Late lessons from early warnings for nanotechnology

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A new technology will only be successful if those promoting it can show that it is safe, but history is littered with examples of promising technologies that never fulfilled their true potential and/or caused untold damage because early warnings about safety problems were ignored. The nanotechnology community stands to benefit by learning lessons from this history.

Nanotechnology is the latest in a long series of technologies that have been heralded as ushering in a new era or even the next industrial revolution. Since 2001, nanotechnology has grown from little more than a gleam in the eyes of researchers to a technology projected to be worth $2.6 trillion in manufactured goods in 2014[1].

So as new nanomaterials move from the lab to the marketplace, have we learnt the lessons of past technologies, or are we destined to repeat the mistakes made with previous technologies? In 2001 an expert panel commissioned by the European Environment Agency (EEA) published a report, *Late Lessons from Early Warnings: The Precautionary Principle 1896–2000*, which explored 14 case studies, all of which demonstrated how not heeding early warnings had led to a failure to protect human health and the environment[2].

Covering topics as diverse as asbestos, chlorofluorocarbons, non-ionizing radiation and 'mad cow disease', the EEA report examined the delay between the emergence of scientific evidence of harm and action being taken to reduce risks in each case. The expert group identified 12 "late lessons" (see Box 1) on how to avoid past mistakes as new technologies are developed. These lessons bear an uncanny resemblance to many of the concerns now being raised about various forms of nanotechnology.

A comparison between the EEA recommendations and where we are with nanotechnology shows we are doing some things right, but we are still in danger of repeating old, and potentially costly, mistakes. This commentary explores these 12 lessons in the context of nanotechnology.

LESSONS 1–3: HEED THE 'WARNINGS'

According to the EEA report "No matter how sophisticated knowledge is, it will always be subject to some degree of ignorance [that is, inevitable surprises, or unpredicted effects]. To be alert to — and humble about — the potential gaps in those bodies of knowledge that are included in our decision making is fundamental."

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Perhaps more than any preceding technology, the early development of nanotechnology has been characterized by discussions of potential risks. Such discussions have always been an integral part of the government-led National Nanotechnology Initiative (NNI) in the US, for example, while a report published by the Royal Society and Royal Academy of Engineering in the UK in 2004 emphasized the need to address uncertainties regarding the risks of nanomaterials[3]. Currently, most economies investing in nanotechnology pepper discussions about future directions in research with questions concerning potential risks — and how to manage them.

However, despite some moves to respond to ignorance and uncertainty rather than simply discussing them, coordinated action seems slow in emerging. The EEA report recommends looking out for "warning signs" such as materials that are novel, biopersistent, readily dispersed or bioaccumulative, and/or materials that lead to irreversible action (for example, thousands of mesothelioma caused by the inhalation of asbestos dust).

These warning signs are clearly relevant to many nanomaterials, some of which have novel properties, are capable of being incorporated in highly diverse products, may be transported to places in new ways, and may be designed to be persistent. Too little is known to predict the environmental fate of nanomaterials, and feasible documentation of environmental dispersion through monitoring is not expected in the short term[4]. The extent to which specific nanomaterials are bioaccumulative or lead to irreversible impact is largely unknown, but the current state of knowledge suggests that the potential exists for such behaviour under some circumstances[5].

The global response to these warning signs has been patchy, with governments being slow to gather essential data on production and use patterns and personal protection equipment. Arguably, efforts have been better than those seen with many technologies but they are still far from ideal.

A number of reports make specific recommendations on developing responsive research strategies[6–8]. Calls for proposals in the European seventh framework programme reflect some of these recommendations, and a number of countries are beginning to develop integrated environment, health and safety (EHS) research programmes, such as the cross-agency risk-research strategy[9] recently published by the NNI. However, there are still critical gaps[10] in our knowledge that are not being addressed by existing EHS research programmes.

Research strategies that target recognized areas of uncertainty should be relatively easy to develop as the critical questions to be addressed are generally agreed upon[11]. But the EEA report highlights the dangers of missing important areas entirely because the right questions have not been identified, leading to "blind spots" in our understanding. The report cites the widespread use of antimicrobials as growth promotors in food animals, the use of methyl tert-butyl ether as an additive to gasoline and the use of tributyltin as a biocide as three examples where conventional thinking resulted in the adverse effects of substances not being recognized until it was too late.

LESSONS 4 AND 11: FACILITATE LEARNING

Even when research throws up useful information, it can be ignored and overlooked through what the EEA authors call "institutional ignorance". They cite cases where regulators made inappropriate appraisals because of the blinkers imposed by their specific disciplines — such as the preoccupation of medical clinicians with acute effects when dealing with radiation and asbestos. There is a real danger of similar errors being made with nanotechnology, which crosses many fields of expertise. One needs to draw on physics, chemistry, computer sciences, health and environmental sciences to understand nanomaterial properties and risks[12]. Consequently, a number of multidisciplinary centres for nanoscience and nanomanufacturing have been established around the world, but only a few of these address health, environmental, and social aspects. Setting aside resources to create an infrastructure that gets people working together across disciplines is critical[13].

Interdisciplinary obstacles also affect regulatory oversight in decision-making[2]. In a recent discussion on the regulation of nanomaterials, the US Environmental Protection Agency (EPA) appears to be constrained by a world view rooted in chemistry, stating that the sole factor that determines whether a nanomaterial is legally classified as 'new' depends on whether it has a unique molecular identity[14]. However, it is now clear that characteristics other than molecular identity — such as particle size and shape — can affect exposure and response to engineered nanomaterials[4].

LESSONS 5 AND 8: STAY IN THE REAL WORLD

The assertion made by the EEA panel that "it is often assumed that technologies will perform to the specified standards. Yet real life practices can be far from ideal" echoes claims made of nanotechnology. In 2006, Rick Weiss of *The Washington Post* visited a nanomaterial company expecting to see a high-tech work environment. Instead, he found that "the future looked a lot like the past with men in grease-stained blue coats […] story-tall spray-drying machines […] noisy milling operations and workers with face masks covered by a pale dust stemming from emptying buckets of freshly made powders"[15].

It is often assumed that nanotechnology will be conducted with small quantities of material, within sealed processes. Reality can be very different and the past tells us that persistent substances used in closed settings (like PCBs) will eventually end up in the environment. Moreover, there is evidence that the research and development community is entrenched in the philosophy that 'basic' research will ultimately solve real-world problems through a one-way process of knowledge diffusion, and that they do not need to worry about EHS issues. This is a mistake in our view. Clearly, basic researchers — those working on technology for applications in the real world — as well as the EHS community need to be involved in informing policy decisions. According to the EEA, this includes making use of the information that workers and users can bring to regulatory appraisal process. Such a process needs as much critical appraisal as specialist knowledge, so non-specialists intimately involved with a technology can bring unique insight to the table.

Nanotechnology is complex, and it could be argued that non-experts have little to contribute to its safe development and use at this point in time. Yet it is frequently those who make and use a product that have some of the clearest ideas about what is important and what works and what does not. This insight often goes beyond idealized text-book knowledge. Moreover, these are often the people who have the greatest stake in the technology being as safe as possible[16].

LESSONS 6 AND 9: CONSIDER WIDER ISSUES

Concerns have often been raised that speculation on risks overshadows real benefits, or that an unbalanced

Box 1 The 12 lessons outlined by the EEA[2]

1. Acknowledge and respond to ignorance, uncertainty and risk in technology appraisal.
2. Provide long-term environmental and health monitoring and research into early warnings.
3. Identify and work to reduce scientific 'blind spots' and knowledge gaps.
4. Identify and reduce interdisciplinary obstacles to learning.
5. Account for real-world conditions in regulatory appraisal.
6. Systematically scrutinize claimed benefits and risks.
7. Evaluate alternative options for meeting needs, and promote robust, diverse and adaptable technologies.
8. Ensure use of 'lay' knowledge, as well as specialist expertise.
9. Account fully for the assumptions and values of different social groups.
10. Maintain regulatory independence of interested parties while retaining an inclusive approach to information and opinion gathering.
11. Identify and reduce institutional obstacles to learning and action.
12. Avoid 'paralysis by analysis' by acting to reduce potential harm when there are reasonable grounds for concern.

promotion of possible benefits will prevent potential risks from being critically scrutinized. Nanotechnology is at a similar position to both of these scenarios. 'Pros' include economic benefits, improved materials, reduced use of resources and new medical treatments[3,17,18], whereas 'cons' mainly revolve around worker health and end-of-life environmental impacts (for example, comparisons have been made between nanoparticles and ultrafine particles in the atmosphere, which are known to cause health problems[3,7,11]).

> The global response to these warning signs has been patchy.

It is generally hard to evaluate whether proclaimed pros and cons are valid both in the short and the long term. However, the process of determining more likely scenarios is vital to the future development of sustainable nanotechnologies. As we emerge from the first flush of nano-enthusiasm and begin the hard work of translating good ideas into viable products, this is a lesson that is more relevant than ever if an appropriate balance between benefits and risks is to be struck.

If proclaimed 'pros' do not materialize in the foreseeable future, despite heavy public investments, or if projected 'cons' are not investigated but later prove to be significant, decision-making processes will be undermined, and public trust compromised.

A key feature of the public reaction to the emerging evidence for bovine spongiform encephalopathy (BSE) in the late 1980s was the surprised revulsion that cows and other ruminants were being fed on offal and bodily wastes. The EEA panel speculates that accounting for wider social values at an earlier stage might have limited the scale of BSE problems. The extent to which societal interests and values can avoid real risks with emerging technologies is debatable. Yet these interests and values influence what is considered acceptable, and consequently what is accepted — or rejected. Nanotechnology is proclaimed to have a tremendous potential to address major global challenges like cancer, renewable energy and provision of clean water. Yet precisely because of the widespread applications of nanotechnology, citizens around the world are as much stakeholders in the technology as the governments and industries promoting it. But so far their engagement has been very limited.

LESSON 7: EVALUATE ALTERNATIVE SOLUTIONS

This lesson may simply be summed up by saying "don't become so enamoured by a new technology that you are blinded to alternative solutions". Past lessons have shown there is a tendency to justify heavy investment in a new technology by promoting its application to every conceivable problem — with the result that alternatives are insufficiently scrutinized, and the most appropriate solution not always selected.

Although nanotechnology is diverse and widely applicable, this would seem a potential pitfall as the number of nanoscale solutions looking for a problem continues to grow. And with international nano-fever running high, everyone wants to be at the forefront of the nanotechnology revolution. In many cases, nanotechnology will provide the means to overcome challenges, but the lesson to be learnt is to find the best solution to a given problem, rather than squeeze a solution out of the latest technology. And this means that, in some cases, although nanotechnology could be used, it will be questionable whether it should be used.

LESSON 10: RETAIN REGULATORY INDEPENDENCE

The EEA panel found "evidence in the case studies that interested parties are often able to unduly influence regulators. As a result, decisions that might reasonably have been made on the basis of available evidence were not taken." In many countries, the organizations responsible for overseeing the development of nanotechnologies through research and development are the same as those that are addressing health and environmental issues, and many campaigners are uncomfortable with this situation.

In a recent testimony to the US Congress House Committee on Science and Technology, Richard Dennison of the Environmental Defense Fund, a non-profit environmental campaign group, wrote that "we have become convinced that a conflict of interest has arisen from the decision to house within NNI the dual functions of both seeking to develop and promote nanotechnology and its applications, while at the same time aggressively pursuing the actions needed to identify and mitigate any potential risks that arise from such applications. That conflict of interest is both slowing and compromising efforts by NNI and its member agencies and departments to effectively address nanotechnology's implications."[19]

Although an integrated approach to understanding the risks and benefits of nanotechnology is critical, when the promoters of nanotechnology — whether government or industry — have a strong influence on oversight, independent regulatory decision making becomes compromised. Perhaps more insidiously, research and development decisions end up being influenced by what will ultimately promote the technology, rather than what will protect producers, users and the environment.

LESSON 12: AVOID PARALYSIS BY ANALYSIS

In the face of uncertainty, a frequent response is to call for more research before action is taken. Yet as the EEA panel note, "Experts have often argued at an early stage that we 'know enough' to take protective action"[2]. Deciding when to act and when to refrain from taking action is often a difficult call. Good policy depends on identifying the right balance between information and action while keeping the end-point (preventing harm) in mind, and building in review procedures for course corrections.

It is over 15 years since first indications of nanomaterial harm were published[20], and in the intervening time, an increasing body of literature has been developed on how nanomaterials interact with people and the environment[21]. Yet many governments still call for more information as a substitute for action, and there are indications that understanding and managing the risks of engineered nanomaterials is being paralyzed by analysis. It is clear that more scientific information is needed, but we need to act on what we know now to enable industry to produce and market nanotechnology-enabled products that are as safe as possible. Engineered nanomaterials are already on the market, and in some cases the risks are poorly understood and ineffectively regulated. Applying current knowledge to nanotechnology oversight will not solve every problem, but it will help prevent basic mistakes being made while the knowledge needed for more effective oversight is developed.

One way to facilitate decision making on nanomaterials may be to develop design criteria to identify which nanomaterials are of higher or lower concern owing to their intrinsic properties, use or exposure characteristics. Furthermore, a thorough consideration of health and safety implications at the design phase of a nanomaterial, including a consideration of possible safer production methods and alternatives to the material, will facilitate decisions because economic interests are not fully entrenched at that point.

SO HAVE WE LEARNT THE LESSONS?

Although the EEA panel was writing about existing technologies and some of the 12 lessons learned are not directly applicable to emerging technologies, many of the lessons are directly relevant to nanotechnology. Yet the picture is not as bleak as it could be. Although progress towards developing sustainable nanotechnologies is slow, we do seem to have learnt some new tricks: asking more critical questions early on; developing collaborations that cross discipline, department and international boundaries; beginning the process of targeting research to developing relevant knowledge; engaging stakeholders; and asking whether existing oversight mechanisms are fit for purpose.

But are we doing enough? The question seems not to be whether we have learnt the lessons, but whether we are applying them effectively enough to prevent nanotechnology being one more future case study on how not to introduce a new technology. Despite a good start, it seems that we have become distracted because nanotechnology is being overseen by the same government organizations that promote it; research strategies are not leading to clear answers to critical questions; collaborations continue to be hampered by disciplinary and institutional barriers; and stakeholders are not being fully engaged. In part this is attributable to bureaucratic inertia, but comments from some quarters — such as "risk research jeopardizes innovation" or "regulation is bad for business" — only cloud the waters when clarity of thought and action are needed.

Many governments still call for more information as a substitute for action.

If we are to realize the commercial and social benefits of nanotechnology without leaving a legacy of harm, and prevent nanotechnology from becoming a lesson in what not to do for future generations, perhaps it is time to go back to the classroom and relearn those late lessons from early warnings.

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