant protection products to be authorised in their territory.'

London International Maritime Organisation Convention on the control of Harmful Anti-fouling Systems on Sips, 2000, Articles 6(3) and (4): 'Where the Commission is of the view that there is a threat of serious irreversible damage, lack of full scientific certainty shall not be used as a reason to prevent a decision to proceed with the evaluation of the proposal … (which involves considering) whether the proposal has demonstrated a potential for unreasonable risk of adverse effects on non-target organisms or human health.'

Box 27.1 International treaties relevant to the case studies illustrating key elements of the precautionary principle (cont.)

European Court of Justice in the BSE case (Case C-157/96, National Farmers Union and others, 1998, ECR 1-2211): 'Where there is uncertainty as to the existence or extent of risks to human health, the institutions may take protective measures without having to wait until the reality and seriousness of those risks become fully apparent.'

Stockholm Convention on Persistent Organic Pollutants, 2001: 'Acknowledging that precaution underlies the concerns of all the Parties and is embedded within this Convention …'

WTO Agreement on Sanitary and Phytosanitary Measures (SPS Agreement), Article 5(7): 'In cases where relevant scientific evidence is insufficient, a Member may provisionally adopt sanitary or phytosanitary measures on the basis of available pertinent information, including that from the relevant international organizations as well as from sanitary or phytosanitary measures applied by other Members.'

European Commission communication on the precautionary principle, 2 February 2000: 'The precautionary principle applies where scientific evidence is insufficient, inconclusive or uncertain and preliminary scientific evaluation indicates that there are reasonable grounds for concern that the potentially dangerous effects on the environment, human, animal or plant health may be inconsistent with the high level of protection chosen by the EU.'

of applying the PP; and the inclusion of elements such as provisions on costs and benefits or public participation.

The EEA's working definition of the PP

It is not surprising that many debates about the PP are confused and lengthy, given the variations apparent in the instruments and statements listed in Box 27.1. During the last decade of discussions arising out of Volume 1 of *Late lessons from early warnings*, the EEA has produced and refined a working definition of the PP that has proved useful in helping to achieve a more common understanding of the PP:

> 'The precautionary principle provides justification for public policy and other actions in situations of **scientific complexity, uncertainty and ignorance**, where there may be a need to act in order to avoid, or reduce, potentially serious or irreversible threats to health and/or the environment, using an **appropriate strength of scientific evidence**, and taking into account **the pros and cons of action and inaction** and their distribution.'

This definition is explicit in specifying situations of uncertainty, ignorance and risk, as contexts for considering the use of the PP. It is expressed in the affirmative rather than the triple negatives found in, for example, the Rio Declaration. It explicitly acknowledges that the strength of scientific evidence needed to justify public policy actions is determined on a case-specific basis, and only after the plausible pros and cons, including their distribution across groups, regions, and generations, have been assessed.

The three key sets of issues highlighted in the EEA definition above are explored in Sections 27.4–27.6 below.

27.4 Complex biological and ecological systems

The *Late lessons from early warnings* case studies cover a vast range of complex systems so it is useful to focus on reproductive and developmental hazards as an illustration of such systems.

Many of the case studies have demonstrated developmental and reproductive harm from exposures to agents such as mercury at Minamata, TBT, DES, PCBs, tobacco, lead, VCM, ethinyl oestradiol from the contraceptive pill, BPA and radiation from X-rays.

These cases have shown that serious damage to health can be initiated in the early life stages of humans and other species but may not become apparent until much later in adult life, and even

Box 27.2 Reproductive and developmental harm

Developmental periods are highly sensitive to environmental factors, such as nutrients, environmental chemicals, drugs, infections and other stressors. 'Many of the major diseases — and dysfunctions — that have increased substantially in prevalence over the last 40 years seem to be related in part to developmental factors associated with either nutritional imbalance or exposures to environmental chemicals …The conditions that are affected by nutritional or environmental chemical exposures during development include the pathophysiologies, diseases, and syndromes that constitute major public health problems across the globe: obesity, diabetes, hypertension, cardiovascular disease, asthma and allergy, immune and autoimmune diseases, neurodevelopmental and neurodegenerative diseases, precocious puberty, infertility, some cancer types, osteoporosis, depression, schizophrenia and sarcopenia' (Baruoki et al., 2012).

The mechanisms of biological action in each of these earlier experiences are not yet well established, despite decades of research. However, it seems clear that it is more the timing of the dose, rather than the dose itself, which, inter alia, distinguishes harmful from harmless exposures to reproductive and developmental toxicants (Gee, 2006, 2008; Grandjean et al., 2008; Kortenkamp et al., 2011; Chemtrust, 2008; EEA, 2012).

Such harm is often irreversible and sometimes multigenerational, causing life-time personal and societal costs that cannot be offset by any benefits to the individual from intrauterine exposures. Thus, biology, economics, equity and morals all justify early actions to prevent developmental and reproductive harm. However, establishing sufficient evidence for action on such complex hazards is much more difficult than it was for tobacco and lung cancer, where there was clear evidence that just one agent, albeit a complex mixture like tobacco smoke, caused a specific cancer that was relatively rare before smoking became widespread.

in subsequent generations, as in the DES case (see EEA, 2001). Such examples illustrate the realities of complex biological and ecological systems that are characterised by multi-causality, scientific uncertainty, ignorance and scientific 'surprises'.

From monocausality to multicausality

The biological processes that lead to chronic diseases such as breast or prostate cancer, or to reproductive or developmental harm, appear to involve some or all of at least eight main events in the disease process: preparation within the host; initiation; promotion; retardation; progression; disease onset; the strengthening or weakening of severity; and prevalence of the disease. These steps in the causal chain of the disease process can be affected by many interdependent, co-causal risk factors, where the timing of exposures is usually critical. Some factors, including chance, may operate at one or several stages of the same disease process.

It is therefore a challenging task to identify the 'causal' and often co-causal factors needed to prevent or reduce the population burden of such ill health, given that exposures occur at different developmental stages; are often interactive, mixed, and usually low level; and affect people with specific environmental histories and susceptibilities.

Within the history of the public health sciences there has long been a tension between the monocausal, reductionist approach to investigating disease causation and multicausal, more holistic approaches. A similar tension exists within ecology between 'diversity' and 'variable ' approaches to complex ecosystems — see Chapter 17 on ecosystems. Some scientists frame their studies around the view that it is the germ, or the gene, the oncogene, or a single risk factor, which is mainly 'responsible' for disease. Others look to the overall environmental history of the host for the many factors and influences that, if taken together, may explain disease causation (Sing et al., 2004).

Concentrating research on particular parts of the puzzle, rather than on the causal puzzle itself, may inhibit the clarification of causality. For example, some 4 000 chemical substances have been identified in tobacco smoke, of which more than 100 are classified as toxic. However, the precise disease process that leads to cancer or heart disease in some smokers but not in others is still largely unknown after more than 40 years of research.

Despite ignorance about the disease process associated with mixtures of chemicals, it has still been possible to prevent some harm by reducing exposures to the whole mixture, such as smoke from burning tobacco and fossil fuels, from complex welding and rubber fumes, and from fine particles of air pollution.

The practical difficulties of studying and understanding complex multicausal biological processes have meant that the attraction of a monocausal approach remains strong. Reductionism and the metaphor of the body as a machine are powerful paradigms that continue to support the idea of linear relationships between specific causes, long after knowledge about irreducible uncertainties, emergent properties and non-linear dynamics became available (Di Guiliio and Benson, 2002).

From confounders to co-causal factors?

The tools available to unravel multicausal, complex and dynamic disease processes are not well developed or used (Cory-Slechta, 2005). As a consequence, most epidemiologists try to identify specific risk factors while eliminating possible confounding factors via various statistical techniques. Such 'statistical surgery' or 'context stripping' may remove many confounders from the analysis that are really co-causal factors. If the focus is on just one toxicant, then other 'environmental properties tend to be regarded as marginal and designated as covariates or confounders: treating such environmental conditions as confounders is equivalent to defining genetic differences as confounders. 'A true evaluation of toxic potential and its neurobehavioral consequences is inseparable from the ecologic setting in which they act and which creates unique, enduring individual vulnerabilities that warrant the same status as genetic predispositions and are imprinted as forcefully' (Weiss and Bellinger, 2006).

Even with a well-studied phenomenon, such as lead poisoning, there is a growing realisation that lead exposure, environmental deprivation and enrichment, and neurotoxicity are complex and 'perhaps bidirectional' (Bellinger, 2007). For example, an enriched and intellectually stimulating home environment seems to reduce the harmful effects of a toxicant such as lead, while lead exposure can reduce the benefits of such enriched environments. Similarly, a deprived socio-economic environment can increase the harmful effects of lead while reducing the beneficial effects of a reduction in lead exposure. More fundamentally, scientists have also noted that bidirectional relationships, such as cell signalling and crosstalk, imply that causality may be circular (Soto and Sonnenschein, 2006).

Similar scientific challenges emerge from the field of endocrine disruption in wildlife, as well as within ecotoxicology more generally (Newman, 2001). These arise from having to investigate and draw inference across biological scales, from population level to lower levels of biological organisation and back again, in order to show, for example, whether harm to individual fish can cause fish population decline (Chapter 13 and Kidd et al., 2007).

It would seem then that the 'key to understanding these causal processes is clearly the ability to elaborate and understand complexity: the interacting systems involved will always overwhelm predictions of independent effects of any single factor, reducing them to very limited and uncertain information' (Bellinger et al., 1985).

It also follows that in complex systems very small changes in key variables can have profound effects. 'Small' can be very significant in finely balanced non-linear systems, where, as Heraclitus observed centuries ago, there is a 'harmony of opposites'. Removing even the 'smallest' link in an interdependent causal chain can sometimes break at least pathway to disease.

Such complex and multi-causal factors are also evident in ecological systems and species as illustrated in Chapter 14 on climate change, Chapter 16 on bees, Chapter 17 on ecosystems and Chapter 20 on invasive alien species.

How then can we identify possible or probable causality from observed associations in such complex biological and ecological systems, so that some co-causal priorities for public health and environmental protection can be agreed?

Multicausality and the Bradford Hill 'criteria' for causality

'With preventive medicine in mind the decisive question is whether the frequency of the undesirable event B will be influenced by a change in the environmental feature A' (Bradford Hill, 1965). Building on the tobacco controversy, Bradford Hill identified nine characteristics of scientific evidence that, if taken together, could help scientists to move with some confidence from observing associations to asserting causation. His

Box 27.3 The Bradford Hill 'criteria' for identifying causation

1. Strength of association
2. Consistency
3. Specificity
4. Temporal relationship (temporality)
5. Biological gradient (dose-response relationship)
6. Plausibility (biological plausibility)
7. Coherence
8. Experiment (reversibility)
9. Analogy

Source: Bradford Hill, 1965.

subsequently misnamed 'criteria' are still widely used today in both the health and environmental fields (WHO, 2002; Collier, 2003; Maxim and van der Sluijs, 2010).

Bradford Hill's explicit approach to deriving causation from association was essentially based on monocausality, that is, on finding the specific cause of a specific disease.

He was aware that several factors would be implicated in disease but that removing one of them may reduce its frequency, or incidence, without necessarily eliminating the disease entirely. He also acknowledged the other, simpler type of multicausality, which is where one disease can have several different independent causes, noting that: 'diseases may have more than one cause. It has always been possible to acquire a cancer of the scrotum without sweeping chimneys or taking to mule spinning in Lancashire' (Bradford Hill, 1965).

The Bradford Hill 'criteria' need to be reappraised in the light of multicausality and complexity. This is particularly important because the absence of some or all 'criteria' is often used in current controversies to deny the possibility of causality. More generally, the criteria seem less robust now as reasons for dismissing associations than they did in the world of the 1960s, when issues were perceived in largely monocausal terms.

For example, the criterion of **consistency** between the results of different studies into the same phenomena, when present, clearly adds much confidence to assertions of causality. However, multi-causality can make consistency very difficult to achieve: 'if all studies of lead showed the same relationship between variables, one would be startled, perhaps justifiably suspicious' (Needleman, 1995). The sources of variability arise both from the study and the investigator, such as the framing and initial assumptions; the models, methods and statistical analyses used; the choice of population group; the presence of susceptible sub-groups; and the data selected. Other sources of variability and bias have been noted (Bailar, 2007) and the limitations of conventional epidemiology have been explored from a precautionary perspective (Grandjean, 2008). In addition, there are the sources of variability in populations arising from the 'sociomics' of environments and the epigenetics of individuals.

It is hardly surprising therefore that, after decades of research, most lead studies can still only 'explain' 30–40 % of the variance in most lead-linked biological end-points, and sometimes far less (Bellinger, 2007). As inconsistent results are to be expected from complex biological and ecological systems the absence of consistency between studies does not imply an absence of causality.

Bradford Hill included a **linear dose-response relationship** between a toxicant and its effects as another important criterion. However, where the timing of exposure is more important than the dose itself, and where non-linear, 'low-dose' effects are present, the absence of a linear dose-response relationship does not provide robust evidence against causality.

The condition of **temporality** anticipates that a cause must precede the effect. This is obviously so, except where there are multiple causes arising at different times, and with varying rates of increase or decrease, which may therefore reverse, stabilise, or accelerate the overall disease trend, depending on their relative strengths. If this feature of reality is not taken into account then some widely used interpretations of temporality in relation to overall disease trends can lead to shaky conclusions.

For example, in a review of the evidence on falling sperm counts and endocrine-disrupting chemicals, it was concluded that, as overall sperm counts began to fall in some countries in advance of the rise of chlorine-based chemistry, such chemical exposures could not be a cause of change in the overall trend (WHO, 2002). In the context of multicausality, where the combined effects of several causes together determine the overall time trend of a disease, such a conclusion is not soundly based.

Such time-dependent factors within multicausal systems also mean that obtaining evidence based on the **experiment** criterion — i.e. demonstrating the impact of removing one cause of a disease affected by many causes — can be very difficult, as with changes in IQ or sperm counts.

Less weight should also be placed on **specificity** as a criterion, given the widespread prevalence of 'many to many' cause and effect relationships, and the capacity of many substances, such as tobacco PCBs, asbestos, lead and mercury, to cause many types of harm.

The **strength of association**, which Bradford Hill put first in his list of features, is clearly still very relevant but with caveats that arise from multicausality. Even a 'low' relative risk of say, 1.5, if replicated in several studies, can be very robust for a multicausal disease as is the case with smoking and heart disease. Such a 'low' relative risk will also represent much harm if the background rate of the disease is large.

The criteria of **biological plausibility** and **coherence** are dependent on the established knowledge of the day and therefore are not robust criteria for dismissing early warnings, where relatively novel science, at the frontiers of scientific knowledge, is often used.

Whereas multicausality seems to weaken most of the criteria, **analogy** becomes more necessary given the difficulties of establishing clear causality from complex systems. If precautionary actions are needed then analogies from past experiences may be particularly valuable. Box 27.4 provides some 'criteria for action' to complement the criteria for causation, based on experiences of past ecological and biological hazards, including by analogy, which may provide quite robust evidence of emerging potential hazards.

In judging strength of association, Bradford Hill also warned against the overuse and misuse of statistical significance testing: 'we waste a deal of time, we grasp the shadow and lose the substance, we weaken our capacity to interpret data and to take reasonable decisions whatever the value of P. And far too often we deduce "no difference" from "no significance".'

Although similar cautions have been repeated regularly since then (Cohen, 1994; Poole, 2000; Hooper, Stang and Rothman, 2011), the misinterpretation of statistical significance and the relative neglect of confidence intervals continue (see also Chapter 26 on science for precautionary decision-making).

In the circumstances of multicausality and complexity the Bradford Hill criteria are characterised by a strong element of asymmetry. The presence of the criteria can be robust evidence for a causal association, whereas the absence of the criteria is not robust evidence that there is no causal association. Bradford Hill drew attention to this asymmetry with several of his criteria but some of his followers have forgotten

Box 27.4 Criteria for precautionary action: some features of evidence about the hazardous potential of agents that may justify precautionary action

1. Intrinsic toxicity/ecotoxicity data
2. Novelty (i.e. where there is a low 'knowledge/ignorance ratio')
3. Ecological or biological persistence
4. Potential for bio-accumulation
5. Large spatial range in the environment e.g. potential for global dispersion.
6. Seriousness of potential hazards
7. Irreversibility of potential hazards
8. Analogous evidence from known hazards
9. Inequitable distribution of hazardous impacts on particular regions, people and generations
10. Availability of feasible alternatives
11. Potential for stimulating innovation
12. Potential and time scales for future learning

this in their use of the criteria to dismiss possible hazards (Ashby, 1997; WHO 2002). When addressing biological and ecological complexity, such asymmetry in the application of the Bradford Hill criteria is even more pronounced than it was when he introduced them.

Another barrier to early action arises from the systemic biases towards not finding a causal link, specifically biases within the epidemiology and toxicology methods that tend to generate false negatives (i.e. assertions that something is safe when it turns out not to be). These methodological biases are illustrated by Grandjean in Chapter 26.

Both policymakers and scientists need to acknowledge and take account of these main directions of methodological error when they evaluate the methods and results of research. Many scientists do (Grandjean, 2004 and 2005) but awareness of these methodological biases among many stakeholders appears to be low.

Finally, the issue of funding bias, whereby research results can be closely associated with the source of funding, has been observed in the tobacco literature (Barnes, 1998) and then identified in other fields such as pharmaceuticals (Goldacre, 2012; Lexchin, 2003) the food and beverage industry (Levine, 2003) BPA, (Vom Saal, 2005), mobile phones (Huss et al., 2007), food, (Levine, 2003), biomedics (Bekelman, 2003), GMOs (Diels, 2011). The explanation for this bias is not clear (Krimsky, 2006, 2010). Funding bias is also to be found in the transport and constructions fields, where underestimation of costs and construction times by the developers is routine, and in cost-benefit analysis where the direction of bias is routinely in the direction of those who fund the study.

Other concepts related to the PP and complexity are likewise often understood differently by different actors. An important example is the distinction between uncertainty and ignorance, which constitute quite different states of knowledge. For example, both the asbestos-induced mesothelioma cancer and the hole in the ozone layer caused by CFCs were complete scientific 'surprises', arising from a state of ignorance. They were not gaps or uncertainties in existing states of knowledge.

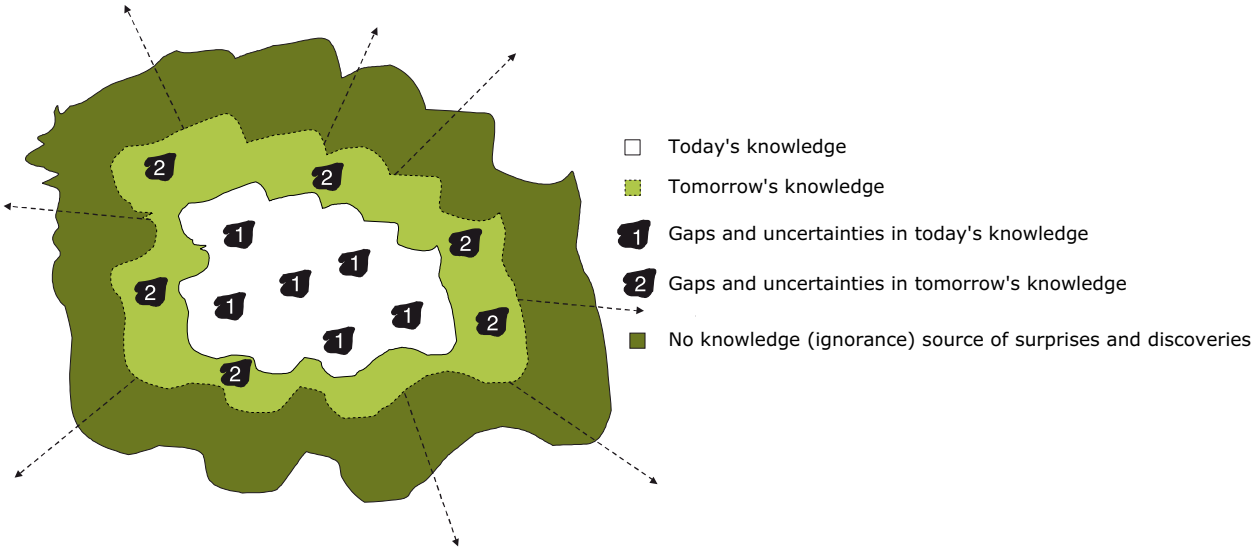
To be uncertain one has to be uncertain about something and any 'gaps' in knowledge relate to current knowledge. Both 'uncertainty' and 'gaps' relate to a stock of existing knowledge. 'Ignorance', on the other hand (or more elegantly, 'nescience', i.e. 'no knowledge') relates to 'unknown unknowns'.

More research can close some gaps in knowledge and reduce some uncertainties but such research will also uncover new sources of uncertainty and gaps in knowledge, as well as raising awareness about new areas of ignorance. Learning to live with and manage irreducible uncertainties is as necessary as trying to reduce them.

The knowledge-to-ignorance ratio

Acknowledging ignorance raises questions about how much knowledge we have in a given field

Figure 27.1 Expanding knowledge, continuing uncertainties



compared to ignorance. This issue was noted in the World Conservation Strategy (IUCN, 1980), which advised people to :

> 'keep in mind that, in spite of present knowledge, **what we know about the biosphere, ecosystems and their interrelationships is less than what we do not know.** Consequently, it is often difficult to accurately predict the effects of human actions. Gaps in knowledge should be filled where possible.. but in the meantime risks should be reduced' (emphasis added).

This may be dismissed as a trivial observation but it does draw attention to the need for scientific humility even when considering the large stocks of current knowledge on many hazards. Scientists in many of the case studies failed to show scientific humility, instead being guilty of what has been termed 'the sin of hubris' in the context of marine ecosytems and fisheries science (MacGarvin, 1994).

While the knowledge-to-ignorance ratio cannot be quantified, it is possible to get an informed qualitative appreciation of the balance in the various fields covered by the case studies. For example, there is clearly a difference between the current stock of accumulated knowledge, on, say, asbestos, ionising radiations and tobacco, compared to our stock of knowledge on nanotechnology, GM food, or on non-ionising radiations when used in recent consumer products such as mobile phones. And while there will still be a lot of new knowledge that could be gained about even a well known substance like asbestos ([2]) the practical need to search for more knowledge about asbestos is very minimal, as we know more than enough to avoid its dangers successfully.

In contrast, there is a vast ocean of scientific ignorance surrounding nanotechnologies, biotechnologies and non-ionising radiation technologies and chemicals used in consumer and other products. This remains to be explored. What is known in these relatively immature fields can perhaps be likened to the few 'pebbles' of knowledge that Sir Isaac Newton gathered from his scientific work and that he contrasted to that 'great ocean of undiscovered truth', which remained to be explored and which encouraged scientific humility ([3]).

Where the 'knowledge-to-ignorance ratio (KIR)' is high (implying much knowledge and little practically necessary ignorance), as with, for example, lead, asbestos and mercury, there is little need for either more research or for precautionary (as distinct from merely preventative) measures. Where the KIR is low, however, there is a need for both precautionary measures following credible early warnings and for novel research, rather than the 'scientific inertia' of excessive research on well known substances described in the Chapter 26. As de Sadeleer (2010) has observed, 'it may be impossible to carry out a full risk assessment because such investigations operate at the frontiers of scientific knowledge, ... (where scientists) must even point to the limits of their knowledge or, where appropriate, to their ignorance.'

The limitations of scientific knowledge imply moral courage in taking precautionary action in time to avert harm. As Lewontin has observed: 'Saying that our lives are the consequence of a complex and variable interaction between internal and external causes does not concentrate the mind nearly so well as a simplistic claim; nor does it promise anything in the way of relief for individual and social miseries. It takes a certain moral courage to accept the message of scientific ignorance and all that it implies' (Orrell, 2007).

Table 27.1 attempts to clarify concepts such as ignorance and uncertainty that often arise in debates on the PP.

27.5 Conflicts between the high strength of evidence needed for scientific causality and the lower strength of evidence needed for timely public policy

All responsible applications of the precautionary principle require some plausible evidence of an association between exposures and potentially harmful impacts. For example, the European Commission's communication on the precautionary principle (EC, 2000) specifies that 'reasonable grounds for concern' are needed to justify action. However, it does not explain that these grounds will vary with the specifics of each case, nor does

([2]) It is only recently that new Dutch analyses of the epidemiological data on asbestos has shown that the difference in harmful potency between blue and white asbestos, claimed by some scientists, practically disappears when the exposure estimates are scrutinised more carefully (Lenters et al., 2012).

([3]) 'I do not know what I may appear to the world, but to myself I seem to have been only like a boy playing on the sea-shore, and diverting myself in now and then finding a smoother pebble or a prettier shell than ordinary, whilst the great ocean of truth lay all undiscovered before me' (Newton, 1855).

Table 27.1 Some common concepts used in PP debates

Situation	Nature of knowledge	Type of action taken
Risk	**'Known' impacts** and **'known' probabilities**, e.g. regarding asbestos from 1930.	**Prevention**: action to reduce known hazards, e.g. eliminating exposure to asbestos dust
Uncertainty (*)	**'Likely' impacts** but **'unknown' probabilities**, e.g. regarding antibiotics in animal feed and associated human resistance to those antibiotics, from 1965.	**Precaution**: action taken to reduce exposure to plausible hazards, e.g. the EU ban on antibiotic growth promoters in 1999.
Ignorance	**'Unknown' impacts** and therefore **'unknown' probabilities**, e.g. the then unknown but later 'surprises' of the ozone layer 'hole' from CFCs, pre-1974; the mesothelioma cancer from asbestos pre 1959; the rate of Greenland ice sheet melting pre-2007.	**Precaution**: action taken to anticipate, identify earlier, and reduce the extent and impact of 'surprises' e.g. by using intrinsic properties of chemicals e.g. persistence, bioaccumulation, spatial range; using analogies; long-term monitoring; and using robust, diverse and adaptable technologies that can help minimise impacts of 'surprises'.
Ambiguity	Concerning the different **values and interpretations** about information used by stakeholders. E.g. in invasive alien species cases where a species can be welcomed by some but not others.	**Participatory precaution:** stakeholder engagement in decision- making about innovations and their potential hazards.
Variability	The natural differences in population or ecosystem exposures and sensitivities to harmful agents.	**Obtain more information** in order to minimise simplistic assumptions about average exposures and sensitivities
Indeterminacy	Unpredictable uses of technologies e.g. use of X-rays in children's shoe shops in the 1950s.	**Pre-market benefit assessment** of novel uses of a technology with potential hazards.

Note: * Different types, sources and levels of uncertainty can be identified (Walker, 2003).

it explicitly distinguish between risk, uncertainty and ignorance as important factors in judging the 'reasonableness' of the grounds for action.

The strength of evidence deemed to be reasonable justification for action varies between different jurisdictions and cases and can be quite low. In Sweden, for example, a 'scientific suspicion of risk' constitutes sufficient evidence for restricting an existing chemical substance. Similarly, for the World Trade Organization, 'pertinent scientific information' can be sufficient to justify protective measures under the Agreement on Sanitary and Phytosanitary Measures whenever there is an insufficiency of science to permit a comprehensive and robust risk assessment.

The strength of scientific evidence appropriate to justify public policy or other actions depends on the pros and cons of action or inaction in the specific circumstances of each case. These circumstances include the nature and distribution of potential or plausible harm; the justification for and the benefits of the agent or activity under examination; the availability of feasible alternatives; and the overall goals of public policy. Such policy goals include 'high levels of protection' of the public, consumers, and the environment, as required by the Treaty of the European Union.

The use of different strengths of evidence for different purposes is not a new idea. Legal practice has long employed several tests, such as 'beyond all reasonable doubt' in criminal courts and the lower 'balance of probabilities' used in many civil courts.

Moreover, public health practitioners have long advocated the use of varying strengths of evidence in different circumstances. For example, Bradford Hill (1965) concluded his classic paper on association and causation in environmental health with a 'call for action' in which he proposed the use of case-specific and differential strengths of evidence, observing that:

> 'It almost inevitably leads us to introduce **differential standards** before we convict. Thus on **relatively slight evidence** we might decide to restrict the use of a drug for early-morning sickness in pregnant women. If we are wrong in deducing causation from association no great harm will be done. The good lady and the pharmaceutical industry will doubtless survive. On **fair evidence** we might take action on what appears to be an occupational hazard, e.g. we might change from probable carcinogenic oil to a non-carcinogenic oil in a limited environment and without too much injustice if we are wrong. But we should need **very strong evidence**

> before we made people burn a fuel in their homes that they do not like or stop smoking the cigarettes and eating the fats and sugar that they do like' (emphasis added).

In the field of cancer, the International Agency for Research on Cancer also uses several types of scientific evidence to categorise their strengths of evidence on carcinogens (Cogliano, 2007).

Failing to acknowledge the reality of different strengths of evidence for action has led to several ill-founded debates. For example, opponents of the PP often cite the North Sea Ministerial Declaration, which calls for: 'action to avoid potentially damaging impacts of substances, **even where there is no scientific evidence to prove a causal** link between emissions and effects' (emphasis added).

Critics claim that this definition justifies action even when there is 'no scientific evidence' that associates exposures with effects. However, the North Sea Declaration clearly links the words 'no scientific evidence' with the words '**to prove a causal link**'. There is a significant difference between the evidence needed to show a **plausible link** between a pollutant and harm, and evidence which is robust enough to 'prove' a causal link. Once evidence reaches the level of 'proving' a causal link there is no need for the PP as the issue is then firmly in the 'prevention principle' area where the risks are well characterised.

Similar confusion arose in interpreting the different strengths of evidence for association and causality set out in a 13-country study of brain cancers and mobile phones (the Interphone study) (see Chapter 21 on mobile phones).

The confusion of commentators, including the media, in these cases arose because scientists were not transparent and clear about the difference between the very strong evidence needed to establish 'causality' and the suggestive evidence of plausible risks.

For example, the Interphone concluded that:

> 'There were **suggestions of an increased risk** of glioma, and much less of menigioma, at the highest level of exposure….. (but) biases and errors limit the strength of the conclusion we can draw from these analyses and **prevent a causal interpretation**'.

One consequence of not clarifying the difference between the low and high strengths of evidence embedded in these two sentences was that readers of the Interphone conclusion, particularly the media, interpreted the study as providing either no evidence of cancer or evidence of cancer. Both conclusions were strongly cited by different and similarly weighty parts of the media.

In the United Kingdom, for example, the *BBC* (17 May 2010) reported that 'No proof of mobile cancer risk, major study concludes'. On the same day, *The Telegraph* asserted that 'Half an hour of mobile use a day increases brain cancer risk'.

Beneath the strong evidence of 'scientific causality' there is a large evidentiary space containing a continuum of strengths of evidence that can be used to justify action under the precautionary principle, depending on the case-specific circumstances. The question remains, however, where, in that continuum, is 'sufficient evidence' located?

Identifying an appropriate strength of evidence for action has been an important issue in climate change debates. The Intergovernmental Panel on Climate Change (IPCC) discussed this issue at length before formulating its 1995 conclusion that 'on the balance of evidence' mankind is disturbing the global climate. It further elaborated on this issue in its 2001 report, which identified seven strengths of evidence that can be used to characterise the scientific evidence for a particular climate change hypothesis (see Panel 14.1 in Chapter 14 on climate change). By 2007 the IPCC was able to conclude with 'high confidence' that the evidence for human-induced climate change had strengthened to 'very likely' (IPCC, 1995, 2001 and 2007).

Table 27.2 presents five of these strengths of evidence based on the IPPC approach and illustrates their practical application to a variety of different societal purposes.

The decision about when there is sufficient evidence to justify preventive action clearly involves more inputs to decision-making than merely science. The strength of evidence that is deemed appropriate depends on such non-scientific criteria as the costs of being wrong with actions or inactions (including their nature and distribution between different groups and generations); the justification for, and benefits of, the agents or activities that pose potential threats to health; and the availability of feasible alternatives.

The term 'no established or conclusive evidence' is often used to characterise the absence of some strength of evidence that would convince the particular scientists doing the risk assessment that an agent causes harm. The different consequences

Table 27.2 Different strengths of evidence for different purposes: some examples and illustrations

Strength of evidence	Illustrative terms	Examples of use
Very strong (90–99 %)	Statistical significance	Can be part of strong scientific evidence of 'causation'
	Beyond all reasonable doubt	Most criminal law, and the Swedish Chemical Law 1973, for evidence of 'safety' of substances under suspicion — placing the burden of proof on manufacturers
Strong (65–90 %)	Reasonably certain	US Food Quality Protection Act, 1996
	Sufficient scientific evidence	To justify a trade restriction designed to protect human, animal or plant health under World Trade Organization Sanitary and Phytosanitary Agreement, Art. 2, 1995
Moderate (33–65 %)	Balance of evidence	Intergovernmental Panel on Climate Change 1995 and 2001
	Balance of probabilities	Much civil and some administrative law
	Reasonable grounds for concern	European Commission Communication on the Precautionary Principle 2000
	Strong possibility	British Nuclear Fuels occupational radiation compensation scheme 1984 (20–50 % probabilities triggering different awards up to 50 % + which triggers full compensation)
Weak (10–33 %)	Scientific suspicion of risk	Swedish Chemical Law 1973, for sufficient evidence to take precautionary action on potential harm from substances — placing the burden of proof on the regulators
	Available pertinent information	To justify a provisional trade restriction under World Trade Organization Sanitary and Phytosanitary Agreement, Art. 5.7, where 'scientific information is insufficient'
Very weak (1–10 %)	Low risk	Household fire insurance
	Negligible and insignificant	Food Quality Protection Act, 1996 (USA)

for those for whom the evidence is 'not established' (i.e. risk takers or risk makers) is seldom discussed. Nor are the purposes for which the evidence could be conclusive discussed, for example to justify warning labels, or low cost exposure reductions, or a ban.

Decision-makers must also be aware of the common mistake of assuming that 'no evidence of harm' is 'evidence of no harm', when the relevant research has not been done, a feature of many case studies which is picked up in Chapter 26, where 'authoritative but unsubstantiated assertions of safety' are described.

Finally, interpreting 'convincing evidence' only as the high strength of evidence needed to establish 'scientific causality' is of little practical use in helping to apply the precautionary principle or in averting, as opposed to observing, future harm. This means that risk assessment committees may need to consider the consequences of their judgements as well as just causation, as Bradford Hill and the IPCC have demonstrated. It may be argued that it is for risk managers to deal with the consequences of decisions about causation. Nevertheless, scientists involved in risk assessments are well placed to contribute to analysis of consequences, as was acknowledged by the European Court when it noted that a scientific risk assessment should provide the competent public authority with sufficient, reliable and cogent information so that it also understands:

> '…the **ramifications** of the scientific question raised and can decide upon a policy in full knowledge of the facts' (ECR, 1999 and 2002) (emphasis added).

27.6 The pros and cons of actions and inactions

The EEA definition of the PP widens the conventionally narrow and quantifiable interpretation of costs and benefits to embrace wider and sometimes unquantifiable 'pros and cons'. These include, for example, a loss of trust in science after the public experiences harm that scientists had assured them would not occur. Such unquantifiable costs can sometimes be as significant as the economic costs, as in the case of BSE (EEA, 2001) and the nuclear accidents at Chernobyl and Fukushima (Chapter 18).

Chapter 23 on costs of inaction illustrates how the costs and benefits of action and inaction are

skewed towards the tangible short-term compliance costs of regulatory action, which usually fall on specific, often powerful actors, and against the long-term diffuse benefits to society as a whole of timely actions. The polluter pays principle and the internalisation of external costs are essential components of approaches to achieving a more economically efficient and equitable distribution of the pros and cons of action and inaction. Such measures would bring the market prices of hazardous agents into line with their real costs, encouraging earlier development of substitutes and other economic and technological innovations (EEA, 2012).

Several of the case studies (asbestos, lead, mercury, PCBs, CFCs, benzene) indicate that early actions can stimulate innovations and conversely illustrate how late actions have consolidated technological monopolies for products, at unrealistically low prices, which served to keep smarter substitutes out of the markets for many years.

Other work has demonstrated the role that strong and smart environmental regulations, tax incentives and other measures can play in stimulating innovation (Porter, 1995; Ambec, 2011; Ashford, 1979, 2011a, 2011b and 2012).

27.7 Political and financial short-termism

The time horizons of democratic politics are very short in comparison to the long timescales associated with successfully managing the harm to environments and people illustrated in the case studies. This is a deep-seated problem but some countries have begun to devise some institutional responses to protect the long-term interests of society. For example, countries like Finland, Israel, New Zealand and Hungary have been experimenting with nominating ombudsmen or committees charged with caring for the long term (Roderick, 2010; Ward, 2012).

The financial sector is even more limited by short termism but since the financial crash there has been some effort to establish more long-term perspectives (Mainelli and Giffords, 2009).

27.8 Public participation in hazard and options analysis

There are many value judgements involved in hazard and risk analysis, from the framing of the issue and the questions to be addressed to the ethical choice of the appropriate strength of evidence that should justify action to reduce hazards in a particular case.

As several authoritative bodies have highlighted in recent years, the public should be involved in decisions about serious hazards and their avoidance, and at all stages of the risk analysis process (US PCR, 1997; RCEP, 1998; German Advisory Council on Global Change, 2001; Codex Alimentarius Commission, 2007; JRP/IPCS, 2007; Health Council for the Netherlands, 2008; NAS, 2009)

Figure 27.2, based on the above reports, illustrates the circular, iterative nature of risk assessment, risk management and risk communication; the links and feedback loops between them; and the involvement of stakeholders at every stage, albeit with different intensities of engagement — greater at the problem framing and options choice stages, less so at the scientific risk assessment stage.

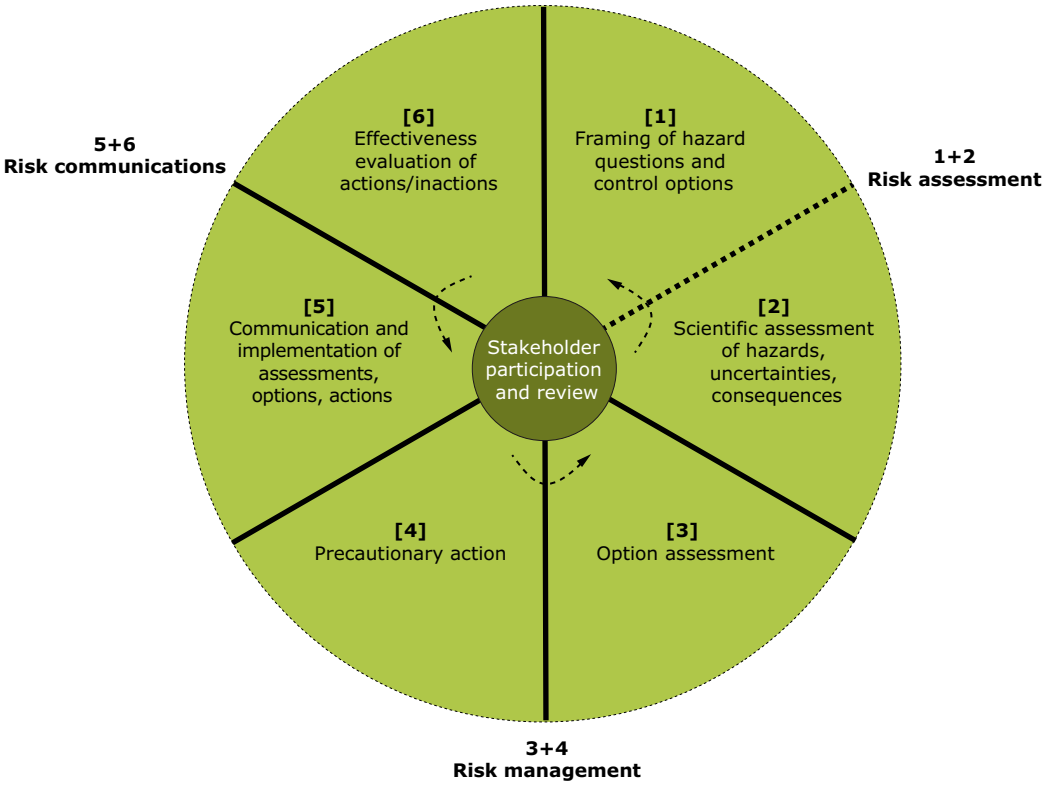
The report from the US National Academy of Sciences on Risk Assessment, *Science and decisions: advancing risk assessment* (NAS, 2009), strongly recommends such stakeholder involvement, especially at the crucial problem framing stage.

These recommendations for enhancing stakeholder participation in the hazard and options analysis process do not appear to be reflected in most existing international and European arrangements for analysing risks and setting public exposure limits e.g. relating to contaminants in food (JRC/IPTS, 2007). European authorities are continuously improving, albeit at speeds that fail to satisfy all stakeholders.

Changes are nevertheless in the air. The European Commission increasingly involves stakeholders in risk assessment by, for example, asking for public comments on the questions to be put to risk assessors and holding stakeholder consultative meetings ([4]). There have also been recent improvements in the way that uncertainties are handled in the food (EFSA, 2009; Hert, 2010) and emerging issues fields (SCENIHR, 2012), building on the earlier work of the IPCC on

([4]) See the stakeholder dialogue procedures in EC (2009). The European Food Safety Authority (EFSA), for example, organises a Stakeholder Consultative Platform for food industry stakeholders and widely publishes agendas, minutes, and scientific opinions as part of its response to Articles 38 and 39 of its founding regulation on openness and transparency in the governance of food safety risks.

Figure 27.2 A participatory and precautionary framework for analysis of hazards and options



Note: The dotted line indicates feedback.

Source: EEA, based on NRC (1996), US Presidential Commission on Risk (1997), UK Royal Commission on Environmental Pollution (1998) and NAS, 'Science and Decisions' (2009).

how to manage and communicate uncertainty. As Chapter 15 on floods illustrates, balancing timely early warnings against false alarms is a very challenging task for decision-makers under conditions of complexity, uncertainty and ignorance.

There have also been improvements in the transparency of risk assessments, including, most recently, improved public access to the scientific data submitted by companies to regulatory authorities for product authorisations (EFSA, 2013). The need for this openness has emerged as a strong lesson from several case studies — from Minamata to the bio- and nanotechnology fields — and the improvements follows recent controversies over the food additive aspartame and GM maize (Seralini et al., 2012; Genewatch, 2012).

From uncertain risks to relevant and responsible innovation?

In the introduction to this chapter the debates in France on GMOs were used to illustrate the potential of the PP to trigger or facilitate debates that go well beyond the issue of risks and into the area of responsible and socially relevant innovation.

One or two other case study chapters also raise this question. For example, the Chapter 3 on leaded petrol reviewed the technological 'roads not taken' and Chapter 19 on GM crops analysed 'top down' and 'bottom up' innovation pathways to agricultural futures. Chapter 5 on Minamata disease and Chapter 16 on bees also raised questions concerning the value of current democratic institutions in dealing with complex socio-technical issues. More involvement of the public in hazard and options analysis, discussed above, may also lead to wider discussions about technological choices and directions of innovation.

Richard Owens, co-author of the Chapter 13 on the 'birth pill' has further developed these ideas in a forthcoming book on 'responsible innovation' (Owens et al., 2013).

Box 27.5 Responsible research and innovation

Responsible research and innovation is a transparent, interactive process by which societal actors and innovators become mutually responsive to each other regarding the ethical acceptability, sustainability and social desirability of the innovation process and its marketable products. Social desirability is currently essentially determined by market mechanisms, however, as universal principles on what counts as socially desirable are not easily agreed upon.

The 'Innovation Union' flagship initiative is a central part of the EU's Europe 2020 strategy and is seen as means to deliver 'smart growth', defined as 'developing an economy based on knowledge and innovation' (EC, 2011).

From this macroeconomic perspective, innovation is assumed to be steerless but inherently good, as it produces prosperity and jobs and meets societal challenges, addressed through market mechanisms.

Modern societies lack a specific forum or policy for evaluating particular technologies in terms of benefits and risks within the legislative context. We only have formal safety, quality and efficacy assessment procedures evaluating the properties of products in the course of passing these three market hurdles.

The benefits of technologies are 'demonstrated' only by market success, whereas the potential negative consequences are evaluated under formal risk assessment schemes. The state is responsible for defining the risks of technologies under product authorisation procedures and product liability law and ensuring market operators compliance, whereas society lacks a particular responsibility for what could count as positive impacts of technologies.

Modern 'Frankensteins' are not intentionally created by a single actor. If they arise they are more likely the unforeseen side effects of collective action. Indeed, techno-scientific applications can remain ethically problematic even in cases where scientists and engineers have the best possible intentions and users have no conscious intention to misuse or abuse ([5]).

This situation constitutes the major ethical challenge we face today. Ethics focused on the intentions and/or consequence of actions of individuals are not appropriate for allocating responsibilities for the impacts of innovations.

Responsible innovation therefore requires ethics of co-responsibility for ensuring the right impacts and avoiding negative consequences, whether these impacts are intentional or not and whether they can be fully foreseen or not.

The challenge is to arrive at a more responsive, adaptive and integrated management of the innovation process. A multidisciplinary approach involving stakeholders and other interested parties should lead to an inclusive innovation process whereby technical innovators become responsive to societal needs and societal actors become jointly responsible for the innovation process. That includes contributing to defining socially desirable products that reflect basic needs and public values, for example by focusing on the great challenges of our times such as climate change and food security.

Effecting such changes requires a paradigm shift in innovation policy. The state must assume responsibility for positive outcomes of innovation, reflect basic public values beyond consumer market preferences and move away from technology-oriented research and innovation policy and towards an issue-oriented approach.

Source: Edited extracts from von Schomberg, 2013 ([6]).

([5]) The concept of collective co-responsibility in response to the shortcomings of professional roles — responsibility in science and engineering is outlined in von Schomberg (2007).

([6]) René von Schomberg is at the European Commission, Directorate General for Research. The views expressed here are those of the author and may not in any circumstances be regarded as stating an official position of the European Commission.

Box 27.5 includes a short description of responsible innovation written by Rene Schomberg, a contributing author to the Owens book (Owen et al., 2013). Innovation 'with a human purpose' is also being proposed as a means to rebalance market-focused innovation and to meet the environmental challenges posed by meeting human needs in a resource-, energy- and water-constrained world (van den Hove, 2012).

The field of public engagement on risks, hazards and innovations is large (Wynne, 2007; Stirling, 2008 and 2010; Wesselink and Hoppe, 2011; Wesselink, 2011; Hoppe, 2012) and extends well beyond the bounds of the present study. However, the evidence from *Late lessons from early warnings* provides further grounds for boosting public and corporate engagement in responsible innovation.

27.9 Conclusion

The case studies and this chapter have illustrated the need for wider use of the PP both as a justification for timely actions on early warnings and as a trigger for broader debates about technological pathways to the future. Mistakes will be made, surprises will occur. But if the quality of the scientific and stakeholder processes used to arrive at such decisions are sound, and the best of science is used, then living with the consequences, of such decisions, both pleasant and unpleasant, will be more acceptable.

The capacity of people to foresee and forestall disasters appears to be limited, however, especially when such action is opposed by powerful economic and political interests, as the case studies in *Late lessons from early warnings* illustrate. It is not just corporations that have the capacity for denial when confronted with evidence of impending disaster — as the financial collapse of 2009 demonstrated. 'Wilful blindness' and human 'folly' are general human traits that thwart our capacities to do the right thing (Heffenan, 2010; Tuchman, 1984).

If we adopt optimism of the will to counter pessimism of the intellect, however, it is possible to believe that human behaviour could improve. Decision-makers could heed the lessons of past experience. Armed with more humility in the face of scientific uncertainty and ignorance, and supported by broad and effective public engagement, they could apply the precautionary principle more widely. In so doing, they would help anticipate and minimise many future hazards, while stimulating innovation.

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28 In conclusion

Since 2001: many changes, crises and lessons relearnt

The first volume of *Late lessons from early warnings* was published in 2001. Since then, the world has changed significantly. It is larger in population but smaller in interconnectivity; faster in terms of technology adoption but slower in terms of policy action in the face of complex interlinked problems; more volatile in terms of economic and environmental changes, yet more static in terms of political reflexivity and adaptations in governance. Beyond the current financial and economic crises, there are several long-term, systemic and interconnected challenges, such as depletion of natural resources, climate change, a 2-billion person increase in the world population by 2050, and diminishing ecosystem resilience (EEA, 2011a; OECD, 2012; WEF, 2012).

These developments point to two important realities. First, the systems of governance misrepresent the socio-ecological system, making societies and the environment subordinate to the economy — essentially serving as sources of human and natural capital. This misrepresentation ignores the reality that any civilisation is ultimately dependent on its ecological and social foundations and that economies function to sustain and enhance human well-being (Passet, 2001). Second, the scale, interconnectedness and sheer complexity of feedbacks between nature and human interventions have outstripped society's capacity to understand, recognise and respond to these effects.

The first volume ended with a call to action for policymakers. How much progress has been made since then? One important area is that of innovation and the effect that precaution can have on it. In Volume 1, the difficulties of balancing precaution with technological innovation were recognised. However, there is now increasing evidence that precautionary measures do not stifle innovation, but can encourage it, in particular when supported by smart regulation or well-designed tax changes (EEA, 2011b, 2011c; Ambec et al., 2011; Ashford and Hall, 2011).

Volume 1 also invited policymakers to take more account of a 'richer body of information from more diverse sources'. It identified public health and the environment as two fields of science that were separate and polarised. And it suggested involving a wider range of stakeholders to expand the information base and to 'improve public trust in society's capacity to control hazards, without stifling innovation or compromising science'. These are all areas where improvements have been made since 2001.

There has been less progress with other lessons, particularly the call to 'identify and reduce institutional obstacles to learning and action'. Both political and scientific 'bureaucratic silos' do not seem to have disappeared, despite the frequent calls for policy integration and inter-departmental coordination (Hamdouch and Depret, 2010; Phoenix et al., 2012).

Worryingly, warnings of impending hazards are, in many areas, still not being heeded and the resulting damage is far more widespread, geographically, across species and extending to future generations, who will particularly suffer many of the harmful effects of our current energy systems, chemicals and technologies. Damage is now shown to be occurring at increasingly lower levels of exposure to pollution, and the polluters, for the most part, are still not paying the full costs of their pollution, partly because of a lack of incentives to do so. At the same time we see the destruction of the stocks of natural capital that underpin human well-being. It is easy to lose sight of the crucial dependence of economies on a diverse, healthy and resilient natural environment, especially in times of economic crises.

A key message in the 2001 report was the notion that 'the growing innovative powers of science seem to be outstripping its ability to predict the consequences of its applications, while the scale of human interventions in nature increases the chances that any hazardous impacts may be serious and global.' This is happening at an ever-greater pace, with globalised industries racing to introduce new technologies but with limited understanding

of what their impacts might be. National governments now have less control over globalised technologies.

More positively, however, new transformative approaches are emerging for managing the systemic and interconnected challenges that we face (e.g. Gladwell, 2012; Stirling, 2008). They are building in particular on the increasing use by consumers, citizens and shareholders of the power of the internet and social media to demand and foster increased participation, responsibility, accountability and transparency.

Such approaches also need longer-term perspectives. Greater complexity, uncertainties, scientific ignorance, broader risks and the irreversibility of many harmful impacts together necessitate the increased use of long-term scenarios and strategy analysis by citizens, governments and corporations alike (EEA, 2011a). The long-term interests of society as a whole, distinct from the partial interest of particular stakeholders and individuals, also require new political and financial institutions that can help overcome the short termism of most politics and much finance (Ward, 2012; Roderick, 2010; Mainelli and Giffords, 2009; RMNO, 2009).

The case studies in this second volume of *Late lessons from early warnings* provide some new insights from the lessons of the past that can help stimulate actions to reinforce, complement and put into practice the emerging transformative approaches, mindful of the observation that 'those who cannot remember the past are condemned to repeat it' (Santayana, 1905).

2001–2013: what new insights emerge?

Many of the cases in this report reveal similar lessons to those in the 2001 report. Some insights have been strengthened, however, as the body of evidence has increased and our understanding of ecological and biological systems has improved. The case studies in the two volumes of *Late lessons from early warnings* cover a very diverse range of both recent and historical chemical and technological innovations and their impacts on humans and nature. All cases have unique characteristics stemming from the type of the innovation, the origins and nature of the hazards, the prevailing approaches to policymaking, and the cultural influences of time and place. The studies also share common features, such as key decisions on innovation pathways made by a few people on behalf of many; a lack of institutional and other mechanisms to respond to early warning signals; misleading market prices that do not properly reflect all costs and risks to society and nature; and inadequate accounting for assets and liabilities across different types of capital.

Such features from the past raise questions for the future. How, for example, can the innovations that are driving knowledge economies, such as nanotechnologies, be developed without repeating the mistakes of the past? How can the wider and wiser application of the precautionary principle support decision-making in the face of uncertainties from within complex systems that defy prediction and where 'surprises' are inevitable? How can we ensure that the lack of 'perfect' knowledge is not a justification for inaction in the face of 'plausible' evidence of serious harm? How can conflicting interests (including public and private ones) be balanced in the development, use and impact phases? How can the distribution of costs and benefits over time be made more equitable?

The *Late lessons from early warnings* case studies demonstrate the complexities of handling the interactions between the many actors and institutions involved — governments, policymakers, businesses, entrepreneurs, scientists, civil society representatives, citizens and the media. Each comes to the debate with different and often conflicting knowledge, perceptions, interests and priorities; balancing these numerous and often antagonistic positions should be seen as a prelude to making decisions on those innovations that have broad societal implications.

The opportunities are manifold but can be boiled down to three main ones:

- to correct the prioritisation of economic and financial capital over social, human and natural capitals through the broader application of the policy principles of precaution, prevention and polluter-pays, and improved accounting systems across government and business;
- to broaden the nature of evidence and public engagement in choices about crucial innovation pathways by balancing scientific efforts more towards dealing with complex, systemic challenges and unknowns and complementing this knowledge with lay, local and traditional knowledge;
- to build greater adaptability and resilience in governance systems to deal with multiple systemic threats and surprises, through

strengthening institutional structures and deploying information technologies in support of the concept of responsible information and dialogues.

Taken together the case studies provide some lessons to support action, supplementing the conclusions of Volume 1. These findings are presented in the remainder of this section.

Reduce delays between early warnings and actions

Most of the case studies in both volumes of *Late lessons from early warnings* illustrate that if the precautionary principle had been applied on the basis of early warnings, many lives would have been saved and much morbidity and damage to ecosystems would have been avoided.

Today, several factors related to the speed, scale and breadth of technological innovation exacerbate the tendency to delay action. First, by the time evidence of harm is confirmed, the technology has often changed, leading to assumptions that, unlike yesterday's technology, today's technology is now safe. Second, for some technologies (e.g. broad-scale energy production systems or chemical plants), the huge initial investments mean that yesterday's investments will be redeemed before any serious risk reduction is implemented, creating *de facto* technological lock-ins. Third, the scale of technological development puts very difficult demands on those attempting to monitor and respond to the risks before they have become serious, widespread and irreversible.

These features of contemporary life further strengthen the case for taking early warning signals more seriously and acting on lower strengths of evidence than those normally used to adduce 'scientific causality'.

The case studies have shown that the main barriers to timely action include the short-term nature of many political and financial horizons; the novel and challenging nature of the technologies and the scientific problems that arise from their interactions with complex biological, ecological and social systems; the conservative nature of much environment and health science; the ways in which scientific and other evidence is evaluated; the different perspectives and interests of many stakeholders and the vested interests of some powerful ones; and the broader cultural and institutional circumstances of public policymaking that often favour the status quo.

Addressing these causes of delay can help to reduce the negative impacts that arise from many innovations. But tackling them is not easy. For example, the problem of the unequal distribution of political power between citizens, business and financial actors, and governments is a persistent problem of politics, which has increased through globalisation and the rise of multinational corporations, yet it is an issue that is well beyond the scope of this report. Some of the other causes of delay are more amenable to change and these are addressed in the rest of this section.

In evaluating the pros and cons of using the precautionary principle, it is important to remember that the harm from most hazards analysed in the case studies turned out to be more diverse and widespread than anticipated and such damage is often found to occur at exposures lower than initially considered dangerous.

For example, it has been known since 1960 that asbestos causes the mesothelioma cancer, in addition to lung cancer (identified in 1955) and asbestosis (identified in 1906–1929). Similarly, it is now known that smoking causes a wide range of cancers, heart disease and foetal damage, beyond the harm of lung cancer identified in 1951. PCBs are now known to cause neurological problems in children, and cancer, in addition to harming the reproduction of eagles (identified in the 1960s). Lead has also been demonstrated to be more broadly chronically harmful — it was initially recognised as damaging children's IQ but it is now known to cause heart disease in adults. Radiation has gone through a similar expansion of known hazards.

This phenomenon of 'harm expansion' is rendered more problematic by the discoveries that harm from all of the above agents has been found to occur at lower and lower levels, such that, more often than not, no 'safe' threshold of exposure can be identified. This knowledge needs to be taken into account when evaluating the potential pros and cons of future precautionary action on emerging issues. Continuous, anticipatory reductions in exposures to emerging hazards could help to avoid repeating these histories of harm expansion.

More and better prospective and retrospective analyses of the costs of action and inaction, across the full lifecycle of a technology, would highlight the value of precautionary and preventive actions, particularly the value of 'secondary benefits and costs' which can be substantial, such as the health benefits from reduced fossil fuel use, where the main objective is to mitigate climate change. They

should also consider the psychological and societal costs of both false alarms concerning a health hazard, e.g. the over-reaction to swine flu in the US in the 1970s, and misplaced reassurances concerning the safety of a technology, such as the downplaying of risks associated to nuclear power plants by Japanese authorities and utilities. Such pro and con analyses should be independent of interested parties, both commercial and political, as they often have a 'natural' tendency to exaggerate costs of hazard reduction and to underestimate the benefits of action.

As case studies from both volumes have also shown, the timely use of the precautionary principle can often stimulate rather than hamper innovation, in part by promoting a diversity of technologies and activities, which can also help to increase the resilience of societies and ecosystems to future surprises. Keeping options open and following multiple paths means that a particular option can be terminated if it turns out to pose high risks, and avoids situations of technological monopolies such as those experienced, for example, in the cases of asbestos, CFCs and PCBs.

In contrast, technological monopolies hamper innovation. For example, it was the monopolies of lead in petrol, asbestos, CFCs and PCBs that both prolonged the harms they caused and made those harms widespread. These monopolies contributed to technological 'lock-in' but also to institutional and ideological lock-ins, which further hampered innovation and the development of alternatives. These technologies and their products were also 'cheap' in the market place, bearing little relation to their real costs in terms of harm to the environment, human health and financial compensation to victims. These artificially low market prices in turn helped to stifle the development of smart substitutes.

This past experience should be taken into account with the emerging technologies such as GMOs and nanotechnologies, where there are already signs of technological monopolies, driven by the high costs of research, development and production involved and the patent protections for developers on many of their products and processes (Stirling, 2007; van den Hove et al., 2012).

When applying the precautionary principle, there are, therefore, not only scientific issues to be considered but also ethical choices, concerning the appropriate strength of evidence for action; the equity implications arising from the costs and benefits of action and inaction; the appropriate balance between generating false negatives and false positives; and the social necessity of large-scale innovations.

Clearly, acting to avoid or reduce harm on lower strengths of evidence than that used to establish scientific causality will sometimes increase the number of false alarms — although the review of 88 cases of alleged false positives in Volume 2 of *Late lessons from early warnings* confirmed just four actual cases, suggesting that the risks are considerably less than sometimes claimed. Moreover, it is important to recognise that, in cases where there are damages over a long time span that may irreversibly alter the system, there is a fundamental asymmetry between the competing policy and scientific options of avoiding false negatives and avoiding false positives. Examples of such situations of irreversibility include climate change, modification to the genetic make-up of humans or other species, persistent chemical or radioactive contamination, and species loss.

If an early warning signal triggers a double reaction of precautionary policy measures and more intensive research on risks and alternatives, then at some point the research may show that this was a false alarm and the precautionary measure can be cancelled. The loss in this case will be a delay in economic and social benefits from the technology (or the cost of mitigating actions in cases such as climate change) during the time it took to show that there was no cause for concern. But the system will not be irreversibly altered. In contrast, if the early warning triggers no precautionary action but more research shows, only much later, that there was indeed real cause for concern then irreversible systemic damages will already have taken place. Acknowledging this asymmetry is central to understanding when precautionary and preventive approaches are best deployed.

Tipping the overall balance of public policy towards avoiding harm, even at the cost of more false alarms, would seem to be a price that is well worth paying, given the costs of being wrong in acting or not acting. This is one of the strategic and ethical societal choices, similar to the choice of strengths of evidence to be used in civil or criminal court cases, that needs to be openly debated.

Acknowledge complexity when dealing with multiple effects and thresholds

The world is drawing down its natural capital through an over-reliance on fossil-fuel-based,

synthetic chemicals that are compromising the health and resilience of ecosystems and key organisms such as fish and bees, in combination with other stressors such as climate change and invasive alien species. There is also evidence that some types of genetically modified crops (and the agrochemical substances used alongside them), which are released into the environment and the food chain, present a threat to human health, some species and ecosystems, and food security. Human health is being further compromised by chemicals that threaten health from before birth, through childhood and into adulthood. (Barouki et al., 2012; EEA, 2012; Kortenkamp et al., 2011).

Such exposures appear to contribute to increases of many types of cancers, birth defects, male infertility, and cardiovascular, neurological and immunological dysfunctions and diseases. The impacts of these hazards are being supplemented by the harmful effects of unhealthy eating habits and lifestyles in many parts of the world, and resulting in epidemics such as diabetes and obesity. Taken together, these multiple stressors have profound public health significance.

Growing scientific knowledge clearly shows that the causal links between stressors and harm are more complex than was previously thought and this has practical consequences for minimising harm. Much of the harm described in Volumes 1 and 2, such as cancers or species decline, is caused by several co-causal factors acting either independently or together. For example, the reduction of intelligence in children can be linked to lead in petrol, mercury and PCBs as well as to socio-economic factors; bee colony collapse can be linked to viruses, climate change and nicotinoid pesticides; and climate change itself is caused by many complex and inter-linked chemical and physical processes.

In some cases, such as foetal or fish exposures, it is the timing of the exposure to a stressor that causes the harm, not necessarily the amount; the harm may also be caused or exacerbated by other stressors acting in a particular timed sequence. In other cases, such as chemicals like BPA, low exposures can be more harmful than high exposures; and in others, such as asbestos with tobacco, and some endocrine disrupting substances, the harmful effects of mixtures can be greater than from each separate stressor. There are also varying susceptibilities to the same stressors in different people, species and ecosystems, depending on pre-existing stress levels, genetics and epigenetics. This variation can lead to differences in thresholds or tipping point exposures, above which harm becomes apparent in some exposed groups or ecosystems but not others. Indeed there are some harmful effects that occur only at the level of the system, such as a bee colony, which cannot be predicted from analysing a single part of the system, such as an individual bee.

The increased knowledge of complex biological and ecological systems has also revealed that certain harmful substances, such as PCBs and DDT can move around the world via a range of biogeochemical and physical processes and then accumulate in organisms and ecosystems many thousands of kilometres away. The practical implications of these observations are threefold. First, it is very difficult to establish very strong evidence that a single substance or stressor 'causes' harm to justify timely actions to avoid harm; in many cases only reasonable evidence of co-causality will be available. Second, a lack of consistency between research results is not a strong reason for dismissing possible causal links: inconsistency is to be expected from complexity. Third, while reducing harmful exposure to one co-causal factor may not necessarily lead to a large reduction in the overall harm caused by many other factors, in some cases the removal of just one link in the chain of multi-causality could reduce much harm.

A more holistic and multi-disciplinary systems science is needed to analyse and manage the causal complexity of the systems in which we live and to address long-term implications. For example, there would be substantial benefits from exploring, much earlier and more systematically, the multiple effects on people and ecosystems of chemical and other stressors, their cumulative effects, chemical metabolites, and their mixture effects. Exposures to low doses of contaminants and their effects, particularly in susceptible sub groups in populations, should also be more fully investigated, accompanied by more biological monitoring that would improve the detection of the precursors of disease.

Several case studies provide examples of where assertions that 'no evidence of harm' have been interpreted as 'evidence of no harm', which may not be the case if appropriate research over relevant time periods is missing. Examples include leaded petrol in the 1920s-60s, and risks to children from mobile phones before 2011, when the first study on children was published. Such authoritative but unsubstantiated assertions of safety have led to much harm, for example, in cases such as asbestos, tobacco, lead and mercury.

Acknowledging both uncertainties and scientific ignorance is particularly important where the science is relatively immature, as with such emerging technologies as GM crops, mobile phones, nanotechnology and invasive alien species and where exposures are widespread. Recognising uncertainty also helps to avoid putting too much reliance on simple models of complex systems as in the cases of floods, nuclear accidents, climate change, ecosystems resilience and multi-pollutant human exposures

Uncertainty, though, can be a two-edged sword, being used as the basis for challenging both assurances of safety and evidence of a hazard. In particular, uncertainty has been misused, exaggerated, or even 'manufactured' in order to delay and undermine regulatory measures to protect health and environments. Examples include climate change, tobacco, lead, honeybees and beryllium (Michaels, 2008; Oreskes and Conway, 2010).

There is also an asymmetry between the high levels of proof of harm demanded by proponents of a technology as sufficient to justify remedial or preventive actions compared to the level of evidence they deem sufficient to claim that their products are 'safe'. Waiting for high levels of proof of harm before acting not only leads to much harm but also to a stifling of innovation, as the case studies on asbestos, lead, mercury, PCBs and CFCs illustrate.

Rethink and enrich environment and health research

The need for research to focus more on the potential hazards of emerging technologies in addition to research on product applications has already been noted. It would also be helpful if there were a greater focus on emerging hazards rather than on well-known risks. Recent research (Grandjean et al., 2011) indicates that much environmental health research still focuses on well known hazards, such as lead and mercury, and tends to ignore newly emerging threats to health. The top ten substances studied are all metals such as copper, lead, zinc and cadmium. These established hazards account for approximately half of all the journal articles on impacts of chemical substances of the last ten years (Grandjean et al., 2011). This disproportion has crowded out research into other dangerous hazards and risks, such as on endocrine-disrupting substances and other hazards where less is known about their pathways and impacts (despite over EUR 100 million of EU research funding on endocrine disrupting compounds in the last decade) but where the evidence is growing of widespread impacts on humans and nature (EEA, 2012; Kortenkamp et al., 2011).

A major reason for this imbalance may relate to the prevailing regulatory science paradigm, where solid conclusions depend on replication and verification. Other likely contributing factors to scientific inertia are the effective use of costly infrastructure to ensure value for money; the desire of policymakers for more certainty from science regarding politically difficult choices; and the tendency of funding agencies to be conservative in their research strategies.

In order to identify hazards that may only appear over decades, there needs to be more long term monitoring of biological and ecological systems, focusing on 'surprise sensitive' parameters such as bees, amphibians, invertebrates, foetuses etc. Such monitoring will also be essential to evaluate the effectiveness of the precautionary and later measures to avoid harm. Monitoring can be supported in part by citizen scientists, using the latest geographical information systems (GIS) and monitoring technologies.

Several cases highlight the benefit of having lay and local knowledge alongside scientific evaluation of harm so that a broader knowledge base can support decision-making. For example, when a mother hypothesised that neurological signs observed in her son were due to exposure to mercury in her womb, this was dismissed by experts who did not question their assumption that the placenta provided protection (see Chapter 5 on Minamata disease). Patients, fishers, wives (e.g. in the sperm damaging, described in Chapter 9 on DBCP), mothers (see Chapter 5 as well as and the chapter on DES in Volume 1 (EEA, 2001, Ch. 8)), factory workers, and bee keepers, as well as clinicians and factory inspectors are amongst those non-scientists who have reliably provided early warnings in the case studies.

Precautionary actions are justified by lower strengths of evidence than those conventionally used for establishing scientific causation, yet in their search for 'certainty' scientists are cautious in attributing causation to an agent while some scientists may sometimes be less cautious when asserting 'safety'. The case studies show that in the past there have been premature assertions of safety based on inadequate scientific methods, such as an over-reliance on studies that were conducted over too short a period to reveal long-term effects for example.

Also evidence of harm has often had to reach the high standard of 'causality' as is the standard for

less complex situations, rather than precautionary strengths of evidence based on plausible association between hazards and harms. The strength of evidence chosen can range from 'a scientific suspicion' of harm to 'beyond all reasonable doubt', depending on the complexity of the system, the level of protection required and the pros and cons of being wrong in acting or not acting.

To avoid waiting for strong evidence of harm in humans and ecosystems, data from animal or other species and methods (ECVAM), should be more widely used to justify precautionary action. This is particularly needed where the potential damage is irreversible — as with some cancers, species and ecosystems losses, and reproductive or developmental effects.

Research, precaution, and exposure control also need to be applied to the substitutes or alternatives to hazardous agents. The chapters on perchloroethylene (Chapter 4), leaded petrol (Chapter 3), DDT (Chapter 11) and booster biocides (Chapter 12) as well as the chapters on CFCs and MTBE in Volume 1 (EEA, 2001, Ch. 7 and Ch. 11) illustrate the hazards that some alternatives have brought in the wake of banned substances, especially when the alternatives are chemically very similar (e.g. HFCs for CFCs). Minimising the hazards of alternatives could be helped by the avoidance of such chemical characteristics as persistence, bioaccumulation, and large spatial range; by the hazard screening of alternatives; and by the greater use of the knowledge to be found in smarter and greener chemistry and technology.

Greater awareness of the complexity, interconnectedness, multi-causality and uncertainties inherent in global environmental issues underlines the need for greater humility about what science can and cannot tell us. Framing issues as purely scientific and technical inappropriately places scientific perspectives above equally valid social and ethical contributions that should be part of decision-making. A shift is needed to more explicitly integrative environmental science approaches in support of public policy, in which systemic considerations and early warnings feature strongly. This shift has started to take place in discourses but often not in practices.

The case studies in Volume 2 of *Late lessons from early warnings* also illustrate how regulatory health and environmental science is still defined in very narrow terms, which obstructs it from being able to identify the complex multifactorial stresses on environmental systems and humans. There is therefore a need for environmental science to become more attuned to the inherent complexities of socio-ecological systems by, for example, balancing a traditional disciplinary focus with more holistic cross-disciplinary scientific research, thereby complementing precision with relevance and comprehensiveness (Phoenix et al., 2012). Such science would often embrace longer timescales, more end-points, and multi-causality.

Since the first volume of *Late lessons from early warnings*, scientific approaches such as 'sustainability science', 'systems biology' or 'futures research' have continued to emerge to help deal with some of the challenges arising from the interconnections and dynamics of socio-ecological systems, focusing on analysis and interventions at the systems level. These emerging disciplines can also help build bridges between research, policy communities, other stakeholders and the public (Kates, 2011).

Last but not least, the case studies show that early warners — scientists and others — have often been harassed for their pioneering work which threatened economic interests and often challenged conventional scientific paradigms. This harassment can include bans on speaking out or publishing; loss of funding; legal or other threats; demotion; transfer to other work and character assassination in scientific and other media (McCulloch and Tweedale, 2007; Martin, 1999, 2008; UCS, 2012). Such early warners should receive better protection via the extension of 'whistle blowing' and discrimination laws; by more active support and protection from scientific societies in the case of scientists; and by awards that acknowledge the value of their work.

Improve the quality and value of risk assessments

Volume 1 stressed the differences between risk, uncertainty and scientific ignorance, and the need to acknowledge and identify all three when doing evaluations of evidence, as in formal risk assessments. Since 2001, some considerable progress has been made in characterising uncertainties in risk assessments, for example, in the food industry (EFSA, 2006, 2013), the field of emerging risks (SCENIHR, 2012), and in climate change (IPCC, 2010). This recognition of uncertainty and ignorance is particularly important where there is much reliance on modelling, as in climate change, invasive alien species, or exposure assessment.

The majority of case studies indicate that it is often inappropriate to use a narrow conception of 'risk' to manage the complex issues at hand with their inevitable features of ignorance, indeterminacy

and contingency. The increasing awareness of the complexity of biological, ecological and technological systems, calls into question the relevance and prevalence of some of the simplistic methods, models and assumptions used in risk assessments. For example, linear dose response curves can be inappropriate when low doses are more harmful than high doses, as in the BPA story; the dictum that the dose alone 'makes the poison' is inaccurate when it is the timing of the dose that makes the dose harmful, as in the TBT and DES cases; assuming uni-causality is too simplistic when multi-causality is the reality, as in the lead case study and many ecosystems such as fisheries; testing for single substances is inadequate when mixtures are present as in all cases of chemical exposures; and there can be an over-reliance on statistical significance when use of confidence limits would be more appropriate.

Simplistic assumptions are also observed in technological risk assessments. As the Fukushima Investigation Committee (NAIIC, 2012) concluded, 'the accidents present us with crucial lessons on how we should be prepared for 'incidents beyond assumptions'. With its failure to plan for the cascade effects beyond design–base accidents 'the regulatory emphasis on risk based probabilistic risk assessment has proven very limited'.

In other words, narrow risk assessment approaches are now outstripped by the realities that they cannot address, recognise and communicate. Too often this contributes to effective denial of those risks that do not fit the risk assessment frame. It is therefore urgent to transform risk assessment practices to make them broader-based, more inclusive, transparent and accountable. That should also enable more transparent communication of diverse scientific views, especially on emerging issues where the uncertainties and ignorance are high and genuine differences of scientific interpretations are likely, desirable, and defensible (Stirling, 2010).

In practice, risk assessments could be improved by including a wider range of stakeholders when framing the scientific risk agenda, through ensuring all available evidence is readily accessible, by broadening the scope and membership of risk evaluation committees, by increasing the transparency and consistency of committee approaches and methods, and by ensuring their independence of vested interests. Improvements in transparency were recently announced by EFSA, who wish all data submitted as part of the product authorisation procedure to be made publicly available, (EFSA, 2013).

The case studies on mercury, nuclear accidents, leaded petrol, mobile phones, BPA and bees, have shown that there can be significant divergence in the evaluations of the same, or very similar, scientific evidence by different risk assessment committees. It is often not clear from their published reports why this is so. It would be helpful if each risk assessment report explained the committee's choice of paradigms, assumptions, criteria for accepting evidence, weights placed on different types of evidence, and how uncertainties were handled. This would also help reduce the confusion amongst users of such divergent risk assessments when they are faced with very different evaluations of essentially the same evidence. It would also help people to recognise the difference between 'settled fact, majority opinion, legitimate minority view, and unsubstantiated assertions' (Weiss, 2002). Moreover, it is helpful if the sources of finance for the research studies under consideration are made explicit because of the 'funding bias' that has been observed in research on issues such as tobacco, pharmaceuticals, food, BPA, GM products and mobile phones.

The case studies on bees, lead, BPA and nuclear accident risks have shown that the scope and membership of some risk assessment committees have been too narrow, and they have sometimes been dominated by one discipline or paradigm with shared assumptions which are not therefore questioned. Risk assessments can be made more reliable if they embrace all relevant scientific knowledge and approaches. For example endocrinology currently brings new insights into hormonally active biological systems that complement conventional toxicology. Toxicity test methods and risk assessments can benefit from more recent yet reliable scientific knowledge emerging from academic research fields.

The case studies also show that toxicity tests designed for acute effects are unlikely to be relevant to chronic effects, and that novel technologies, such as systemic pesticides that replace sprayed pesticides or new chemical compounds replacing earlier ones, usually need novel risk assessments.

The value of being transparent about what is known and not known and about uncertainties and disagreements is equally pertinent. Scientific conclusions should not be portrayed as if there is consensus when there is not. Science by its nature progresses by building on critical appraisal. Several cases show that disagreement can be helpful to decision-makers with a broader picture of the

alternative directions and options available before making a decision.

The whole process of risk analysis which includes risk assessments, risk management and risk communication, would benefit from the involvement of stakeholders, particularly when framing the risk assessment and identifying options for risk management. This is illustrated in Ch. 27 on the precautionary principle.

Foster cooperation between business, government and citizens

An element that is often missing from innovation policies and practice is the recognition that innovation should be considered as a means, not an end in itself, and desirable to the extent that it improves human health and well-being while maintaining ecological resilience. Policy formulation should start from these premises and from a broader concept that includes not only technological innovation but also non-technological, social, institutional, organisational and behavioural innovation (van den Hove et al., 2012).

In this framework, governments have at least three roles: first, providing direction by putting in place smart regulations and consistent market signals; second, ensuring that the distributional consequences of innovations are balanced between risks and rewards across society; and third, fostering a diversity of innovations so that the wider interests of society take precedence over narrower interests.

Numerous case studies show that decisions to act without precaution often come from businesses. There are, however, several impediments to businesses acting in a precautionary manner, including a fundamental economic focus on creating and increasing short-term economic value for shareholders. There are also a number of psychological factors involved that lead to a so-called 'ethical blindness' or a 'self-serving bias' whereby people largely (and often unconsciously) tend to interpret ambiguous situations in their own interests.

This report reveals interesting parallels between older case studies and fast emerging issues such as nanotechnologies, genetically modified crops, new chemicals, and the possible link between brain tumours and non-ionising radiation from mobile phones. For example, only a very small number of actors were involved in making strategic decisions about lead in petrol in the USA in 1925 yet the technology spread all around the world before being phased out some 60 years later. With issues such as GMOs in food and energy options for a low carbon future, only a relatively few actors are involved in choosing innovation pathways that will shape the future of agriculture and energy supply and use for many decades.

Governments and businesses could collaborate more with citizens and civil society on publicly disclosing and analysing the potential value conflicts entailed in acting on early warning signals. Public disclosure and a culture of transparency and open discussion can in turn promote positive business attitudes and innovations. As stressed above, in many cases, accurate determination of risk is difficult and open to disagreement, making engagement, openness and transparency all the more important.

Involving the public can also help in choosing between those innovation pathways to the future (WBCSD, 2010; EC, 2011; WBGU, 2012); identifying and prioritising relevant public research (e.g. Diedrich et al., 2011); providing data and information from other knowledge holders — including NGOs, lay observers and citizens — in support of monitoring and early warnings; improving risk assessments; identifying and considering both alternatives to potentially hazardous agents and the unintended consequences of both actions and inactions on such agents; striking appropriate trade-offs between innovations and plausible health and environmental harms; and, making decisions about risk-risk trade-offs, such as the health benefits of consuming fish which contains mercury and PCBs. In particular, a feature of the studies is the top-down nature of innovations — the history of antibiotics in animal feed and lead in petrol, for example, show how a very small number of people can take decisions which have a major impact on millions. The public should help shape the future, including helping to choose strategic innovation pathways, for example, to sustainable agriculture and low impact renewable energy systems, by 2050.

The case studies also illustrate that there is often a lack of public accountability and access to the private research on which public protection authorities rely. Such access would help to increase independent verification of data submitted for licensing and would increase public trust in the regulatory authorities at a time when such trust in elites is very low.

Information and communications technologies (ICT) and their role in transforming social behaviour can help to engage the public on these issues. ICT has spawned a wide range of new collaborative

tools and approaches, which, as we saw above, are already transforming the dynamics of governance and innovation, fostering two-way interactions, and which can be used to support a more diverse approach to engaging with citizens. Less positively, ICT developments and access to knowledge may be building barriers to collaboration by fostering more hectic interactions and competition in the pursuit of enhanced productivity, less face-to-face contact, and less space for thinking through possible solutions to complex realities. Creating the space for more deliberative thinking and innovation could contribute to more collaborative problem solving.

For public engagement to be effective there needs to be adequate procedures for identifying and including the relevant stakeholders and public interest groups and for the provision of adequate educational and financial resources to enable such groups to play an effective role. Public engagement can be encouraged and supported by substantially improved and simpler access to relevant data and information, building on the provisions of the Aarhus Convention and national freedom of information laws. Business concerns about confidentiality and competitiveness can be overcome through judicious use of information technologies to manage access rights while maintaining transparency on how such information has been used and the insights drawn.

Today there are large imbalances within publicly financed research between product development and the study of potential hazards, an imbalance that seems to repeat the histories of better-known hazards. In Europe for example, in the period 2002–2013, about 1 % of the total amount that the EU Framework Programmes of Research and Development allocated to developing products from nanotechnologies, biotechnologies and ICT was spent researching their potential hazards. Research carried out by private industry may well show a similar imbalance, but data is not easy to obtain.

Correcting this imbalance between researching innovations and their applications, and anticipatory researching of potential hazards posed throughout their life cycle (production, use, recycling and disposal) can help avoid unequal distribution of costs and benefits further down the line and support a better public acceptability of such technologies.

Correct market failures using the polluter pays and prevention principles

When evidence of initial harm emerges, the costs of such harm need to be internalised into the prices of polluting products, via taxes and charges, in line with the polluter pays principle. The revenues could be devoted partly to stimulating research into less hazardous alternatives, as was the case in the US with CFCs, and partly to reducing taxes and charges on labour.

The pollution taxes/charges would rise or fall in line with knowledge about increasing/decreasing harm and this would help to level the market playing field for innovative alternatives to the harmful products that are otherwise subsidised by the external costs of their pollution. Tax shifts from labour to pollution and inefficient use of resources bring other benefits such as increased employment, a stimulus to innovation and a more efficient tax system (EEA, 2011b and 2011c).

More realistic market prices, that reflect the true economic, environmental and social costs, can help encourage more sustainable behaviours by governments, businesses and citizens. More broadly, firms and governments need to extend their accounting systems beyond economic and financial capital considerations to incorporate the full human and natural capital impacts of their activities, building on developing practices worldwide (UN, 2012; EEA, 2011d; Puma, 2011).

Many case studies also demonstrate the long time lags between evidence of harm and the additional injustice and time of forcing victims to pursue their case through civil compensation claims. In the case of Minamata this took over 50 years. Prompt and anticipatory no-fault compensation schemes for victims of harm and damage to ecosystems could be set up and financed in advance of potential harm by the industries that are producing novel and large-scale technologies, thereby helping to correct this market failure. These schemes increase incentives for innovating companies to carry out more *a priori* research into the identification and elimination of hazards.

Precedents exist for such schemes in some countries, for example for nuclear accidents, oil spills, some radiation exposures, and some environmental liability laws, including contamination by GM crops of adjacent non-GM farms. Within the schemes there needs to be provision for penalising gross negligence, which under a tort system justifies punitive damages. Consideration also needs to be given to the use of anticipatory liability bonds by innovating companies so as to increase their incentive to minimise hazards and to provide adequate funds to compensate those who may suffer from any harm that may arise from their

products. Re-insurance schemes are also playing a role in helping to anticipate long tail liabilities from emerging technologies.

Attributing responsibility and sometimes negligence to corporations and others active in the history of hazards has relied mainly upon evidence uncovered by the legal processes of document discovery in civil compensation cases. The further use and development of freedom of information laws and the Aarhus Convention could provide a speedier means of accessing documented history. This will be even more necessary if no-fault administrative schemes replace some civil compensation cases.

Governance of innovation and innovation in governance

This chapter opens with a picture of unprecedented global change and interdependence. Such change provides many benefits to societies but also exposes them to more shocks and surprises. Scientific and technological innovations proceed apace, more often than not on trajectories that exacerbate risks and threats. At the same time, those researching and developing technological innovations often fail to acquire relevant existing knowledge from other disciplines. Governments tend to use structures and methods from the past to monitor the potential hazards of future technologies, rather than implementing more advanced, flexible and relevant approaches.

Failures, such as those presented in the two volumes of *Late lessons from early warnings*, provide numerous valuable insights, yet it appears that memories fade quickly. Typically, a hazardous event generates a sense of urgency and enthusiasm for strengthening preparedness systems, initiating research and implementing long-term monitoring, and heavy expenditure often follows. In the aftermath of an event, relevant authorities elaborate ambitious plans and launch works, but lessons are soon forgotten. After some time without adverse events, willingness to invest in risk research, long-term monitoring etc. decreases sharply and projects are downscaled or suspended. Chernobyl and Fukushima are cases in point.

This cycle of events is termed the 'hydro-illogical cycle' in the case study on floods but could perhaps be called the 'homo-illogical cycle' as it seems to be a recurrent pattern for humankind, which is found across many cultural, political, social and economic systems. Despite its prevalence, this pattern need not be inescapable. Humans can learn, change and transform and there is enormous potential in human creativity and its capacity to inspire cultural, social, political, institutional, organisational and behavioural innovation, beyond 'mere' technological innovation. If, as Plato said, necessity is the mother of invention, then the crises we are facing create a level of necessity that will hopefully engender the needed innovations.

Crucially, governance systems also need to better recognise the value conflicts that are underpinning all societal and environmental issues. They are unavoidable and are even desirable as they are constitutive of the human condition. What is often missing is the institutional space to have a much more systematic, and non-judgmental, analysis of such conflicts so that they can be made explicit, enabling policymakers and other actors to start working together on the problems along the lines described in this chapter.

Of course such analysis already takes place (in part) in some quarters — examples include some parliamentary commissions and non-governmental organisations — but it is not sufficiently systematic and does not always focus on value conflicts. There could be merit in establishing a place in formal institutional frameworks where such value conflicts (and consequent conflicts of interests) could be analysed and proposals offered for their resolution.

The ideas for the governance of innovation and innovations in governance presented in this chapter will remain at the level of good intentions unless they are translated into institutional arrangements and practices. This is the task that lies ahead.

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In memory of Masazumi Harada, 1935–2012

Masazumi Harada, a physician involved for many years in the study of the mercury poisoning Minamata disease, died in June 2012 of acute myelocytic leukemia at his home in Kumamoto City. He was 77.

Harada conducted medical examinations on the disease's sufferers for the first time in the summer of 1961 in Minamata city in Kumamoto Prefecture while he was a student at Kumamoto University's graduate school.

Shocked by their miserable lives, Harada devoted himself to the study of the disease from that time. Harada published a thesis on congenital Minamata disease in 1964. The work had a significant impact as it disproved the conventional belief at the time that the placenta does not pass poisons. He received an award from the Japanese Society of Psychiatry and Neurology for the thesis in 1965.

He then established the Open Research Center for Minamata Studies at the university in 2005, becoming the center's head. He continued to lead the disease's research from non-medical perspectives as well. Harada visited Brazil, China and native Indian communities in Canada to discover those suspected of suffering from the disease.

Author of many books, Harada wrote 'Minamata Byo' (Minamata Disease), which raised awareness on the issue around the world.

Dr. Masazumi Harada first came to Asubpeeschoseewagong (Grassy Narrows) and Wabaseemoong (White Dog) First Nations in Canada in the early 1970s. Harada's death came at the end of River Run 2012, five days of actions by members and supporters of Grassy Narrows in Toronto, who are seeking to have Minamata disease recognized in Canada and Ontario. Harada's final report for the Grassy Narrows community was released on 4 June 2012 after 30 years of research, showing mercury deposited in the river by the Dryden paper mill in the 1970s is impacting those who were not yet born when the dumping ceased.

In memory of Poul Harremoës, 1934–2003

Poul Harremoës was a key player in environmental issues in Denmark and internationally for more than 30 years until his death, at 69, in 2003. In that time, those who worked closely with him benefited from a continuous, almost daily flow of excellent ideas for new research projects.

He was a member of the Danish Pollution Council, which prepared the first framework national law on environmental protection and advised on the establishment of a Ministry of Environment from 1971. He was a key participant in numerous settings, including the first Scientific Committee of the European Environment Agency from 1995.

He had a civil engineering degree from the Technical University of Denmark. He specialised early on in geo-technics and constructed dams on the Faroe Islands. While teaching geo-technics he wrote a textbook that was used for more than 40 years. However, he was able to quickly change his research direction and develop new areas of excellence. So, for example, he got a grant to study at Berkeley, California, from where he received a M.Sc. degree in environmental engineering.

In 1972, he became professor in environmental engineering at the Technical University of Denmark where he originally worked with wastewater discharge to the sea and the biological processes of wastewater treatment. He became a world leading scientist in the theories of biofilms for removal of organics and nitrogen from wastewater before turning to sewer design and modelling. In 2000, Poul was awarded the *Heineken prize for Environmental Sciences* for his contributions to the theory of biofilm kinetics in relation to biological waste water treatment and for his successful organisation of the international scientific community in water pollution research and control.

As a result of his work with sewers and storm water he went into the area of risk analysis and the role of the precautionary principle. In a short time he became an international expert in this field and was highly demanded for lectures in all parts of the world. A key outcome of his interest was his contributions as chairman of the editorial team for the first volume of *Late lessons from early warnings* published in 2001.