Part C Emerging issues

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Contents — Part C

18 Late lessons from Chernobyl, early warnings from Fukushima 464
18.1 Introduction 465
18.2 Chernobyl 465
18.3 Fukushima Dai-ichi 469
18.4 Nuclear liability 477
18.5 Nuclear risk: probabilistic risk assessment and beyond design-based accidents ... 479
18.6 Conclusion 480
References 481

19 Hungry for innovation: pathways from GM crops to agroecology 490
19.1 Introduction 491
19.2 Innovation: what kinds and for whom? 493
19.3 GM crops as a top-down path out of poverty and hunger 495
19.4 The bottom-up path towards sustainable farming 503
19.5 Case example: Contrasting top-down and bottom-up innovation solutions to water stress 506
19.6 Conclusions 507
19.7 Lessons learned 509
References 510

20 Invasive alien species: a growing but neglected threat? 518
20.1 Introduction 519
20.2 The difficulty of defining invasive alien species 519
20.3 Emergence of awareness of an old problem 520
20.4 A new discipline with its own approaches and research agenda 522
20.5 A wealth of initiatives worldwide 523
20.6 Obstacles to a common understanding 525
20.7 The limits of governance on the complex issue of IAS 528
20.8 Applying the precautionary principle to invasive alien species 529
20.9 Addressing invasion pathways: a late engagement with the stakeholders 530
20.10 Lessons learnt on invasive alien species: towards more transdisciplinarity in a rapidly changing world? 531
References 535

21 Mobile phone use and brain tumour risk: early warnings, early actions? 541
21.1 Introduction 542
21.2 The Hardell group studies — 1999–2011 542
21.3 First Hardell group study on mobile phone use and brain tumours — 1999 542
21.4 Second and third Hardell group studies — 2002–2006 543
21.5 Fourth Hardell group study — 2010 544
21.6 Some Swedish responses to the Hardell group studies 545
21.7 A pooled analysis of the Hardell group studies 545
21.8 Risks to children 546
21.9 The Interphone study 2000–2010: disagreements and delays 549
21.10 Some reviews and discussions of the Hardell group and Interphone studies 550
21.11 IARC evaluation of the carcinogenicity of RF-EMFs 2011 552
21.12 Some responses to the IARC conclusion 552
21.13 Some further studies published since the IARC conclusion 553

21.14 Need for monitoring long term trends in country wide nervous system tumours ..555
21.15 Concluding remarks 555
21.16 Epilogue 556
References.....557

22 Nanotechnology — early lessons from early warnings 562
22.1 What is nanotechnology and what are nanomaterials? 563
22.2 Development of nanotechnology and nanomaterials 565
22.3 Current production and application of nanotechnology and nanomaterials.....565
22.4 Signs of early warnings 566
22.5 Current (lack of nano-specific) regulation for nanomaterials 569
22.6 Late lessons from early warnings for nanotechnology.....574
22.7 So have we learnt the lessons?.....579
22.8 Precautionary strategies for nanomaterials.....581
References 584

18 Late lessons from Chernobyl, early warnings from Fukushima

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The nuclear accident at Fukushima in Japan occurred almost exactly 25 years after the Chernobyl nuclear accident in 1986. Analysis of each provides valuable late and early lessons that could prove helpful to decision-makers and the public as plans are made to meet the energy demands of the coming decades while responding to the growing environmental costs of climate change and the need to ensure energy security in a politically unstable world.

This chapter explores some key aspects of the Chernobyl and Fukushima accidents, the radiation releases, their effects and their implications for any construction of new nuclear plants in Europe. There are also lessons to be learned about nuclear construction costs, liabilities, future investments and risk assessment of foreseeable and unexpected events that affect people and the environment.

Since health consequences may start to arise from the Fukushima accident and be documented over the next 5–40 years, a key lesson to be learned concerns the multifactorial nature of the event. In planning future radiation protection, preventive measures and bio-monitoring of exposed populations, it will be of great importance to integrate the available data on both cancer and non-cancer diseases following overexposure to ionising radiation; adopt a complex approach to interpreting data, considering the impacts of age, gender and geographical dispersion of affected individuals; and integrate the evaluation of latency periods between exposure and disease diagnosis development for each cancer type.

Given the degree of uncertainty and complexity attached to even the most tightly framed and rigorous nuclear risk assessment, attempts to weight the magnitude of accident by the expected probability of occurrence have proven problematic, since these essentially theoretical calculations can only be based on sets of pre-conditioning assumptions. This is not an arcane philosophical point but rather a very practical issue with significant implications for the proper management of nuclear risk. With its failure to plan for the cascade of unexpected beyond design-base accidents, the regulatory emphasis on risk-based probabilistic assessment has proven very limited. An urgent reappraisal of this approach and its real-life application seems overdue.

Whatever one's view of the risks and benefits of nuclear energy, it is clear that the possibility of catastrophic accidents and consequent economic liabilities must be factored into the policy and regulatory decision-making process. In the context of current collective knowledge on nuclear risks, planned pan-European liability regimes will need significant re-evaluation.

18.1 Introduction

The chapter on climate change has demonstrated the need to plan for a low-carbon energy future, and an ambitious long-term target of 80–95 % reductions in greenhouse gases by 2050 has been set by the European Union (EU) (EU, 2011). Although some scenarios suggest that future energy demands could be met without nuclear electricity production ([1]) (IPPC, 2011; SRU, 2011b), others suggest greater reliance on new nuclear capacity in Europe ([2]), as well as Asia (Yi-chong, 2011).

At present, nuclear energy is used in 30 countries and Taiwan, producing roughly 13 % of the world's commercial electricity, and currently 14 countries and Taiwan are in the process of planning the building of new nuclear capacity. There are 435 nuclear power reactors in operation around the world — at the peak of nuclear generation in 2002 there were 444 — of which 189 are in pan-Europe and the Russian Federation, comprising about one third of the world's 146 civil reactors, with France alone generating close to half of the EU's nuclear production from 58 plants (Schneider et al., 2011).

With mounting public concern and policy recognition over the speed and pace of low carbon energy transition needed to mitigate climate change, nuclear power has been reframed as a response to the threat of global warming. Proponents conclude that nuclear provides a secure supply of low carbon base-load energy, safe in operation and powered by a reliable source of uranium supplies (IAEA, 2000; EDF, 2012; NIA, 2012; WNA, 2012). However, at the heart of the question of nuclear power are differing views on how to apply foresight, precaution and responsibility in the context of the possibility of accidents.

18.2 Chernobyl

On the 26th April 1986 an explosion at the Chernobyl Nuclear Power Plant No. 4 in Northern Ukraine resulted in widespread cross-boundary atmospheric pollution by fission-product radioisotopes. Following what is understood to have been a misconceived reactor experiment, a positive void coefficient caused reactivity excursion, resulting in a steam explosion that destroyed the plant. Over the six days of open containment 30–60 % of the Chernobyl reactor core's fission products were released to the atmosphere, 6.7 tonnes of material from the core. This material was projected high into the atmosphere, spreading radioactive isotopes over more than 200 000 square kilometres (km^2) of Europe (UNDP, 2002). In response, the authorities evacuated and subsequently relocated around 115 000 people from areas surrounding the reactor; after 1986, a further 220 000 people from Belarus, the Russian Federation and Ukraine were re-settled (UNSCEAR, 2008).

Each day some 3 500 workers enter the 30 kilometre exclusion zone, established by the Ukraine, to monitor, clean and guard the site, where remediation work is likely to continue until 2065 — although less than half the resources needed to fund the remediation have been raised, and the completion date has slipped by a decade. The work includes managing the long-term storage of waste from Reactor 4, and more than 20 000 spent fuel canisters from the site's other reactors. Significant quantities of radioactive waste continue to be generated — partly due to ongoing flooding in some areas of the waste-storage buildings and Reactor 4's turbine hall, forcing the pumped discharge and on-site storage of around 300 000 litres of radioactively contaminated water per month (Peplow, 2011).

18.2.1 Post-Chernobyl meta-analyses

Whilst it is outside the remit of this discussion to rehearse in detail the very broad literature on radiation risk epidemiology, it is sufficient to note that the precise estimation of acute and long-term health effects as a result of the Chernobyl accident remains problematic and subject to ongoing critique. This is because epidemiological evidence on health impacts is contradictory and conflicting. The link between radiation and the aetiology of cancer and leukaemia is well established — but the debate continues about the risks of those diseases, in particular childhood cancer and leukaemia, from Chernobyl releases and in the vicinity of other operational nuclear installations elsewhere (Box 18.1).

It is therefore unsurprising to see significant differences in the understanding and interpretation

([1]) The German governments Energiekonzept involves a reduction in primary energy consumption by 50 % between 2008 and 2050, a reduction in electricity consumption of 25 %, and a reduction in carbon emissions by 80 % (SRU, 2011a).

([2]) Planning for the same carbon target as the German government, the UK government's National Policy Statement on Energy envisages a doubling of electricity demand by 2050 and a potential trebling of total installed capacity (DECC, 2011). As a result, the policy foresees the construction of a series of new nuclear plants in the United Kingdom.

Box 18.1 Low level radiation epidemiology

There are significant uncertainties associated with the choice of differing models used to interpolate radiation risk between populations with different background disease rates; for the projection of risk over time; for the extrapolation of risks following primarily a single external high dose and a high dose-rate in contrast to cumulative low dose and low dose-rate exposures (ARCH, 2010). Despite this, the analysis of incidence and distribution of disease (epidemiology) remains fundamental to radiation-risk determination and standard setting. Epidemiological investigations ranging from the Japanese atomic bomb life span survivor studies to more numerically and temporally limited studies have provided a weight of evidence about the effects of ionizing radiation on humans. Whilst a range of studies suggests no causal or associative link between routine discharges from operating nuclear plants (Jablon et al., 1991; Yoshimoto et al, 2004; Evrard et al., 2006; COMARE, 2011), this important debate is ongoing.

One of the most significant data sets in this debate comprises a national case-control study, funded and published by the Federal Office for Radiation Protection on behalf of the German Federal Ministry for the Environment and conducted by the German Childhood Cancer Registry on childhood cancer near nuclear installations. This study investigated childhood leukaemia and cancer incidence near nuclear plants from 1980 to 2003, providing evidence of a significant increase in childhood leukaemia and cancer risk near to nuclear plants in Germany (Kaatsch et al., 2007; Kaatsch et al., 2008a; Kaatsch et al., 2008b; Spix et al., 2008). The German Federal Office for Radiation Protection formally confirmed these findings, stating that 'in the vicinity of nuclear power plants, an increased risk of 60 % was observed for all types of childhood cancer, and for childhood leukaemia the risk doubled equaling a risk increase of approximately 100 %' (BfS, 2008). In response, the UK scientific advisory body Committee on Medical Aspects of Radiation in the Environment (COMARE) 14th Report (2011) critiqued the German study, and discounted the findings, noting that COMARE's primary analysis of the latest British data had revealed no significant evidence of an association between risk of childhood leukaemia and living in proximity to a UK nuclear facility (COMARE, 2011). The Committee also pointed to the role of unidentified viral infections rather than radiation exposure in the aetiology of childhood leukaemia near nuclear power plant (Kinlen, 2011).

Subsequently, in early 2012, a further nation-wide case-controlled investigation by Institut Nationale de la Santé et de la Recherche Medicale (INSERM) on behalf of France's nuclear safety research body, Institut de Radioprotection et de Sûreté Nucléaire (IRSN), demonstrated a statistically significant doubling of the incidence of leukaemia near to nuclear plants in France between 2002 and 2007 (Sermage-Faure et al., 2012). However, neither a causal link nor an association between gaseous discharges and ill health were established.

of Chernobyl health effects. The problem may be exacerbated by the nature of previous studies, which have been described as forming a patchwork rather than a comprehensive, structured attempt to delineate the overall health consequences of the accident (ARCH, 2010). Nevertheless, despite differences in the types of exposure, doses, dose rates and applied methodologies, data on the health consequences of the Chernobyl accident add to knowledge collected from atomic bomb victims and from populations over-exposed during nuclear accidents and nuclear weapons testing. Integration of the available data on related health risks gives added value in preparing radiation protection protocols and in the management of subsequent nuclear accidents, such as Fukushima.

Focusing only on Belarus, Ukraine and the Russian Federation, and no other exposed countries and populations, the International Atomic Energy Authority (IAEA) convened the Chernobyl Forum (2005) that predicted a potential total mortality of about 4 000. Discounting the significantly raised childhood thyroid cancer incidence ([3]), the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 2008) found no evidence of increases in overall cancer incidence or mortality rates or in rates of non-malignant

([3]) In Belarus, the Russian Federation and Ukraine nearly 5 000 cases of thyroid cancer have now been diagnosed to date among children who were aged up to 18 years at the time of the accident (WHO, 2006).

disorders that could be related to radiation exposure. Both of these estimates were subject to critical analysis by Yablokov et al. (2006), who suggested a higher death toll as a consequence of the Chernobyl fall-out. Based on Belarus' national cancer statistics, the study predicted approximately 270 000 cancer incidences — of which 93 000 would prove fatal. A follow-up meta-analysis, which included Belarus, Russia and Ukraine, suggested further increased predicted premature deaths as a result of the radioactivity released (Yablokov et al., 2007).

It is worth noting that UNSCEAR (2008) decided not to use models to project absolute numbers of effects in populations exposed to low radiation doses from the Chernobyl accident, because of unacceptable uncertainties in the predictions. Given that UNSCEAR (1993) and IAEA (1996) estimate a total world-wide collective dose of 600 000 person-Sieverts over 50 years from Chernobyl fallout, and the standard risk estimate from the International Commission on Radiological Protection (ICRP, 2005) is 0.057 fatal cancers per Sievert, this suggests an estimate of about 34 000 fatal cancers over that time period (Ramana, 2009). Given the widely accepted linear no-threshold radiation risk model may overstate or understate risks by a factor of two (BIER VII, 2006) — then estimates for post-Chernobyl cancer mortality extrapolation may range from 17 000 to 68 000 over 50 years.

These differences in meta-analysis estimates also obtain around post-Chernobyl leukemia aetiology: Whilst UNSCEAR (2008) suggests that the incidence of leukaemia in the general population, one of the main concerns owing to the shorter time expected between exposure and occurrence compared with solid cancers, does not appear to be elevated, the UK government scientific advisory Committee Examining Radiation Risks of Internal Emitters (CERRIE, 2004) concluded that, in the judgment of a large majority of committee members, it is likely that radioactive fallout from the Chernobyl accident resulted in an increased risk of infant leukaemia in the exposed populations.

In addition, there were immediate deaths of emergency workers and firefighters resulting from acute radiation exposure. Treatment of these people also placed hospital staff and funeral workers at risk of radiation over-exposure (Box 18.2).

18.2.2 Post-Chernobyl cancer risk

The most susceptible populations for thyroid disease development after nuclear overexposure are pre- and post-natally exposed children, young people and women (Shimizu, 1991; Nagataki and Nystrom, 2002; McCarthy, 1997, Prysyazhnyuk, 2007). As both external and internal exposure to ionizing radiation can cause thyroid cancer, similar incidences were detected amongst those exposed in Hiroshima, Nagasaki, and following the Chernobyl accident, with a much higher prevalence in children than adults (Larsen et al., 1982; Pacini et al., 1999). Increased levels of anti-thyroid antibodies, hyper- or

Box 18.2 Acute medical care of Chernobyl radiation casualties

'By May 5, 10 days after the accident, 172 individuals, 47 of them fire fighters, had been admitted Hospital #6 with the most severe form of radiation sickness. All had visible burns, were in severe pain and had little chance of survival. It should be remembered that all medical staff entering the rooms of irradiated patients were also exposed to intensive radiation from victims whom they were supposed to treat. We should express deep gratitude to all personnel, from the reception area, sterile rooms, specialized offices and laboratorie, to dosimeter controllers for their tireless service and sacrifice. As experienced radio-biologists, we understood that some of our patients would not survive — they had received radiation doses of more than 1 000 rad, which resulted in large and deep radiation burns and the penetration of their bodies by significant amounts of radioactive material. Therefore, we planned for their funerals, including the selection of appropriate location(s) and estimates of the necessary depth of tombs to avoid increases in the radiation level above the tomb. We needed to equip vehicles that would transport the dead bodies with strong protection layers quickly so as not to harm the drivers and to avoid radiation pollution between the hospital and the cemetery' (Grigoriev, 2012).

Despite these challenging circumstances it is important to note that, thanks to round-the-clock care over many months by a dedicated team of doctors, and through a wide range of holistic treatments, the lives of many patients with acute radiation sickness were saved (Grigoriev, personal communication, 2012).

hypothyroidism and thyroid cancer have different latency periods after exposure, even at relatively low doses of less than 1 Sv (Nagataki, 1994), and the data from the Chernobyl and atomic bomb victims should be of significance in bio-monitoring exposed subjects following the Fukushima accident.

In recent years, an increased incidence of leukaemia has been described among clean-up workers and the population aged 0–5 years at the time of the Chernobyl accident (Noschenko et al., 2010; Romanenko et al., 2008). Such a trend may continue as the latency period for leukaemia can exceed more than 40 years, as shown for myelodisplastic syndrome (pre-leukaemia) and the related increased risk for acute myeloid leukaemia after the Hiroshima and Nagasaki A-bomb detonations (Iwanaga et al., 2011).

Lactating women may be more susceptible to ionizing radiation, as breast tissue bio-accumulates iodine as part of the physiological process of its accumulation in breast milk. These levels of accumulated radioiodine in breast milk may also increase the risk of thyroid cancer in newborns (Bland et al., 1969; Tazebay et al., 2000; Hatch et al., 2005). This information may prove necessary and significant for breastfeeding sub-populations in cases of increased radioiodine levels. Similar results were shown for breast cancer incidence after Hiroshima and Nagasaki, as the highest dose-specific excess relative risk was among women exposed prior to the age of 20 years (Land et al., 2003), with the latency period for breast cancer development at approximately 10 years for both those affected by the atomic bombs and Chernobyl (Tokunaga, 1979; Pukkala et al., 2006), with raised incidence of breast cancer found among young and pre-menopausal women exposed during the Chernobyl accident.

In order to improve preventive measures following over-exposure to ionizing radiation, it is imperative that the latency period between exposure and disease development be re-evaluated for each cancer type; as the currently approved 10-year latency period of international radiation protection agencies does not seem in accord with data reported for certain solid cancers, with a 4-year latency period reported post-Chernobyl (UNSCEAR, 2008; Ivanov et al., 2009). The question of latency in cancer induction is further complicated through radiation biology discoveries about the underlying complex cellular response mechanisms by which radiation interacts with living organisms (Box 18.3).

18.2.3 Post-Chernobyl non-cancer health consequences

Evaluation of health risks relating to accidental overexposure to ionizing radiation is usually limited to estimations of increased cancer incidence; however, current knowledge of complex interactions of ionizing radiation and living systems demonstrates that in addition to increasing cancer risk, exposure to radiation may disturb a number of other biological pathways. For example, analyses of the Japanese A-bomb survivor Life Span Studies mortality data (1950–1997) show a statistically significant dose-response pattern for death from diseases other than cancer, and these excesses do not seem limited to any particular disease (Preston et al., 2003; Yamada et al., 2004). Disturbance of pathways by ionizing radiation may be modified by age, gender, psychological status of a person (stress) or diet, all of which impact on the final increase of health risk and its duration.

Correspondingly, the Chernobyl nuclear accident also caused non-cancerous diseases, such as cardiovascular and immunological disorders, and cataracts (Hatch et al., 2005; Cardis, 2011). In children exposed to long-term low doses after the Chernobyl nuclear accident, a significant increase of cardiovascular diseases was reported, followed by decreased physical status (Kostenko, 2005). A significant increase in cardiovascular disorders was also recorded among adults (Bebeshko et al., 2007; Eglite et al., 2009), which was compatible with atomic bomb survivor data (Zubovksi and Tararukhina, 1999; Shimizu et al., 2010).

Immunological disturbances have been reported for both clean-up workers and the environmentally exposed population affected by the Chernobyl accident. In children, marked immune disturbances were detected after Chernobyl, with significant differences between directly exposed children and children born to irradiated parents (Baleva et al., 2011). In children residing in the zone 30–90 km from the Chernobyl site, immunological disturbances arising more than 20 years after the nuclear accident are still clinically presenting (Sajjadieh et al., 2009). Additionally, immunological disorders are combined with inflammations and an increased risk of cardiovascular disease in both those exposed to radiation following atomic bomb and the Chernobyl accident (Kusunogi et al., 1999; Hayashi et al., 2003; Kusunoki et al., 2010; Timoshevskiĭ et al., 2011). It has also been suggested that data regarding cataracts in subjects participating in the clean-up and building of sarcophagi in Chernobyl may fail to support the ICRP 60 risk guideline assumption of a

Box 18.3 Genomic instability and the bystander effect

The theoretical underpinning of the biological effects of ionizing radiation is based on sophisticated variants of target theory, such as track structure theory. Target theory stipulates that the biological targets damaged in the cell are relevant to the endpoint: for example, damage to a tumour suppressor gene might lead to cancer. Target theory holds for single locus hereditary disease but there were problems in applying it to somatic cell endpoints such as cancer. However, in 1992 evidence inconsistent with target theory emerged in the form of two effects, genomic instability (Khadim et al., 1992) and the bystander effect (Nagasawa and Little, 1992). Such effects are collectively known as non-targeted effects because the target is large enough to encompass the whole nucleus of the cell, and radiation does not directly affect the damaged cell. Genomic instability is characterised by the acquisition, *de novo*, of various kinds of damage, mostly to DNA, up to several cell generations after the exposure. Damage associated with genomic instability may not be directly caused by the radiation but is a secondary response of the cell to radiation insult. The bystander effect occurs in cells that experienced no radiation events, but are neighbours of cells that have.

These phenomena pose a set of significant research questions for the understanding of the underlying mechanisms involved, and could imply the need for a re-appraisal of the target theory approach, and the emergence of a new theoretical framework for the biological bases of the effects of radiation. Perhaps the most worrying aspect from the public health perspective is the potential for trans-generationally inherited genomic instability. A number of mechanistic hypotheses have been proposed to explain genomic instability (ARCH, 2011), and Baverstock and Karotki (2011) have suggested a further explanatory conceptual framework.

Whilst two European Commission projects, RISC-RAD (http://riscrad.org/) and NOTE (http://www.note-ip.org), specifically directed at obtaining a better understanding of genomic instability, have reported — so far no replacement for the underpinning framework based on target theory has emerged. This may be because, as usual with radiation biology, the picture is complex, especially in distinguishing between the interpretation of results from *in vitro* and *in vivo* studies. Yet more recent work indicates that additional mechanisms may also be important for the understanding of the impact of genomic instability and bystander effects on radiation protection regulation: Mukherjee et al. (2012) suggest that radiation-induced chromosomal instability may also result from inflammatory processes having the potential to contribute secondary damage expressed as non-targeted and delayed radiation effects. Lorimore et al. (2011) conclude that complex multi-cellular interactions resulting from bystander effects may influence carcinogenic susceptibility, with inflammatory processes responsible for mediating and sustaining the durable effects of ionizing radiation. Given that the genotype of each individual is a key determinant of carcogenic susceptibility, then genotype-directed tissue responses may be important determinants of understanding the specific consequence of radiation exposure in different individuals (ibid). One potentially significant implication of these finding is that differing people may have differing responses and susceptibilities to radiation insult.

5-Gy threshold for detectable opacities, but rather point to a dose-effect threshold of under 1 Gy (Worgul et al., 2007; Chumak et al., 2007).

One of the most at risk groups is infants and children (Box 18.4).

Although increased levels of stress and depression have been found in children and teenagers born to exposed parents (Panchenko et al., 2005); in general, post-Chernobyl psychological disturbances, stress, depression and suicides in children and adults have been poorly described. The significance of psychological impacts on survival rates after exposure may prove important, as there has been increased suicide rates among clean-up workers (Rahu et al., 1997).

18.3 Fukushima Dai-ichi

On 11 March 2011, the Japanese Great Easter Earthquake, involving 5 to 10 metres of slip motion on fault zones more than 100 kilometres in length along the Japanese Trench Subduction Zone, struck the east coast of Japan triggering the shut down of 10 operating nuclear power plants. At the time of the earthquake, Fukushima Dai-ichi units 1, 2, and 3 were operating at full power (Marshall and Reardon, 2011). The plants, designed to withstand a maximum 8.2 earthquake on the logarithmic Richter scale, received a seismic shock 9–15 times higher than the design limit (Park, 2011). At the time of the accident, the radiological inventory at risk within the 6 reactor cores comprised 487 tonnes of uranium, of which 95 tonnes include 6 %

Box 18.4 Infants and children: susceptible sub-populations

Children are generally more susceptible to ionizing radiation and other environmental pollutants, and may suffer from life-long health consequences, some of which may be pre-natally determined (EEA, 1999; BCPT, 2008; Fucic et al., 2008). Pathological changes in reproductive function, peri-natal illnesses and mortality were reported several years after the Chernobyl nuclear accident. The birth rate was additionally influenced by migration of the population, use of contraceptives, stress and induced abortions (Kulakov et al., 1993), and a peak in Down Syndrome cases was observed in newborns born in 1987, one year after the Chernobyl nuclear accident (Zatsepin, 2007). New DNA mutations in children born after the accident to irradiated parents and living in non-contaminated territories confirm the long-term health risks in the exposed population (Aghajanyan and Suskov, 2009; Weinberg et al., 1997). Additionally, trans-placental exposure to radioisotopes may significantly increase the rate of spontaneous miscarriages without clinical symptoms in mothers or difference in level of genome damage between women exposed to external and internal radiation by radioisotopes (Fucic et al., 2008).

plutonium from the MOX assemblies ([4]). There were a further 1 838 tonnes of stored spent fuel on the site, including 1 097 tonnes in the central pool store (Large, 2011a).

At the Fukushima Dai-ichi No. 1 plant, site emergency diesel generators provided on-site power to the reactor cooling pumps and other essential services of the three operating nuclear plants, as well as cooling for the six-reactor unit spent fuel ponds, and also for the central spent fuel store (Brumfiel and Cyranoski, 2011a). On-site power supplies continued in operation for just over one hour until the entire site was swamped by a 15 metre tsunami with the total wave height amplified by the backwash as the tsunami wave was contained and reflected by the heavily terraced western section of the site. This part of the site contained four reactors, three of which had been fully operational at the time of the earthquake, resulting in the failure in two or three of the nuclear power plants robust sealed containment structures as water poured into the plants (Large, 2011b) ([5]) (Box 18.5).

The collapse of the Japanese electricity distribution grid resulted in the shut-down of individual nuclear power plant's electricity systems, resulting in loss of essential reactor fuel cooling and crucial instrumentation and control systems. This loss of offsite power and onsite AC power combined with the rapid discharge of DC batteries led to a complete station blackout which disabled the emergency core cooling systems which, in turn, disabled the monitoring of critical parameters such as reactor water levels and open critical

Box 18.5 Japanese earthquakes and tsunamis

Minoura et al. (2001) conclude that traces of large-scale invasion tsunami recorded in the coastal sequences of the Sendai plain show an approximate 1 000-year re-occurrence interval, noting that more than 1 100 years have passed since the historic Jgan tsunami and, given the reoccurrence interval, the possibility of a large tsunami striking the Sendai plain was high. Their findings indicated that a tsunami similar to Jgan would inundate the present coastal plain for about 2.5 to 3 km inland. More recently, post-Fukushima, the University of Tokyo's Earthquake Research Institute concluded that risk of a large-scale earthquake in the region has risen considerably since the Great East Japan Earthquake of 2011. This implies that, since neither practical nor theoretical models can properly determine the dynamics of imminent large earthquakes, much greater emphasis may need to be placed on natural hazards for nuclear risk assessment (Park, 2011).

([4]) MOX (mixed oxide) is a form of nuclear fuel designed for use in breeder reactors, consisting of a blend of uranium and plutonium oxides.

([5]) According to the Japanese Commission tasked with reviewing the disaster, the tsunami that struck the plant was twice as high as the highest wave predicted by previous risk assessments, and the assumption made by Tokyo Electric Power Company (TEPCO) that the plant's cooling system would continue to function after the tsunami struck worsened the disaster (The Investigation Committee, 2011).

safety valves, cascading to significant fuel and containment overheating and damage (Buongiorno, 2011). As Tokyo Electric Power Company (TEPCO) was unable to restore either on or off-site power; the entire Fukushima Dai-ichi nuclear complex went into, and remained, in station blackout.

The blackout meant that no safety systems remained intact, just passive design features and defense in depth layers — representing a beyond design base accident. In Unit 1, steam was bubbled through the suppression pools, further increasing water temperature, and water leaving the core was not replaced. As the water dropped below the top of the fuel, the temperature in the fuel and cladding began to rise rapidly, causing fuel degradation. The zirconium in the cladding oxidized, releasing hydrogen into the containment dry-well, and after a short time, pressure levels in the containment were at or above the design pressure, raising risk of containment rupture. In response, operators manually opened valves to release steam from containment into the reactor building, and the vented steam containing hydrogen violently and exothermally ignited, destroying the reactor building, allowing gaseous fission products to escape, and exposing elements of the spent fuel to open containment.

Units 3 and 4 soon experienced similar beyond design-based cascading conditions. At this point, elevated radiation levels of several fission products including Caesium 137 and I-131 were detected at the reactor buildings, and the plant boundary; providing the first indication that some fuel in the reactor had already melted (Butler, 2011). The presence of hydrogen and these volatile fission products in the released steam suggested that the temperature had severely damaged the fuel cladding inside the reactor pressure vessel (Bonin and Slugen, 2011).

Backup generators and batteries arrived some hours later, restoring partial power to plant, but these were insufficient to power any of the cooling pumps; instead smaller ad hoc fire pumps were used to pump boranated seawater into the reactor core and containment.

Within a few hours the reactor cores of the three operating units were subject to varying degrees of meltdown. The molten fuel had slumped to the bottom of the reactor pressure vessels, the reactor pressure vessels themselves had failed and, in various degrees, the primary containment of the pressure suppression system had failed. What remained of the reactor instrumentation clearly indicated an ongoing and deteriorating situation — with thermal activity within the reactor buildings resulting in sharp perturbations in containment pressure and radiation levels, particularly within what remained of the primary containment. Doubts about the effectiveness of water injection, and increasing concerns about the volumes of highly contaminated water have been linked to TEPCO's necessary emergency seawater cooling strategy, which also involved unconventional cooling efforts with helicopter and water cannons over the period of a week.

18.3.1 Fukushima Dai-ichi radiation releases: cross boundary pollution

The multiple meltdown of reactors at the Fukushima Daiichi nuclear plant released more radiation than any accident since Chernobyl. Japanese regulatory officials initially assessed the accident as Level 4 on the International Nuclear Event Scale (INES), with the risk level successively rising to 5 and eventually to the maximum of 7 — a rating equal to the Chernobyl disaster. Of primary concern were fission products, readily absorbed by the human body, and the actinides, which act as heavy metal poisons. Caesium 137 (Cs-137) represents the most significant long-term hazard since it is readily taken up in human metabolic, environmental, and agricultural systems.

Early measurements reported from the United States, more than 7 000 km from Fukushima, confirmed maximum concentrations of radioxenon (Xe-133) in excess of 40 becquerel per cubic metre (Bq/m^3) — more than 40 000 in excess of normal expected average concentration (Bowyer et al., 2011). High activity concentrations of several man-made radionuclides (I-131, I-132, Te-132, Cs-134 and Cs-137) were detected along the Iberian Peninsula from 28 March to 7 April 2011, deduced through back-trajectories analysis, and verified by activity concentrations (Lozano et al., 2011). Other elevated levels were recorded in air sampling, rainfall and sheep's milk at Thessaloniki, Greece (Manolopoulou et al., 2011). In April and May 2011, fallout radionuclides (Cs-134, Cs-137, I-131) were detected in environmental samples in Krasnoyarsk, Russian central Asia. Similar maximum levels of I-131 and Cs-137/Cs-134 and I-131/Cs-137 ratios in water samples collected in Russia and Greece suggested the high-velocity global movement of radioactive contamination from the Fukushima nuclear accident (Bolsunovsky and Dementyev, 2011); as did results from the Russian rapid response Typhoon monitoring system (Box 18.6).

Box 18.6 Typhoon monitoring system

For hazardous facilities located close to larger cities, early stage accident detection, monitoring and warning systems are critical — as they allow for better impact prediction and mitigation of human and environmental consequences. During the Fukushima accident, Typhoon, the early monitoring network associated with the Russian Early Warning and Emergency Response System (REWERS), carried out operational analysis and forecasting for this large-scale radioactive emergency. The monitoring was achieved through a network of observational stations, with radiometric laboratories providing the measurement data for environmental samples. The first Fukushima air mass transfer dispersion calculations made by Typhoon's experts were carried out on the evening of 11 March and on 12 March 2011 — the radiation monitoring network of Roshydromet in the Russian far east was set to rapid measurement mode to obtain radionuclide dose rate measurements every hour. Throughout the accident period at Fukushima, Typhoon cooperated with the IAEA and the World Meteorological Institute in performing calculations and assessments of trans-boundary emissions (Shershakov, 2011).

18.3.2 Post-Fukushima Dai-ichi radiation releases: Japan

The very high population density near the damaged reactors and spent fuel dispersions implies increased risk for local communities. The regulators conducted an initial evacuation of 100 000 people from around Fukushima, and after some hesitation, Japan's Nuclear Safety Commission established a new 20 km evacuation zone, with a further 90 000 people evacuated. Because damaged plant monitoring proved unreliable — on at least four occasions TEPCO retracted findings on the amount and composition of radionuclides in areas in and around the plant, or on reactor parameters — it has been suggested that more complete analyses of reactor-event scenarios and release fractions can be derived from outside Japan (Nature, Editorial, 2011a).

The radiation releases dispersed according to the wind direction and weight of the particles. The radionuclides of interest were I-131, primarily linked to thyroid cancer; Cs-134 and Cs-137, primarily linked to bladder and liver cancer; and strontium, primarily linked to bone disorder and leukaemia. Significantly, there is confirmed isotopic evidence for the release of plutonium into the atmosphere and deposition on the ground in northwest and south of the Fukushima nuclear site (Zheng, 2012).

In September 2011, Japan's Nuclear and Industrial Safety Agency (NISA) estimated that the Fukushima Daiichi plant had released 15 000 terabecquerels Cs-137 to air. Other estimates vary. However, it may well be too early to accurately estimate or determine the scale of the damage and radiological releases (Cyranoski and Brumfiel, 2011). A meta-analysis comprising radionuclide measurement data and atmospheric dispersion modeling (Stohl et al., 2011), reported in Nature (Brumfiel, 2011), suggested that the disaster at Fukushima Daiichi may have released far more radiation than Japanese regulatory estimates; concluding that the emissions started earlier, lasted longer, and were therefore higher than earlier official estimates assume. The study noted that:

> 'While at first sight it seemed fortunate that westerly winds prevailed most of the time during the accident, a different picture emerges from our detailed analysis. Exactly during and following the period of the strongest Cs-137 emissions on 14 and 15 March as well as after another period with strong emissions on 19 March, the radioactive plume was advected over Eastern Honshu Island, where precipitation deposited a large fraction of Cs-137 on land surfaces. The plume was also dispersed quickly over the entire Northern Hemisphere, first reaching North America on 15 March and Europe on 22 March. In general, simulated and observed concentrations of Xe-133 and Cs-137 both at Japanese as well as at remote sites were in good quantitative agreement with each other. Altogether, we estimate that 6.4 TBq of Cs-137, or 19 % of the total fallout until 20 April, were deposited over Japanese land areas, while most of the rest fell over the North Pacific Ocean. Only 0.7 TBq, or 2 % of the total fallout were deposited on land areas other than Japan' (Stohl et al., 2011, p. 28 322).

In other words, Fukushima releases may have contained an estimated 3.5 × 1 016 Bq Cs-137 — roughly twice the official government figure, with almost one fifth falling on the Japanese mainland. This means that the Fukushima release can be

estimated to equal to 40 % of the Cs-137 release from Chernobyl.

By November 2011, the air radiation level in Ibaraki Prefecture was about 0.14 microsievert per hour, equivalent to an annual dose of about 1 millisievert, the safety limit for exposure under normal standards (Ishizuka, 2011). On 14 December 2011, the Japanese Science Ministry assessed caesium fallout in Fukushima Prefecture in the four months after the March 11 disaster at 6.83 MBq/m^2 — 94 % of which was concentrated in March, an indication of the severity of radiation discharge shortly after the onset of the accident (Asahi Shimbun, 2011).

Fallout attaches strongly, through ion exchange, to soil — in particular to clay soils common throughout Fukushima. From there the radiocaesium will move slowly into plants, at a rate, and level of risk, that remains unclear. Cs-137 strongly contaminated the soil in large areas of eastern and northeastern Japan, whereas western Japan was relatively sheltered by mountain ranges. The soils around the Fukushima nuclear site and neighboring prefectures have been extensively contaminated with depositions of more than 100 000 and 10 000 megabecquerel per square kilometre (MBq/km^2), respectively (Yasunaria et al., 2011).

Correspondingly, it was reported that Fukushima Prefecture survey conducted in June and July 2011 found 33 Cs-137 hot-spots in excess of 1.48 MBq/m^2, the level set by the Soviet Union for forced resettlement after the Chernobyl accident. A further 132 locations had combined Cs-137/134 of more than 0.555 MBq/m^2, the level at which the Soviet authorities called for voluntary evacuation and imposed a ban on farming (Obe, 2011). Further reports suggest that radiation pollution is widely dispersed in Japan, with the Japanese Science Ministry confirming that Cs-134 and Cs-137 fallout was present in all prefectures, with the highest combined cumulative density of Cs-134 and Cs-137 found in Hitachinaka, Ibaraki Prefecture, at 0.0408 MBq/m^2, followed by 0.0226 MBq/m^2 in Yamagata, the capital of Yamagata Prefecture, and 0.0174 MBq/m^2 in Tokyo's Shinjuku Ward (Ishizuka, 2011). Further reports indicated that the Japanese Environment Ministry estimated the contaminated zones at circa 2 400 km^2 over Fukushima and four nearby prefectures, with Cs-134 and Cs-137 the dominant contaminants, mainly contained in the topsoil layer. By definition, shorter-lived isotopes decayed promptly (Reuters, 2011).

The Fukushima accident contaminated large areas of farmland and forests, albeit not as severely or extensively as at Chernobyl. But lacking land for resettlement and facing public outrage over the accident, the Japanese government has embarked on an unprecedented decontamination effort. The Japanese Ministry of the Environment estimates disposals of 15–31 million m^3 of contaminated soil and debris by the time the decontamination projects finish (Bird, 2012). The total remediation programme may cover about 500 km^2 where radiation dose levels are above 20 millisieverts per year (mSv/year), and about 1 300 km^2 where radiation dose levels are between 5 mSv/year and 20 mSv/year (IAEA, 2011a). In order to cope with this level of contamination, and in contradiction to international radiation protection standards, Japanese regulators have raised dose constraints to 20 mSv/year — thereby subjecting schoolchildren to exposures normally only tolerated by adult nuclear workers.

Over the time of the accident, the amount of highly contaminated water on the site rose from 10 000 to 100 000 tonnes, presenting storage capacity difficulties (Reardon, 2011). The French Institute for Radiological Protection and Nuclear Safety estimated that between March and mid July, the amount of radioactive Cs-137 discharged into the Pacific from the Fukushima Daiichi plant amounted to 27.1 million megabecquerels — the greatest amount known to have been released to water from a single accident (Brumfiel and Cyranoski, 2011b).

18.3.3 Fukushima Dai-ichi aftermath

The Japanese government established an independent Investigation Committee on the Accident at the Fukushima Nuclear Power Stations of Tokyo Electric Power Company on June 7, 2011. The Committee's December 2011 Interim Report strongly criticised both central government and TEPCO, noting that both seemed unequal to the task of making decisions in order to stem radiation leaks as the situation at the coastal plant worsened in the days and weeks following the disaster. The Interim Report also noted that Japan's response to the crisis was flawed by poor communication and delays in releasing data on dangerous radiation leaks at the facility, and was critical of the regulatory authorities' 'inappropriate preparation' of nuclear disaster emergency planning (Investigation Committee, 2011).

In a commentary published in *Nature*, committee members Tomoyuki Taira and Yukio Hatoyama, both also members of the House of Representatives in the Japanese Diet, with Hatoyama having served

as Prime Minister of Japan from 2009 until 2010, noted that their investigation had

> 'shown that key pieces of evidence remain incomplete… Particularly important is finding out whether the worst-case scenario occurred: that is, whether self-sustaining nuclear reactions were re-ignited in the core (re-criticality), creating more fission products and heat damage; whether the explosions that rocked the plant days after the earthquake were nuclear in origin, releasing radioactive metals from damaged fuel rods; and whether molten fuel has broken through the reactor's base, threatening environmental contamination' (Tomoyuki and Hatoyama, 2011).

These internal critiques were compounded by others, questioning the relative independence of Japanese regulators:

> 'The Japanese government's main sources for scientific information for Fukushima were the industry ministry's Nuclear and Industrial Safety Agency and the Nuclear Safety Commission. Although these bodies might have expertise in nuclear reactor physics, they also have ties to the nuclear industry that create a conflict of interest. And they were not an effective and prompt source for quick decisions on decontamination or health risks' (Nature, Editorial, 2011b).

Despite these ongoing difficulties, on 16 December 2012, the Japanese Prime Minister, Yoshihiko Noda, declared that the Fukushima nuclear plant had entered the state of cold shutdown; with cold shutdown confirmed by IAEA in their Status Report (IAEA, 2011b) ([6]). However, whilst the reactor temperatures had fallen, there still remained uncertainty about a series of ongoing problems, including the state and level of the nuclear fuel, particularly after confirmation that molten fuel may have eaten through three-quarters of the concrete under unit 1 and damaged the bases of two of the other reactors (TEPCO, 2012). A revised TEPCO timetable suggests that decommissioning, including melted reactor fuel, fuel rod removal, and repair of containment vessels, will take up to 40 years (ibid).

Extrapolating from monthly trade ministry data, the average Japanese nuclear power plant utilisation rate fell to 15.2 % in December 2011 from 67.9 % a year earlier (Reuters, 2012) and, following a further reactor shut-down in January 2012, to 10.3 % (Japan Times, 2012). With almost all of Japan's 54 reactors either offline in early 2012, or scheduled for shutdown, the issue of structural safety looms over any discussion about restarting them. Japan, traditionally a pro-nuclear country, derived about 30 % of its electricity from nuclear plants in 2010 — however opposition has been emerging as an important political issue, and the country's nuclear industry has been repositioning itself for a significantly less attractive market, halting plans to build 14 further reactors by 2030 (Crooks, 2011).

Although post-Fukushima plans for bio-monitoring and epidemiological assessment are still not finalised, it is clear that there will need to be a significant assessment of a wide range of environmental risk factors. Because some of the evacuees have started to settle across the country, long-term follow-up of the victims will need to account for geographic dispersion (Sugihara and Suda, 2011).

The final Report of the National Diet of Japan noted the severity of the future decontamination challenges that Japan faces, and strongly criticised the underlying organisational, institutional and legal framework that resulted in the 'regulatory capture' of safety systems. The Independent Investigation Commission also concluded that the Fukushima accident was a man-made disaster, pointing to the key role of human agency in radiation risk controversies, see Box 18.7.

18.3.4 Post-Fukushima nuclear policy impact

Before the Fukushima accident, most planned nuclear power plant projects were in Asia and Eastern Europe, extending a trend from earlier years, including a dispersion of proposed new reactors around the Pacific seismic region. Between 2009 and April 2011 construction started on nine units; and where projects are going ahead, they do so with strong government support, including implicit or explicit public subsidy (Box 18.8).

Since the Fukushima accident, the number of operating reactors fell from 441 at the beginning of 2011 to 435 in early 2012, with a total net installed

([6]) 'Cold shutdown' normally refers to a state in which a reactor has become subcritical, with the temperature having been brought to a stable level below 95 °C through the operation of normal systems.

Box 18.7 The Fukushima Nuclear Accident Independent Investigation Commission (NAIIC, 2012)

'The earthquake and tsunami of 11 March 2011 were natural disasters of a magnitude that shocked the entire world. Although triggered by these cataclysmic events, the subsequent accident at the Fukushima Daiichi Nuclear Power Plant cannot be regarded as a natural disaster. It was a profoundly manmade disaster.'

'The Commission recognizes that the residents in the affected area are still struggling from the effects of the accident. They continue to face grave concerns, including the health effects of radiation exposure, displacement, the dissolution of families, disruption of their lives and lifestyles and the contamination of vast areas of the environment. There is no foreseeable end to the decontamination and restoration activities that are essential for rebuilding communities. The Commission concludes that the government and the regulators are not fully committed to protecting public health and safety; that they have not acted to protect the health of the residents and to restore their welfare.'

capacity of just more than 368 gigawatts (GW), representing a decrease in installed nuclear capacity of around 10 GW or 3 %. Similarly, construction starts fell from 15 in 2010 to just 2 in 2011. New nuclear plant construction is progressing in Brazil, China, India, and Russia. Iran has recently completed its first reactor. New-build orders have been placed in the United Arab Emirates and the United States, with a planned call for tender in South Africa. Ordering continues in China, India, Korea and Russia.

In Europe, Finland and France are completing their new Generation III European Pressurized Reactor (EPR) at Olkiluoto and Flammanville (Box 18.9), with the Finnish parliament and regulators having granted permits for construction of the country's sixth and seventh commercial reactors to Teollisuuden Voima (TVO) and Fennovoima (a subsidiary of E.ON), with a further reactor to be built at Olkiluoto by TVO. In October 2011, Fennovoima announced that it had chosen Pyhäjoki, in northern Finland, as a site for further nuclear expansion, with construction expected to start in 2015. Elsewhere, the United Kingdom's government, excluding Scotland, has in principle approved the concept of a new generation of up to eight nuclear power plants, subject to reactor generic design approvals; Bulgaria has begun detailed planning for a reactor at Belene; Romania has issued a planned call for tender; Poland's state utility, PGE, has shortlisted three sites as possible locations for their first nuclear power plant; and the Czech Republic is progressing with planning new-build — despite downsizing the proposed Temelin site tender from five to two reactors and Austria's strong objection to the expansion of the Temelin plant, which is situated near the border of the two countries.

Although Sweden formerly had a nuclear phase-out policy aiming to end nuclear power generation by 2010, on 5 February 2009, the Swedish Government announced an agreement allowing for the replacement of existing reactors. However, the

Box 18.8 Nuclear costs

A key challenge for nuclear power has been the high cost of construction (Davis, 2011). Nuclear new builds are high value and high risk construction projects with a marked tendency for significant delay and delay claims, cost growth and investor risk (KPMG, 2011). Based on the experiences of 52 United States investor-owned utilities that built nuclear power plants in 1960–2011, the Texas Institute (2011) concluded that building nuclear power plants provide significant economic risks involving a 70 % certainty that a power utility would see borrowing costs rise due to the downgrading of credit rating once construction began, with plant construction marred by significant cost overruns and electricity tariff increases. Nuclear plants, which are among the largest and most complex engineering projects in the world, also carry high technical and regulatory risks, with World Nuclear Association figures showing very significant cost overruns for most projects, implying that utilities may only be able to pay for new plants if governments guarantee their income (Thomas, 2010a). Thus, costs and risks associated with nuclear construction may mean that plants may only be built with implicit and explicit public subsidy, including long-term power purchase agreements (Professional Engineering, 2011).

Box 18.9 European Union Nuclear New-build Experience

The Olkiluoto 3 EPR in Finland was originally planned to go online early in 2009, but is now predicted to start generating in late 2014 (Thomas, 2010c). The new 1.6 GW AREVA designed EPR is conceived as first of type, with Siemens responsible for steam turbines and electricity generators. Originally priced at EUR 3 billion, the project is now estimated at EUR 5.7 billion and rising. The fixed price turn-key contract is subject to an ongoing dispute between the French manufacturer AREVA and TVO with the former claiming compensation of EUR 1 billion for alleged failures, and the latter demanding EUR 2.4 billion in compensation for delays (Thomas, 2010b). Similarly, in France, EDF confirmed the EPR Flamanville project was running late and increased its estimate of the cost. Originally scheduled to start operating in 2012, it is hoped that the reactor may be operational by 2016. Originally priced at EUR 3.3 billion, the reactor completion is currently estimated at EUR 6 billion (Thomas, 2011).

Fukushima disaster may have reversed prior public support of nuclear power, with a BBC World Service — Globescan (2011) poll showing that 64 % of Swedes opposed new reactors while 27 % supported them. Similarly, whilst Spain has no plans for expansion or closure, public opposition to new nuclear build remains very high at 55 %. The United Kingdom is more favourable towards the use of nuclear energy than any other European country, with 37 % in favour of building new nuclear infrastructure (ibid).

Given that Germany uses around 20 % of all EU electricity, the government's March 2011 decision to close 7 of its 18 reactors, followed in June by the German Parliament vote to phase out nuclear power by 2022 and to invest in renewables, energy efficiency, grid network infrastructure, and plan for trans-boundary pumped-storage hydroelectricity (PSH), may prove significant for European energy policy as a whole. In June 2011, Italian voters also passed a referendum to cancel plans for new reactors, with over 94 % of the electorate voting in favour of the construction ban. Because 55 % of the eligible voters participated, the vote is binding. Elsewhere, six months after the Fukushima plant catastrophe, strong Swiss public opposition to nuclear led to a decision not to replace the country's five reactors when they come to the end of their operation in 2034. Belgium also confirmed a nuclear phase-out, with no firm date set for end of operation, whilst the only Dutch reactor at Borssele will remain open until 2033 if it can comply with the highest safety standards. It is also worth noting that, at a ministerial meeting in Vienna; ministers and heads of delegations of Austria, Greece, Ireland, Latvia, Liechtenstein, Luxembourg, Malta and Portugal, observed by ministers from Cyprus, Denmark and Estonia, concluded that nuclear power was not compatible with the concept of sustainable development, suggesting that nuclear power does not provide a viable option in combating climate change (Vienna Declaration, 2011).

Before Fukushima, the IAEA had predicted that around the world nuclear plants would add 360 GW of generating capacity by 2035, the equivalent of over 200 new reactors. Post-Fukushima, it has halved this forecast, partly due to diminishing public acceptance of nuclear energy, but also to the increased costs of nuclear security improvements and of insurance premiums for accident-related damages (Leveque, 2011). France has set radical safety standards for the industry. However the required plant upgrades are both technically difficult and expensive, with the French nuclear authority, ASN, estimating the cost of necessary improvements at the country's 58 nuclear reactors at around EUR 10 billion (Nature, Editorial, 2012).

Western European Nuclear Regulators Association (WENRA) 'Stress Tests' comprised a targeted reassessment of the safety margins of nuclear power plants in the light of Fukushima, including extreme natural events which challenge plant-safety functions, leading to severe accident (WENRA Task Force, 2011). However, since the European Nuclear Safety Regulators Group (ENSREG, 2011) decided that security issues were outside WENRA's remit, post-Fukushima stress tests of EU's 143 nuclear power reactors did not include accident and incident from an aeroplane strike or terrorist attack. The exclusion of these security issues seems unfortunate given that, for example, all UK civil nuclear infrastructures are uniquely implicated in all four high priority tier-one threats identified in the UK National Security Strategy (HM Govt., 2010).

Despite further new-build plans in e.g. Finland, France and the United Kingdom; the general post-Fukushima situation in the EU implies that the limited construction of nuclear new-build since 2000, and potentially in the coming decade, combined with the ageing of nuclear power

plants and the finalisation of nuclear phase-out in Germany and other European countries, will lead to a relative decreasing share of electricity production sourced from EU nuclear energy after 2020. The emphasis is likely to shift towards maximizing output of existing reactors through extension, up-grade and retrofit (Leveque, 2011; Coenen and López, 2010).

The energy futures landscape within Europe is one of major national differences between state and market, choices and trade-offs over supply-side, demand-side, transmission and load-balancing infrastructure (Schiellerup and Atanasiu, 2011). Although EU Member States diverge in terms of cultural and industrial landscapes, public opinion, technological structures, institutions, regulatory practice and energy mixes (Box 18.10), the European energy policy offers a fairly open and flexible framework in which some Member States could develop collective action on energy issues. The development of sustainable and affordable low carbon energy remains a growing economic sector with huge potential for job creation (Andoura, 2010).

18.4 Nuclear liability

The risk to people, the environment and to the future of nuclear energy as a consequence of a major incident is significant. The cost of the Chernobyl accident can only be roughly estimated, but a variety of government estimates from the 1990s put the cost of the accident, over two decades, at hundreds of billions of dollars.

More recent events at Fukushima tend to support the conclusion that reactor accidents may prove the single largest financial risk facing the nuclear industry, far outweighing the combined effect of market, credit, and operational risks. Perhaps unsurprisingly, liability estimates vary with ongoing events. Japanese replacement power costs in 2011 alone have been estimated at EUR 6.5 billion (JPY 700 billion), with decommissioning costs for the six reactors are estimated at EUR 9 billion (JPY 1 trillion). On 20 May, 2011, TEPCO reported a net loss for the fiscal year ending in March 2011 of EUR 11.5 billion (JPY 1.25 trillion), the largest corporate loss in Japanese history outside the financial sector. By mid 2011, Bank of America Merrill

Box 18.10 Cultural and policy diversity in energy governance

Finland: The Finnish discussion culture can be summarised as one in which decisions are preceded by an open public and policy debate, but once the decision has been made, according to the rules and regulations in force, there should no longer be room for complaints and further debate. Provided that proper procedures have been followed, changing course would mean loss of face and identity. Correspondingly, nuclear power has acquired the reputation of being the cheapest, safest, and most reliable source of electricity generation. This is primarily because there have been no serious nuclear accidents in Finland, and their reactors maintain a high reliability and load factor. These advantages are coupled with arrangements under the Mankala Principle, whereby large industrial corporations such as forest and heavy industry — as shareholders in nuclear power companies — can buy electricity at cost price (Lehtonen, 2010a; Lehtonen, 2010b).

Germany: Decisions on nuclear power cannot be separated from prior energy policy choices, and Germany has demonstrated a very strong, historic commitment to renewables, with renewable electricity production doubling between 1998 and 2003 and again between 2003 and 2008. By 2010 renewables contributed 17 % of total electricity production, and there are plans to increase this to at least 35 % by 2020 (BMU, 2011). Innovative German practice includes the first implementation of a fixed price feed-in-tariff, and huge purchases of solar photo voltaics (PV), which have driven down the world price of modules. Energy futures have also devolved to the local level, with communities securing political agreements under which the *Bundesländer* (federal states) are enabled to set goals and locations for renewable generation. This ensures that local energy resources and financial subsidies — paid for by customers (through feed-in tariffs) or taxpayers (through cheap loans provided by the government development bank (KfW)) — benefit not only the energy companies but also the local people, with profits and employment kept in the region. Germany's non-nuclear energy policy is framed in the context of national pride and scientific-technological achievement, twinned with economic expansion: 'As the largest industrialized (European) nation, we can achieve a transformation toward efficient and renewable energy, with all the opportunities that brings for exports, and the development of new technologies and jobs' (Chancellor Angela Merkel, in German, 2011).

Lynch reported that compensation claims could total EUR 93–102 billion (JPY 10–11 trillion) over the next two years, with liabilities far exceeding the current market cap (Maloney, 2011). By September 2011, Fukushima liabilities stood at anywhere between EUR 76–152 billion, with the Japanese Centre for Economic Research estimating clean-up remediation at EUR 190 billion over the next 10 years (Kobayashi, 2011).

Currently, individual European nuclear accident liabilities are capped at EUR 169 million for operators. However, the Paris Convention on Nuclear Third Party Liability and Brussels Convention (2011) ([7]) aims to raise this to ensure that victims of a nuclear incident are compensated for resulting damage. Under the proposals, nuclear operators would be liable for the first EUR 700 million for any accident, with the national government having the option of adding a maximum of a further EUR 500 million towards the company's liabilities. Collectively, other signatory states could contribute a further EUR 300 million, potentially bringing the total available to EUR 1 500 million for any one accident.

Yet actuarial analysis suggests that even this level of cover may fail to account for liability in case of major accident. Versicherungsforen Leipzig GmbH (2011), a company that specialises in actuarial calculations, concluded that these costs were not adequately internalised, suggesting that full insurance against nuclear disasters would increase the price of nuclear electricity by up to EUR 2.36 per kilowatt hour (kWh) — a sum that may weaken the economic case for nuclear power compared to other low-carbon sources.

Both the required liability (EUR 6.09 trillion), based on an estimate of the average maximum damage and corresponding variance, and the resulting insurance premium, are significantly higher than the financial resources currently legally required of nuclear power plant operators. Versicherungsforen Leipzig's study estimated that future damage and liability insurance costs would exceed the financial resources that nuclear power plant licensees are currently required to maintain by several orders of magnitude. In this context, nuclear disasters seem uninsurable, due to a combination of methodological difficulties in estimating the probability of occurrence of damage, insufficient size of the risk pool, and the extent of potential maximum damage (ibid).

To the extent that liability rules provide incentives for prevention, the financial limit on the liability of an operator may lead to under-deterrence — since, as a result of the financial cap on liability, the potential complementary function of liability rules in providing additional deterrence may be lost. The financial limit, and the resulting nuclear subsidy, may also distort competition by unduly favoring nuclear energy compared to other energy sources (Faure and Fiore, 2009).

The issue of nuclear waste liability has also been subject to intense and prolonged debate, especially in the context of high burn-up fuel proposed for Generation III reactors (Box 18.11).

Box 18.11 High burn-up fuel

Following the liberalisation of the EU energy market, it was realized that a decrease in nuclear costs could be achieved if reactor power could be optimized by using more uranium as reactor fuel and keeping the fuel rods in longer. This means that generation III reactor high burn-up spent fuel will be significantly more radioactive than conventional spent fuel. Five years after discharge, each square metre of spent fuel in the proposed EPR cooling ponds may generate up to 17 kW of heat compared with 11 kW from more conventional spent fuel pool. And the high density of spent fuel racks from the proposed Westinghouse AP1000 reactor implies that 24–36 kW of heat may need to be removed from each square metre. Safety could depend on the effective and continuous removal of the significant thermal power of high burn-up spent fuel, potentially requiring additional pumps, back-up electricity supplies and back-up water supplies: all systems potentially vulnerable to mechanical failure or deliberate disruption. It is also likely that densely packed high burn-up spent fuel may require additional neutron absorbers, and greater radiation shielding during encapsulation and storage (Richards, 2009).

([7]) Note, not all EU Member States are signatories. Belgium, Denmark, Finland, France, Germany, Greece, Italy, the Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, the United Kingdom and Turkey are signatories to the Paris Convention on Nuclear Third Party Liability and Brussels Convention.

18.5 Nuclear risk: probabilistic risk assessment and beyond design-based accidents

Key to the analysis of nuclear safety is the analytical concept of probabilistic risk assessment (PRA) or probabilistic safety analysis (PSA). Whilst PRA calculations are not taken as absolute, but rather as significant indicators of plant weaknesses, they do underpin the concept of acceptable risks and tolerable consequences under fault conditions. In this context, the risk of an accident must be acceptable, and the radiological consequences tolerable, with more frequently occurring incidents countered by greater resilience through enhanced safety systems grounded in robust engineered structures. However, PRA has proven structurally limited in its ability to conceive and capture the outcomes and consequences of a nuclear accident resulting from a cascading series of events, as described in the Fukushima disaster and all previous major nuclear accidents. This implies that relatively simplified chain-of-event fault-tree models may not be sufficient to account for the indirect, non-linear, and feedback relationships common for accidents in complex systems. Here, modeled common-cause, common-mode, and dependent failures have proved problematic; partly due to data limitation (since major failures occur infrequently), and because failure mechanisms are often plant specific (Ramana, 2009).

Most PRAs assume failure likelihood can be captured through identical, independent log-normal failure distributions. Since strong independence assumptions employed in PRAs assume that reactor safety systems are duplicated and reliable, core damage frequency estimates are typically very low. Because of this, there may be good reason to question the conceptual and theoretical completeness, and empirical and practical reliability of PRA models. This is partly because PRA is prone to under-counting accident scenarios — since risk is estimated for enumerated reactor states, failure to account for unknown and serially cascading beyond design-base accident scenarios leaves an un-measurable model error in the core damage frequency estimate (Maloney, 2011).

Before the Fukushima accident, for example, the Japanese Nuclear Regulatory Commission Guidance (NSC, 2006), updated in early 2011, concluded that 'robust sealed containment structures would prevent damage from a tsunami… and no radiological hazard would be likely'. Whereas after the accident, the Chairman and President of the European Nuclear Society High Scientific Council stressed that 'the magnitude of the tsunami that struck Japan was beyond the design value to which the reactors were supposed to withstand' (Bonin and Slugen, 2011). These pre- and post-facto statements suggest that, although reactor design can prove relatively robust against specific accidents and specific modes, safety cannot be guaranteed for cascading beyond design-base accidents. In the case of Fukushima, because the cascade from earthquake, through tsunami, to reactor and spent fuel fault condition was discounted, no account was taken for the need to respond to the failure of three nuclear reactors and spent fuel ponds.

Pre-Fukushima probability estimates of a major nuclear accident were around 1:100 000 for the 440 reactors in operation over the next 20–25 years. Since Fukushima, estimated probabilities of major nuclear accidents have increased significantly. However, estimation of core melt and containment failure may still prove problematic. Chernobyl and Fukushima together comprise catastrophic meltdown in four nuclear reactors over the past few decades, implying that that the probability of a major accident in the current worldwide fleet over the next 20–25 years is around 1:5 000. Thus, whereas earlier estimates assumed a probability of one major nuclear accident over a 100-year period, reoccurrence of these events can be expected once every 20 years (Goldemberg, 2011). This reassessment of nuclear risk has been particularly apparent in Germany, where Chancellor Angela Merkel concluded that Fukushima 'has forever changed the way we define risk' (Schwägerl, 2011); an analysis echoed by Norbert Röttgen, Germany's Environment Minister, who noted that Fukushima 'has swapped a mathematical definition of nuclear energy's residual risk with a terrible real-life experience… we can no longer put forward the argument of a tiny risk of 10–7, as we have seen that it can get real in a high-tech society like Japan' (ibid).

Importantly, the governmental German Advisory Council on the Environment also concurred with this critique, suggesting that: 'The widespread view that the extent of the damage due even to major incidents can be adequately determined and limited in order to be weighed up… is becoming considerably less persuasive… The fact that the accident was triggered by a process which the nuclear reactor was not designed to withstand… casts a light on the limitations of technological risk assessment… based on assumptions, and that reality can prove these assumptions wrong' (SRU, 2011b, p.11).

Levels of reliability required for a complex interactive and tightly coupled nuclear power plant are very great (Perrow, 1984), with the range of

operating reactors having differing sets of designs and configurations. Because of their complexity and the physical conditions during reactor operation, the understanding of the reactor design and operation is always partial. Additionally, as system components and external events can interact in unanticipated ways, it is not possible to predict all possible failure modes. It follows that numerical estimates of probabilities of significant accidents remain deeply uncertain. As the Fukushima Investigation Committee concluded (2011, p. 22): 'The accidents present us (with) crucial lessons on how we should be prepared for… incidents beyond assumptions'.

18.6 Conclusion

Because it is likely that post-Fukushima health consequences may start to arise and be documented over the next 5–40 years, a key lesson to be learned concerns the multi-factorial nature of this event. It can be expected that a number of chemical agents were released and, hence, the final biological effect may depend on the consequential complex radiochemical environment. Thus, in planning future radiation protection, preventive measures and bio-monitoring of exposed populations, it is of great importance to:

- integrate the available data on both cancer and non-cancer diseases following overexposure to ionizing radiation;
- take a complex approach in the interpretation of data — considering the impacts of age, gender, and geographical dispersion of affected individuals, and the psychological, educational and social status of victims; and
- integrate the evaluation of latency periods between exposure and disease diagnosis development for each cancer type.

Bunn, the former adviser to the US Office of Science and Technology Policy, and Heinonen, the former Deputy Director General of the IAEA, also conclude that there is a need for more stringent nuclear safety standards, and propose six areas for improvement involving substantial cost and time investment:

- operators must plan for events beyond design bases;
- more stringent standards for protecting nuclear facilities against terrorist sabotage;
- a stronger international emergency response;
- international reviews of security and safety;
- binding international standards on safety and security; and
- international co-operation to ensure regulatory effectiveness (Bunn and Heinonen, 2011).

In addition, there is also the need to defend and adapt the coastal sites of nuclear plants to the hazards of rising sea levels, storm surges, flooding and the possibility of eventual nuclear site islanding (IME, 2009; Kopytko and Perkins, 2011). It should also be understood that it is very unlikely that current major accident liability regimes will prove adequate, and a significant re-adjustment may be essential.

This wide-ranging set of recommendations constitutes a significant step forward in radiation protection philosophy. However, there seem to be no resounding new revelations over the vulnerability of nuclear power to unforeseen natural disasters like earthquakes and tsunamis, or through human or engineering based fault conditions, including accidental or deliberate harm. Accidents are by nature, accidental, and the cost of ignoring this common-sense axiom can prove radiologically catastrophic (Stirling, 2011).

Whilst the imaginative use of foresight and precaution are key to the management of nuclear risks, a further paradox lies at the heart of the debate: Whereas fundamental radiation protection science is characterised by very real uncertainty, indeterminacy and contingency, the regulation and operation of nuclear facilities is based on the language of certainty. The nearer one gets to the fundamental science and engineering of complex technological systems, the greater the uncertainty and complexity; yet the nearer one gets to regulation and operation, the greater the certainty and simplicity. Since somewhere along this continuum, uncertainty has been translated into certainty, and risk has been translated into 'safety', the question remains: when, how, and why does this transformation happen?

Given the degree of uncertainty and complexity attached to even the most tightly framed and rigorous nuclear risk assessment, attempts to weight the magnitude of accident by the expected probability of occurrence has proven problematic, since these essentially theoretical calculations can only be based on sets of pre-conditioning assumptions. This is not an arcane philosophical point, but rather a very practical issue with

significant implications for the proper management of nuclear risk. With its failure to plan for the cascade of unexpected beyond design-base accidents, the regulatory emphasis on risk-based probabilistic assessment has proven very limited. An urgent re-appraisal of this approach, and its real-life application seems overdue.

Whatever one's view of the risks and benefits of nuclear energy, it is clear that the possibility of catastrophic accidents must be factored into the policy and regulatory decision-making process. In the context of current collective knowledge on nuclear risks, both the regulation of operating nuclear reactors and the design-base for any proposed reactor will need significant re-evaluation.

Given the size of the long-term investments that are now needed across the options of nuclear, carbon based fuels, renewables, energy efficiency and conservation, grid network infrastructure development and load balancing; it is clear that European public needs to play a key role in taking these critical, social, environmental and economic decisions ([8]). Here, public values and interests are central, and the role of public dialogue and the participatory practices that enable it are core to the building of mutual understanding between European states, governments, industry and people. If carried out in a truly involving way, the integration of public, policy, and expert scientific knowledge allows for greater accountability, transparency, and much better take-up of necessary change and improved long-term likelihood of problem resolution. This conclusion mirrors those from many chapters in this publication — from leaded petrol to nanotechnology: that wider public engagement in choosing strategic innovation pathways is essential.

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19 Hungry for innovation: pathways from GM crops to agroecology

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Innovation's potential to deliver food security and solve other agriculture-related problems is high on the agenda of virtually all nations. This chapter looks at two different examples of food and agricultural innovation: genetically modified (GM) crops and agroecological methods, which illustrate how different innovation strategies affect future agricultural and social options.

GM crops are well suited to high-input monoculture agricultural systems that are highly productive but largely unsustainable in their reliance on external, non-renewable inputs. Intellectual property rights granted for GM crops often close down, rather than open up further innovation potential, and stifle investment into a broader diversity of innovations allowing a greater distribution of their benefits.

Science-based agroecological methods are participatory in nature and designed to fit within the dynamics underpinning the multifunctional role of agriculture in producing food, enhancing biodiversity and ecoystem services, and providing security to communities. They are better suited to agricultural systems that aim to deliver sustainable food security than high external input approaches. They do, however, require a broader range of incentives and supportive frameworks to succeed. Both approaches raise the issue of the governance of innovation within agriculture and more generally within societies.

The chapter explores the consequences of a 'top-down transfer of technology' approach in addressing the needs of poor farmers. Here innovation is often framed in terms of economic growth in a competitive global economy, a focus that may conflict with efforts to reduce or reverse environmental damage caused by existing models of agriculture, or even deter investment into socially responsible innovation.

Another option explored is a 'bottom-up' approach, using and building upon resources already available: local people, their knowledge, needs, aspirations and indigenous natural resources. The bottom-up approach may also involve the public as a key actor in decisions about the design of food systems, particularly as it relates to food quality, health, and social and environmental sustainability.

Options are presented for how best to answer consumer calls for food quality, sustainability and social equity in a wide sense, while responding to health and environmental concerns and securing livelihoods in local small-scale agriculture. If we fail to address the governance of innovation in food, fibre and fuel production now, then current indications are that we will design agriculture to fail.

19.1 Introduction

Would it not be a loss to humanity if society's science and policy institutions delivered wonderfully sophisticated technological tools for agricultural innovation, but yet were out of touch with the needs for food security, poverty alleviation and ecological sustainability? In agriculture, as in other industries, research and development is guided by innovation policies. Within these policies, the incentive systems set at the highest levels of policymaking largely determine who is innovative and what innovative products will look like. They also favor those who will most benefit. Under the current innovation policies for industrial agriculture, continuous increases in wealth, sufficient food production to more than feed the current population, and ongoing investment in particular kinds of research and technology fail nearly a billion people who are undernourished or hungry, well above Millennium Development Goals (FAO, 2010, 2011a). Has modern agriculture, despite good intentions, been unwittingly designed to fail?

A confluence of issues surround agriculture and its existing problems: Ongoing societal and trade issues, food price volatility (FAO, 2008), inefficient energy utilisation, harvesting/storage and production systems (Nellemann, 2009) as well as retail/consumer level waste (Gustavsson, 2011) to name a few. These challenges are building on decades of environmental degradation from high-external input farming, and centuries of environmental damage from inefficiencies within traditional farming that have exacerbated social inequities (IAASTD, 2009a). The extent of these environmental and social consequences of current agricultural practices in food-wealthy and food-poor countries alike means that food production must be rethought in order to achieve greater resilience and sustainability within these systems. The new goal for agricultural innovations is a transition towards social, economic, and environmental sustainability that can support needed production levels (De Schutter, 2010; EU-SCAR, 2011; UNEP, 2011).

Scientific and technological advances within agriculture have the potential to alleviate hunger and increase food security, particularly where food productivity and sustainability are solely limited by simple technical issues or their availability, rather than by institutional or societal constraints (Heinemann, in press). Science and technology have the capacity to produce valuable outcomes from investments in research and development. However, the efficacy of innovation is more than merely invention; it must also meet real needs and be effectively accessed, supported and adopted by farmers who, like retailers, consumers and community members must share in the benefits.

Agriculture is multifunctional (IAASTD, 2009a). It provides food, fibres and fuel for local and international needs, income for producers who purchase education, health and consumer goods, calories and nutrients for families, and cultural and social identity. Through its practice skills are transferred and developed, biodiversity and greenhouse gas emissions are changed — depending on how agriculture is practiced (Hoffman, 2011; IAASTD, 2009c). However, food production remains local. Local needs must be met through both technological and non-technological advances which can be adapted to fit local conditions through ongoing innovation (Altieri, 2011b; Vanloqueren, 2009).

In the global context, the policy focus on agricultural development and food production is shifting from 'how much' through to 'how long' to just 'how'. Some see the problem as not enough production to feed the world. Others note that we have a global food surplus, but the lack of good infrastructure, conflicts and appropriate tools for local farmers cause food shortages and insecurity in many places (MEA, 2005).

Even other commentators see farmers no longer as producers of food, but more accurately of biomass, as part of an economic system that can vary the usage of this biomass as human food, animal feed, biomaterial or biofuels (Pengue, 2005a). Competition among different markets (for energy, industrial products, food production or animal fodder) is creating further constraints on food availability in some parts of the world. Moreover, with the predominant food production practices, there are also concerns that current demands on yields require an unsustainable level of environmentally damaging external inputs of agrochemicals and supply of exogenous energy. For example, industrial agricultural practices on average require 10 calories of exogenous energy (used for everything from petrochemical production, extraction, transport etc.) for every 1 calorie of food produced (Giampietro, 1993; UNEP, 2011). Growing populations, competing demands for crop biofuels and demand for meat will continue to intensify these pressures on agricultural food production. This insight draws us full circle: food security will follow not only from producing more food, but how we produce and consume it (IAASTD, 2009c).

The role of innovation to end food insecurity and solve other problems caused by, and for, agricultural is high on the agenda of virtually all nation states. More and more frequently, governments are framing innovation as a means for economic competitiveness by using the promise of returns on intellectual property (IP) as incentive for both public and private innovators (Heinemann, 2009). As a result, those that innovate by inventing technologies — mainly products — that can be commodified in a form that meets the criteria for IP instruments, e.g. patents or patent-like plant variety protections, are incentivised by the prospect of financial rewards. Moreover, the problems identified for solution will tend to be those that can be packaged and sold — usually to the largest/wealthiest/most lucrative market and largely bypass the poor (Spielman, 2007). This was perhaps the most evident early warning of the so called 'Green Revolution', where supplying technological product packages of seed and agrochemical inputs for monocultures on large tracts of land in some developing countries would increase yields and production for cash crops (e.g. in Asia but not Africa), but would prove to be incompatible with the cultural and social structures surrounding farming practices in many places that it was implemented (e.g. Africa). Indeed, its successes for decreasing hunger and malnutrition was a useful stop-gap solution, yet has not shown to be a sustainable approach for contributing to local food security or diet diversity for resource-poor small tract farmers or generate sufficient surplus income for many to be a path out of poverty (IAASTD, 2009b). Meeting these needs for a healthy and diverse diet would require the development of locally adapted varieties that are tailored to local environments, agricultural practices and needs for a range of nutrient dense foods from local food crops (Reynolds, 2006). 'Although the world food system provides an adequate supply of protein and energy for over 85 % of people, only two-thirds have access to sufficient dietary micronutrients. The supply of many nutrients in the diets of the poor has decreased due to a reduction in diet diversity resulting from increased monoculture of staple food crops (rice, wheat and maize) and the loss of a range of nutrient dense food crops from local food systems.' (IAASTD, 2009d).

Those who might invest in research or invent solutions that are not derived from a technology or technological process leading to a product that can be licensed under existing IP instruments are often left out of the innovation development and support system. Instead of a view of agricultural innovation focused on seed products from genetic improvement or developing external inputs, the neglected innovations are often locally adaptable practices and services related to complex and dynamic ecological processes that do not lend themselves to commodification—at least not in the way current IP instruments require—but are transferable knowledge that can undergo further innovation at the local level by the end user. A good example of this is the 'push-pull' systems developed at the ICIPE in Kenya (Cook, 2006; Hassanali, 2008).

For this case study on innovation, we have chosen to contrast genetically modified (GM) crops and agroecological methods as two examples of innovation outputs and strategies that have very different outcomes in the way we produced food. We illustrate how these contrasting innovation strategies shape, and in some cases limit, future social options. The former is driven by production goals and short-term profit maximisation incentives, where the predominant types of GM crops developed thus far are economically profitable within a system of high-input industrialised monoculture that is largely unsustainable in its reliance on external, non-renewable inputs. In such systems, economies of scale allow the farmer to outweigh the higher costs of production of such farming practices ([1]). The latter innovation strategy, based on an understanding of co-evolution and dynamics at ecological and social levels of agriculture, is better suited to agricultural systems that are in transition to sufficient production and socio-ecological sustainability, and requires a broader range of incentives and shelters to succeed (Tilman, 2002). That is, agroecological systems may be better suited than the current practice with GM crops to answer the call from affluent consumers for food quality, sustainability and social equity in a wide sense, responding to health and environmental concerns as well as securing livelihood in local small-scale agriculture. These issues may be crucial for the future of diverse agricultural practices needed to address improvements to the resilience and sustainability of agricultural systems. If we fail to address the governance of innovation in food and fibre production now, then current indications are that we will surely design agriculture to fail.

([1]) While hypothetically not all GM crops would necessarily require high-input or monoculture farming methods, their development to date has focused on 'technology traits' amenable to agricultural practices focused on high-input and monoculture production methods.

19.2 Innovation: what kinds and for whom?

Agriculture has not escaped the wave of new policies behind the banner of 'innovation'. The European Commission (EC) is running the 'Innovation Union' campaign (EC, 2011). The explicit claim is that innovation 'speeds up and improves the way we conceive, develop, produce and access new products, industrial processes and services. It is the key not only to creating more jobs, building a greener society and improving our quality of life, but also to maintaining our competitiveness on the global market.' The EC further endorses innovation as a means for stimulating economic growth investment in knowledge generation where 'innovative ideas that can be turned into new marketable products and services help create growth and quality jobs' (EU-Council, 2011). Similar initiatives and campaigns will be found in most developed and developing countries (Kiers, 2008) ([2]).

How innovation is conceived shapes how it is promoted, and who benefits from the promotion. The EC sees 'expensive patenting, market fragmentation, slow standard-setting and skills shortages' as barriers to innovation because they 'prevent ideas getting quickly to market' (van den Hove, 2011). This preoccupation with how efficiently technology products flow from knowledge holders to technology users is what Altieri (2002) called the 'top-down transfer-of-technology approach' in the context of addressing the needs of poor farmers. Here innovation is often framed in terms of economic growth in a competitive global economy, a focus that may conflict with efforts to reduce or reverse environmental damage caused by existing models of agriculture, or even disincentivise investment into socially responsible innovation (Tilman, 2002). This is an aspect deserving of representation in European innovation discourses, policies, and actions (van den Hove, 2012).

Kiers et al. (Kiers, 2008) argue for a more comprehensive approach to innovation: '[i]nnovation is more than invention. Success is not based on technological performance in isolation, but rather how technology builds knowledge, networks and capacity…innovation demands sophisticated integration with local partners'. This emphasis on the appropriateness of the technology for the target user is what Altieri (2002) called 'a 'bottom-up' approach, using and building upon the resources already available: local people, their knowledge and their autochthonous natural resources. It must also seriously take into consideration, through participatory approaches, the needs, aspirations and circumstances of smallholders'. The bottom-up approach also may involve the public as a key actor in decisions in the design of food systems, particularly as it relates to food quality, health and environmental sustainability.

Either pathway could lead to policy decisions to drive efficiencies in food production, lower food costs through increased supply, and become a means out of poverty. Where these pathways differ is in *who is considered the critical innovator and thus who should primarily benefit from innovation policies*. The key innovator in the top-down approach is usually a specialist technology producer, such as an agroindustrial company that builds technologies optimised for a specific type of farming system that shape the agroecosystems in which they are to be applied. For example, the use of herbicide tolerant GM plants coupled with the application of a specific herbicide creates a type of farming suited towards low agrobiodiversity and high capital inputs (e.g. multi-row spraying equipment) to maximise efficiency, and demands a scale investment and specialised farmer. However, this approach is incompatible with the available resources and needs of the subsistence and small farmer (see Box 19.1), the key innovator in the bottom-up approach and the target of strategies to feed the world through local production (IAASTD, 2009a). Bottom-up approaches place emphasis on the ability of the small-scale farmer to innovate to address critical local needs.

Will the predominant top-down approaches to agricultural innovation— and the science policies and legal instruments which support them — be better pathways to achieving the Millennium Development Goals, namely, to sustainably feed the world nutritious and desirable food, and through the production of this food, provide pathways out of poverty for the poor? Or might there be alternative strategies better suited to meeting these needs?

Our focus here will be whether top-down innovation produces the necessary benefits to small-scale farmers as well as income- and food-insecure countries as has been claimed. And in this attempt to create a consistent set of common regulatory and market incentives

([2]) For example, New Zealand defines it this way: 'Innovation is defined as the introduction of any new or significantly improved goods, services, processes, or marketing methods' (see Statistics-NZ, 2012).

Box 19.1 Herbicide tolerant GM crops: a technology for developing country agriculture?

Starting in the 1990s, the agroecosystems adopting herbicide tolerant GM crops simplified weed management through a near exclusive reliance on a single agrochemical product ('Roundup'), with its active ingredient glyphosate. The Roundup and Roundup-tolerant GM crop package promises lower labour costs through a simplified weed management strategy. It is also compatible with no-till practices that can reduce soil erosion (Duke, 2008).

These advantages are, however, disappearing (Service, 2007; Pengue, 2005b;Benbrook, 2012). Extensive and continuous use of glyphosate with the introduction of GM crops (Powles, 2008) has led a rapid evolution of glyphosate-resistant weeds (Binimelis, 2009; Duke, 2008; Heap, 2012; Heinemann, 2008; NRC, 2010). This has a negative overall effect on sustainability, where minimising the use of external inputs such as agrochemicals is key. Since glyphosate tolerance can be overcome by using more glyphosate, farmers have entered into a treadmill where overuse of a single product leads to tolerance and tolerance is overcome with more product, leading to ever higher levels of tolerance in weeds and an increase in the number of species that display tolerance (Binimelis, 2009; Duke, 2008; NRC, 2010). In some cases, farmers are returning to tilling and using other (and possibly more toxic) herbicides (Binimelis, 2009; Duke, 2005; Heinemann, 2008b; Mortensen, 2012). Further, indications of harm stemming from the widespread and intensive use of glyphosate for the environment and human health has been documented in the scientific literature and remains a concern (Greenpeace, 2009; Séralini 2012).

The herbicide-GM crop package is not compatible with how most people farm, and especially with small and subsistence farming practices. The package is most economical when herbicide can be sprayed in great quantities using mechanised delivery (e.g. airplanes) or expensive, multi-row sprayers and this would not be possible in a mixed cropping landscape (Binimelis, 2009).

Moreover, this top-down solution to the problem of weeds threatens long-term retention of alternative weed control skills. 'Although seed and chemical companies can generate enormous revenues through the packaged sales of herbicides and trans- genic seeds, the [integrative weed management] approaches… are based on knowledge-intensive practices, not on saleable products, and lack a powerful market mechanism to push them along' (Mortensen, 2012). The farming system is 'deskilling' and losing the know-how to implement other pest management approaches (Binimelis, 2009). A second problem with this package is that it is encouraging the expansion of damaging agricultural practices. For example mixed agriculture/animal husbandry instead would require animal production further out into marginal lands or necessitate clearing new lands and accelerating rates of deforestation (Morello, 2007).

A bottom-up innovation for addressing weed problems is integrative weed management (IWM). The advantages of this system are that it uses, maintains and improves local knowledge of weed dynamics and ecology to develop multiple weed management approaches (Liebman, 2001) and is affordable to poor farmers. 'IWM integrates tactics, such as crop rotation, cover crops, competitive crop cultivars, the judicious use of tillage, and targeted herbicide application, to reduce weed populations and selection pressures that drive the evolution of resistant weeds' (Mortensen, 2012). IWM improves agrobiodiversity conservation, soil-quality, on farm energy efficiency — all of which enhance a more multifunctional system of agriculture that produce important environmental services (Boody, 2005). Farmers benefit from the same high yields and profits (Anderson, 2010; Liebman et al., 2008; Pimentel, 2005). Further, the soil-building under IWM helps to achieve conservation goals and improves soil quality even above no-till approaches based on herbicides (Venterea, 2006). This does not cause resistance problems of the magnitude seen with simplified chemical controls (Davis, 2007).

'Stacking additional herbicide tolerance genes into existing plants is not an alternative to IWM or other pest management strategies. They are likely to undermine sustainable agriculture further because 'the new traits will encourage continued neglect of public research and extension in integrated weed management' (Mortensen, 2012).

The transfer of herbicide tolerant GM crops to poor farmers, which has demonstrated not to be a sustainable approach for addressing the needs of developed country agriculture, appears to be another example of a top-down approach that has not, and will not produce the beneficial outcomes for the poor farmer (Heinemann, 2008b). However, there are already viable bottom-up approaches; all that is lacking is the political will and institutional capacity to make them available.

Box 19.1 Herbicide tolerant GM crops: a technology for developing country agriculture? (cont.)

Finally, the adoption of these crops is not leading to uniform or sustainable increases in income for farmers (Botta, 2011). The highest yielding varieties of GM crops are so because of ongoing and intensive genotype improvement through traditional breeding, rather than through the development of genetically engineered traits (Gurian-Sherman, 2009). Even in the most mature GM agroecosystems, such as cotton plantations in the US south, GM-farmers have not enjoyed a net economic benefit for adopting these plants compared to other high yield varieties (Jost, 2008). The high rent of patent-protected seeds is an upfront cost to farmers who may not realise a benefit from the trait each year, or would have to purchase other inputs, such as expensive agrochemicals, to gain any benefit. Here again, especially for poor farmers, those initial costs can be too high (Delmer, 2005).

(itself a top-down approach) if it in tandem will be suited to promoting the kind of innovation needed in countries with conditions favouring small-scale farms as well as those that are poor and food insecure. Building on the late lessons from prior top-down innovations in agriculture, we find that the promise of this approach to deliver the expected benefits will continue to be elusive when the pace and scale of innovations are prioritised over considerations for the intertwined institutional, governance and societal issues. Critically, innovation pathways that do not include such considerations may condition innovation directions, diversity and distribution away from the very kinds of innovation that are best adapted to meet local needs (STEPS, 2010). With this in mind, the lure of short-term wealth production from predominantly productivist frameworks for innovation must be re-balanced with those that prioritise long-term goals for sustainability — including financial sustainability and nutritional goals of small and subsistence farmers. This means supporting not just innovations which create new technology, but also those that create social good by addressing the non-technological, social, institutional, organisational and behavioural aspects along with new technology (van den Hove, 2012).

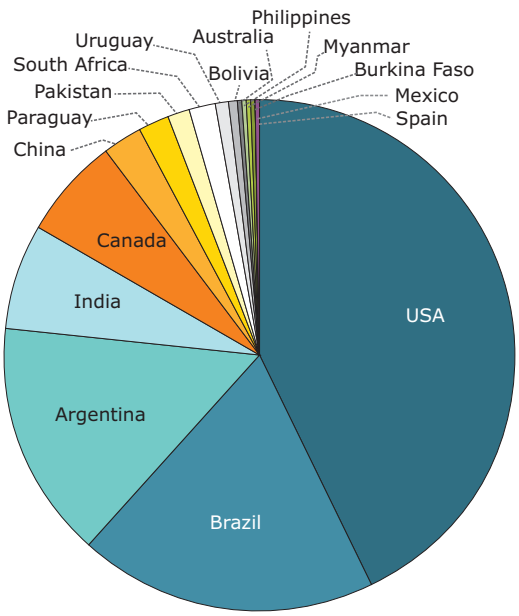
There is increasing evidence that the top-down approach to innovation will not achieve the expected stimulus to innovation (Baldwin, 2011), where an approach reliant on private incentives (primarily through IP protections) may actually have a negative effect on the progress in certain fields, including biotechnology (Murray, 2007).

19.3 GM crops as a top-down path out of poverty and hunger

The use of genetic engineering to produce commercially viable GM agricultural products is so far and for the foreseeable future restricted to crop plants (Heinemann, 2009). The crops are predominantly cotton, maize, rapeseed (canola) and soybeans ([3]) (James, 2011). Despite more than 30 years of research and development and nearly 20 years of commercialisation of GM crops, surprisingly only two traits have been significant in the marketplace — herbicide tolerance and insecticide production. And they are grown at scale only in a small number of countries. Industry-derived figures (James, 2011) report a large number of global hectares under GM cultivation, but when examined by country indicate an uneven global commitment to GM crops. The five countries USA, Brazil, Argentina, India and Canada account for 91 % of the global GM crop production, with the next five largest GM-cultivating countries accounting for another 8 %, leaving a total of 1 % of all GM acreage produced annually among just seven other countries. The proportion of agricultural land with GM varied from < 1 % to 17 % per country (Figure 19.1). These 17 so-called GM 'mega-countries' combined had 159 million hectares under GM cultivation in 2011 — seemingly a large figure, but in reality is just 3 % of the world's agricultural land (Figure 19.2). Some crop types have been converted entirely (or effectively entirely) to GM production in some countries. For example, nearly 100 % of the soybean crop in Argentina and the US is GM, sugarbeet in the US, and cotton in India at the present time is almost exclusively GM.

([3]) However GM papaya, sugar beet and possibly alfalfa are grown commercially in the US, with tomato and peppers reported in China yet at very low levels.

Figure 19.1 Ranked commitments to GM by the 17 largest producing countries



Hectares

Ranked order of countries by proportion of agricultural land under GM crop cultivation

12–17 %	5–9 %
USA	Pakistan
Argentina	Uruguay
Paraguay	India
Canada	Philippines
Brazil	

1–3 %	< 1 %
Myanmar	Mexico
Burkina Faso	Spain
South Africa	
Australia	
Bolivia	
China	

Note: Left: Countries range from a high of 69 million (USA) to < 50 000 hectares. Lowest level shown in graph is Spain at an industry estimated 100 000 hectares.

Right: Countries range from a high of 17 % (USA, Argentina) to under 1 % conversion from conventional to GM plants in commercial production. The rankings by proportion differ from the rankings by absolute number of hectares showing significantly different commitments to GM for primary production.

Source: GM hectares data taken from the industry source ISAAA (James, 2011). Agricultural land values taken from FAOSTAT (FAOSTAT, 2012).

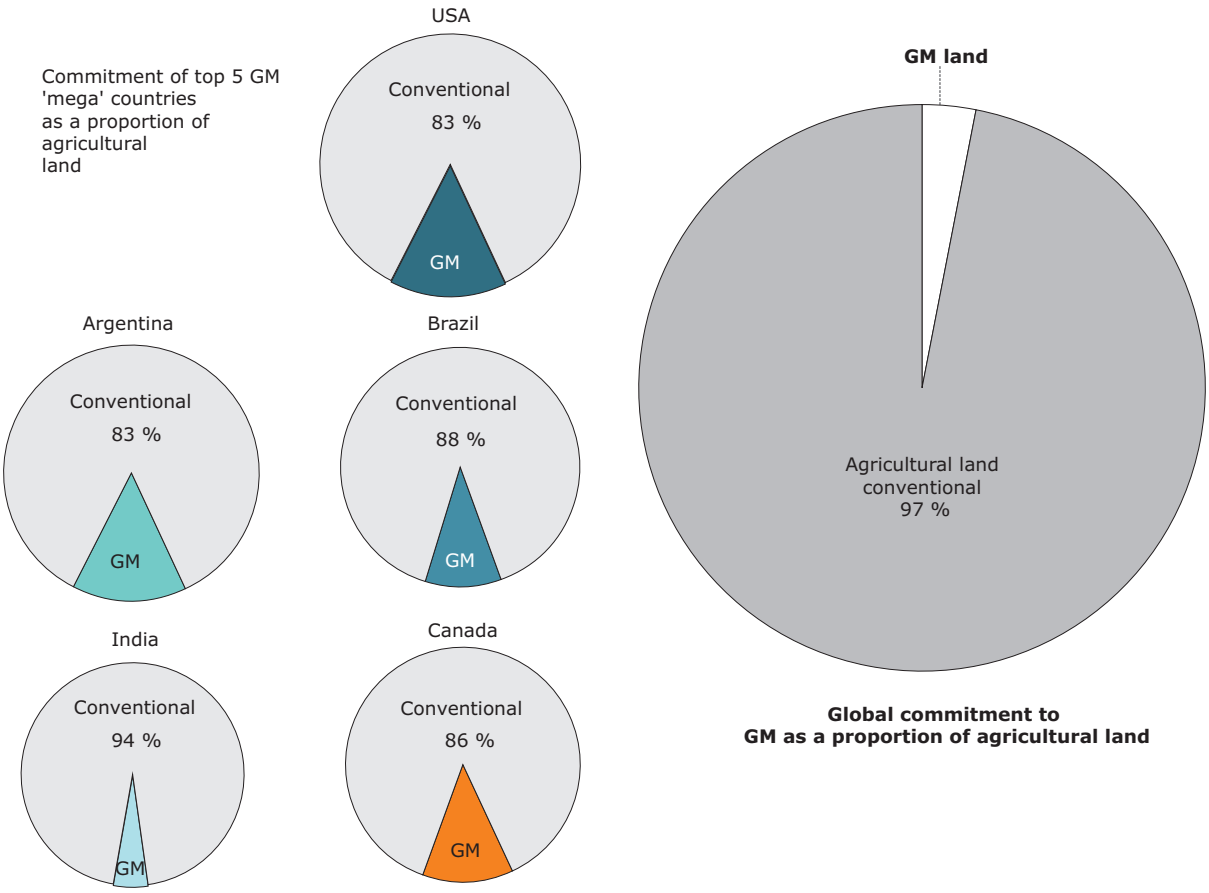
Why this patchy and limited global adoption of GM? There are several reasons. First, significant markets of high-income consumers have rejected GM (Gaskell, 2010). Given that the types of crops being commercialised, and the types of traits on offer, provide no direct benefit to consumers and may be introducing unintended adverse effects (see Box 19.2), in some places there exists skepticism on claims of net benefit. The main argument for adoption is the indirect benefits, financial and management-related, that GM crops offer to certain kinds of farmers (Heinemann, 2009).

Among the GM-adopting farmers are usually large-scale commodity growers that cultivate monocultures (e.g. soybeans in Argentina) or are in two-crop rotations (e.g. maize/soy in the US Midwest). The US and other OECD countries produce plenty of food or have the income to purchase it. While their agricultural systems deliver what they need, the OECD agroecosystems rely on heavy taxpayer subsidies to remain viable (Kiers, 2008).

It is perhaps no surprise that GM crops, the paradigmatic examples of top-down products, are most commonly crops that benefit from subsidies, such as maize, soy and cotton in the US (Pechlaner, 2010). These subsidies lead to the second reason for patchy adoption, where their use in developed countries undermines the market for these crops in developing countries. 'The average support to agricultural producers in the major developed countries as percentage of gross value of farm receipts was at 30 % for the period 2003–2005, representing an amount of almost USD 1 billion per day (OECD, 2006). These developed-country agricultural policies cost developing countries about USD 17 billion per year — a cost equivalent to five times the recent levels of ODA [official development assistance] to agriculture' (Hoffman, 2011).

The incentive brought by subsidies give a third reason for patchy adoption. The high rent of GM seeds and associated management inputs, such as proprietary agrochemicals, and other high costs of high external farming, confines these tools for agriculture to countries that redistribute wealth to farming for export, whether rich or poor (Delmer, 2005). Such capital and management intensive

Figure 19.2 Proportion of land in GM production



Note: Left: Charts indicate the proportion of total agricultural land per country in GM cultivation. The 5 countries shown have the highest absolute number of hectares in GM.

Right: Global value of GM production as a function of global agricultural land.

Source: GM hectares taken from the industry source ISAAA (James, 2011). Agricultural land values taken from FAOSTAT (FAOSTAT, 2012).

agricultural practices simply are not well adapted to use by small and subsistence farmers (see Box 19.1).

Poor countries that adopt this export lead are in danger of being caught on a loss leading treadmill where they produce agricultural goods at a net social loss and must continue to bear this debt as agriculture becomes a leading source of export income (Heinemann, in press; Pengue, 2005b). GM crops have not migrated to countries that have yet to commit to this strategy or are avoiding it, because the upfront costs are too high (Delmer, 2005).

19.3.1 Top-down incentives homogenise tool building

Too often the 'how to feed the world debate' (possibly a shorthand for the Millennium Development Goals) is presented as if it were an either/or choice between genetic engineering and agroecological science (Marris, 2008; Vanloqueren, 2009). Advocates for or against these technologies often are distinguished by their beliefs on whether it is genes or the environment that is the right substrate to manipulate to improve agriculture.

This dichotomy is in essence artificial, because few when pressed would argue against the relevance of both genotype and environment for meeting agricultural production and sustainability goals. However, there is an underlying truth to this division. The emphasis on genetics, or seed-based tools (Lal, 2009), is an unavoidable outcome of how innovation in the top-down model works. Modifying genotypes and capturing them as IP through plant variety protection and patent instruments is a far easier means of capturing financial benefits than

attempting to commodify management-based innovations, such as cover crops, rotation schedules and composting, farmer-initiated training and education and small scale marketing and credit programs. When a singular, centralised and highly specialised approach to agricultural development is followed, such as through genetic engineering, it can stifle other approaches that might produce even more desirable outcomes.

The size of the market available to genotype-manipulated tools may also be larger than for management-based approaches ([4]). Provided that the agroecosystem can be homogenised through the use of external inputs (e.g. fertilisers, agrochemicals), then a small number of varieties based on a proprietary genotype can be sold to a large number of farmers. In contrast, management-based techniques are knowledge- rather than product-intensive and must be customised to the location and often the circumstances of the farmer (e.g. whether irrigated or non-irrigated land, mixed or monocropping, combined crop and livestock production) and thus require more investment relative to the size of the market. Yet the benefits of these investments to promote and sustain management-based agricultural improvements are better distributed because they are not concentrated back to a seed producer. However, these asymmetries in investment incentives mean that management-based approaches do not receive the same levels of support and investment as do approaches that are easily recaptured in the marketplace.

To some degree, however, the environment does offer commercial opportunities through top-down innovation yet even then it comes from selling farmers tools that homogenise the environment to support proprietary genotypes. These tools are usually in the form of external inputs such as fertilisers and agrichemicals. The success of the green revolution was its ability to convert very different lands into similar agroecosystems using external fertilisers and other inputs to achieve high yields, but at great long term environmental costs, fossil fuel consumption and greenhouse gas emissions (Giampietro, 1993; Pretty, 2011; UNEP, 2011). Indeed, the unsustainability of the green revolution shows it will not be the model for future agriculture.

The editor of Nature magazine summed up the duality of genotypic and environmental sources of technology for addressing future needs in agriculture when he said: 'A second green… revolution will require a wholesale realignment of priorities in agricultural research. There is an urgent need for new crop varieties that offer higher yields but use less water, fertilisers or other inputs — created, for example, through long-neglected research on modifying roots — and for crops that are more resistant to drought, heat, submersion and pests. Equally crucial is lower-tech research into basics such as crop rotation, mixed farming of animals and plants on smallholder farms, soil management and curbing waste. (Between one-quarter and one-third of the food produced worldwide is lost or spoiled.)' (Editor, 2010).

That is, the tools and knowledge needed to transform agriculture towards a more sustainable path are not sufficiently prioritised in research and development. The failure of current top-down approaches to deliver on promises of a wide range of trait innovations needed by farmers, for example those that are tolerant to various environmental stresses (i.e. salt tolerance, water stress tolerance) requires a fundamental shift in agricultural innovation priorities towards improvements in genotype and environmental management approaches.

19.3.2 Effects on the knowledge pipeline

At the start of the 21st century public sector spending on agricultural research and development was just under twice the amount spent by the private sector (IAASTD, 2009b). Developing countries invested the majority of public funding at around USD 12 billion per year while high-income countries invested only around USD 10 billion. To see the investment imbalance another way, consider that the Consultative Group on International Agriculture Research, the world's largest international public sector research body, has an annual budget of only 12 % of the combined research and development budgets of the world's 6 largest breeding and genetic engineering companies (Spielman, 2007). Private funding in agricultural research is largely focused on innovations that will allow a high return on that investment to shareholders.

These statistics require deeper analysis to be fully understood. First, the shift in responsibility for agricultural research and development from

([4]) While both classical breeding and genetic engineering are different ways to create plant varieties, the latter creates novelty through the use of modern biotechnology (involving the in vitro manipulation of nucleic acids or fusions across the taxonomic boundary).

public research institutions to the private sector is unequivocal in high-income countries. This shift has profound effects on what comes from innovation. Second, high income countries have cited the need for increasing their economic competitiveness through instituted 'industry-driven' priorities into the research and development spending that they still do, thereby further leveraging the public contribution toward (often privately held) top-down innovation. This compromises the unique function and capacities that public funding supports pro-poor agriculture (Spielman, 2007), which may lack sufficient financial incentives to attract investment from the private sector (Tilman, 2002). Third, much of the existing public funding has direct or indirect ties to industry. Direct ties can take the form of private-public partnerships at universities and indirect ties include preferential relationships with institutions that maintain long-term industry-friendly cooperation (Knight, 2003; Lotter, 2009b; Seabrook, 2011).

Top-down innovation is guided by patent and patent-like plant variety protection (PVP) instruments, many newly applied to agriculture only in the last decades of the 20th century (Heinemann, 2009). Patents 'provide more control since (PVP) certificates have a research exemption allowing others to use the new variety for research purposes' (Fernandez-Cornejo, 2006; Mascarenhas, 2006).

The general argument for this approach is that patent and patent-like IP rights instruments on biotechnology create net social benefits, by encouraging and then capturing wealth for developers whether they be private or public (Pray, 2007). The main limitation here is that such an approach ignores significant effects on the innovation pipeline (Heinemann, 2006b; Kleinman, 2003; Krimsky, 2004; Shorett, 2003b; Wright, 2000) which shift innovation priorities towards economic policies and financial incentives. Leading international institutions have dismissed prevailing IP instruments as agents of constructive economic or food security change in developing countries at least at their stage of development (WHO, 2005; WorldBank, 2007). Furthermore, they impede practices that uphold and improve both food security and sovereignty. For example, seed savings and exchanges have become incompatible with these more severe IP instruments as shown in the conversion of behaviour in the US, and would, if adopted by developing countries, undermine what is now seen as an important source of bottom-up innovation: farmer by farmer breeding and adaptation of germplasm (Bellon, 2011; Borowiak, 2004; Mascarenhas, 2006; WHO, 2005).

The patenting of germplasm is concentrating IP rights-based control of the seed supply under a very small number of multinational corporations (Adi, 2006; Barlett, 2008; Sagar, 2000; Howard, 2009). The consolidation of the seed industry also has resulted in lower competitiveness (Pinstrup-Andersen, 1999) as the 'concentration of the top four' (CR4) seed companies breached a critical threshold (WorldBank, 2007). For example, the UK Parliament now says that:

'The use of patents on genes is controversial. There are concerns that in countries where GM technology is widespread in agriculture, seed companies may have reduced incentives to develop conventional varieties, as the market for these varieties is reduced, and they tend to have weaker IP rights than the patents usually used with GM crops. In the US, this is the case for soy, with conventional breeding now mainly left to universities and to small seed producers who focus on niche markets. The presence of patents may also limit public-sector research in some areas' (POST, 2011).

Is the answer to empower public institutions to secure IP instead? If the goal is to stimulate innovation across the board, history to date indicates that it does not seem to be so. Intriguingly, the flow of IP to the private sector has been fuelled by an unprecedented accumulation of IP claims in biotechnology made by public sector institutions whose behaviour is consistent with top-down innovation models despite their historic public-good role (Graff, 2003). This creates a feedback loop in which the best-funded researchers are those with top-down innovation interests, and they in turn out-compete other researchers — and their possible innovations — from future funding. This loop can decrease bottom-up innovation, even products that would provide much greater benefit. The downstream effects are stifling of public-good knowledge commons, upon which the modern agroecosystems of North America and Europe were initially built, and neglect of the needs of poor and subsistence farmers who are key to feeding the world.

'[F]or scientific knowledge subject to both Open Science and private property institutional regimes, the granting of IP [rights] is associated with a statistically significant but modest decline in knowledge accumulation as measured by forward citations (in academic publications)…Overall, we are able to reject the null hypothesis that IP [rights] have no impact on the diffusion of scientific knowledge… These patterns provide a novel perspective on the economic consequences of the privatisation of the

Box 19.2 GM crops: a late lesson case in the making?

The benefits and harms of GM crops are still being verified, despite there being science-based calls for greater scrutiny concerning the release of genetically engineered organisms from early on in the US FDA ([5]) (Drucker, 2012) and elsewhere (Traavik, 1999). The literature is accumulating indicators both of inflated benefit claims and of evidence of adverse effects (Bøhn, 2008; Botta, 2011; Hilbeck, 2012; Jost, 2008; Mesnage, 2012; Rosi-Marshall, 2007; Service, 2007). The benefits that may have been overstated are the reduction in pesticide use (Service, 2007), the reduced use of more toxic pesticides (Mesnage, 2012; Séralini, 2009), higher yields (Gurian-Sherman, 2009) and farmer income (Jost, 2008).

While GM crops are not found at scale in many places (see Figure 19.1), because they dominate as commodity crops they can be present at low levels in many types of food and feed, fibres and industrial products. Thus, exposure is global even if production is mainly in a few countries.

At what point is there sufficient evidence to be concerned and take action about the effects of GM crops on human health and the environment? How strong is the evidence of safety vs. risks?

The outcomes of many risk assessment studies equate the conclusions of 'no evidence of harm' to be synonymous with safety. The troubling outcome is that the safety of GM crops is presumed when there is a lack of evidence of harm, as if this were equivalent to evidence of lack of harm, when it clearly is not. Hence many of the safety conclusions arising in risk assessments stating 'no evidence of harm' are assumptions-based, rather than evidence-based, reasoning (Spök, 2004). Critically, when this lower standard of safety assurance is followed, as is the case with the mainstream risk assessment approaches today, important effects may be missed.

Of course, it is plausible that there simply are no effects to be found. Yet, what is the likelihood that the existing risk assessment approaches would capture an adverse effect caused by a particular GM plant? Are there particular challenges to detecting biologically important but difficult to detect effects? If so, what regulatory approaches can help avoid or overcome these challenges?

Emerging from the experience with biosafety research and risk assessment is a number of obstacles and limitations in policy or methodology that can limit or underestimate the detection of potential harms that may be present.

Obstacles to conducting biosafety research

Biosafety research and the safety investigations required for regulatory approval are the two main means for identifying potential adverse effects. However, a number of obstacles may limit or prevent the observation adverse effects in research, if they were indeed occurring:

- Industry contracts with researchers and farmers restrict access to material for safety testing. For example, 26 scientists released a public statement criticising that confidentiality and material transfer agreements made conducting any independent research on GM foods virtually impossible (Pollack, 2009).

- GM innovation research and development is outpacing biosafety research necessary to evaluate for safety. When it comes to research funding for biotechnology (including genetic engineering research), biosafety-related research has been lagging behind. From 1992 to 2002 the USDA disbursed USD 1.8 billion for biotechnology research, yet only approximately 1 % (USD 18 million) of this went to risk-related research (Mellon, 2003).

- Safety interested scientists face tough career choices. Researchers who have published scientific evidence unfavourable to the interests of GM crop developers have experienced personal and professional attacks on their work (Delborne, 2008; Editor, 1999; Waltz, 2009a, 2009b), and in some cases leading to threats or loss of research funding and dismissal (Lotter, 2009a, 2009b).

([5]) FDA Memos. FDA Memos 1991, 1992a and 1992b above are 3 of 24 internal FDA documents obtained through a FOIA (Freedom of Information Act request by the Alliance for Bio-Integrity, see http://www.bio-integrity.org/list.html).

Box 19.2 GM crops: a late lesson case in the making? (cont.)

Risk assessment: barriers to detecting adverse effects

The release of a GM crop into the environment, or for use in feed or food, is preceded in many countries by a pre-market risk assessment. The principles, concepts and methodologies of assessment vary, but most countries use international guidance (e.g. OECD/Codex Alimentarius, Cartagena Protocol on Biosafety) as a basis of their systems. Scientific and other information may also inform the risk assessment or secondary evaluation by expert committees.

Policies can undermine the effectiveness of risk assessment (Pavone, 2011) by allowing risk standards which increase the likelihood that adverse effects, if occurring, would not be identified during the appraisal.

Key examples:

- Many jurisdictions require scientific testing to be done by the developer and supplied to the regulator, who often lacks any capacity to perform independent testing. This lack of independence in the testing sets up the situation of bias in the studies outcomes as a result of 'the funding effect' — where results tend to correlate with the wishes of the funder (Krimsky, 2004). Various research efforts have found that the funding effect reaches well into the public research community and especially into biotechnology (Diels, 2011; Heinemann, 2006a; Shorett, 2003a).

- Often there is a provision to keep secret information that the developer claims is of proprietary value. When regulators agree to keep some information in the risk assessment confidential, review or reproduce the study by independent scientists is prevented (Fontanarosa, 2005). Transparency is a fundamental principle of good science reporting and practice but lacking in many risk assessments (AHTEG, 2012).

- Risk research conducted for the purposes of a risk assessment by the developer often lacks sufficient methodologies to allow statistical rigor that would yield meaningful results. Risk studies with low sample numbers lack statistical power, and bias the outcome towards no observation of differences/ effects between treatment groups (for examples, see Marvier, 2002). Further, they might not have been designed to test for potential hazards that the regulator has not asked the developer to test, or to the sensitivity that the regulator might find valuable (Séralini, 2009) or which have long lag time frames (Marvier, 2007).

- The regulator's policies on what to test will also affect what might be found. This approach may miss unintended changes to other gene products or metabolites or the effects of cooking and processing. For instance, applicants are often allowed to use a transgenic protein 'surrogate' (derived from a source other than the transgenic organism for which environmental release or consumption is being sought) in the place of the actual transgenic protein in safety testing from which regulatory approval is sought. Often the protein used in safety testing is that produced in bacteria, which is not going to be released into the environment or used as food — leaving the actual protein produced by the GM plant untested for safety. Since there can be significant biological differences in how the transgenic protein is produced in different hosts (e.g. in plants vs. bacteria), any differences would not be possible to detect (Freese, 2004).

- Currently, no regulatory framework requires mandatory toxicity or allergenicity testing from the consumption (or inhalation, see Kroghsbo 2008) of GM crops or their products. Commonly, only 90-day (usually rat) feeding trials are conducted and conclusions of long-term risk are based on these short-term tests, despite their critical deficiencies in revealing sub-chronic and chronic effects (Séralini, 2009; Spiroux de Vendomois, 2010). Research has indicated the importance of life-time studies for health affects where indications of adverse health impacts only manifested after 120 days (Séralini, 2012).

- A common practice in risk assessment is a comparative approach: the new GM plant is compared to a similar plant to see if there is any evidence of additional potential to cause harm. In actual practice, however, developers will often further include 'reference lines' (usually genetically less similar and grown under different environmental conditions) in the comparison which will expand background variation where any potential signals to be drowned in statistical noise and thusly concluded as 'within the range of biological variation' (Antoniou 2012; Dolezel and Gaugitsch 2009).

Box 19.2 GM crops: a late lesson case in the making? (cont.)

- Ongoing risk assessment may not be benefitting as much as it could from new information, because of a general lack of comprehensive post-release monitoring efforts. As pre-market risk assessments are based on information acquired over short term and/or small scale investigations, they are not designed to capture effects that may occur when exposure is on a larger scale, or for longer time periods, or result from unanticipated interactions with other GM plants post release. While monitoring is mandated in some jurisdictions there is very little information on its effectiveness and no uniformity in design or methodology (Züghart, 2008, 2011; AHTEG, 2012; Heinemann, 2012).

Can the precautionary principle make scientific risk assessments more scientific?
The precautionary principle has been legitimised as an important objective in GMO legislation (e.g. European Union, Cartagena Protocol on Biosafety). Nonetheless, it thus far has mainly been considered as a risk management tool and not part of the scientific risk assessment. While critics of the precautionary principle consider it easily misused as a barrier to trade and the cause of more regulation, this misrepresents how precaution may be appropriately applied. Importantly, precaution has a role to play in the scientific risk assessment itself in two fundamental ways. First, applying precaution within risk assessment practice also means applying more robust scientific standards — that is, the need for precaution and the need for scientific rigor are not incompatible but complementary (Groth, 2000). Second, particularly when testing hypotheses, value judgements within science practice (Funtowicz, 2003; Rudner, 1953) may be informed by precaution, including levels of evidence, directions of error (Brosi, 2009; Lemons, 1997), and by acknowledging and communicating what we know, do not know, and cannot know with existing methodologies (Aslaksen, 2006; Myhr, 2002). The formal acknowledgment of uncertainties and the choice of error type from the risk assessment and their communication to decision-makers are key components of rigorous science-based risk assessment.

Conclusion: avoiding old lessons from earlier late lessons
The critical late lesson that may be emerging from GM crops is not the evidence of harm — the early indications of harm are just emerging — but the persistence of the same institutional patterns that led to the old late lessons already learned from asbestos, benzene and BSE (Harremoes, 2001). In these cases, weak risk assessment standards were implemented that prevented identifying the harm and taking precautionary action. To avoid this old lesson, the appropriate application of the precautionary approach to risk standards would help ensure we are not repeating the same error with GM crops, and thus avoid a late lessons case in the making.

scientific commons. Rather than simply serving to facilitate a 'market for ideas,' IP may indeed restrict the diffusion of scientific research and the ability of future researchers to 'stand on the shoulders of giants,' at least for research of the type published in *Nature Biotechnology*' (Murray, 2007).

This has been a brief review of the predominant top-down innovation models that characterise the main policy developments of wealthier and food rich nations (Heinemann, 2009). We have found that if this framework of innovation for agricultural development is followed, the outcome is likely contrary to the stated objectives to create a global food production capacity that delivers on calories and nutrients to all. It will fail in the long run to produce food security because it does not have the necessary incentives to create resilient and sustainable production systems. If the demands on agriculture are reasonably expanded to include delivery of culturally diverse foods, produced locally by those most in need, and which serves as a path out of poverty, then the top-down innovation models of today are the wrong pathways to achieve it.

In coming to these stark realisations, we do not argue that top-down innovation is irrelevant at all times and in all countries. Indeed, the right mix of innovation is essential. Likewise, seed-based versus environmental approaches both have value in all agroecosystems at all times. The question is more complex. When industries or private providers become out of balance in scale, power or access to information, then one can smother the other. At the heart of it, most farmers are private sector, even if they are feeding themselves with the products of their labour and capital. But there is a difference between the economic scale of the large US farming unit and the farmer, especially the one most prone to hunger, and the one searching for long-term

agroecosystem sustainability. Similarly, there is a difference in scale between the university and the multinational corporation, and between both and the farmer. When public institutions must act in a way that is consistent with how companies must act, then the imbalance between farmer and knowledge access grows.

19.4 The bottom-up path towards sustainable farming

A core quality of bottom-up approaches is that they can generate, harness and exchange information and innovation in a multitude of ways that bring users of innovations into the process so that local adaptation and shaping of technologies fit the ecological, socio-cultural and technical dimensions of the system (STEPS, 2010; Wagner, 2007).

Bottom-up innovation is demonstrating its potential to build not just sustainable farming systems, but also sustainable communities through the support of local food production and local markets (Altieri, 2011a; UNEP-UNCTAD, 2008). Discussions on increasing agricultural sustainability tend to put the emphasis on biodiversity, soil and water management and ecological principles to improve productivity and energy efficiency (including reductions in greenhouse gas emissions). This is a specialty of the science of agroecology. Instead of engineering nature to fit into our desired technological system, agroecological innovations fashion our technological solutions to fit nature (Schumacher, 1973) by applying ecological concepts and principles to the design and management of agroecosystems (Altieri, 1995). Agroecology strives to increase the sustainability of agriculture by minimising the use of agrochemical and energy inputs and instead leverage ecological synergisms and interactions between biological components of the agroecosystem to produce their own productivity, crop protection and soil fertility. This type of production system has also been captured as a means for transitioning to more sustainable agricultural practices under the banner of 'green agriculture' (UNEP, 2011).

While this science also values the importance of conventional breeding and genotype optimisation, it tends to address yield problems using management solutions, often through a modification of agricultural practices that remove, rather than adapt to, the problem (Lal, 2009). Biodiversity is important to create greater system resiliency within the agricultural environment (Enjalbert, 2011; Ensor, 2009; Li et al., 2009). Enhancing on-farm biodiversity and soil organic matter can make agriculture more resilient to climate change (drought, flooding, severe weather, and temperature change) and enhance ecosystem services (Hajjar, 2008). In a recent survey, of agricultural productivity after hurricane Mitch in Central America revealed that farms that engaged in agroecological practices such as intercropping, cover crops and agroforestry incurred less damage than neighbouring conventional monoculture farms (Altieri, 2011a). Hence, increasing the adaptive potential of agricultural systems will be vital in the face of global climate change (Bellon, 2011).

We have chosen to use agroecological science (including compatible organic certification schemes) as an example of an outcome of bottom-up innovation because this science is delivering excellent results in the farming systems most in need of innovation (Altieri, 2011b; De Schutter, 2010; FAO, 2011b; Pretty, 2011; UNEP-UNCTAD, 2008 (Khan et al., 2008)). The main feature of the bottom-up approach is that it decentralises solution providers and their solutions, thereby facilitating the transfer of products, services or information that allows continued innovation at the hands, skills and knowledge of the local user. In contrast to top-down approaches, the real innovation potential does not stop with the farmer, but often starts there. In addition, consumer concerns and desires for food quality, health and environmental concerns are facilitated by initiating discussions over agricultural innovations as a bottom-up approach (SCAR, 2012).

It is important to distinguish between traditional farming approaches and agroecological science. The former can, yet in different ways be as destructive to the environment, and unsustainable, as any high external input industrial 'modern' farm (IAASTD, 2009a). While in general agroecological science utilises a 'low tech' toolbox, it is far more sophisticated, knowledge intensive, and integrative both on environmental and institutional levels than simple kitsets of seeds, fertilisers and agrochemicals that characterise industrial farming operations. That is, this approach creates a strong need for farmer support through extension services and farmer-lead educational initiatives, calling for broad participation across a range of scientific disciplines and policy actors.

19.4.1 Bottom-up incentives homogenise productivity and resilience rather than tools

Rather than sell farmers packages of tools that bring in improved seed and convert their soils to near replicas of those for which elite varieties of

plants have been optimised, agroecological science facilitates local development of soil conservation practices and supports farmer seed exchanges for breeding of local varieties or local elite varieties (Badstue, 2007; Jarvis et al., 2008). These practices support agrobiodiversity, which contributes to sustained productivity by creating resilience to unpredictable changes at the local level, such as to resource availability, or changes to climate, all the while making the farm less likely to attract pests (Bellon, 2011; Jarvis, 2000). Here the emphasis is on the farmer rather than the breeder, where they are different (Reynolds, 2006).

The focus on farmers is a viable alternative to the focus on genotypes. As the UN FAO have argued, '75 % of the additional food we need over the next decades could be met by bringing the production levels of the world's low-yield farmers up to 80 % of what high-yield farmers get from comparable land' (Molden, 2007). This suggests that the future of sustainable, low impact agriculture is one in which products and methods are developed at landscape rather than global or even national levels. In this way we agree that 'there is a need to invest in science and practice which gives farmers a combination of the best possible seeds and breeds and their management in local ecological contexts' (Pretty, 2011).

19.4.2 Bottom-up innovations are participatory

Bottom-up approaches often include participatory activities built on open collaborative models, with the aim to address problems that are relevant to the local ecological and sociocultural context through experimentation and education (Baldwin, 2011; Ceccarelli, 2006; Toomey, 1999; Witcombe, 1996). Even where the incentive systems are tuned towards generating IP, such as in plant breeding, the choice of relevant instrument can encourage ongoing innovation through participatory innovation development.

For example, legal instruments such as patent-like PVP and patents restrict farmer use of this legally protected germplasm from breeder innovation unless they negotiate permission for use from the license holder. Poor and subsistence farmers who may most benefit from their own local innovation are unlikely to have access to either public or private patent holders who reside in urban centres far away, often out of country (Howard, 2009). In contrast, PVPs which recognise breeder's rights allow farmers and others to continue development including making locally adapted varieties for sale or for exchange (Figure 19.3). PVP allows a wave of innovation to extend from an initial variety and contributes to the speed of technology transfer within an institutional context that supports agricultural sustainability (Gyawali, 2007; Steinberg, 2001). Thus breeding innovation that is centrally controlled by contracts between the license holder and selected breeders can bottleneck technology transfer. This phenomenon has been associated with the 'yield gap' experienced by GM varieties because of the use of patents to control these products (Fernandez-Cornejo, 2006).

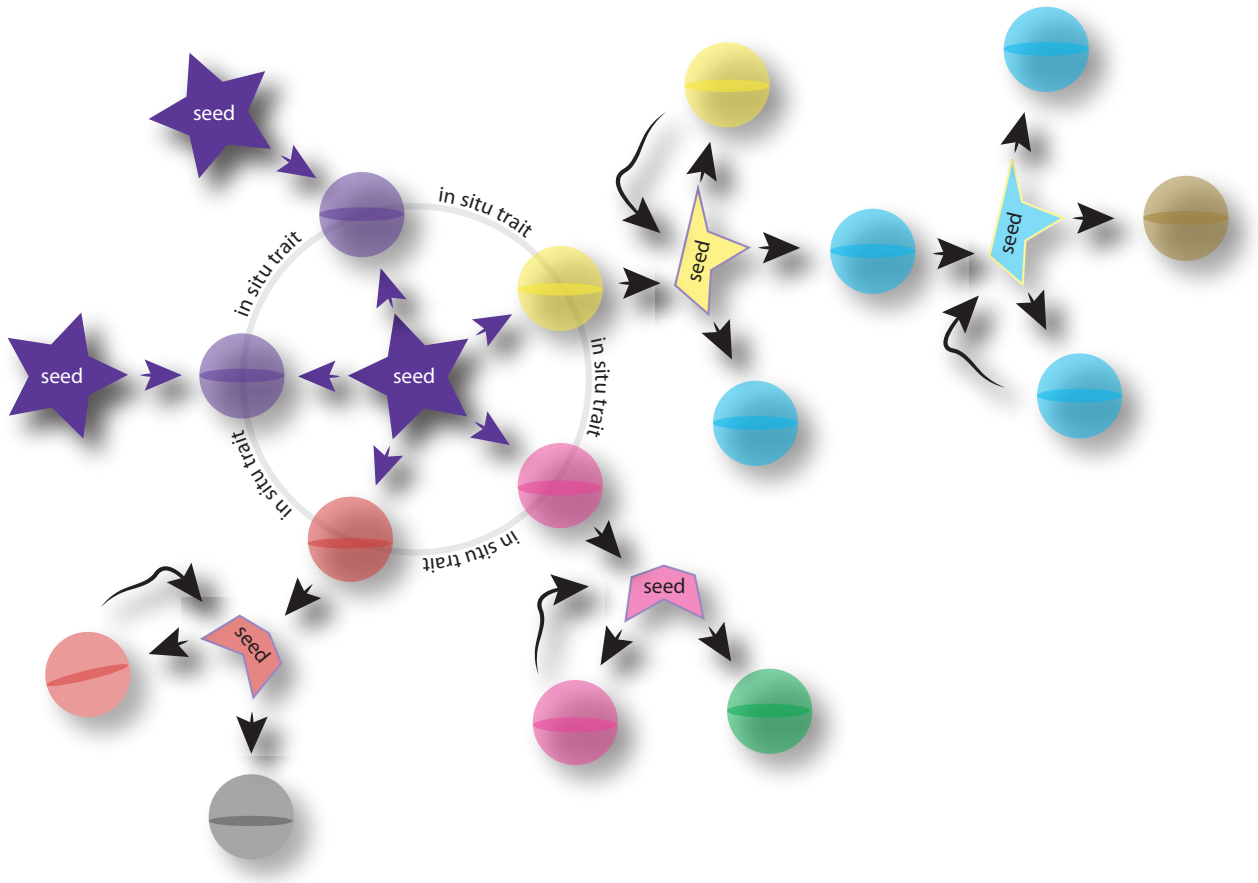
The knowledge required to select and save seed, and the infrastructure for exchanges, are also social resources that if (or when) lost may be difficult to re-establish (Howard, 2009). In a future of climate change, decentralisation of public breeding and in situ conservation are likely to be fundamental to the survival of billions of people (Bellon, 2011; Ceccarelli, 2006; McIntyre, 2011).

'Farmers (including pastoralists and agro-pastoralists) should not simply be seen as maximisers of food and agricultural commodity production, but also as managers of the food and agricultural commodity-producing eco-systems' (Hoffman, 2011). That role requires farmers to have freedom to innovate as well as the confidence of governments in the value of that innovation.

Participatory research that leads to new innovations in agriculture often starts from a point of co-inquiry, whereby farmers and scientist work as partners and bring their own, complementary knowledge, experience and insights to developing innovations that are relevant to the needs of farmers. That is, participatory research treats farmers as experts with their own scientific knowledge and experience that is complementary to more formalised training expertise. In participatory breeding initiatives, traits of value to local farmers might be identified and often are different than those valued by national and international breeders: 'Professional breeders, often working in relative isolation from farmers, have sometimes been unaware of the multitude of preferences — beyond yield, and resistance to diseases and pests — of their target farmers. Ease of harvest and storage, taste and cooking qualities, how fast a crop matures, and the suitability of crop residues as livestock feed are just a few of the dozens of plant traits of interest to small-scale farmers…' (Toomey, 1999).

Another example of participatory innovation models, the farmer field schools, have been instrumental in designing new ways to decrease

Figure 19.3 Participatory IP instruments



Note: When farmers and breeders can continue to innovate on seed or propagule stock, the benefits of elite varieties are more quickly adapted to local conditions and other desirable traits and may inspire new breeder income. Consider seed with a novel genotype (purple star) being sold to farmers who find a variety of phenotypes after planting (pink, yellow, orange circles) due to local gene x environment interactions. Some of these new phenotypes may be desirable and could inspire the farmer or professional breeder to capture the new variety for ongoing sale. Other farmers may wish to return to the original seed stock (purple stars to the left). The new varieties may be purchased by other farmers or the same farmer and additional breeding may bring new and some desirable traits (blue, brown, blue, green and black circles).

insecticide use in studies from Indonesia, Bangladesh and Vietnam, and increases in crop yield in China, India and Pakistan (Van den Berg, 2007). These programmes teach farmers how to problem solve and experiment independently through interactive learning, which will help adapt technologies to their specific environmental and management needs (Vasquez-Caicedo, 2000).

19.4.3 Bottom-up approaches deliver the right kind of innovation to the right kind of users

Agroecological bottom-up innovations are relevant and work. By focusing on locally adapted and developed integrative innovation over remotely developed standardised innovation they can help create sustainable farming systems that deliver more food, nutrition and wealth to the farmers and their communities that are needed to feed the world. There is mounting evidence that the scale-up of these approaches may offer, beyond improvements to crop productivity, enhanced environmental benefits, e.g. reductions in chemical inputs and soil erosion, improved water conservation and soil organic matter content, and higher levels of biodiversity (Pimentel, 2005). Further, bottom-up approaches offer a means to tackle issues related to land degradation to restore soil fertility (de Jager, 2005).

The world's largest meta analysis comparing science-lead industrial and agroecological (organic) farming systems found that the latter could match

the former in the common metric of yield (Badgley, 2007). Critically, this intensification of farming systems through agroecological science achieved the same or superior yields with a concomitant reduction of external inputs, including a much lower dependence on agrichemicals and fossil fuel-derived fertilisers. Finally, this study also provided evidence to suggest that mature agroecological conversions (those in excess of five years old) consistently out produced industrial operations. This study exposed the reason for other studies reporting that agroecological farms are less productive: it takes about five years of intensive work to rehabilitate soils converted from traditional or industrial farming management to agroecological and past studies lumped young and mature conversions together.

International projects to initiate organic and sustainable agriculture have shown excellent overall results. UNEP-UNCTAD reported an average crop yield increase of 116% for organic and near-organic projects involving more than 1.9 million African farmers on roughly 2 million hectares of cultivated land within the 114 cases analysed. The benefits were not just in yield — improvements in natural, social and economic capital associated within these farming systems led to an array of benefits that have increased food security. The report authors concluded: 'Organic agriculture can increase agricultural productivity and can raise incomes with low-cost, locally available and appropriate technologies, without causing environmental damage. Furthermore, evidence shows that organic agriculture can build up natural resources, strengthen communities and improve human capacity, thus improving food security by addressing many different causal factors simultaneously' (UNEP-UNCTAD, 2008), and can be more economically profitable than conventional farming (Edwards, 2008; Nemes, 2009).

Another synthesis study investigated the increases in productivity since the implementation of 286 sustainable agriculture initiatives from the FAO, which covered 37 million hectares in 57 countries (Pretty, 2008). They found increased productivity on 12.6 million farms with an average crop increase of 79 %, and a rise in key environmental services.

A commissioned report from the Foresight Global Food and Farming Futures Project of the UK government (Foresight, 2011) appraised 40 sustainable intensification projects developed in the 2000s, from 20 countries in Africa. The projects were developed based on a range of bottom-up approaches to agriculture, including participatory plant breeding, integrated pest management, agro-forestry and agroecological soil conservation measures. The results speak for themselves: by 2010 the projects had led to a range of documented benefits and improvements to 12.75 million hectares for the 10.39 million farmers and their families, including a doubling of crop yields, on average (2.13-fold increase) spanning a 3–10 year period (Pretty, 2011).

Results from bottom-up approaches are also evidenced in the global North. In Wisconsin, USA, a 12-year study on productivity of organic vs. conventional cropping systems found that diverse, low-input systems can be as productive per unit of land as that of conventional ones (Posner, 2009). A 30-year study by the Rodale Institute in the US compared organic and conventional agricultural methods and found yields, economic viability, energy efficiency and human health indexes improved with organic farming (Rodale, 2011).

Scaling up these successes will require policies that stimulate investment into key sectors that support bottom-up approaches. In one modeling study (UNEP, 2011), the outcomes of targeted 'green' investments over a 40 year period are compared to the same amount of financial investment into conventional and traditional 'business as usual' agriculture of today. Overall, the green investments lead to numerous comparative benefits, including increased yield, soil quality, greater water efficiency and land use, increased GDP growth and employment, and reduced CO_2 emissions and energy consumption. Therefore the potential scale-up for agroecological based bottom-up approaches appear to be immense.

19.5 Case example: Contrasting top-down and bottom-up innovation solutions to water stress

Consider the anticipated application of top-down innovation to address the challenges of agricultural water stress. Agriculture is already the largest user of water among human activities and lack of access to water is an increasing problem (Hoffman, 2011; Marris, 2008). Climate change is expected to further exacerbate the problem (Schiermeier, 2008). The most likely top-down product for addressing this problem will be genotypic changes to germplasm to enhance traits that confer drought tolerance. Already progress is being made in some crops through classical breeding (CIMMYT, 2012; Heinemann, 2009), especially augmented through

marker-assisted selection ([6]). Yet similar genotypic approaches using genetic engineering have not been as successful. As drought tolerance depends on the action of multiple genes, drought tolerant varieties require changes in multiple genes all at once, rather than adding genes singularly (as with genetic engineering). Developing adapted varieties will require more responsive breeding and development than can be offered through the extensive process for creating a commercially viable genetically engineered drought tolerant product (Gurian-Sherman, 2009; Heinemann, 2008a, in press). Further, plants with ever more extreme adaptation of genotypes will likely continue to exacerbate the depletion of the water table. Nevertheless, any seed (or propagule)-based product that is better adapted to drought stress would be amenable to prevailing IP instruments such as plant variety protection (PVP), patent-like plant variety protection, or patents and therefore it is no surprise that genotype innovation receives so much emphasis, especially from industry.

In contrast, bottom-up environmentally based management solutions, some of which have been in practice for decades, tend to raise latent water levels and retention capacities in soil as well as improve the genetics of crop plants (Heinemann, 2008a; Lotter, 2003; Pimentel, 2005; Scialabba, 2007). Environmental management using locally-adapted drought tolerant varieties, cover crops, polycropping, rotating in fallow years, compost and soil conservation to raise organic matter levels, agroforestry and building small dams all raise water levels (Altieri, 2002; Lal, 2006). The resiliency of this kind of system is equally affected: In fact, it may not be possible to feed the world in 2050 unless soil quality and water retention capacity are raised regardless of how efficient plants can become at extracting water (Hoffman, 2011). 'If soils are not restored, crops will fail even if rains do not; hunger will perpetuate even with emphasis on biotechnology and genetically modified crops' (Lal, 2008). Many of these improvements would be considered innovations by our bottom-up definition (Kiers, 2008), but by their nature could not be easily described or protected by patents or similar IP instruments in order to facilitate the knowledge transfer to the commercial sector, and thus are not innovations in the currently practiced top-down model. By following the top-down approach, the private sector will offer solutions to a problem that either possibly cannot be solved using technologies that are described under prevailing IP instruments or which will only shift the problem in time or space, addicting us to finding and producing even more extreme genotypes through genetic modification.

19.6 Conclusions

We have attempted to contrast two pathways to innovation and their relative opportunities and costs for agricultural development. We find limitations to top-down innovation because of largely productivist objectives. These tend to shut down rather than open up innovation and options, particularly those for addressing social welfare issues. Further, science and its role as a public good become conditioned within certain notions of progress (Callo, 1994). This framework will only continue to create technological lock-ins and path dependence to specific research choices at the expense of others (Stirling, 2007).

We find that both top-down and bottom-up approaches will have their roles to play, but getting them in the right mix, order and framing is critical to ensure their benefits and risks are more evenly distributed if we are to produce the kinds of innovations capable of achieving the Millennium Development Goals. This will require rebalancing innovation towards the public good, further requiring that innovation frameworks focus not only on scientific and technological developments, but also on the interlinked institutional, organisational and social changes. In terms of agriculture, taking these issues seriously means operationalising the outcomes from the IAASTD (2009a) and SCAR (2012) reports. The recent recommendations on research, innovation and agricultural knowledge coming from the European Commission's Standing Committee on Agricultural Research (SCAR) call for 'increased support be provided for research on the economic and social dimensions of these new technologies and farming practices. Approaches that promise building blocks towards low-input high-output systems, integrate historical knowledge and agro ecological principles that use nature's capacity should receive the highest priority for funding' (SCAR, 2012). To achieve this, a public sector free from political incentives for top-down innovation is an essential capacity. However, the small business and the farmer, while still private sector and benefiting from proprietary knowledge, will be an essential source of creativity, problem solving and income for their communities.

([6]) Marker-assisted selection is a breeding technique that uses biotechnological tools to concentrate particular traits within the existing plant by traditional breeding. This allows for a more efficient breeding process for achieving varieties with specific traits of interest. It does not involve the use of in vitro modified nucleic acids as with genetic engineering.

Further, scientists are not passive members of the scientific enterprise, but a powerful force from within that influences the techno-sciences and the options available to society to benefit from scientific research. The modern techno-science culture took shape just after WWII in an unusual convergence of thinking across the East-West geopolitical divide. Nuclear power in the United States and space travel in the Soviet Union become exemplars of a new form of conceiving and doing science, and witness a deep transformation in its ethos and political economy. The convergence of internal culture, economic and political power was and is an irresistible force. Scientists today cannot shirk from their role and their responsibility on how science is done and governed, as practitioners and frequently as participants, entrepreneurs and citizens.

Lastly, top-down innovations will be most effective when scientific knowledge from specialised fields within biology, chemistry, ecology, genetics, soil microbiology, etc. converge with bottom-up approaches to innovate locally optimised solutions. In this way, the benefits of advanced scientific knowledge will naturally become be much more diverse and widely distributed.

We have made the case that the future of agriculture and global food security is one that requires a truly long-term vision, attendant to the environmental and social costs of production, and with an emphasis on the small and subsistence farmer. Long term, there will be enough food if agriculture both intensifies and remains local. We have found that if the bottom-up approach is followed, the transfer of knowledge and further innovation potential is augmented, and success far more likely, than the outcomes witnessed to date from the prevailing top-down approach, where the innovation potential downstream is severely limited. Conversely, the proceeds of bottom-up innovation disproportionately flow to adopters rather than the providers. By their very distributive and participatory nature, bottom-up innovation strategies do not tend to concentrate power, financial or political, into providers which otherwise are easily displaced by wealthier and more powerful champions of top-down policies.

If the policy demands on agriculture are reasonably expanded to include delivery of culturally and nutritionally diverse foods, produced locally by those most in need, and which serve as a path out of poverty and malnutrition, then the bottom-up innovation models are the responsible innovation models, and require investment and support (De Schutter, 2011).

On the one hand, we have explored a path directed by top-down innovation models. As a type of black-box technology that is protected by particularly restrictive IP instruments (patents and patent-like PVPs), so-called 'biotech' crops (GM and similar) and their co-technologies are expensive to buy, destroy local seed savings and exchange practices, and prevent further farmer tinkering and improvement of innovations. When working as advertised, we find that top-down innovation as promoted by the large market economies, directed at advancements in agriculture (which ironically is maintained by extra-market subsidies), undermines the stated national and international goals of poverty reduction, sustainability, and increases food insecurity. They contribute to a feedback loop that continues to concentrate wealth and power into a smaller number of companies and large farms (Botta, 2011; Spielman, 2007; USDA, 2009; World Bank, 2007). Top-down providers are invariably attracted to the largest markets (real or subsidised), the most uniform agroecosystems, and the highest volume farmer. They therefore will always serve last those who are foremost needed to feed the world in the future: the presently small and subsistence farmer on < 2 hectare plots of land where highly diverse and intermixed crops and livestock production work best to meet local needs.

On the other hand, bottom-up approaches emphasise the contextual role of innovation, even when the product is technology (van den Hove, 2012). Bottom-up innovation is the kind that provides useful tools, methods and knowledge that can be adapted to and by the farmer and farming system. Products that depend on ecosystem, cultural and financial homogenisation damage biodiversity and ecosystems, but also cultural identities as they eliminate the need for local knowledge (in the short term) and shift communities away from traditional foods and ethnobiological knowledge. Obstacles to taking bottom-up approaches need to be addressed and overcome by policy makers seeking to create a sustainable agricultural system (De Schutter, 2009, 2011).

If there is a solution to the global mal-distribution of access to sufficient quantities of nutritious foods, how do we find it? In the process, how do we build agriculture into a pathway out of poverty without also raising greenhouse gasses and increasing soil erosion? How can we support agricultural systems that are resilient and sustainable? A commitment and investment of public resources as incentives to promote strategies for agricultural and ecological sustainability will require a radical shift on how we think about and perform innovations in the future,

where 'business as usual' in agriculture is no longer an option. As Einstein said, 'The solution will not come the same kind of thinking that created the problem'…

Innovations in agricultural food production have been deeply part of the human experience for over 10 000 years. They will continue to be central to how we feed the world. The agricultural innovations of the future will have to be more 'hands on' and local if we are to meet our goals of food security, poverty alleviation and environmental sustainability (Benessia, 2012). For as long as the problems needing products are framed as technological rather than social, behavioural or political, then innovation will be directed toward technological products (van den Hove, 2012). The technological 'solutions' are often just responding to symptoms of the underlying cause of existing socio-ecological solutions. As the late Nobel Laureate Joshua Lederberg said: 'Our imperfect solutions aggravate every problem.' (Lederberg, 1970).

We find the '3D Agenda' of the STEPS Centre (2010), cognisant of the ways which the directions, distribution and diversity of innovations affect their use, to be a compelling model for the future thinking of innovation in agricultural development.

As we have discussed, where the directions of innovation that follow top-down approaches — highly specialised, centralised and capital intensive — tend to shape innovation towards technological lock-ins. Economic and political forces that promote these innovation trajectories then become hard to reverse, or crowd out alternative approaches, such as agroecology. In contrast, bottom-up approaches facilitate participation of the user to shape the directions that innovation will take. The innovation direction further moulds the potential distribution of benefits, costs and hazards brought by the adoption of the innovation pathway. Often top down approaches leverage legal instruments of knowledge control that close down access to knowledge or further innovation, defines who indeed innovation is for, who can access it, based on who can afford to pay for it. An important consequence here is that top-down approaches marginalise those for whom innovations are more critically needed to increase the productivity and sustainability of agriculture. Lastly, these two aspects of innovation — direction and distribution — further determine the diversity of innovation possible, not only the scientific and technical aspects of innovation, but the social, organisational and innovations that support it. Diversity in innovation buffers against lock-ins and creates the potential for local adaptation within the ecological and economic contexts for which they are designed. This means a more integrative focus of the agroecosystem, beyond the genotype approaches towards augmenting biodiversity within agro-environments to develop sustainable and resilient agroenvironments as protection against future uncertainties.

19.7 Lessons learned

In 1961, outgoing President of the US Dwight D. Eisenhower warned society to be vigilant of the large, concentrated interests in technology when he said: 'The prospect of domination of the nation's scholars by Federal employment, project allocations, and the power of money is ever present — and is gravely to be regarded. Yet, in holding scientific research and discovery in respect, as we should, we must also be alert to the equal and opposite danger that public policy could itself become the captive of a scientific technological elite' (Wikisource, 2012).

The early warning, or perhaps late lesson, to be heeded here is that if one follows the top-down, usually technologically oriented, approaches to innovation,the desired outcomes for addressing food insecurity will not be achieved. Top-down approaches will most likely fail to deliver on the large promises of food security and alleviation of poverty, mainly because these approaches contribute to a feedback cycle that concentrates resources, knowledge, and influence as witnessed in the seed and agrichemicals sector (Adi, 2006; De Schutter, 2009; Fernandez-Cornejo, 2006; Howard, 2009). Through this power, top-down providers can artificially homogenise both the conception of the problem to be solved and the solutions — such as GM crop plants — they propose. All too often questioning the *rationality* of the approach gets lost in the background of the unquestioning discussion over the *use* of the approach (Pavone, 2011 and see discussion in Boxes 19.1 an 19.2). Perhaps greater reflection and social deliberation into why and for whom agricultural innovations should be produced is needed if we are truly going to follow more sustainable pathways in the production of food and fibre.

In the path ahead, societies will have to make more conscientious choices of how to define and shape innovation to produce solutions that are appropriate for meeting global challenges related to agriculture. Bottom-up approaches are proving capable of getting sustainable, participatory and locally adapted solutions into the hands of those that need them most (Altieri, 2011a;

De Schutter, 2011), but are incapable of flourishing where invention is limited to what can be easily described by prevailing IP instruments. Change the directions, distribution and diversity of innovation, and you change the world.

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20 Invasive alien species: a growing but neglected threat?

Sarah Brunel, Eladio Fernández-Galiano, Piero Genovesi, Vernon H. Heywood, Christoph Kueffer and David M. Richardson

Biological invasions are one of the five major causes of biodiversity loss as global human travel and trade have moved, and continue to move, thousands of species between and across continents. Some species of alien origin have a high probability of unrestrained growth which can ultimately lead to environmental damage.

An alien species — animal, plant or microorganism — is one that has been introduced, as a result of human activity, either accidentally or deliberately, to an area it could not have reached on its own. A common definition of the term 'invasive' focuses on its (negative) impact, while other definitions consider only rate of spread and exclude considerations of impact.

Despite the growing amount of legislation being adopted at the global scale, biological invasions continue to grow at a rapid rate, with no indication yet of any saturation effect. Decision-making in this area is very challenging. The overall complexity of the problem, its interdisciplinarity, the scientific uncertainties and the large number of stakeholders that need to be informed and involved, together demand governance actions that are difficult to see emerging at the regional scale (as in the EU), let alone globally.

It is widely agreed that preventing biological invasions or tackling them at a very early stage is the most efficient and cost-effective approach. Harmless species can be confused with harmful invasive species, however, leading to a waste of resources. Even more seriously, harmful invaders can be mistaken for innocuous species — so-called 'invaders in disguise' — and no appropriate action may be taken to counter the threats they pose.

Even with a very good risk assessment system, new outbreaks of invasive alien species could still occur, necessitating a system of rapid early warning and effective eradication response. The decision on where to draw the line on the acceptable environmental risks versus the introduction of new species or new communities that may carry invasive alien species then becomes a value judgement.

There is lively debate within the scientific community regarding the most appropriate strategies for managing invasive alien species. Governments and institutions charged with making decisions have access to considerable knowledge on the topic, but the lack of rules of interactions between multiple parties regularly thwarts effective decision-making.

20.1 Introduction

Biological invasions are one of the five major causes of biodiversity loss, alongside habitat destruction, over-exploitation, climate change and pollution (Millennium Ecosystem Assessment, 2005). Global human travel and trade have moved, and continue to move, thousands of species between and across continents (McNeely, 2001). Only a small proportion of alien species become established, some of these spread, and a small subset produce major ecological, economic or social effects (generally termed 'impacts'). Ecological impacts include local extinction or a reduction in the diversity of native species, and various types of ecosystem-level changes such as modifications of nutrient cycling or water quality. As an example, in an analysis of 680 recent animal extinctions worldwide, causes were compiled for about 25 % of these. Ninety-one (54 %) included invasive species among the causes of extinction, and in 34 cases they were the only known cause (Clavero and Garcia-Barthou, 2005). For example, feral cats on islands are responsible for at least 14 % of global bird, mammal, and reptile extinctions in recent times (Medina et al., 2011). All types of organism, from micro-organisms, including microbes and diseases, to mega-herbivores, can become invasive, and all can cause impacts on biodiversity and ecosystem functioning. All types of ecosystem are affected: terrestrial, freshwater and marine.

Biological invasions are receiving increased attention in many countries, some of which have already set in place comprehensive legislation or national strategies to deal with various aspects of invasions, in particular concerning their management (e.g. Australia, Great Britain, Mexico, New Zealand, South Africa and USA) (Pyšek and Richardson, 2010). As regards the management of invasive alien species (IAS), it is widely agreed that preventing biological invasions or tackling them at a very early stage is the most efficient and cost-effective approach. For example, the cost of eradicating weeds can increase at least 40 times if action is not taken promptly (Harris and Timmins, 2009), and in most cases eradication quickly becomes unfeasible (Genovesi, 2007). Preventive management calls for a precautionary approach, because prompt response often does not permit full assessment of the risks connected to a newly detected invasion (Genovesi et al., 2010). Despite widespread agreement on these principles, the full range of problems associated with IAS still lacks political recognition and too few government-coordinated actions are in place, or are effective, in most parts of the world, including in the European Union.

There is nevertheless a lively debate within the scientific community regarding the most appropriate strategies to adopt for managing invasive alien species. Aspects of this debate offer important pointers to dimensions that need to be better studied and the measures needed to make the phenomenon of biological invasion better understood by all stakeholders. Invasive alien species represent a growing threat, in particular in a globalised world, as they are introduced and spread by people (McNeely, 2001). This is more a human-driven environmental problem than a strictly biological one. Inherent uncertainties remain about what species will be introduced and which will become invasive. Consequently, making decisions is very challenging. The overall complexity of the problem, its interdisciplinarity, the scientific uncertainties, and the large number of stakeholders that need to be informed and involved, together demand governance actions that are difficult to see emerging at the regional scale (as in the EU), let alone at the global scale. Lessons already learnt in different parts of the world need to be considered when seeking to improve management regimes for IAS in different environments and at different scales.

20.2 The difficulty of defining invasive alien species

The terminology applied to organisms involved in biological invasions is complex, often confusing, and there is no universally accepted definition of IAS (Riley, 2005; Falk-Petersen et al., 2006; Richardson et al., 2011a); all this has serious practical consequences. The term 'alien' (exotic, foreign, non-indigenous, non-native) requires a geographical, biogeographical or ecological context to have a useful meaning — an alien species is one which has been introduced as a result of human assistance, either accidentally or deliberately, to an area it could not have reached on its own. The area in question has to be specified since a species 'may be alien to any definable area, e.g. continents, islands, bio- or eco-regions, or any political entity (e.g. countries, states, provinces)' (Lambdon et al., 2008). The terms alien and invasive both have political overtones. The Convention on Biological Diversity (CBD) requires its Parties, through Article 8(h) to 'prevent the introduction of, control or eradicate those alien species which threaten ecosystems, habitats and species' and uses the term 'invasive alien species' to refer to such species and defines these as 'alien species whose introduction and/or spread threaten biological diversity'. The term 'invasive' is therefore defined by the CBD in terms of (negative) impact, while other definitions

employ ecological and biogeographical criteria, i.e. invasive species are defined as alien species that sustain self-replacing populations, often in very large numbers at considerable distances from the site of introduction such as in natural areas, and explicitly exclude considerations of impact (see Richardson et al., 2011a; Blackburn et al., 2011 and references therein). Other definitions also include economic impacts, for example on agriculture or the use of amenities, and social impacts such as on human health.

In general, the biogeographical concept is more widely used in the academic world, whereas the impact concept is widely used by decision makers (Ricciardi and Cohen, 2006). Such terminological and conceptual problems have contributed to difficulties in developing a coherent and effective political response to biological invasions.

The amount of information on IAS has grown steadily (Gurevitch et al., 2011) in the last 20 years. Since 2000, when the International Union for the Conservation of Nature (IUCN) Invasive Species Specialist Group (ISSG) established the Global Invasive Species Database (http://www.issg.org/database/welcome/, the first web-based, freely accessible database on invasive species), many tools have been created ([1]). However, partly for the reasons discussed above, accurate and comprehensive information on global or regional numbers of invasive alien species is still difficult to obtain and statistics that are available are often ambiguous and difficult to interpret (e.g. see discussion in Richardson and Rejmánek, 2011). Even taxonomic reference works such as *Floras and Faunas* are notoriously bad at distinguishing between native and alien species (Lambdon et al., 2008). The need for accurate identification is an essential prerequisite for detection of IAS, and many cases of misidentification are coming to light. For example, harmless species can be confused with harmful invasive species, leading to a waste of resources and, even more serious, harmful invaders can be mistaken for innocuous species, so-called 'invaders in disguise' (Verloove, 2010), and no appropriate action taken to counter the threats they pose.

Europe is fortunate in having generally good information about invasive alien species, with many countries having prepared lists, although much more critical evaluation is needed in many cases and under-recording remains a problem. An overview is provided by the DAISIE database (http://www.europe-aliens.org/) and its List of Species Alien in Europe although there are still significant gaps in coverage and distribution and many problems of accurate identification remain to be resolved. For example, even well-known plant invaders such as *Heracleum mantegazzianum* and *Fallopia japonica* are frequently confused with related species, and the invasive hybrids often referred to as *Rhododendron ponticum* have now been named *R.× superponticum* (Cullen, 2011). In other taxa such as the genus *Opuntia* it is often unclear which species are involved in particular invasions, with experts disagreeing, for example, about whether *O. maxima* and *O. ficus-indica* are separate species.

However outside Europe, very few countries have comprehensive, regularly updated lists of alien or invasive alien species. For example, the McGeoch et al. (2010) review of available data on invasive alien species for a set of 57 countries found that the number of invasive alien species varied from 9 to 222, reflecting as much a lack of information as real differences of incidence. Furthermore, because of the dynamic nature of biological invasions, the lists that do exist need regular revision. An example of the difficulties of interpretation is the much-cited paper by Pimentel et al. (2005) which estimates that 50 000 alien species have entered the US. This figure is, however, misleading unless broken down. In the case of plants, the figure of 25 000 alien species (compared with a native flora of about 17 500 species) includes agricultural and horticultural crops, timber and ornamental trees, garden plants, and weeds! In addition, although several countries had compiled lists of alien or invasive alien species by the late 1990s, there is general lack of coordination and harmonisation between these lists. Aggregation of lists developed using different criteria and definitions is a complex task which makes the interpretation of data and the planning of common action difficult and laborious.

20.3 Emergence of awareness of an old problem

The effects of IAS have been known for a very long time. As early as 77AD, Pliny the Elder wrote in his *Naturalis Historia* (The Natural History) that the invasion of rabbits in the Balearic Islands, Spain, was a very severe problem requiring effective control (see Scalera and Zaghi, 2004). In the 19th century,

([1]) See http://www.cbd.int/doc/meetings/sbstta/sbstta-15/information/sbstta-15-inf-14-en.pdf for a very partial overview of main global data providers.

Charles Darwin noted the invasive behaviour of some alien species during his explorations on the *Beagle*. Indeed, Darwin's musing on invasive alien species contributed to the development of his theory of the 'survival of the fittest' (Darwin, 1859). In most cases, however, alien species at that time were regarded as curiosities, rather than a significant threat to global or even regional biodiversity. Concerns regarding the impacts of alien species on native vegetation, particularly on islands (Kiehn, 2011; Kueffer et al., 2010), started to be voiced in the 19th century (Inderjit et al., 2005; Cadotte, 2006). For example, J D Hooker wrote in 1864: 'Among the most interesting phenomena connected with the distribution of plants, are those that concern the rapidity with which some species of one country will, when introduced into another, rapidly displace the aborigines and replace them' (Hooker, 1864). It was not, however, until the 20th century, especially in the second half, that they began to be recognised as a rapidly growing threat to global biodiversity.

A key figure in the history of invasion biology was the British zoologist and ecologist Charles S. Elton (1900–1991) who not only made seminal contributions to modern population biology and community ecology but also set the scene for the emergence of invasion ecology as a separate discipline. His influential monograph *The Ecology of Invasions by Animals and Plants*, published in 1958, set out his concerns about the escalating impacts of IAS on natural ecosystems and the need to conserve species diversity from their adverse impacts. Elton's landmark publication is seen by many as a starting point for the understanding of invasion biology as a distinct field of study, and has been very widely cited (Richardson and Pyšek, 2008), although Kueffer and Hirsch Hadorn (2008) note that the European tradition of research on biological invasions is actually older and is rooted in floristic studies of adventive species in the 19th and early 20th centuries which already considered the role of humans as agents in biotic invasions.

The circumstances in the mid-20th century when Elton formulated his ideas were very different from those of today. The book *Fifty years of Invasion Ecology. The legacy of Charles Elton* documents the radical changes in the extent and nature of invasions since the 1950s and in the ways in which humans perceive and consider managing alien species (Richardson, 2011a). In Europe, in particular, these concepts were slow to manifest themselves widely; for many biologists and conservationists, biological invasions were still perceived as happening 'somewhere else' (rabbits in Australia, water hyacinth in African lakes and waterways, etc). It was not until the last two decades of the 20th century that the significance of biological invasions and the threats they pose to native biological diversity became widely acknowledged at both global and national levels.

An international research programme on the Ecology of Biological Invasions ran in the 1980s under the auspices of the Scientific Committee on Problems of the Environment (SCOPE) (see Drake et al., 1989). This initiative ('SCOPE I') had a strong conservation focus ([2]), and was important in shaping the research agenda on IAS in its framing of the problem and in the core questions that the programme set out to examine. SCOPE I was a global research programme, and collated case studies and syntheses from around the world, thereby providing clear evidence of the global scale of the problem.

Another landmark was the Convention on Biological Diversity (CBD) which entered into force at the end of 1993. IAS was established as a cross-cutting issue and the CBD adopted a set of Guiding Principles for the Prevention, Introduction and Mitigation of Impacts of Alien Species that Threaten Ecosystems, Habitats or Species (COP decision VI/23).

A second SCOPE research programme ('SCOPE II') on IAS was launched in 1997. This was more inter/transdisciplinary than SCOPE I, and considered economic valuation, stakeholder participation, pathway analysis and management (Mooney et al., 2005). SCOPE II was run under the auspices of a consortium of scientific organisations including SCOPE, IUCN, and CABI which developed the Global Invasive Species Programme (GISP), with the explicit objective of providing new tools for understanding and coping with IAS. The report *Invasive Alien Species: a Toolkit of Best Prevention and Management Practices* (Wittenberg and Cock, 2001) gives a good synthesis of the concepts current in the 2000s on biological invasions. In 2011 GISP was closed down, for financial reasons.

In Europe, research on IAS was limited and uncoordinated until the late 1980s. Ambitious research programmes, focussing on risk analysis, inventories and the management of IAS, were launched in the early 2000s, including the EU

([2]) The outcomes of SCOPE 1 were published in a special issue of the journal Biological Conservation, volume 44, parts 1 and 2, published in 1988.

programme 'Delivering Invasive Alien Species Inventories for Europe' (DAISIE; http://www.europe-aliens.org) and 'Assessing Large Scale Risks for Biodiversity with Tested Methods' (ALARM; http://www.alarmproject.net/alarm) to cite only two important European initiatives.

The amount of information on IAS that was accumulating and the need to make it widely available to an audience of managers and scientists led to the development of national, regional and international databases and information systems, web portals and clearing house mechanisms such as the Global Invasive Species Information Network (GISIN) ([3]), the Global Invasive Species Database ([4]), the Invasive Species Compendium (ISC), the Inter-American IABIN Invasives Information Network (I3N) ([5]) for the Americas and NOBANIS ([6]) for North Europe and the Baltic.

20.4 A new discipline with its own approaches and research agenda

The global approach of the SCOPE I project in the 1980s consolidated the recognition of the study of biological invasions as a new scientific discipline. Kueffer and Hirsch Hadorn (2008) reviewed and analysed the state of research on biological invasions, and distinguished different approaches. The research topics have been further divided to make the distinctions clearer, but all these elements have coexisted over time.

The **classical model** of biological invasions that emerged from the SCOPE 1 programme in the 1980s examined case studies of invasions to attempt to answer three main questions: the traits that determine whether or not a species is an invader, why some habitats are more vulnerable to invasion than others, and how management systems using this knowledge can be developed (Drake et al., 1989; Williamson, 1996). During this phase, research on invasions was restricted mainly to population and community ecology, and was based mostly on biogeographic comparisons of invasions, the underlying assumption being that the alien origin of species was important for explaining their behaviour. Despite many studies, and advances on many fronts, no single/common list of traits emerged that distinguish invasive from non-invasive species. The most informative criterion that emerged is that a species becoming invasive elsewhere (assuming that it has had the opportunity to do so), is a powerful predictor of whether that species will become invasive, although this criterion must be used with great caution in a world of rapid global change (Kueffer, 2010).

Invasions were then considered according to the different phases characterising their successive ecological and evolutionary processes. '**Phase transition models**' break biological invasions down into at least the following steps: entry of a species into a new area, establishment after a possible lag phase during which the population size of the species remains small, and spread. Although the idea is older (Usher, 1986), considering invasions as a sequence of distinct phases has become a central piece of biological invasion theory since around 2000 (Richardson et al., 2000; Kolar and Lodge, 2001) and has since guided much synthetic thinking in the field (e.g. Dietz and Edwards, 2006; Blackburn et al., 2011). The development of risk-assessment systems also emerged (e.g. Pheloung et al., 1999). Risk-assessment schemes seek to identify alien species (including those not yet introduced into a territory) that are likely to become invasive, as a basis for preventive measures or prioritised management action. The phase transition model also represents a conceptual basis for a multi-stage management approach involving prevention of entry at borders as a priority, plus early detection and eradication as key responses when prevention fails, or sustained containment and mitigation of impacts as the last option if the former steps fail (Wittenberg and Cock, 2001). Such a model also facilitates taking into account climate and global change.

As a result of SCOPE II and GISP, the **study of pathways of introduction** became an active research area, integrating natural and human sciences, since human activities are the central cause of movement of species (e.g. global trade and travel by rail, road, sea and air, wars, shipping movements and ballast waters, trade in animals and plants, intentional introductions for economic reasons or by tourists, accidental introductions) (McNeely, 2001; Ruiz and Carlton, 2003). A landscape-scale perspective on biological invasions was largely neglected, focusing initially on spatial models of spread, and

([3]) GISIN website: http://www.gisin.org.
([4]) GISD website: http://www.issg.org/database/welcome.
([5]) IABIN website: http://i3n.iabin.net.
([6]) NOBANIS website: www.nobanis.org.

did not became prominent until around 2000 (With, 2002). Such types of study also included the role of land-use change in invasions (Vilà and Ibañez, 2011).

There is now increasing acceptance that biological and social factors interact in complex ways to initiate and sustain different facets of biological invasions (Kueffer and Hirsch Hadorn, 2008), and several studies have in particular highlighted the role of economic factors in the introduction and spread of invasive species (e.g. Kueffer et al., 2010; Pyšek et al., 2010; Essl et al., 2011; Jeschke and Genovesi, 2011). Lately, research on the impact of invasive alien species on ecosystem resilience and ecosystem services has been gaining importance (EFSA, 2011).

Indeed the advances in understanding the mechanisms and the correlates of invasions have had a significant influence on awareness of the issues, and on the development of innovative and more effective response strategies. For example, the recent engagement of European institutions ([7]) to adopt more stringent measures to deal with IAS may also have been helped by an assessment showing that, in addition to the ecological impact, the economic costs of invasive alien species in the region exceed EUR 12.5 billion/year (Kettunen et al., 2009). Furthermore, several assessments have shown the efficacy of eradication of invasives for the recovery of native species affected by IAS at a global scale, with eleven birds, five mammals and one amphibian species having improved their conservation status as a result of the successful removal of IAS (McGeoch et al., 2010). These results contributed to the increased implementation of this management option, with more than 1 100 campaigns being carried out in the world (Genovesi, 2011). However, although some eradications are being undertaken in Europe (e.g. *Carpobrotus* spp. in Menorca or Ruddy Duck *Oxyura jamaicensis* in the United Kingdom, France and Spain), they are uncommon.

20.5 A wealth of initiatives worldwide

Many initiatives focussing on IAS, dealing with legislation, management and communication, have emerged from international organisations, non-governmental organisations, governments and universities across the world. The case of the EU is detailed in Box 20.1. Some are listed below to illustrate their diversity (the listing is in no way exhaustive):

International treaties and agreements

As Riley (2005) notes, at least 42 treaties dealing with environmental issues, the marine environment and international quarantine refer to the regulation of IAS in the world. As regards terrestrial IAS, one of the major treaties is the International Plant Protection Convention (IPPC), setting international standards for phytosanitary measures (although it only covers non-marine invertebrates and plants). The IPPC initially focused mainly on the protection of cultivated plants, but extended its scope in 1999 to include issues relating to wild plants and the environment. The CBD also recognises the need to address invasive alien species in Article 8(h). In 2004, the two Conventions signed a Memorandum of Understanding to avoid duplication of efforts on IAS (Tanaka and Larson, 2006). This required a revision of the glossaries and procedures of the two Conventions for dealing with the analysis of environmental impacts associated with IAS. These organisations have counterparts at the regional scale, and countries are obliged to implement legislation on IAS.

Governments

Governments and parliaments play a major role in preventing the entry and controlling the spread of IAS, in particular through the adoption and enforcement of legislation (both national and international), conducting or financing the eradication of some IAS through appropriate agencies, and promoting research and public awareness of the issue. Within countries, responsibility for the topic is usually divided between ministries of the environment and of agriculture (including farming, forestry, hunting and fisheries, although some aspects may fall within the ministries of health, energy, infrastructure and transport, etc.), with the ministries of agriculture also being responsible for plant and animal health and the associated legislation. Although the environmental and agricultural sectors cooperate at the international level, the mandates are not always clear at the national level. This reflects the fact that pest management (under the plant and animal health regimes) has a longer history than control of invasions, as well as the multiple impacts that IAS may have and the difficulty of categorising these.

Many countries have implemented dedicated legal instruments that relate to the entry and control of IAS (e.g. Australia, New Zealand, USA, South Africa, the United Kingdom), and as a result the number of legal tools has increased steadily in recent decades (McGeoch et al., 2010). For

([7]) See European Commission Environment website: http://ec.europa.eu/environment/nature/invasivealien/index_en.htm).

Box 20.1 Varying European approaches for dealing with IAS

The current situation in Europe is that despite many studies to assess the impacts of IAS, and possible solutions (e.g. Miller et al., 2006), no comprehensive regulation or legislative framework for the EU is yet in place. Partly as a result of the lack of coordinated action, Europe houses a very large number of alien species (around 11 000 according to DAISIE http://www.europe-aliens.org), of which about 10 % (1 094) have ecological impacts and 12 % (1 347) have economic impacts (Vilà et al., 2010). Moreover, many of the invasive alien species of plants and animals that countries spend millions of Euros in managing and controlling can still be freely purchased in some outlets. For instance, the water hyacinth (*Eichhornia crassipes*), which caused spectacular invasions in Portugal, Italy and along 75 km of a Spanish river — which took a few months and 18 million Euros to control (Cifuentes *et al*., 2007) — can still be bought and traded freely in the EU. Another example is the American grey squirrel (*Sciurus carolinensis*) which is known to have replaced the native European red squirrel (*Sciurus vulgaris*) in most of Britain and yet was released in the wild in Italy at three sites, in 1948, 1966 and 1994. Even though the Bern Convention (see below) requested the government of Italy to eradicate the introduced population 'without further delay' and prohibit the trade in the species in 1999, and appropriate plans were made, twelve years later it is still legally offered for sale in pet shops, while the invasive population continues to grow in the absence of any efforts to control or eradicate it (Standing Committee to the Bern Convention, 2011).

Europe has a complex, fragmented and continually developing network of legislative instruments and regulations aimed at prohibiting the introduction and spread of alien species that pose a threat to native biodiversity (Miller et al., 2006). The European and Mediterranean Plant Protection Organization (EPPO) establishes regional standards on phytosanitary measures, and the Convention on the Conservation of European Wildlife and Natural Habitats, generally known as the Bern Convention (1979), commits its contracting parties to a strict control of the introduction of alien species (article 11) and since 1993 has established a working group aimed at supporting states in the implementation of their obligations concerning IAS (see Brunel et al., 2009 for further details). These plant health and environment organisations work closely together, and have, for example, jointly published the *European Code of Conduct on Horticulture and Invasive Alien Plants* (Heywood and Brunel, 2009).

European states have developed national legislation on IAS but often in an un-coordinated manner. For example, Norway has adopted comprehensive and coordinated legislation on invasive species, Germany and Austria are developing a list of regulated species (Essl et al., 2011), the United Kingdom is working on a similar list, Spain adopted legislation in November 2011 which includes a list of regulated species, and Switzerland adopted similar legislation in September 2008. However, given that the regulation of trade in the EU lies within the European Commission, all these efforts will only have limited effectiveness until there is a legal tool that can be applied across the EU. No coordinated legal instrument is yet in place despite the many studies undertaken on the topic, but the European Commission is preparing a dedicated legislative instrument to be ready by the end of 2012 (see European Commission, COM, 2011). However, there will always remain matters that are more appropriately regulated on a national basis because of climatic or other country-specific contexts.

One of the reasons for the lack of a coordinated European approach is that neither of the European legal instruments on nature conservation that deal with IAS — the Bern Convention, covering 45 European States, and the Habitats Directive, applied in all the EU-27 Member States — are very specific on the topic of IAS. They were formulated in 1979 and 1992 respectively, before IAS became a major concern of governments. The Bern Convention simply asks governments to '**strictly control the introduction of non-native species**' and the Habitats Directive requires Member States to '**ensure that the deliberate introduction into the wild of any species which is not native to their territory is regulated … and, if they consider it necessary, prohibit such introduction**', without giving much information on how to deal with the IAS issue as a whole i.e. dealing with the prevention of new entries, pathways, unintentional introductions, containment or eradication of introduced species, early detection and rapid response systems, etc. Although the Bern Convention's 'European Strategy on Invasive Alien Species' (2003) and the European Commission's technical documents produced during the preparation of the EU Strategy on Invasive Alien Species (2011) do contain sufficient guidance for precise government action, they are not legally-binding documents and their application has been patchy. Within the framework of a revision of the Plant Health regime, European national plant protection organisations have identified the inclusion of invasive alien plants having detrimental effects on biodiversity as one of their first concerns (Agra CEAS Consulting et al., 2010).

Europe, no coordinated legal instruments are yet in place, despite the many studies undertaken on the topic, but the EU has committed to presenting a draft dedicated legal tool by the end of 2012, and an assessment of the different legal options was published in December 2011 ([8]).

Countries with national strategies on IAS include Canada (Gouvernement du Canada, Environnement Canada, 2004), South Africa, for the Cape Floristic region (CAPE Partnership Program, 2009), Mexico (Comité Asesor Nacional sobre Especies Invasoras, 2010), the Bahamas, (see Pyšek and Richardson, 2010), and a number of European countries (see Box 20.1).

A few governments have also established large interdisciplinary programmes for dealing with invasive species 2011).

Non-governmental organisations
Non-governmental organisations cooperate in the management of IAS through the preparation of strategic documents and gathering of information, or directly by managing sites to conserve native species and restore ecosystems. The Invasive Species Specialist Group (ISSG) of the International Union for the Conservation of Nature (IUCN) is one of the oldest organisations active in this field ([9]). ISSG has long worked with all the main global initiatives, including SCOPE and the Convention of Biological Diversity, providing technical support for improving the ability to prevent and mitigate the impacts of invasive species on biological diversity.

Other major institutions active in the field include CABI, Birdlife, The Nature Conservancy, Wildlife Conservation Society, and Island Conservation (whose mission is specifically to prevent extinctions by removing invasive species from islands). Across the world, at the national and local scale, thousands of associations or foundations are also involved in controlling IAS, for example in nature reserves.

Universities
Many universities and research institutes across the world are engaged in research on IAS, within the disciplines of biological science, weed science, agronomy, and more recently social science. Dedicated research centres and networks have been created in several parts of the world. Networks of scientists are also very active and organise conferences (e.g. NEOBIOTA, see http://cis.danbif.dk/neobiota2010 or EMAPI, Ecology and Management of Alien Plant Invasions).

Thus, despite the growing amount of legislation being adopted at the global scale, invasions continue to grow at a rapid rate, with no indication yet of any saturation effect (Butchart et al., 2010). In addition to the more than 42 international treaties dealing with environmental issues referring to the regulation of IAS (Riley, 2005), there is much reliance on voluntary codes of conduct which by definition lack sanctions for non-compliance, the latest in Europe being the European Code on Pets and Invasive Alien Species (Davenport and Collins, 2011). None of this is helped by the inherent difficulties of defining and tackling IAS and the consequent continuing confusion and debate over terminology and the lack of an agreed core definition of IAS. It is therefore not surprising that the scientific community recurrently undergoes soul-searching over these issues.

20.6 Obstacles to a common understanding

The issue of the extent to which IAS adversely affect the natural environment has long been a subject of controversy, not just between stakeholders with different interests (e.g. conservationists versus horticulturists/foresters) but also within the scientific community. Dissenting voices periodically challenge the extent to which IAS represent a major threat to biodiversity, and the measures that should be taken (see for example the exchange between Sagoff, 2005 and Simberloff, 2005).

The obstacles to reaching a common agreement about the threats posed and measures needed are reflected in the scientific debates on the topic. Although debates and discussion are inherent to the development of any discipline, too much focus on these controversies can have a deleterious effect. A more extensive discussion of the valuation of invasive alien plants can be found in Larson (2007), Kueffer and Hirsch Hadorn (2008), Hattingh (2011) and Rotherham et al. (2011). Some of the key issues that are a cause of conflicting expert views are reviewed in the next section.

([8]) Document available at http://ec.europa.eu/environment/nature/invasivealien/index_en.htm.
([9]) Founded in 1993, it was the first thematic (as opposed to taxonomic) specialist group of the IUCN SSC to be created. ISSG is a voluntary global network of about 1 000 scientists and practitioners working to mitigate the impacts of biological invasions.

Dissenting voices about the 'pros' and 'cons' of managing IAS

As already noted, IAS are broadly defined according to the negative impacts they cause (cf. the CBD definition and definitions extending to economic impacts). The very definition of IAS along these lines is therefore somewhat of a hybrid, mixing biological elements (a species), the effects on the environment that we are able to detect, and human perceptions of its economic, environmental or social impacts. Assessment of these impacts, specially when considering those on the environment (which in some cases are not easy to quantify or qualify, not to mention the dynamic nature of the environment), are subject to multiple interpretations. The assessments are particularly difficult in the context of a precautionary management approach that builds on an ability to predict potential future impacts. It is widely acknowledged that some IAS can have major impacts and that in these cases it would, in principle, be ideal to prevent these invasions before they happen. However, there are divergences in our perception of how common problematic alien invaders are and whether the alien origin of a species is a reliable heuristic for predicting problematic spread. Davis et al. (2011) question whether conservation money is efficiently spent on preventing the introduction of any new alien species until such species are proved innocuous, as a strict interpretation of the precautionary principle would require. In effect, they highlight the opportunity costs of a strict prevention of introduction of alien species, including the opportunity costs of losing the benefits that some alien species might provide.

The IUCN Invasive Species Specialist Group (ISSG) (2011) responded to these points by explaining that the escalating loss of biological diversity is the motivation for invasive management action on alien species. They also recalled that alien species may not manifest invasiveness till decades after their introduction, and draw attention to species that may only have a subtle immediate impact but which eventually affect entire ecosystems, for example through their effect on soil properties. In addition, invasions and impacts appear to be context-dependent. This is particularly true for plants: for example, while an alien species of cinnamon (*Cinnamomum verum*) has been considered as potentially beneficial for restoring novel mid-elevation forests in the Seychelles, it is a major invader in nearby montane cloud forests (Kueffer et al., 2010). The ISSG (2011) argues that, irrespective of how common problematic invasions of alien species are, prevention is needed because of the huge impacts of the invasions that do happen.

Based on such a perspective, the cost of inaction has been estimated at up to USD 1.4 trillion per year, representing about 5 % of global GDP (Pimentel et al., 2005). Examples are also available for countries: USD 138 billion per year for the US, USD 14.45 billion for China (figure for 2000, representing 1.36 % of Chinese GDP) and over EUR 12 billion per year in Europe. While the cost of inaction in Europe is EUR 12 billion per year, the cost of action is estimated at EUR 40–190 million per year, depending on the possible policy options (Kettunen et al., 2009). The management of IAS is therefore, according to this perspective, considered a very cost-effective investment.

It is not, however, obvious how to decide on priorities and what actions should be taken to address the benefits or harm to native biodiversity, human health, ecological services and economies that species might pose when such benefits and harm cannot be predicted. The solution may come from a pragmatic approach that involves prevention or mitigation of the worst impacts of invasives through a combination of preventive measures, early detection and rapid response to new incursions, with permanent management as only the last option.

The lack of acceptance by society of some management actions

Measures to manage IAS may also be subject to criticism, in particular when they involve the killing of animals, or the use of biological control agents or phytosanitary products (i.e. herbicides or pesticides) (see Boxes 20.2 and 20.3). Opponents of the management of invasive alien plants may also oppose the use of herbicides or pesticides, which they perceive as a bigger threat than the actual impacts of the invasives.

Native vs. alien: a polemical topic to explain to the public

A misunderstanding that is pervasive when talking about IAS lies in not differentiating between invasive species and alien species, as already mentioned above, and using this to justify interventions against alien species in general. While conservation biologists and ecologists refer to the threats from alien species because of evidence that indicates that some of them entail particular ecological and economic risks, some social scientists such as Larson (2007) and Warren (2007) have pointed out the problematic social and cultural connotations of such 'prejudice' against

Box 20.2 The grey squirrel and the ruddy duck: too cute to be killed

A good example of protest by animal welfare groups is the case of the grey squirrel (*Sciurus carolinensis*) in Italy. The two officers in charge of the eradication of grey squirrel were brought to court and charged with cruelty toward animals and illegal methods of capture, despite consultations with animal welfare groups and exercising caution in killing the animals. The legal case delayed the enforcement of any action, ruining the whole eradication campaign, and the grey squirrel is now expected to spread across Europe, with huge impacts on biodiversity as well as the economy of the entire region (Bertolino and Genovesi, 2003; Bertolino et al., 2008).

Another relevant case is the control of the American ruddy duck (*Oxyura jamaicensis*) which escaped from captivity in the United Kingdom and, after reaching a population of several thousand, spread throughout Europe and started to hybridise with the endangered native white-headed duck (*Oxyura leucocephala*). In Spain it threatened the very intense efforts of the conservation authorities to prevent the extinction of the native species. Selective shooting of ruddy ducks and hybrids soon started in Spain, but this was only a temporary measure. Realising that the long-term solution for the Spanish populations of white-headed duck could only come from the eradication of the ruddy duck in the United Kingdom, a European eradication plan was proposed by the Bern Convention and its eradication financed by the UK government and the European Union from 1997. The problem was that shooting attractive ruddy-ducks caused a public and vociferous outcry in that bird-loving country, until the support of the Royal Society of the Protection of Birds for the controls was decisive in getting the project started. That courageous decision cost the society the loss of probably a few thousand members, but by December 2011 the number of birds in the United Kingdom had been reduced to a few hundred and there are good chances of eradicating the species from the wild in Europe by 2015 (Standing Committee to the Bern Convention, 2011; Consulting et al., 2010).

species of non-native origin. Some consider that environmentalists, conservationists and gardeners are 'xenophobic' when dealing with IAS.

Invasive species may indeed be flagged in the press with pejorative names such as 'the yellow peril' for water primroses (*Ludwigia grandiflora* and *L. peploides*) in the south of France. But from a scientific point of view, the focus on alien species is not xenophobic but has a scientific basis (Simberloff and 141 scientists, 2001). The focus lies on alien species not because they are considered unwanted *per se*, but because they show that some species of alien origin have a higher probability of unrestrained growth which can ultimately lead to environmental damage. One reason why some alien species differ ecologically from native species is that they are not subject to the control of natural enemies (diseases, pests, herbivores) that are not present in the newly colonised area.

An even greater difficulty in defining what is 'natural'

The debate on native versus alien goes beyond the species level and touches on the definition of ecosystems and on what conservationists or society decide to protect. The definition of an 'alien' species in an era of accelerated global change is also a challenge. Davis et al. (2011) call for management approaches that recognise that the 'natural' ecosystems of the past have changed forever due to drivers such as climate change, nitrogen eutrophication, increased urbanisation and other land-use changes. They argue that most human and natural communities now contain both long-term residents and new arrivals, and that ecosystems with combinations of species that never existed before are emerging as a consequence of climatic and other global change ('novel ecosystems' *sensu* Hobbs et al., 2006; 'no-analogue ecosystems' *sensu* Williams and Jackson 2007).

These arguments only represent a part of the emerging challenges in the struggle against invasions (Kueffer, 2010). For example, the increasing use of novel alien crops such as those used for biofuel and biomass present a risk of favouring new invasions (Genovesi, 2010; Sheppard et al., 2011); and synthetic biology may in the near future produce still more fundamentally novel species. To overcome the effects of climate change, some authors have proposed translocating native species to areas outside their natural ranges (so called assisted migration (McLachlan et al., 2007) or assisted colonisation (Hunter, 2007; Hoegh-Guldberg et al., 2008): see Seddon et al., 2009; Stanley-Price, 2010), with the possible risk of causing further impact on native species, as in the case of the proposed translocation of the Iberian lynx into the British Isles (Thomas, 2011; Vilà and Hulme, 2011).

Box 20.3 Fear of biological control agents

Biological control is a management method that triggers reluctance in decision makers and the public, though generally supported by scientists if proper and conclusive research has first been carried out. Such caution prevents this efficient technique from being used when IAS are widespread. The mistrust of biological control agents springs from the fear that the agent may not prove specific enough and end up attacking non-target native species, thus aggravating the problem instead of solving it. The public also finds it odd and risky to introduce a new non-native species into a complex ecosystem, particularly in a psychological context of negative feelings towards alien species. Often scientists are not fully trusted either. The use of the lepidopteran *Cactoblastis cactorum* (Pyralidae) to manage the invasive *Opuntia* species that threatens endemic plants in rocky habitats is a typical example that is used to oppose biological control. While the introduction of the Lepidopteran had proved successful in managing millions of hectares of invasive *Opuntia* species in Australia, South Africa and then in Hawaii and the Caribbean Islands, *Cactoblastis cactorum* was then accidentally introduced in Florida where it threatened a native *Opuntia* species (Sforza, 2006). In this case, the potential for accidental spread of the species in areas where it could be detrimental had not been assessed accurately.

Another well-known example of the introduction of a biological control agent that itself became invasive is that of the cane toad (*Rhinella marina*) which was introduced in Queensland (Australia) to control insects that feed on sugarcane and other crops. Cane toads became naturalised and spread, and have detrimental impacts as they feed on many terrestrial animals and compete with native amphibians for food and shelter (Global Invasive Species Database http://www.issg.org/database/species/ecology.asp?fr=1&si=113). In this case, the potential adverse impacts of the species on native fauna had not been assessed accurately.

Even if successful, the method may be susceptible to criticism. The recent release of *Cibdela janthina* in Reunion Island in 2009 to combat the highly invasive plant *Rubus alceifolius* (Le Bourgeois and Della Mussia, 2009) triggered intense debate in the media. Apiculturists and fruit producers feared that the biological control agent would outcompete bees, jeopardising fruit production on the island. The issue even reached the French Senate (JO Sénat, 21/05/2009). After undertaking additional studies and dialogue with stakeholders, it finally appeared that *Cibdela janthina* had no impact on bees, and was efficient at controlling the targeted plant. Many other biological control programmes have proved successful, and the selection of an agent is nowadays carefully studied through formal risk assessment protocols (the same as those used for IAS) that greatly reduce the chance of unexpected behaviour of released species.

At a European level, legislation on the introduction of biological agents is quite stringent, while legislation against the introduction of any other species, including acknowledged invasive ones is non-existent.

In the case of the control of the water hyacinth (*Eichhornia crassipes*) in Spain, mentioned above, the authorities ruled out the introduction of a biological control agent, used successfully in Africa, because of the complex European legislative framework impeding the release of agents.

It should be noted, however, that after extensive research and discussion, the biological control agent *Aphalara itadori* was released in the United Kingdom to control the highly invasive Japanese knotweed (*Fallopia japonica*) whose management and control costs more than GBP 150 million a year. This represents the first classical biological control release against an invasive alien plant in Europe. CABI had carried extensive testing on this insect over the past five years to verify that it can be safely released into the environment. A public consultation was launched: 20 respondents were against the release, 42 in favour (CABI, 2010).

20.7 The limits of governance on the complex issue of IAS

The interdisciplinary nature of the skills required for dealing with IAS is a challenge and can slow action and cooperation. An IAS may, for example, have both environmental and agricultural impacts as well as providing other agricultural benefits. This raises the question of which legislative framework should be in charge. At a macro scale such as the EU, various principles, terminologies and legislative frameworks need to be aligned before any decision can be taken, complicating and slowing the effective application of legislation and management measures. This has been of particular concern in the case of ragweed (*Ambrosia artemisiifolia*). The pollen of this plant is very allergenic, and the species is also a weed in crops,

particularly of sunflower. Discussions on which department — health or agriculture — should deal with the problem has much delayed measures to control the species.

Managing an invasive alien species is difficult not only because of its intrinsic biological characteristics and technical difficulties, but also because of the very many stakeholders that need to be involved for coordinated action. Classical environmental management tools (i.e. habitat protection, liability for environmental damage or mediation in environmental conflicts) prove of little use for IAS. Indeed, before becoming invasive, a species may remain unnoticed in an area for several decades, the so-called 'lag phase'. This can makes the application of a liability approach very difficult, as the traceability of who introduced a species may be lost with time. Environmental mediation that would permit a consensus between conflicting interests about the introduction of a particular species is handicapped by uncertainty in the potential invasive behaviour of an introduced species, as the decision on whether or not to introduce a species needs to be taken far in advance of the species becoming effectively invasive. For example, the potential impacts had not been assessed accurately before introducing the signal crayfish (*Pacifastacus leniusculus*) into Europe. When the Scandinavian fisheries of European crayfish (*Astacus astacus*) were damaged by a crayfish plague, signal crayfish, originating from North America, were introduced to Norway and Finland for recreational and commercial crayfish capture. It turned out that signal crayfish was not only the carrier of the crayfish disease, but it also became invasive, threatening the European crayfish as well as macro-invertebrates, benthic fish and aquatic plants. The species has spread widely and is now out of control (Global Invasive Species Database, *Pacifastacus leniusculus*, http://www.issg.org/database/species/ecology.asp?fr=1&si=725). The species nevertheless has beneficial effects for crayfish production, resulting in a conflict of interest between those who want to control the species and those who want to breed it. Clearly a decision should have been taken long before allowing the introduction of this species in Europe.

These complex and difficult decisions are taken on the basis of risk assessment, which is a time-consuming exercise. Furthermore, even with a very good risk assessment system, new outbreaks of IAS could still occur, making the need for a system of rapid early warning and effective eradication response necessary. The decision on where to draw the line on the acceptable environmental risks versus the introduction of new species or new communities that may carry invasive alien species then becomes a value judgement to be taken by governments. The question of the proportionality of the measures to be taken (allowing the entry of any species versus prohibiting the entry of all non-native species) is very delicate and should involve, in addition to the strategic position of governments, a societal debate. This would imply, in the first place, a good knowledge by the public of the phenomenon and of the impacts of invasive alien species. The stakeholders involved in introducing IAS, and the public who are often responsible for the entry or further spread of these species, both need to be engaged in the debate. Another element of 'proportionality' that makes legislative measures complex lies in the geographical range over which measures should be taken. A species might be a problem only in a given bioclimatic area, but free movement and trade might occur between this area and others, particularly in the free-trade space of the EU. Should this species therefore be prohibited in the whole free movement and trade area, even if it only has detrimental effects in part of it? Such concern is being raised for the development of a European legislative framework on IAS. In other words, should the attractive water hyacinth (*Eichhornia crassipes*), which in Europe may only become naturalised and be invasive in Mediterranean countries, be prohibited from trade in the United Kingdom where it is harmless? The UK nursery industry might like to make use of a plant that does not threaten UK biodiversity, but its introduction, given the free movement of persons and goods within the EU, might compromise management efforts in areas at risk. The question of balance between legislative and voluntary approaches in dealing with IAS is crucial. As many stakeholders are involved, both approaches are needed, the one reinforcing the other.

20.8 Applying the precautionary principle to invasive alien species

Because of the lack of robust criteria for predicting invasiveness, and because most research on biological invasions assumes that alien species are 'guilty until proven innocent', rigid application of the precautionary principle in managing biological invasions is problematic in the context of free-trade agreements. New Zealand, for example, requires that every species imported to the country is assessed for risks, and only if found to pose a low risk can an authorisation be issued. Some countries, however, regulate the introduction only of species

on a list of 'unwanted' invasive or potentially invasive species ([10]). This approach is also proposed by the International Plant Protection Convention (IPPC).

Another way of applying the precautionary principle, while not preventing the entry of IAS, is to eradicate new invaders in a timely manner. The case of *Caulerpa taxifolia* is a good illustration of a missed opportunity to undertake early action in Europe. The alien alga was detected in France in 1984 at a very early stage of invasion, and could have been quickly removed. However, the management of *C. taxifolia* only started when it had already expanded to a large portion of the Mediterranean, when eradication was no longer possible. When the same species was recorded in California in 2000, eradication started only 17 days after its discovery, leading to its successful removal (Genovesi, 2007).

The precautionary principle is the first of the CBD's Guiding Principles for the Prevention, Introduction and Mitigation of Impacts of Alien Species ('The Guiding Principles' Annex Decision VI/23 ([11])) (see Cooney, 2004). It is applied to some extent by the IPPC, when considering all sources of uncertainty in performing a pest risk analysis. Biosecurity is a very dynamic field of research that seeks to integrate the latest techniques and concepts in its methods to assess risks: the modelling of a species' potential area of establishment, pathway analysis, etc. Such techniques face the challenge of identifying species that may be invasive, and also those that may be invasive under novel conditions created by climate change and/or other facets of global change. Approaches for addressing such situations are being developed, such as consideration of the impacts of IAS on ecosystem services through the elaboration of different scenarios (EFSA, 2011; Chytrý et al., 2012).

20.9 Addressing invasion pathways: a late engagement with the stakeholders

A pathway for engagement: Codes of conduct

Managing IAS now consists of placing more emphasis on pathways of introduction of IAS, as well as identifying the stakeholders involved, although such aspects have been adopted quite recently considering the history of the discipline. This has shifted the focus away from preventing particular species to managing risks associated with introduction pathways, including the human activities that create, shape and sustain such pathways (Wilson et al., 2009; Richardson, 2011b), involving local knowledge. Researchers in the social sciences have become interested in exploring perceptions of alien and invasive species and their impacts (Menozzi, 2007; Andreu et al., 2009; Kueffer and Hirsch Hadorn, 2008; Javelle et al., 2010). Cooperation with stakeholders involved in introducing and disseminating IAS is becoming increasingly common.

For invasive alien plants, the horticultural trade is the primary invasion pathway (Reichard and White, 2001; Dehnen-Schmutz et al., 2007; Drew et al., 2010; Richardson and Rejmánek, 2011). As a response, some countries have prepared voluntary codes of conduct or good practice for the horticultural industry, for example the United States (Fay et al., 2001) and Europe (Heywood and Brunel, 2009). Such approaches have so far had limited effectiveness and buy-in (Drew et al., 2010), although 12 European countries report initiatives related to the implementation of a code of conduct on horticulture and invasive alien plants. The effectiveness of such voluntary codes depends largely on how well they are promoted (Dehnen-Schmutz and Touza, 2008; Brundu et al., 2011); this requires continuing communication and dialogue with the stakeholders (Gibbs, 2011). When developing this code of conduct in Europe, the International Association of Horticulture Producers (AIPH) was involved in the drafting of the document. For the specific case of invasive alien plants, the industry cannot be seen as preventing legislation from happening, and although playing its role in challenging the issue, it has been collaborative in considering that if some species present a problem, then some alternative can be found.

Pathway approaches are also emerging in the field of plant health. It is increasingly considered that a species-by-species regulatory approach relying on inspections is more and more difficult in today's markets context. As a consequence, the forest entomology and pathology science communities recommend a pathway approach for regulating nursery stock, similar to that adopted for wood packaging material. This is based on the principle that best management practices that effectively

([10]) Such lists used to be called 'Black lists', but such a term is now not considered politically correct.
([11]) See http://www.cbd.int/decision/cop/?id=7197.

prevent known IAS will significantly reduce the risk of also introducing unknown pests. In this regard, the IPPC is developing an international standard for plants for planting (see the UK Forestry Commission website: http://www.forestry.gov.uk/fr/INFD-6YUJRD).

Other initiatives to prepare codes of conduct involve botanical gardens (see Heywood, 2011 for Europe; Fay et al., 2001 for the US), the pet industry, hunting, recreational fishing, zoos and aquaria, aquaculture, marine ballast waters, commercial forestry and other sectors.

Stakeholders: what forces lie behind action and inaction?

Scientists and experts have been active in communicating the dangers of IAS for biodiversity — although not necessarily in the most coherent way, as most scientists are not trained in public relations or communication. Dissenting views have probably had little influence on government decisions on IAS, where the consensus is now that this is a serious problem requiring some degree of attention. Other interest groups have been silently watching the growing interest in IAS with much attention and a degree of reluctance. This includes not only animal welfare activists, alarmed at the possible eradication of animals, but also industries and lobbying groups, for whom restrictions on the trade of some species would hinder or complicate business. Horticulture would have to change its current practices substantially if serious measures to avoid new introductions were put in place. But as they feel that their industry is part of the environment business, they do not want to be seen as environmentally unfriendly. A number of other stakeholders who deal with animals and plants may not welcome restrictions, i.e. foresters, the pet trade, aquaculture, recreational fishing and, to a lesser extent, hunters, zoological gardens, aquaria and botanical gardens. Many of these groups are generally aware of the problem and display in general a cooperative attitude with governments and scientists, but prefer a voluntary approach with agreed codes of conduct to hard laws. The industry may also be divided in some cases. While few businesses are in favour of more bureaucracy, some think they might be at a disadvantage compared with those who decide not to apply codes and therefore that legislation would be fairer. The pet industry is more favourable to a voluntary approach and has been actively engaged in the drafting of a European Code of Conduct on Pets and Invasive Alien Species. It would certainly not welcome some mandatory regulations, for instance any relating to the shipping of all pets, as these would increase costs and imply new complex procedures and operations. Yet it is clear that responsibility for the introduction of many invasive species lies partly with the industry and its activities, although it is also a consequence of the slowness of governments to take action or introduce legislation.

20.10 Lessons learnt on invasive alien species: towards more transdisciplinarity in a rapidly changing world?

During the past few decades, we have acquired greatly increased awareness of the extent of biological invasions, the impacts they have on biodiversity and the economy, and a much better understanding of how to prevent and manage them. Faced with the uncertainties posed by a rapidly changing world, we need to learn lessons from this large body of experience so as to avoid further losses.

Biological invasions currently interest a large and growing body of people, including researchers and students in academic institutions, conservation agencies and NGOs, civil servants, park managers, activists, volunteers and a growing number of concerned citizens in many parts of the world. This network of people, interests and perspectives has assembled over the past 30 years worldwide. The 'game rules' for interactions between different parties are still being defined, tested, and debated. Governments and institutions charged with making decisions have access to considerable knowledge on the topic, but the lack of rules of interactions between multiple parties regularly thwarts effective decision-making. Governance of IAS needs to be achieved before the introduction of species, which means dealing with uncertainties and setting a level of protection. Lessons can, nonetheless, be learnt that could pave the way to more effective interaction and communication between parties, which should result in more effective and transparent decisions. Some of these lessons are late ones (EEA, 2001).

Align concepts for a better understanding by society and public engagement

Public understanding of the threats posed by IAS is fundamental for effective governance. Occasional divergence of opinion among experts in the field of biological invasions may weaken public confidence in the advice of 'experts'. Rather than talking with one voice to the public and insisting on convergent opinions, it is more important to ensure that different opinions are made clearly understandable and transparent to the public and decision makers.

In the historical framing of the phenomenon of biological invasions (see above), it was assumed that the problem could be solved by identifying the biological traits of potentially invasive species and preventing their introduction to new areas. Fifty years of research have shown that the identity (alien or native) and traits of the species are indeed highly relevant, but it has become increasingly obvious that other factors are also involved (e.g. propagule ([12]) pressure, habitat factors, land use). In particular, several studies have shown that biological invasions are strongly correlated with economic factors (Essl et al., 2011; Jeschke and Genovesi, 2011; Pyšek et al., 2010). A comparison of plant invasions on oceanic islands highlighted the fact that economic development (measured as gross domestic product) is the most important predictor of invasive species richness on islands (Kueffer et al., 2010). Human activities are an essential factor in the understanding and solution of the IAS issue, so that public engagement is vital if we are to adopt effective measures and ensure good governance.

Harmonise concepts for improved coordination of on-the-ground actions

The lack of clear and common concepts and definitions of IAS has led to serious problems in obtaining reliable information on species involved in biological invasions and has undoubtedly hampered the development of detailed databases. This is a key element to be addressed when considering ways of strengthening strategies for the management of IAS. This is indeed one of the reasons why some countries do not have a comprehensive list of alien or invasive alien species and is exacerbated by the fact that some countries do not appear to be aware of the extent or seriousness of biological invasions. Another cogent reason is the dynamic nature of biological invasions, so that existing lists need to be regularly updated, requiring budgets and trained staff. A better connection between science and management would help increase and improve policy and legislative action. Initially, most research questions were disconnected from management concerns, and arose from the issues of population and community ecology (Kueffer and Hirsch Hadorn, 2008). Also, impacts were considered without explicitly clarifying the broader human and economic context, and it was often assumed that any detectable effect of an alien species on an ecosystem would be undesirable (Kueffer and Hirsch Hadorn, 2008). Researching global concepts may have hindered the provision of concrete and simple actions. With time, the study of biological invasions has become much more interdisciplinary, and links to management agencies have strengthened. The valuation of costs and benefits associated with alien species (including IAS) and their management has become an important research focus (Kueffer and Hirsch Hadorn, 2008). Consequently, the problem of IAS, initially recognised and brought forward by scientists, is now being more firmly rooted in civil society (e.g. NGO groups).

A late lesson not yet learnt: take account of wider social interests and values

As mentioned in *Late lessons from early warnings* Vol. 1 (EEA, 2001), 'taking account of wider social interests and values' has been overlooked when dealing with IAS. Further social studies are needed to understand human perceptions of biological invasions, so as to eventually adapt the concepts and reconcile diverging opinions between experts and stakeholders. It has for example been shown that the alien origin of a species is of minor importance for stakeholders, while the role that humans play in the spread of a species, its aesthetic and cultural value, or personal experiences with the impacts and management of a particular invasive species in a specific site, are of high importance in their valuation (Bardsley and Edwards-Jones 2007; Bremner and Park, 2007; Gobster, 2011; Selge et al., 2012). Additional care and thought must also be given to the language used in communicating on the topic (Larson, 2010; Hattingh, 2011). For problems associated with IAS, it is crucial to involve all stakeholders, including those who introduce species and members of the public who have divergent ideas about the species. Identifying the pathways of introduction of the invaders and implementing any regulations that affect these demands ongoing dialogue with stakeholders (e.g. in formulating codes of conduct), which, to be effective, should be undertaken at an early stage. It is important to recognise that sociological aspects are very important in addressing this problem, and some of the research questions still need to be explored and the results acted on, such as personal attitudes to IAS and those of interest groups such as animal rights groups.

Another late lesson: avoid paralysis by analysis

Much progress has been made in enhancing the consistency and transparency of protocols for (pest) risk analysis and cost-benefit studies, such as research undertaken for the PRATIQUE project at the European scale (see EPPO, 2011). Such progress in evaluating the risks that species pose has become

([12]) A propagule is defined as any plant organ or part, as a spore, seed or cutting, used to propagate a new plant.

increasingly sophisticated and multidisciplinary, bringing together zoologists, botanists, managers, policy makers and economists (Hulme, 2011a). However, despite the significant advances in predicting the risks related to species introductions, the complexity of the relationships between the many potential explanatory variables still limits the precision of current risk assessment tools (Hulme, 2011b). In addition, the discipline known as 'biosecurity' ([13]) which encompasses all aspects and measures that deal with the prevention of pests will also need to address the emerging challenges of a changing world.

A specific lesson for Europe which concerns the need to act without waiting for coordinated European action is presented in Box 20.4.

Anticipate further challenges and 'blind spots' in a changing world

Kueffer and Hirsch Hadorn (2008) suggest that biological invasions represent a complex societal issue because knowledge is highly uncertain, and because conflicts of interest and values are central to the problem. A wider and more intense debate is expected on options for preventing and managing invasions, and on how to deal with the risks related to novel approaches to conservation and the economy such as biofuel crop planting and managed relocation. Contextual factors are amplified through the global changes that we are currently witnessing: climate change, habitat change, land-use change, etc. Consequently, criteria currently used to consider the invasive behaviour of a species in particular areas are likely to be increasingly challenged (Kueffer, 2010). For example, in montane areas, future invaders may be mountain specialists directly introduced through human activity between high-elevation habitats, rather than the current situation where most invaders of montane regions are climatically plastic species that spread from lowlands (McDougall et al., 2011). As already described, increasing interest in 'novel ecosystems' (Hobbs et al., 2006) as well as novel crops, and in radical conservation measures such as managed relocation, pose new challenges for nature conservation which will demand in-depth discussion.

Box 20.4 A lesson for Europe: do not take the need for European coordination as an excuse for inaction

A particular problem for Europe has been the long time taken by European institutions to propose coordinated stringent measures to control the introduction, trade and spread of IAS and to promote eradication or containment measures. It is likely that a dedicated legislative instrument will be prepared before 2013, to be implemented in the following years, but 2013 is twenty years after scientists alerted governments to the dimension of the problem and the growing risks to European native biological diversity from IAS. During that time the problem has grown worse. Many governments were reluctant to pass legislation on the grounds that the free movement of goods in the EU did not permit them to restrict the import of alien species that might threaten their native biodiversity through national laws. This remains a doubtful claim, as a few European governments did not hesitate to take that step. However many European governments have been slow to act.

As environment is a competence of the EU and resources are scarce, some EU states, when fixing their priorities for conservation action, pay a greater attention to the legal requirement for implementation of EU legal instruments and tend to pay less attention to other issues not specifically covered by European legislation, including much-needed action on IAS. Although the 1992 EU Habitats Directive contains obligations on the introduction of IAS and the European Commission has since the late 1990s invested substantial funds on research, data gathering and eradication operations, government awareness of the need for a more stringent legislative instrument has only come since the growing economic and environmental costs of invasive species have become difficult to ignore. The problem is complex, awareness only relatively recent, government interest limited, and public resources scarce. Hard times for native species!

([13]) The FAO notes that 'Biosecurity is a strategic and integrated approach that encompasses the policy and regulatory frameworks (including instruments and activities) that analyse and manage risks in the sectors of food safety, animal life and health, and plant life and health, including associated environmental risk. Biosecurity covers the introduction of plant pests, animal pests and diseases, and zoonoses, the introduction and release of genetically modified organisms (GMOs) and their products, and the introduction and management of invasive alien species and genotypes. Biosecurity is a holistic concept of direct relevance to the sustainability of agriculture, food safety, and the protection of the environment, including biodiversity.' http://www.fao.org/biosecurity.

Do not allow philosophical debates to create blockages in tackling the problem

Biological invasions occupy a position between 'nature' and 'culture', as they have both biological and social aspects. While many problems that affect biodiversity directly relate to human activities (destruction of habitats, pollution), issues related to IAS are 'nature threatening nature' through human activities, making the role of humans difficult to unravel. This is particularly true in Europe, where ecosystems have been modified since prehistoric times. Such uneasiness sends us back to the classical argument 'it is natural therefore it is safe'. The emerging questioning of IAS reflects the difficulties inherent in defining what nature is and how to protect it, in particular in a context of climate and global change. Global change will increasingly challenge current assumptions and concepts relating to biological invasions. The risk of invasion should be perceived not only as coming from alien species, but rather as a socio-ecological phenomenon in which our perceptions about how humans move species and manage land are considered as a whole (Kueffer, 2010). The response to invasions therefore needs to take into account the human dimension, combining the need to consider the rapidly changing patterns of our society with the urgent need to respond to the threats posed by invasive species.

Table 20.1 Early warnings and actions

77 AD	Pliny the Elder wrote in his *Naturalis Historia* that the invasion of rabbits in the Balearic Islands, Spain, was a very severe problem requiring effective control
1830s	Charles Darwin noted the invasive behaviour of some alien species during his explorations on the *HMS Beagle*, which contributed to the development of his theory of natural selection
1958	Publication by the British zoologist and ecologist Charles S. Elton of his landmark monograph *The Ecology of Invasions by Animals and Plants* which is seen by many as a starting point for the understanding of invasion biology as a distinct field of study
1980s	International research programme on the Ecology of Biological Invasions by the Scientific Committee on Problems of the Environment (SCOPE I) which was important in shaping the research agenda on IAS and led to an explosive growth in invasion biology
1993	Entry into force of the Convention on Biological Diversity (CBD) and of its Article 8(h) on invasive alien species, requiring parties to: Prevent the introduction of, control or eradicate those alien species which threaten ecosystems, habitats or species. Establishment of the IUCN SSC Invasive Species Specialist Group, first interdisciplinary specialist group of IUCN
1997	Launch of a second SCOPE research programme ('SCOPE II') on IAS, which was more inter/transdisciplinary than SCOPE I, and considered economic valuation, stakeholder participation, pathway analysis and management. SCOPE II was run under auspices of a consortium of scientific organizations including SCOPE, IUCN, and CABI which developed the Global Invasive Species Programme (GISP), with the explicit objective of providing new tools for understanding and coping with IAS
2002	Adoption, by the Convention on Biological Diversity (CBD) of Guiding Principles for the Prevention, Introduction and Mitigation of Impacts of Alien Species that Threaten Ecosystems, Habitats or Species (COP decision VI/23)
2000s	Development of national, regional and international databases and information systems, web portals and clearing house mechanisms such as the Global Invasive Species Information Network (GISIN) ([a]), the Global Invasive Species Database ([b]), the Invasive Species Compendium (ISC), the Inter-American IABIN Invasives Information Network (I3N) ([c]) for the Americas, DAISIE ([d]) for Europe and NOBANIS ([e]) for North Europe and the Baltic

Note: ([a]) GISIN: http://www.gisin.org.
([b]) GISD: http://www.issg.org/database/welcome.
([c]) IABIN: http://i3n.iabin.net.
([d]) DAISIE: www.europe-aliens.org.
([e]) NOBANIS: www.nobanis.org.

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21 Mobile phone use and brain tumour risk: early warnings, early actions?

Lennart Hardell, Michael Carlberg and David Gee ([1])

In 2011 the World Health Organization's International Agency for Research on Cancer (IARC) categorised the radiation fields from mobile phones and other devices that emit similar non-ionizing electromagnetic fields (EMFs), as a Group 2B i.e. 'possible' human carcinogen. Nine years earlier IARC gave the same classification to the magnetic fields from overhead electric power lines.

The IARC decision on mobile phones was principally based on two sets of case-control human studies of possible links between mobile phone use and brain tumours: the IARC Interphone study and the Hardell group studies from Sweden. Both provided complementary and generally mutually supportive results. This chapter gives an account of the studies by these two groups — and others coming to different conclusions — as well as reviews and discussions leading up to the IARC decision in 2011. The chapter also describes how different groups have interpreted the authoritative IARC evaluation very differently.

There are by now several meta-analyses and reviews on mobile phones and brain tumours, which describe the challenges of doing epidemiology on this issue, the methodological limitations of the major studies published so far and the difficulties of interpreting their results.

It has been suggested that national incidence data on brain tumours could be used to qualify or disqualify the association between mobile phones and brain tumours observed in the case-control studies. However, in addition to methodological shortcomings, there might be other factors that influence the overall incidence rate such as changes in exposure to other risk factors for brain tumours that are unknown in descriptive studies. Cancer incidence depends on initiation, promotion and progression of the disease. As the mechanism for radiofrequency electromagnetic fields carcinogenesis is unclear, it supports the view that descriptive data on brain tumour incidence is of limited value.

The chapter points to mobile phone industry inertia in considering the various studies and taking the IARC carcinogenic classification into account and a failings from the media in providing the public with robust and consistent information on potential health risks. The IARC carcinogenic classification also appears not to have had any significant impact on governments' perceptions of their responsibilities to protect public health from this widespread source of radiation.

The benefits of mobile telecommunications are many but such benefits need to be accompanied by consideration of the possibility of widespread harms. Precautionary actions now to reduce head exposures would limit the size and seriousness of any brain tumour risk that may exist. Reducing exposures may also help to reduce the other possible harms that are not considered in this case study.

Evidence is increasing that workers with heavy long-term use of wireless phones who develop glioma or acoustic neuroma should be compensated. The first case in the world was established on 12 October 2012. The Italian Supreme Court affirmed a previous ruling that the Insurance Body for Work (INAIL) must grant worker's compensation to a businessman who had used wireless phones for 12 years and developed a neuroma in the brain.

([1]) This chapter was supported by grants from Cancer- och Allergifonden and Cancerhjälpen. Contributions by co-workers in the various Hardell group publications are acknowledged.

21.1 Introduction

On May 31, 2011 the WHO International Agency for Research on Cancer (IARC) categorised the radiation fields from mobile phones, and from other devices that emit similar non-ionizing electromagnetic fields (EMFs), as a Group 2B i.e. a 'possible' human carcinogen. Nine years earlier IARC had also classified the magnetic fields from overhead electric power lines as a Group 2B carcinogen.

The IARC decision on mobile phones was principally based on two sets of case-control human studies: the IARC Interphone study and the Hardell group studies from Sweden. Both provided complementary but generally mutually supportive results.

But why were these case-control studies into possible brain tumours from mobile phones initiated?

21.2 The Hardell group studies — 1999–2011

Sweden, along with Israel, was one of the first countries in the world to widely adopt wireless telecommunications technology. Analogue phones (NMT; Nordic Mobile Telephone System) were introduced in the early 1980's using both 450 and 900 Megahertz (MHz) fields. NMT 450 was used in Sweden since 1981 but closed down in 31 December, 2007, whereas NMT 900 operated during 1986–2000.

The digital system (GSM; Global System for Mobile Communication) using dual band, 900 and 1 800 MHz, started to operate in 1991 and now dominates the market. The third generation of mobile phones, 3G or UMTS (Universal Mobile Telecommunication System), using 1900/2100 MHz RF fields has been introduced worldwide since a few years, in Sweden in 2003. Currently the fourth generation, 4G, operating at 800/2 600 MHz, and Trunked Radio Communication (TETRA, 380–400 MHz) are being established in Sweden and elsewhere in Europe.

Desktop cordless phones (e.g. Digital Enhanced Cordless Telecommunications; DECT) have been used in Sweden since 1988, first using analogue 800–900 MHz RF fields, but since early 1990's the digital 1900 MHz system has been used.

Nowadays mobile phones are used more than landline phones in Sweden. (http://www.pts.se/upload/Rapporter/Tele/2011/sv-telemarknad-halvar-2011-pts-er-2011-21.pdf).

The real increase in use and exposures to their radiation fields has been since the end of the 1990's. Wireless phones emit radiofrequency (RF) EMFs and the brain is the main target organ during use of the handheld phone (Cardis et al., 2008).

One of the author's (LH) interest in this research area was initiated by his involvement in a Swedish committee that evaluated cancer risks from exposure to extremely low frequency (ELF) EMFs from power lines. The conclusion was that there was an increased risk for childhood leukemia based on distance to power lines (Hardell et al., 1995). In 2002 IARC concluded that ELF electric and magnetic fields from power lines etc. is a human Group 2B carcinogen (IARC, 2002).

From a review of the literature there seemed to be an increased risk for brain tumours in the electronics industry (Hardell et al., 1995). It was decided to study it further in a case-control study. However, at that time there was also some media attention to a US lawsuit against cell phone industry companies.

It was alleged that repeated use of mobile phone had caused a fatal brain tumour in a woman. The head line in Los Angeles Times was *'Suit Over Cellular Radiation Raises Hazard Questions'* (Carlo and Schram, 2001). It was therefore decided to add questions on mobile phone use in the first of 4 linked case-control studies that are briefly described below.

This is followed by the results of the other major publications with some data on long-term use, the Interphone study, and the IARC evaluation of the RF and cancer evidence, and related responses and discussions.

The aim is not to give a thorough review of this research area, nor to deal with possible other effects of RF exposures which can be found in other publications including meta-analyses of the risk of brain tumours related to use of wireless phones (Hardell et al., 2006d; 2009; Myung et al., 2009; Kundi, 2009; Cardis and Sadetzki, 2011; Levis et al., 2011; IARC Monograph, in press).

21.3 First Hardell group study on mobile phone use and brain tumours — 1999

In 1999 the Hardell group in Sweden published results from their first case-control study on brain tumours and use of mobile phones (Hardell et al.,

1999a). In total 209 (90 %) of the cases and 425 (91 %) of the controls that fullfilled the inclusion criteria answered the mailed questionnaire. Overall no association between use of mobile phones and brain tumours was found.

A slightly increased (but not statistically significant) risk was found for analogue phone (NMT) use and for a *latency* period greater than 10 years, Odds Ratio (OR) = 1.20 (95 % Confidence Interval; CI = 0.56–2.59). For tumours located in the temporal ([2]), occipital or temporoparietal lobe areas of the brain an increased risk was found for ipsilateral ([3]) exposure, OR = 2.42 (95 % CI = 0.97–6.05) (Hardell et al., 1999a, 2001). However, all results were based on low numbers of exposed subjects and different histopathological types of brain tumours so no firm conclusions could be drawn. Furthermore, in this first study use of cordless phones was not included.

Authors of an Editorial in 2001, in commenting on a 'negative' US study (Inskip et al., 2001) that was published after the first Hardell et al. (1999a) study, stated that *…the use of cellular telephones does not detectably increase the risk of brain tumors'* and that *'This study allays fears raised by alarmist reports that the use of cellular telephones causes brain tumors* (Trichopoulos and Adami, 2001). This statement goes far beyond what was scientifically defensible. For example, among the 782 patients with brain tumours only 22 had 5 years or more of mobile phone use and no data with longer latencies were presented. The Editorial illustrates a common misconception which is that a 'non–positive' study is often assumed to be a 'negative' study when in fact the data do not support this assumption.

21.4 Second and third Hardell group studies — 2002–2006

This initial study by the Hardell group gave some support for an association between use of mobile phones and brain tumours. However, the results were based on low numbers especially regarding tumour type and long-term use. The first study was thus followed by two larger studies with cases diagnosed during the time period 1997–2003. The second study encompassed cases diagnosed during 1 January 1997 to 30 June 2000 and the third study 1 July 2000 to 31 December 2003. The methods were the same including an identical questionnaire in both studies. Results for these two study periods were published separately (Hardell et al., 2002, 2005, 2006a), but here pooled results for the whole study period 1997–2003 are presented (Hardell et al., 2006b, 2006c; Hardell and Carlberg 2009). More details can be found in the different publications.

In short, all cases were reported to a cancer registry and had histopathological verfication of tumour diagnosis. Both men and women aged 20–80 years at the time of diagnosis were included. Matched controls were identified from the Swedish Population Registry. The study included use of both mobile and cordless (DECT) phones (wireless phones), the latter an exposure which most other studies ignore ([4]). Also questions e.g. about occupational exposures were asked. Use of wireless phones was assessed by a self-administered questionnaire. The information was supplemented over the phone, if necessary.

The ear that had mostly been used during calls with mobile phone and/or cordless phone was assessed by separate questions; more than 50 % of the time for one side, or equally both sides. This information was checked during the supplementary phone call. Moreover every person that had used a wireless phone received after that a letter asking them again to specify the ear that had been used during phone calls and to what extent that side of the head was mostly used. There was a very good agreement for the result using these three methods to assess these data.

Separately, tumour localisation was defined by using medical records, such as computer tomography (CT) and/or magnetic resonance imaging (MRI). Use of mobile and cordless phones was defined as ipsilateral (more than 50 % of the time), equally ipsi/contralateral or contralateral (less than 50 %) in relation to tumour side. Calculation of cumulative hours of use over the years was based on information on first and last year of use (time period) and average number of minutes per day during that period. Use in a car with external antenna was disregarded as well as use of a handsfree device. A minimum latency period of one year was adopted. Hence, latency period and cumulative use for the different phone types could be defined.

([2]) A review of 110 phone models showed that exposure to radiations is generally higher in the temporal lobe, which is a part of the brain that is near to the ear, (Cardis et al., 2008).
([3]) i.e. the tumour appears on the side of head at which the phone is normally used.
([4]) The Interphone study (see Section 20.9) had some questions on cordless phone use at least in some countries but that information has never been properly analysed or published.

Box 21.1 Some concepts and tools for identifying cancer risks in human studies

OR: Odds ratio. The odds ratio is an estimate of the relative risk, showing how much more likely it is that someone who is exposed to a factor (e.g. cell phones) will develop an outcome (e.g. brain tumour) compared to someone who is not exposed. An OR of 1 indicates no risk, OR < 1 decreased risk and OR > 1 increased risk. For example, an OR of 1.5 indicates that those who are exposed have a 1.5 times higher risk of developing a disease compared to those who are not exposed.

SIR: Standardized incidence ratio. The SIR compares the observed number of cases in a specific population (e.g. cell phone subscribers) to the number of cases expected would the same rates apply as observed in a reference population (e.g. general population). A SIR of 1 indicates no risk, SIR < 1 decreased risk and SIR > 1 increased risk.

CI: Confidence interval. A confidence interval shows the uncertainty of the statistical estimate. In the case of OR and SIR, if the corresponding CI range does not cover 1.0, the result is considered **statistically significant**. Usually 95 % confidence intervals are reported indicating the range of the true OR/SIR with 95 % statistical confidence. The absence of 'statistical significance' can often be a weak guide to the strength of evidence for a risk compared to the power of a study to detect a risk ([5]).

Latency period. Time between first exposure and identification of the disease. For cancer, particularly the solid tumours like brain cancers in contrast to cancers of the blood, such as leukemia, the latency period can be from 15–45 years on average, depending on age at exposure, type and intensity of exposure ([6]) etc. This means that any study of cancer has to be at least as long as the average latent period for the tumour being studied before there will be any clear evidence of a cancer risk.

21.5 Fourth Hardell group study — 2010

In a review commissioned by the former Swedish Radiation Protection Agency (now called the Swedish Radiation Safety Authority) it was suggested that the exclusion of deceased cases was a source of bias in the Hardell group studies (Boice and McLaughlin, 2002). The scientific reason for this suggestion was not given.

As a response to that critique a fourth study was performed. This included the cases with a malignant brain tumour who had died before inclusion in the case-control studies 1997–2003. These cases represented patients with a poor prognosis, mostly with a astrocytoma grade IV tumour. Controls were selected from the Death Registry in Sweden.

Two groups of controls were included, one group consisted of controls that had died from other types of malignant diseases than brain tumour and one group of controls that had died from other diseases than cancer. Relatives to both cases and controls were identified through the Swedish Population Registry at the Swedish Tax Agency. The study encompassed 464 cases and 464 controls that had died from a malignant disease and 463 controls with other causes of death. A similar questionnaire as in previous studies was used and exposure was assessed by a questionnaire sent to the next of kin to each deceased case and control.

Replies were obtained for 346 (75 %) cases, 343 (74 %) cancer controls and 276 (60 %) controls with other diseases. Use of mobile phones gave an increased risk, highest in the >10 years latency group yielding an OR of 2.4 (95 % CI = 1.4–4.1). The risk increased with cumulative number of life-time hours of use, being highest in the more than 2000 hours group who had an OR of 3.4 (95 % CI = 1.6–7.1).

([5]) See Sir Bradford Hill's classic epidemiology paper, 'The Environment and Disease: Association or Causation?' (Proceedings of the Royal Society of Medicine, 1965) where he warned not to overrate the value of statistical significance since it often led people to 'grasp the shadow and loose the substance' of what was in the data. See Chapter 26 on science for precautionary decision-making.

([6]) Stein, Y., Levy-Nativ, O., Richter, E.D., 'A sentinel case series of cancer patients with occupational exposures to electromagnetic non-ionising radiation and other agents', *Eur. J. Oncol.*, 2011, (16/1) 21–54. It has taken almost 50 years to be sure that the atomic bomb dropped on Japan in 1945 also caused brain cancers: the data before then were not clear or robust enough. (Shibata, Y. et al., 'Intercranial meningiomas among Nagasaki atomic bomb survivors', *Lancet*, 1994, (344) 1 770).

No clear association was found for use of cordless phones, although an OR of 1.7 (95 % CI = 0.8–3.4) was found in the group with more than 2000 hours cumulative use. This investigation confirmed the previous results of an association between mobile phones and malignant brain tumours (Hardell et al., 2010). It was concluded that the critique made by Boice and McLaughlin (2002) was scientifically unfounded.

21.6 Some Swedish responses to the Hardell group studies

The first publication on mobile phone use and brain tumour risk (Hardell et al., 1999a) was quickly followed by a letter to the journal (Ahlbom and Feychting, 1999). They suggested that selection bias of cases might have created the high response rate in the Hardell study. However, the critique was unfounded and easy to rebut (Hardell et al., 1999b). In all of the Hardell et al. studies there has usually been a high response rate to the oncologists who have been trained in cancer epidemiology. This applies as well to studies not related to mobile phone use.

Interestingly in the Swedish part of the Interphone studies, one of the authors (Anders Ahlbom) had stated, even before the study started, that an association between cellular telephones and brain tumours was *biologically bizarre* in an 'opinion' letter (Adami et al., 2001). Ahlbom's own work provided evidence for an association between exposure to magnetic fields from overhead power lines and childhood leukemia: an association that would also have to be regarded as *biologically bizarre* (Feychting and Ahlbom, 1993).

Maria Feychting, who participated in the Swedish part of the Interphone studies, queried whether *'the questions really were placed in the same way to cases and controls'* (Björkstén, 2006). Indeed they were in the Hardell studies, however, different methods do seem to have been used for the interviews with cases and controls in the Interphone study, for example, when bed-side interviews were done of cases only.

Meanwhile, the Hardell studies and other evidence of possible health risks from EMF inspired a group of scientists to summarise this evidence in their BioInitiative Report (BioInitiative Working Group, 2007). This had considerable impact in alerting many people to the emerging evidence of risks and to the presence of a small but growing minority of experts who did not agree with the WHO EMF Project statements and other reports that there was no evidence of risk (e.g. of SCENIHR 2007).

The European Environment Agency (EEA), having produced a report *Late lessons from early warnings* (EEA, 2001) was invited by the Biointiative group to submit a chapter about the relevance of the 14 well known 'Late lessons' case studies to the emerging issue of EMF. Having considered the published evidence, the EEA decided it was timely to issue a guarded early warning about the possible risk of brain tumours from mobile phones in September 2007 (see Box 21.2).

21.7 A pooled analysis of the Hardell group studies

Pooled analysis of the two case-control studies on brain tumour cases (glioma, meningioma and acoustic neuroma ([7]), Table 21.1) diagnosed for the whole time period 1997–2003 was made and results were reported for both malignant (Hardell et al., 2006b) and benign (Hardell, 2006c) tumours. This was possible since the same methods were used in both studies with an identical questionnaire. In this presentation results for glioma in the fourth study were added (Hardell et al., 2010; Hardell et al., 2011a).

Latency was divided in three categories, > 1–5 year, > 5–10 year, and > 10 year from first use of a wireless phone until diagnosis. Both use of mobile and cordless phones gave an increased risk overall for **glioma**, highest in the latency group > 10 years, increasing further for *ipsilateral* use; mobile phone OR of 2.9 (95 % CI = 1.8–4.7) and cordless phone OR of 3.8 (95 % CI = 1.8–8.1). Highest OR was found in the > 10 year latency group for total wireless phone use as well.

Table 21.1 gives the same calculations for **meningioma** (n = 916). There was no consistent pattern of an increased risk, although highest risk was found for ***ipsilateral*** exposure in the > 10 year latency period, mobile phone OR = 1.6 (95 % CI = 0.9–2.9). Also ipsilateral use of cordless phone in the same latency category yielded an increased risk, OR = 3.0 (95 % CI = 1.3–7.2).

Regarding **acoustic neuroma** (n = 243) wireless phone use gave OR = 2.2 (95 % CI = 1.3–3.7) in the > 10 y latency period. *Ipsilateral* use gave higher risks than contralateral use for both mobile phone and cordless phone use.

([7]) Studying especially long-term use and laterality.

21.8 Risks to children

Use of wireless phones is widespread among children and adolescents (Söderqvist et al., 2007, 2008). Children's brain absorbs higher radiation from RF-EMF emissions than adults (Cardis et al., 2008; Christ et al., 2010; Gandhi et al., 2012). This is due to the smaller head, thinner skull bone and higher conductivity of the brain tissue. The developing brain is more sensitive to toxins (Kheifets et al., 2005) and the brain is still developing until about 20 years of age (Dosenbach et al., 2010). The greater absorption of RF energy per unit of time, the greater sensitivity of their brain, and the longer lifetimes within which to develop a brain tumour leaves children at a higher risk than adults from mobile phone radiations.

Analyses of the Hardell group results revealed that first use before age of 20 is associated with the highest risk for glioma and acoustic neuroma, see Table 21.2 (Hardell, Carlberg, 2009).

Three age groups for first use of a wireless phone were used; < 20 years, 20–49 years and 50–80 years. For glioma, first use of a mobile phone < 20 y of age gave OR = 3.1 (95 % CI = 1.4–6.7). A similar pattern was found also for cordless phone use (data not shown). Also for acoustic neuroma the risk was highest in the youngest age group; OR = 5.0 (95 % CI = 1.5–16), but no conclusions could be drawn regarding cordless phones since only 1 case had first use before the age of 20 years. These ORs increased further for *ipsilateral* mobile phone use in the youngest age group; glioma OR = 4.4 (95 % CI = 1.3–15), acoustic neuroma OR = 6.8 (95 % CI = 1.4–3.4). No clear age dependent pattern of increased risk was found for meningioma.

There have been very few other studies of children and mobile phone use except the CEFALO study (Aydin et al., 2011) and that of the EU, Mobikids ([8]), which is ongoing.

The multi-centre case–control study CEFALO, conducted in Denmark, Sweden, Norway, and Switzerland has been commented in detail by Söderqvist et al. (2011) since serious methodological problems exist as exemplified below.

In the summary of the study the authors wrote that they *did not observe that regular use of a mobile phone increased the risk for brain tumors.* This conclusion was accompanied by an editorial stating that the study showed *no increased risk of brain tumors* (Boice and Tarone, 2011) as well as by a news release from the Karolinska Institute in Stockholm that the results of no increased risk were 'reassuring' (Karolinska Institute, 2011). However, the statements go far beyond what the study really showed.

For example the data collection and analyses of use of cordless phones was not valid. Use of cordless phones was assessed only *in the first 3 years* of use, a most peculiar definition for which the authors gave no explanation for or reference to. Furthermore, the study never considered wireless phone use, including both mobile and cordless phones, as an exposure category. IARC categorised wireless phone use as a relevant exposure group (Baan et al., 2011). Instead, Aydin et al. (2011) included use of cordless phones in the 'unexposed' category, so risk estimates for mobile phone use might therefore be underestimated. Similarly mobile phone use was included among the 'unexposed' when considering use of cordless phones and thereby potentially concealing an increased risk.

The study yielded a statistically non-significant increased risk for brain tumours among regular users of mobile phones, OR = 1.36 (95 % CI = 0.92–2.02). This OR increased somewhat with cumulative duration of subscriptions and duration of calls (Aydin et al., 2011). Only latency time of 5 years or more was presented with very few cases within this category. Further support of a true association was found in the results based on operator-recorded use for 62 cases and 101 controls, which for time since first subscription > 2.8 years yielded a statistically significant OR of 2.15 (95 % CI = 1.07–4.29) with a statistically significant trend (p = 0.001).

Although the authors do not emphasize that the results yielded an increased risk, the data indicate a moderately increased risk, in spite of low exposure, short latency period and limitations in study design and analyses. Certainly it cannot be used as reassuring evidence *against* an association, as discussed in the commentary (Söderqvist et al., 2011).

Unfortunately, the CEFALO study (Aydin et al., 2011) was published after the IARC meeting in May 2011. Had it been available at the IARC meeting it would have provided additional evidence to support the IARC conclusion that human exposure to RF-EMF is a group 2B carcinogen.

([8]) Contact: ecardis@creal.cat for details.

Box 21.2 The EEA early warnings on brain tumour from mobile phones, 2007–2011

'There are many examples of the failure to use the precautionary principle in the past, which have resulted in serious and often irreversible damage to health and environments. Appropriate, precautionary and proportionate actions taken now to avoid plausible and potentially serious threats to health from EMF are likely to be seen as prudent and wise from future perspectives' (EEA, 2007).

This early warning was updated in 2009 to include:

'The evidence for a head tumour risk from mobile phones, although still very limited, and much contested, is, unfortunately, stronger than two years ago when we first issued our early warning'.

The evidence is now strong enough, using the precautionary principle, to justify the following steps (EEA, 2009):

1. For governments, the mobile phone industry, and the public to take all **reasonable measures to reduce exposures to EMF, especially to radio frequencies from mobile phones, and particularly the exposures to children and young adults who seem to be most at risk from head tumours**. Such measures would include stopping the use of a mobile phone by placing it next to the brain. This can be achieved by the use of texting; hands free sets; and by the use of phones of an improved design which could generate less radiation and make it convenient to use hands free sets ([9]).

2. **To reconsider the scientific basis for the present EMF exposure standards which have serious limitations** such as reliance on the contested thermal effects paradigm; and simplistic assumptions about the complexities of radio frequency exposures.

3. To provide **effective labelling and warnings** about potential risks for users of mobile phones. Across the European Union, the vast majority (80 %) of citizens do not feel that they are informed on the existing protection framework relating to potential health risks of electromagnetic fields. 65 % of citizens say that they are not satisfied with the information they receive concerning the potential health risks linked to EMF. (Special Euro barometer report on EMF, Fieldwork Oct/Nov 2006, published 2007).

4. To **generate the funds needed to finance and organise the urgently needed research** into the health effects of phones and associated masts (base stations). **Such funds could include grants from industry and possibly a small levy on the purchase and or use of mobile phones**. This idea of a research levy is a practice that we think the US pioneered in the rubber industry with a research levy on rubber industry activities in the 1970s when lung and stomach cancer was an emerging problem for that industry. The research funds would be used by independent bodies ([10]) (http://latelessons.ew.eea.europa.eu/fol572324/statements/Benefits_of_mobile_phones_and_potential_hazards_of_EMF.doc).

This was updated in 2011 when evidence was presented to the Council of Europe hearing on mobile phones, February 2011 (EEA, 2011a).

([9]) The EEA has since noted, with some relief, what appears to be an increased use of hands free devices, particularly in the younger generation, due to enhanced applications.

([10]) The EEA has noted the increasing evidence of 'funding bias' in scientific research whereby results outcomes are strongly linked to source of funding. This observation is based on evidence from pharmaceuticals, tobacco, lead, asbestos, BPA and EMF, as well as on evidence from other fields such as cost-benefit analysis and transport construction project cost estimations.

Table 21.1 Odds ratio (OR) and 95 % confidence interval (CI) for glioma, meningioma and acoustic neuroma and use of wireless phones (mobile phones and/or cordless phones)

	Ipsilateral, > 10 year latency	> 10 year latency	Total, > 1 year latency
	OR, CI	OR, CI	OR, CI
Glioma (n = 1148)			
Wireless phone	-	**2.1** **1.6–2.8**	**1.3** **1.1–1.5**
Mobile phone	**2.9** **1.8–4.7**	**2.5** **1.8–3.3**	**1.3** **1.1–1.6**
Cordless phone	**3.8** **1.8–8.1**	**1.7** **1.1–2.6**	**1.3** **1.1–1.6**
Meningioma (n = 916)			
Wireless phone	-	1.4 0.97–2.0	1.0 0.9–1.2
Mobile phone	1.6 0.9–2.9	1.4 0.9–2.1	1.1 0.9–1.3
Cordless phone	**3.0** **1.3–7.2**	1.6 0.9–2.8	1.1 0.9–1.4
Acoustic neuroma (n = 243)			
Wireless phone	-	**2.2** **1.3–3.7**	**1.5** **1.1–2.0**
Mobile phone	**3.0** **1.4–6.2**	**2.6** **1.5–4.6**	**1.7** **1.2–2.3**
Cordless phone	2.3 0.6–8.8	1.0 0.3–2.9	**1.5** **1.04–2.0**

Note: Bold = statistically significant. Number of controls = 2438 in analyses of glioma (living and deceased controls), 2162 for meningioma and acoustic neuroma (only living controls). Only living cases and controls included in analyses of ipsilateral use of mobile and cordless phones.

Adjustment was made for age, gender, socioeconomic-code and year of diagnosis. For glioma adjustment was also made for vital status.

Source: Hardell et al., 2006b, 2006c, 2010, 2011a.

Table 21.2 Odds ratio (OR) and 95 % confidence interval (CI) for glioma, meningioma and acoustic neuroma in different age groups for age at first use of a mobile phone

	Glioma (n = 1148)	Meningioma (n = 916)	Acoustic neuroma (n = 243)
	OR, (CI)	OR, (CI)	OR, (CI)
Mobile phone	**1.3** **(1.1–1.6)**	1.1 (0.9–1.3)	**1.7** **(1.2–2.3)**
< 20 years old	**3.1** **1.4–6.7**	1.9 0.6–5.6	**5.0** **1.5–16**
20–49 years old	**1.4** **1.1–1.7**	1.3 0.99–1.6	**2.0** **1.3–2.9**
≥ 50 years old	**1.3** **1.01–1.6**	1.0 0.8–1.3	1.4 0.9–2.2

Note: Bold = statistically significant. Number of controls=2438 in analyses of glioma (living and deceased controls), 2162 for meningioma and acoustic neuroma (only living controls).

Adjustment was made for age, gender, socioeconomic-code, year of diagnosis. For glioma adjustment was also made for vital status.

Source: Hardell et al., 2006b, 2006c, 2010, 2011a.

21.9 The Interphone study 2000–2010: disagreements and delays

The Interphone study was an international collaboration on brain tumour risk and mobile phone use conducted under the guidance of IARC, which is an independent agency of WHO. The investigation was inititated by recommendations from several expert groups to study possible health effects of exposure to RF-fields (McKinlay, 1997; Cardis et al., 2007). It was conducted at 16 research centres in 13 countries during varying time periods between 2000 and 2004. It cost nearly EUR 20 million of which industry contibuted 5.5 million (IARC, 2010) ([11]).

Some of the separate country analyses of the Interphone study produced different results, with some being positive i.e. finding increased brain tumour risks, and some negative i.e. finding decreased risks, i.e. seemingly a 'protective' effect of the radiation.

The authors therefore found it hard to come to an agreed conclusion and there was a 4 year delay between publication of the country results and of the overall study results. One group reportedly thought that the Interphone study overall had found indications of a positive link between mobile phone use and brain tumours, especially when the results of the 10+ year exposure group were analysed separately. Another group thought that they had found no indication of a risk and that the apparent excess of brain tumour was an artifact of the study design and methodology. A third group could agree to neither position.

The publication of the overall Interphone results was finally initiated by the Director of IARC, Christopher Wild, who brokered sufficient agreement between the scientists to finally get the results published in May 2010.

No association between mobile phone use and meningioma was found in the overall Interphone results whereas subgroup analyses showed statistically significant increased risk for glioma in the highest exposure group, i.e. those who had used their mobile phones for 1 640 hours or more, which corresponds to about half an hour of use per day for ten years (Interphone Study Group, 2010), OR = 1.40 (95 % CI = 1.03–1.89). The risk increased further for ipsilateral exposure (OR = 1.96, 95 % CI = 1.22–3.16) and for tumours in the most exposed part of the brain, the temporal lobe, (OR = 1.87, 95 % CI = 1.09–3.22) in the highest exposure group for glioma.

However, the compromise reached between the opposing scientists involved the juxtaposition of two contrasting sentences that were pointing in different directions: *There were suggestions of an increased risk of glioma, and much less so meningioma, at the highest exposure levels, for ipsilateral exposures and, for glioma, for tumours in the temporal lobe* followed by *…biases and errors limit the strength of the conclusions we can draw from these analyses and prevent a* ***causal*** [our emphasis] *interpretation* (Interphone Study Group, 2010).

There was no explanation about how the strength of a link between a cause and an effect can vary from a 'scientific suspicion of risk' to a 'strong association' through 'reasonable certainty' and on to 'causality' which requires the strongest of evidence. This continuum in strengths of evidence, which was illustrated in Bradford Hill's paper written at the height of the tobacco and lung cancer controversy (Hill, 1965), was not explained in the Interphone paper. This meant that the media and the public could assume that 'not causal' meant 'no link' between mobile phones and brain tumours. Other epidemiologists did pick up this rather significant nuance.

In an Editorial accompanying the Interphone results (Saracci and Samet, 2010), published in the International Journal of Epidemiology, the main conclusion of the Interphone results, was described as *both elegant and oracular…(which) tolerates diametrically opposite readings*. They also pointed out several methodological reasons why the Interphone results were likely to have underestimated the risks, such as the short latency period since first exposures became widespread: less than 10 % of the Interphone cases had more than 10 years exposure.

None of the today's established carcinogens, including tobacco, could have been firmly identified as increasing risk in the first 10 years or so since first exposure.

The 'oracular' concluding sentences from the Interphone study therefore allowed the media to report opposite conclusions. For example, on 17 May, 2010 the UK Daily Telegraph reported that the Interphone study provided evidence of a brain tumour risk from mobile phones (http://

([11]) The Hardell studies cost approximately EUR 410 000 and were financed by the Swedish Work Environment Fund, Cancer- och Allergifonden, Cancerhjälpen, Telia, Fondkistan, and the Örebro University Hospital Cancer Fund.

www.telegraph.co.uk/health/7729676/Half-an-hour-of-mobile-use-a-day-increases-brain-cancer-risk.html) whilst the BBC News reported on the same day that there was no risk (http://news.bbc.co.uk/2/hi/health/8685839.stm). This conflicting media reporting pattern was widely repeated elsewhere ([12]).

Further confusion for the public and policymakers followed as a result of the differences in the statements of the Interphone scientists reported in the media. For example, Microwave News reported on 17 May that Elisabeth Cardis, the coordinator of the Interphone study, thought that *Overall...the results show a real effect*; Bruce Armstrong, the Australian Interphone participant, thought that *It shows some indication of an increased risk of gliomas, but I cannot say this with certainty;* and Siegal Sadetzki from Israel thought the results had consistency in indicating a risk but, whilst not *strong enough for a* ***causal*** [our emphasis] *interpretation, they are sufficient to support precautionary policies* (http://www.microwavenews.com/Interphone.Main.html).

In contrast, another co-author, Feychting, thought, *the use of mobile phones for over ten years shows no increased risk of brain tumours* (http://www.i-sis.org.uk/EEA_Highlight_Mobile_Phone_Cancer_Risks.php) and Ahlbom, also from the Swedish Interphone part, told Chinese Television that *there is nothing in these data or in previous data, really, to indicate that there is any risk involved in this* (http://www.youtube.com/watch?v=TllmreWZdoA).

In later publications of Interphone data the estimated RF dose from mobile phone use in the tumour area was also associated with an increased risk for glioma in parts of the Interphone group. The OR increased with increasing total cumulative dose of specific energy (J/kg) absorbed at the estimated tumour centre for more than 7 years before diagnosis with an OR of 1.91 (95 % CI = 1.05–3.47) in the highest quintile of exposure (Cardis et al., 2011).

This important result, which for the first time linked amount of radiation absorbed (rather than just its proxy which is years of exposure/cumulative hours of use) to tumour induction, received very little media attention.

A similar study based on less sound methods was later published by another part of the Interphone study group, see below (Larjavaara et al., 2011).

Results have also now been published for **acoustic neuroma** (Interphone study group, 2011). An increased risk was found for start of *ipsilateral* mobile phone use ≥ 10 year before reference date and cumulative use ≥1 640 h; OR = 3.74 (95 % CI = 1.58–8.83).

The total Interphone results for tumours of the parotid gland ([13]) have never been published. Since the IARC has now terminated the Interphone study ([14]) only the results from Sweden (Lönn et al., 2006) and Israel (Sadetzki et al., 2008) are available. Subgroup analyses that considered laterality (side of use and risk of tumour) and/or amount of use (cumulative hours) indicated increased risks. However, results from other studies do not indicate a consistent pattern of increased risk (Auvinen et al., 2002; Hardell et al., 2004; Duan et al., 2011; Söderqvist et al., 2012a). Results on long-term use are, however, scarce.

21.10 Some reviews and discussions of the Hardell group and Interphone studies

There are by now several meta-analyses and reviews on mobile phones and cancer and they describe the challenges of doing epidemiology on this issue, the methodological limitations of the major studies published so far and the difficulties of interpreting their results.

For example, several of the Interphone findings display differential misclassification of exposure due to observational and recall bias which would tend to underestimate the risk. There were low participation rates for both cases and controls in the Interphone studies, for example in some countries only about 50 % of the cases and about 40 % of the controls participated. This is to be compared with 90 % response rate for cases with malignant brain tumours, 88 % for benign and 89 % for controls in the Hardell-group studies on living subjects (Hardell et al., 2006b, 2006c). Deceased cases were included in the calculations of participation in Interphone, but in

([12]) The EEA had anticipated this confusion and had earlier proposed to IARC that the conflicting opinions of the different Interphone groups should be published alongside each other, with their different arguments and data interpretations clearly illustrated in the same scientific article. This would have helped the media and the public to better understand the reasons for the divergent views amongst the Interphone scientists. However, this suggestion was not adopted.
([13]) A tumour in a gland on the cheek in front of the ear.
([14]) According to the official website (http://interphone.iarc.fr/) the Interphone Study was completed in February 2012.

the Hardell studies deceased cases were included in a separate sub-study on malignant brain tumours.

About 40 % of the cases were interviewed at hospitals in the Interphone studies. Further, it was always known to the interviewer if it was a case or a control that was interviewed. Use of cordless phones was not properly assessed in the Interphone study, or at least not reported. Further discussion on these methodological points may be found elsewhere (Hardell et al., 2008; Kundi, 2009).

Myung et al. (2009) subsequently compared methods and results in all the published studies on the use of mobile phones and the risk for brain tumours. They concluded that the Hardell studies were of higher quality compared with the Interphone study based on the Interphone results from different countries that were then available.

However, one important issue was not covered in the Myung et al. (2009) review, namely that the Hardell group also assessed use of cordless phones in contrast to the Interphone study group. RF-EMF emissions from a cordless phone are of the same magnitude as that from a digital mobile phone, something that has been pointed out several times (Hardell et al., 2006d; Kundi, 2009; Redmayne et al., 2010). Moreover cordless phones are typically used for longer calls than mobile phones (Hardell et al., 2006b, 2006c). Including cordless phone use in the 'unexposed' group, as was done in the Interphone study, would bias estimates against a risk.

The use of bedside interviews of cases, as in the Interphone study, can be a major disadvantage and is ethically questionable. At that time the patient has not fully recovered from e.g. surgery, may not have been fully informed about the diagnosis, treatment and prognosis and may even be under sedation by drugs. In fact patients scored significantly lower than controls due to problems in recalling words (aphasia), problems with writing and drawing due to paralysis in the Danish part of Interphone (Christensen et al., 2005). Obviously observational bias could have been introduced thereby during these bedside interviews.

In contrast, the Hardell group cases received a postal questionnaire approximately 2 months after diagnosis and could give the answers in a relaxed manner, a situation similar to the controls. All cases and controls were later interviewed over the phone to verify and clarify different exposures. This was done blinded as to case or control status.

The possibility of recall and observational bias was investigated in the second case-control study by Hardell et al. (2002). Use of a wireless phone was similar among cases and controls regardless if they reported a previous cancer or if a relative helped to fill in the questionnaire. Potential observational bias during phone interviews was analysed by comparing change of exposure in cases and controls after these interviews. No significant differences were found, showing that the results could not be explained by observational bias: for further details see discussion in that publication (Hardell et al., 2002). All interviews were performed by trained persons using structured instructions and protocols.

The article by Myung et al. was commented on by e.g. Rowley and Milligan (2010) representing the mobile phone industry. They claimed that the Interphone studies were independent of industry influence. However, the mobile phone industry provided 5.5 million euro for the Interphone study and additional funding was provided by the industry in some countries. Furthermore, according to the study protocol *Other parties may also be involved in the Study Group as observers or consultants. These may include representatives of industry, other concerned organisations...* In addition, *representatives of industry and other concerned organisations… shall be informed shortly (maximum of seven days) before publication,* and before the scientific community and laymen have access to the study results (IARC, 2001).

Rowley and Milligan claim that there is *evidence of selection, information, and recall bias, and unusually high reported participation rates* in the Hardell studies (Rowley and Milligan, 2010). These ad hoc statements are not substantiated by the authors or in their references. A high participation rate is a pre-requiste for high quality in case-control studies.

Other scientists have analysed the Hardell results more favourably (Kundi, 2009; Myung et al., 2009; Mead, 2009; Cardis and Sadetzki, 2011; Levis et al., 2011) and IARC relied mainly on the Hardell group and Interphone study group results for its evaluation of the RF evidence.

The Cardis review was particulary interesting as she was the coordinator of the Interphone study. In the review with Sadetzki, another Interphone study participant, they concluded, after a full discussion of the methodological strengths and weaknesses of the Hardell and Interphone studies, that:

> *It is not possible to evaluate the magnitude and direction of the different possible biases on the study results and to estimate the net effect of mobile phones on the risk of brain tumours. The overall balance of the above mentioned arguments,*

> *however, suggest the existence of a possible association* (i.e. between mobile phones and brain tumour).

They ended by concluding that:

> *Simple and low cost measures, such as the use of text messages, handsfree kits and/or the loudspeaker mode of the phone could substantially reduce exposure to the brain from mobile phones. Therefore, until definitive scientific answers are available, the adoption of such precautions, particularly among young people, is advisable* (Cardis and Sadetzki, 2011, p. 170).

21.11 IARC evaluation of the carcinogenicity of RF-EMFs 2011

In 2011 IARC evaluated the carcinogenic effect to humans for RF-EMF emissions during a 8 days (24–31 May) meeting at Lyon in France. This included all sources of radiofrequency radiation, not only mobile and cordless phones. Regarding use of wireless phones all of the published studies by the Hardell group were included as well as overall results for Interphone (Interphone Study Group, 2010, 2011; Cardis et al., 2011). The results on glioma are similar in the Hardell group and Interphone studies if the same inclusion and exclusion criteria are used (Hardell et al., 2011b). This is in contrast to widespread claims that the results of the two sets of studies differed significantly.

The IARC Working Group consisted of 30 scientists ([15]) representing four areas: 'animal cancer studies', 'epidemiology', 'exposure' and 'mechanistic and other relevant data'. The different expert groups had initially a draft written before the meeting by some of the experts. Further work was done in the expert groups and a final agreement, sentence by sentence, was obtained during plenary sessions with all experts participating.

The Working Group concluded that there is 'limited evidence in humans' for the carcinogenicity of RF-EMF, based on positive associations between glioma and acoustic neuroma and exposure to RF-EMF from wireless phones. This conclusion was based on the Interphone study and the Hardell group studies. No conclusions could be drawn from the Danish cohort study on mobile phone subscribers due to considerable misclassification in exposure assessment (Baan et al., 2011).

The final conclusion was obtained by voting by all 30 scientists and there was a very large majority for the conclusion that RF-EMF radiation is 'possibly carcinogenic' to humans, Group 2B, based also on occupational studies.

21.12 Some responses to the IARC conclusion

It is interesting to see that even the authoritative IARC evaluation has been interpreted very differently by different groups.

To date, no adverse health effects have been established as being caused by mobile phone use. This was stated in a fact sheet in June 2011 from WHO EMF Program after the IARC decision (http://www.who.int/mediacentre/factsheets/fs193/en/), and furthermore that *Tissue heating is the principal mechanism of interaction between radiofrequency energy and the human body* without acknowledging any of the non-thermal effects that could explain the evidence on brain tumours (Guiliani and Soffriti, 2010).

Michael Milligan from the Mobile Manufacturers Forum (MMF) said:

> *…After reviewing the available scientific evidence, it is significant that IARC has concluded that RF electromagnetic fields are not a definite nor a probable human carcinogen…* (http://www.mmfai.org/public/docs/eng/MMF_PR_310511_IARC.pdf).

Jack Rowley from GSM Association (GSMA) said:

> *…The IARC classification suggests that a hazard is possible but not likely…* (http://www.gsma.com/articles/gsma-statement-on-the-iarc-classification/17567/).

([15]) David Gee of the EEA had been invited by IARC to join the group as 'a representative of your organization, rather than as an observer' (for a definition of representatives and observers, please see the Preamble: http://monographs.iarc.fr/ENG/Preamble/currenta5participants0706.php). However, a few days before the IARC meeting began the EEA wrote to IARC to say they were withdrawing because of further delays in publishing the full Interphone results and because of the intellectual bias of Ahlbom who was then the Chair of the epidemiology group for the meeting. The day before the meeting began Ahlbom was removed from the Chair by IARC as a result of a reported conflict of interest: and the meeting was also given part of the unpublished Interphone data. However, this was too late for the EEA to then participate.

Patrick Frostell from the Federation of Finnish Technology Industries (FFTI) said:

> *…IARC's classification is in line with the dominant interpretation of current research data, according to which radiofrequency electromagnetic fields are neither carcinogenic to humans nor probably carcinogenic to humans…* (http://www.teknologiateollisuus.fi/en/news/announcements/2011-6/no-change-in-international-assessment-of-the-health-effects-of-mobile-phones).

Professor **Dariuz Leszczynski** from the Finnish Radiation and Nuclear Safety Authority (STUK) and member of the IARC expert panel wrote:

> *Recent IARC evaluation of mobile phone radiation potential to cause cancer and classification of it as a 2B carcinogen has caused a stir of pro and contra opinions among the scientists, industry and news media. Unfortunately, the only outcome of this broad attention leads to only one — **confusion**. Regular mobile phone user, whether highly or not so highly educated, can only be **confused** by this flurry of contradictory opinions and spin-statements* (http://betweenrockandhardplace.wordpress.com/2011/06/29/%e2%80%a2viva-confusion/).

The Economist wrote:

> *..your correspondent thinks the whole brouhaha over mobile phones causing brain cancer is monumentally irrelevant compared with all the other things there are to worry about* (http://www.economist.com/blogs/babbage/2011/06/mobile-phones-and-health).

Microwave News has followed this area for a long time. Much of the whole IARC story and the aftermath can be found at its website, for example regarding ICNIRP's standpoint:

> *ICNIRP is a self-perpetuating group that declines to disclose its finances. Its Standing Committee on Epidemiology, which wrote the new commentary, has only welcomed the like-minded. Its previous chairman, Anders Ahlbom, has also registered his opinion that cell phone tumor risks are nonexistent. (He was the lead author of the last ICNIRP review of cell phones and cancer.) Another former member, Maria Blettner, was the lone dissenting voice in the final vote of the IARC working group. Both Blettner and Ahlbom worked on Interphone* (http://www.microwavenews.com/ICNIRP.Interphone.html).

Perhaps even IARC has contributed to this confusion by seeming to agree with the largely non-positive but much criticized Danish cohort study, see below (http://www.microwavenews.com).

No doubt the IARC decision started a world-wide spinning machine perhaps similar to the one launched by the tobacco industry when IARC was studying and evaluating passive smoking as a carcinogen in the 1990s (Ong and Glanz, 2000) ([16]). Sowing confusion and 'manufacturing doubt' is a well known strategy used by the tobacco and other industries (Michaels, 2008; McGarity and Wagner, 2008; Oreskes and Conway, 2010).

21.13 Some further studies published since the IARC conclusion

The Nordic part of Interphone published a study relating brain tumour location to mobile phone radiation (Larjavaara et al., 2011). The results seemed to contradict the findings by Cardis et al. (2011) as discussed above, but used a different, less clear method. Only 42 cases had used the mobile phone for more than 10 years and no analysis was made of the highest exposed group with longest duration of use. Thus, this study is much less informative and less sophisticated that the one by Cardis et al. (2011).

In Denmark a cohort of mobile phone subscribers was designed and started in cooperation between The International Epidemiology Institute (IEI), Rockville, MD, USA, and the Danish Cancer Society. The cohort was established by grants from two Danish telecom operation companies (TeleDenmark Mobil and Sonafon), by IEI, and by the Danish Cancer Society. The source of money for the IEI has not been disclosed.

([16]) In the early 1990s the Philip Morris tobacco company feared that an IARC study and a possible IARC monograph on second-hand smoke would lead to increased restrictions in Europe so they spearheaded an inter-industry, three-prong strategy to subvert IARC's work. The scientific strategy attempted to undercut IARC's research and to develop industry-directed research to counter the anticipated findings. The communications strategy planned to shape opinion by manipulating the media and the public. The government strategy sought to prevent increased smoking restrictions. The IARC study cost USD 2 million over ten years; Philip Morris planned to spend USD 2 million in one year alone and up to USD 4 million on research (Ong and Glanz, 2000).

Box 21.3 IARC and its classifications of carcinogens

IARC evaluates the *hazard* from potential carcinogens, i.e. 'an agent that is capable of causing cancer under some circumstances', while a cancer *risk* is an estimate of the carcinogenic effects expected from an exposure to a cancer hazard. The IARC monographs are an exercise in evaluating cancer hazards, despite the historical presence of the word 'risks' in the title.

IARC has categorised nearly 1000 potentially carcinogenic **hazardous** agents, that it has studied over the last 40 years, into 5 classifications. These are differentiated by different strengths of evidence. In *descending order of strengths of evidence* they are: **Group 1**, which are '**established'** human carcinogens, such as asbestos, diesel engine exhaust, tobacco, and X-rays (*108 agents*); **Group 2A**, which are **probable** carcinogens, such as perchloroethylene (*64 agents*); **Group 2B,** which are **possible carcinogens,** such as other traffic fumes, lead, DDT and now radiofrequency electromagnetic fields, including mobile phones (*272 agents*); **Group 3**, where the agent is **not classifiable** because the evidence is inadequate and does not permit another classification *(508 agents);* and **Group 4**, where the agent is **probably not carcinogenic to humans,** based on fairly strong evidence *against* a cancer effect in both humans and animals (*1 agent*) (IARC, 2012).

It may be helpful to clarify the meaning of the particularly contentious groups. i.e. 2A and 2B.

IARC chooses 3 main different strengths of evidence when it is evaluating the different types of cancer evidence that may be available. The evidence evaluated comes mainly from humans; from animals; and from consideration of the biological mechanisms for cancer causation: this last can provide understanding about *how* carcinogens cause cancer, in contrast to *whether* they cause cancer.

The main strengths of evidence groups used by IARC are: 'sufficient', 'limited', and 'inadequate'. For example, while Group 1 consists of those agents where there is 'sufficient evidence of carcinogenicity' in humans; Group 2A includes those agents where there is 'limited evidence of cancer in humans' but 'sufficient evidence of cancer in animals'; and Group 2B, which is the radiofrequency EMF category, is those agents where there is 'limited evidence of cancer in humans and less than sufficient evidence in animals' and where 'chance, bias or confounding cannot be ruled out with reasonable confidence'. 'Evidence suggesting lack of carcinogenicity' is used for Group 4 (IARC, 2006, p. 19–20).

Different agents in the same classification group are evaluated on the basis of very different kinds of evidence and exposure conditions that are specific for each substance. Some 2B agents will be at the lower end of the probability range, others will be close to the nearly one in two probability and the rest are somewhere in between, depending on their very specific characteristics. By loosely lumping together several randomly chosen carcinogens from the 271 in Group 2B such as dry cleaning fumes and coffee, which invites comparison to mobile phones, journalists and others help to complicate the already difficult discussion about the likelihood of cancer risks. Each agent needs to be considered on its own evidence.

The first results from the Danish study on brain tumour risk among mobile phone subscribers were published in 2001 and updated in 2006 and 2011 (Johansen et al., 2001; Schüz et al., 2006, 2011; Frei et al., 2011). It included subjects from 1 January, 1982 until 31 December, 1995 identified from the computerized files of the two Danish operating companies, TeleDenmark Mobil and Sonafon. A total of 723 421 subscribers were identified but the initial cohort consisted of only 58 % of these subscribers.

The IARC working group's main reason for not using the Danish study as evidence for its evaluation was that it *could have resulted in considerable misclassification in exposure assessment* (Baan et al., 2011).

The authors of the Danish study have themselves pointed out the main causes of such considerable exposure misclassification (Frei et al., 2011): mobile phone subscription holders not using the phone were classified as 'exposed'; non-subscribers using the mobile phone were classified as 'unexposed'; corporate subscribers of mobile phones (200 507 people), which are likely to have been heavy users, were classified as 'unexposed'; persons with a mobile phone subscription later than 1995 (which is over 80 % of the Danish population) were classified as 'unexposed'; and many users of cordless phones, which Hardell et al. have linked to excess risks of brain cancers, were also classified as 'unexposed'.

Other limitations are the absence of analysis by laterality (the side of head were the phone is used in relation to the side of the tumour) and the complete absence of actual exposure data. These and other shortcomings in this cohort study have been discussed elsewhere in more detail (Ahlbom et al., 2007; Söderqvist et al., 2012b).

It is clear from these limitations that the authors conclusion that 'In this update of a large nationwide cohort study of mobile phone use, there were no increased risks of tumours of the central nervous system, providing little evidence for a causal association' is not soundly based (Frei et al., 2011).

21.14 Need for monitoring long term trends in country wide nervous system tumours

It has been suggested that overall incidence data on brain tumours for countries may be used to qualify or disqualify the association between mobile phones and brain tumours observed in the case-control studies (Aydin et al., 2011; Ahlbom and Feychting, 2011; Deltour et al., 2012; Little et al., 2012). In support of the findings that Frei et al. (2011) presented for Denmark, Ahlbom and Feychting (2011) refer to data on overall brain tumour incidence from the Swedish Cancer Registry (which does not show an overall increase in brain tumour incidence since the 1990s) rather than from the Danish Cancer Registry which would have been more relevant.

The quality of the Swedish Cancer Registry in reporting of central nervous system tumours, particularly high grade glioma, has been seriously questioned (Bergenheim et al., 2007; Barlow et al., 2009). In the Deltour et al. paper (2012) Sweden accounted for about 40 % of the population and cases. Thus, underreporting of brain tumour cases to the Swedish Cancer Register would make the conclusions in the Deltour et al. study less valid.

In Denmark a statistically significant increase in incidence rate per year for brain and central nervous system tumours (combined) was seen during 2000–2009, in men +2.7 % (95 % CI = 1.1 to 4.3) and in women + 2.9 % (95 % CI = 0.7 to 5.2) (NORDCAN). Recently updated results for brain and central nervous system tumours were released in Denmark. The age-standardized incidence of brain and central nervous system tumours increased by 40 % among men and by 29 % among women between 2001–2010 (Sundhedsstyrelsen, 2010).

A more recent news release based on the Danish Cancer Register states that during the last 10 years there has been an almost 4-fold increase in the incidence of the most malignant glioma type, glioblastoma (http://www.cancer.dk/Nyheder/nyhedsartikler/2012kv4/Kraftig+stigning+i+hjernesvulster.htm). So far these incidence data are not generally available.

Little et al. (2012) studied the incidence rates of glioma during 1992–2008 in the United States and compared the results with odds ratios for glioma associated with mobile phone use in the 2010 Interphone publication (Interphone Study Group, 2010) and the Hardell group pooled results published in 2011 (Hardell et al., 2011a). However, an important methodological issue that was not stated in the abstract or in Figures, but can be found in the web appendix, is that observed rates were based on men aged 60–64 years from the Los Angeles SEER registry as the baseline category. These data were used to estimate rates in the entire dataset, men and women aged ≥ 18 years and all 12 SEER registries. Thereby numerous assumptions were made. The conclusion by Little et al. that 'Raised risk of glioma with mobile phone use, as reported by one (Swedish) study … are not consistent with observed incidence trends in the US population data...' goes far beyond scientific evidence and what would be possible to show with the faulty methods used in the study. On the contrary, it is of interest that they in fact showed statistically significant yearly increasing incidence of high-grade glioma in the SEER data for 1992–2008, + 0.64 %, 95 % CI 0.33 to 0.95, a result not commented further by the research group.

Much care is needed when using *descriptive* data, as in Aydin et al. (2011), Deltour et al. (2012) and Little et al. (2012), to dismiss results from *analytical* epidemiology. In addition to methodological shortcomings, there might be other factors that influence the overall incidence rate such as changes in exposure to other risk factors for brain tumours that are unknown in descriptive studies. Cancer incidence depends on initiation, promotion and progression of the disease (Hazleton et al., 2005). As the mechanism for RF-EMF carcinogenesis is unclear it supports the view that descriptive data on brain tumour incidence is of limited value.

21.15 Concluding remarks

It is sometimes claimed by the telecommunications industry and others that:

- the scientific basis for the current ICNIRP limits for exposure to EMF is adequate to protect the public from cancer risks;
- that children are no more sensitive than adults to the RF from mobile phones;
- that there are no biologically significant effects from **non-thermal** levels of EMF, and
- that, if there are such effects, there are no acceptable mechanisms of action that could explain these effects.

However the recent 400-page review by the Ramazzini Institute and The International Commission for Electromagnetic Safety (ICEMS) provides a wealth of evidence on the non–thermal biological and ecological effects of EMF (Giuliani and Soffritti, 2010). The EEA summarised the main findings of this report in its evidence to the Council of Europe' hearing on RF and mobile phones in 2011 (EEA, 2011a, 2011b).

Results from the Hardell-group as well as from the Interphone group show an increased risk for glioma and acoustic neuroma associated with long term mobile phone use. Also use of cordless phones increases the risk when properly assessed and analysed. The risk is highest for ipsilateral exposure to the brain of RF-EMF emissions. Adolescents seem to be at higher risk than adults. For meningioma there is no consistent pattern of increased risk.

Furthermore, of interest is that in the same studies different results were obtained for different tumour types. This strongly argues against systematic bias as an explanation of the findings. In that case the results would have been similar regardless of tumour type.

The IARC conclusion that RF-EMF emissions overall, e.g. occupational and from wireless phones, are possibly carcinogenic to humans, Group 2B (Baan et al., 2011) has been questioned by e.g. members of ICNIRP (Swerdlow et al., 2011). That article appeared online 1 July, 2011, one month after the IARC decision, and concluded that *the trend in the accumulating evidence is increasingly against the hypotheses that mobile phone use can cause brain tumors in adults*. There has also been unfounded attacks on individual researchers as exemplified in this article, a pattern that repeats similar experiences in the asbestos, lead and tobacco histories. Published results on health effects are questioned by using obscure methods and citing single results out of context without considering the overall pattern.

There is a lack of investigating journalists who can produce nuanced reports in the media. Most journalists seem to make only reference to news reports or press releases without making their own evaluations or without seeming to have read the original articles. Many limitations of epidemiological studies are to be found in the text, but rarely in the abstract which is most often all that is read. Without accurate and reliable reporting in the media the public do not get a robust and consistent information on potential health risks to make their own judgements about how precautionary they should be.

It is remarkable that the IARC carcinogenic classification does not seem to have had any significant impact on governments' perceptions of their responsibilities to protect public health from this widespread source of radiation, especially given the ease with which exposures can be reduced (i.e. texting, handsfree devices and better phone design).

Independent research into the many unknowns about the biological and ecological effects of RF radiations are urgently needed, given the global exposure of over 5 billion people and many other species, especially those, like bees and some birds whose navigation systems are possibly being affected by such radiations (Balmori, 2005, 2009; Sharma and Kumar, 2010), and effects on breeding of wild birds (Everaert and Bauwens, 2007). Research could be in part funded by relevant industries from levies on phones and masts but used independent from their influence.

The benefits of mobile telecommunications are many, but, as with other case studies in the *Late lessons from early warnings* Volume 1 (EEA, 2001) and the present report, such benefits need not to be accompanied by the possibility of widespread harms. Precautionary actions now to reduce head exposures, as pointed out by the EEA in 2007, and many others since, would limit the size and seriousness of any brain tumour risk that may exist. Reducing exposures may also help to reduce the other possible harms that are not considered in this case study.

21.16 Epilogue

The Italian Supreme Court affirmed a previous ruling that the Insurance Body for Work (INAIL) must grant worker's compensation to a businessman who had used wireless phones for 12 years and developed a neurinoma in the brain (http://www.applelettrosmog.it/public/news.php?id_news=44;

http://microwavenews.com/news-center/italian-supreme-court-affirms-tumor-risk). He had used both mobile and cordless phones for five to six hours per day preferably on the same side as the tumour developed. The neurinoma was located in the trigeminal Gasser's ganglion in the brain. This 5th cranial nerve controls facial sensations and muscles. It is the same type of tumour as the acoustic neuroma in the 8th cranial nerve located in the similar area of the brain. Although neurinoma is a benign tumour it causes persistent disabling symptoms after treatment with neurological impairment that severely affects the daily life. The Italian case fulfils the criteria for a causal association; more than 10 years use of wireless phones, high cumulative exposure on the same side as the tumour appeared, and a tumour type that would be predicted based on previous research on use of wireless phones and brain tumour risk. No further appeal of the Supreme Court decision is possible.

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22 Nanotechnology — early lessons from early warnings

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Nanotechnology is the latest in a long series of technologies heralded as ushering in a new era of technology-driven prosperity. Current and future applications of nanotechnology are expected to lead to substantial societal and environmental benefits, increasing economic development and employment, generating better materials at lower environmental costs, and offering new ways to diagnose and treat medical conditions. Nevertheless, as new materials based on nanoscale engineering move from the lab to the marketplace, have we learnt the lessons of past 'wonder technologies' or are we destined to repeat past mistakes?

This chapter first introduces nanotechnology, clarifies the terminology of nanomaterials and describes current uses of these unique materials. Some of the early warning signs of possible adverse impacts of some nanomaterials are summarised, along with regulatory responses of some governments. Inspired by the EEA's first volume of *Late lessons from early warnings*, the chapter looks critically at what lessons can already be learned, notwithstanding nanotechnology's immaturity ([1]).

Nanotechnology development has occurred in the absence of clear design rules for chemists and materials developers on how to integrate health, safety and environmental concerns into design. The emerging area of 'green nanotechnology' offers promise for the future with its focus on preventive design. To gain traction, however, it is important that research on the sustainability of materials is funded at levels significant enough to identify early warnings, and that regulatory systems provide incentives for safer and sustainable materials.

Political decision-makers have yet to address many of the shortcomings in legislation, research and development, and limitations in risk assessment, management and governance of nanotechnologies and other emerging technologies. As a result, there remains a developmental environment that hinders the adoption of precautionary yet socially and economically responsive strategies in the field of nanotechnology. If left unresolved, this could hamper society's ability to ensure responsible development of nanotechnologies.

([1]) This chapter is based on and in parts identical to Hansen, S.F., Maynard, A., Baun, A., Tickner, J.A. 2008. 'Late lessons from early warnings for nanotechnology', *Nature Nanotechnology*, (3/8) 444–447.

22.1 What is nanotechnology and what are nanomaterials?

Nanotechnology is often described as having roots in a wide range of scientific and technical fields, including physics, chemistry, biology, material science and electronics. The field of nanotechnology is thus broad and covers a multitude of materials, techniques, scientific and commercial applications and products (RS and RAE, 2004). Originally the term nanotechnology, first used by Taniguchi in 1974, referred to the ability to engineer materials precisely at the nanometre (nm) level (Taniguchi, 1974). The term has since been framed and reframed by various actors over the decades and, despite the desire for a unifying all embracing definition of nanotechnology, many versions of the definition exist today. Here, we use the widely-accepted definition suggested by the United States National Nanotechnology Initiative (NNI):

> Nanotechnology is the understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications. Encompassing nanoscale science, engineering, and technology, nanotechnology involves imaging, measuring, modelling, and manipulating matter at this length scale (NNI, 2009).

Chemistry typically deals with large numbers of atoms and molecules acting together. The behaviour of individual atoms and molecules can best be understood within a quantum physics-based framework, while the motion of massive collections of atoms and molecules such as physical objects under the influence of force are best described through classical mechanics or Newtonian physics. Nanotechnology falls between these two domains and holds the possibility of revealing and exploiting unique novel phenomena as a result.

Although the wordings differ, a number of definitions require that two criteria must be fulfilled for materials to be considered as engineered nanomaterials ([2]):

- they must have some purposely engineered structure with at least one dimension in the approximate range 1–100 nm;
- this nanostructure must give the system properties that differ from those of the bulk forms of the same material.

Although the definition is broad, in most materials or systems it can be determined whether they involve nanomaterials or not (Hansen et al., 2007).

The range of nanomaterials that can be manufactured is extremely broad. However the techniques used to produce them can, roughly speaking, be divided into top-down and bottom-up approaches. Top-down techniques involve starting from a larger unit of material, and etching or milling it down to smaller units of desired shape, whereas bottom-up involves progressing from smaller sub-units (e.g. atoms or molecules) to make larger and functionally richer structures (RS and RAE, 2004; BSI, 2007b). Top-down techniques include processes such as high-energy ball milling, etching, sonication and laser ablation, whereas bottom-up techniques include sol-gel, chemical vapour deposition, plasma or flame spraying, supercritical fluid, spinning and self-assembly (Biswas and Wu, 2005). Both approaches pose specific challenges. Creating smaller and smaller structures with sufficient accuracy is a critical challenge for top-down manufacturing, whereas the challenge for bottom-up techniques is to make structures large enough and of sufficient quality (RS and RAE, 2004).

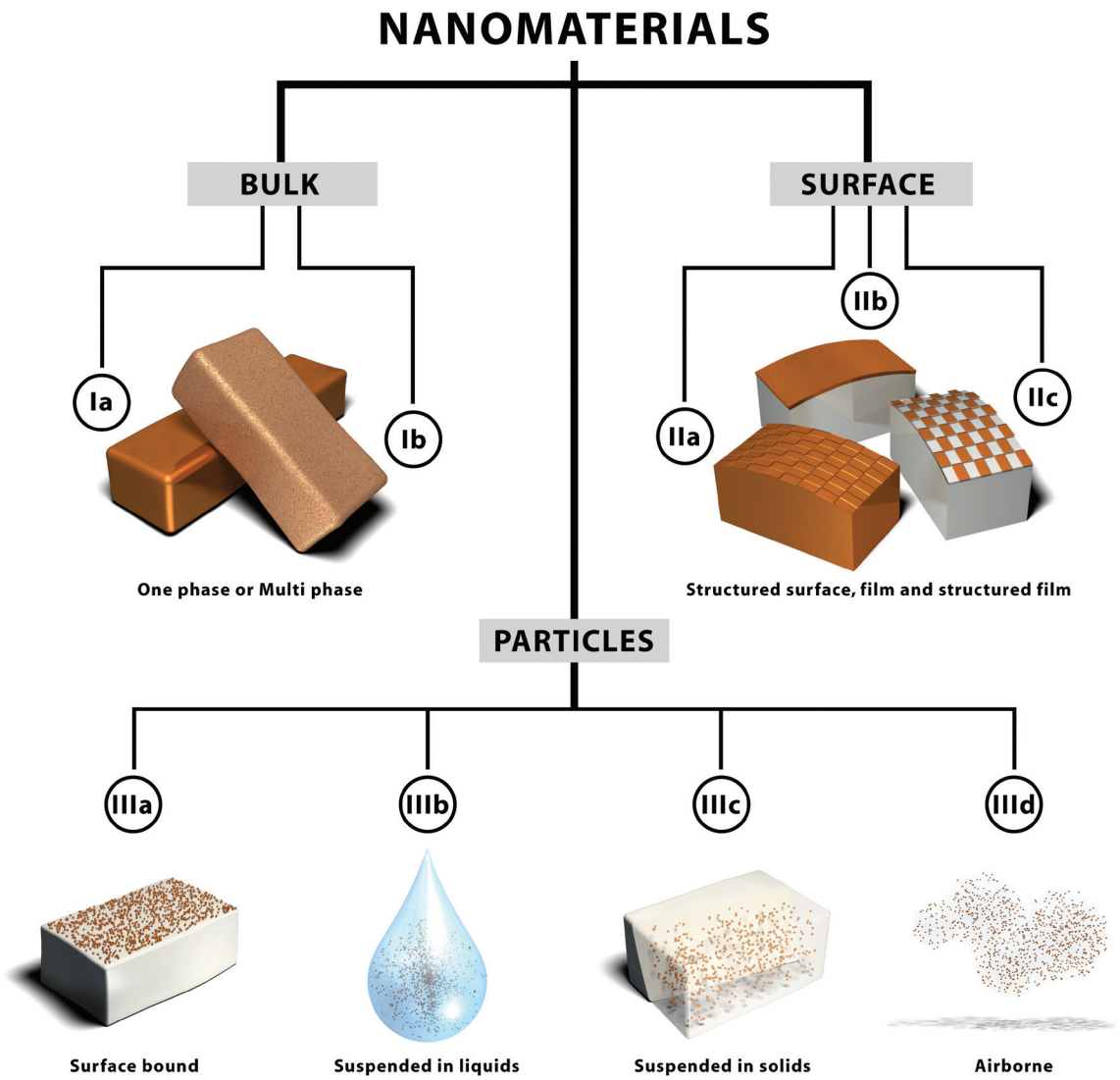
Starting with a palette of conventional materials, new nanomaterials may be formed by subtly altering the shape, size and form of these materials at the nanoscale. A further range of nanomaterials with new properties may be developed by combining two or more nanoscale materials. Familiar chemicals may also be used to construct new nanometre-scale molecules and structures, such as carbon-60 and carbon-70 molecules (C60 and C70), carbon nanotubes, nanoscale liposomes, self-assemble monolayers, dendrimers and aerogels. Various international standardisation institutes have expanded their focus of attention from trying to define nanotechnology to defining the nature of the many different kinds of nanomaterials such as carbon nanostructures, nanorods and nano-objects (BSI, 2007; ISO, 2008).

In order to facilitate hazard identification and focus risk assessment, a procedure for dividing nanomaterials into relevant subcategories has been developed by Hansen et al. (2007), as illustrated by Figure 22.1.

Hansen et al. (2007) suggest categorisation of nanomaterials depending on the location of the

([2]) Nanomaterials in this context specifically refer to materials that have been purposely engineered to have nanoscale structure.

Figure 22.1 The categorisation framework for nanomaterials. The nanomaterials are categorised according to the location of the nanostructure in the material



Source: Hansen et al., 2007, reprinted with permission.

nanoscale structure in the system. This leads to a division of nanomaterials into three main categories:

- materials that are nanostructured in the bulk;
- materials that have nanostructure on the surface;
- materials that contain nanostructured particles.

Nanoparticles have been defined by the ISO (2008) as particles having three external dimensions between 1 and 100 nanometre ([3]). Category III above contains nanostructured nanoparticles that can have various forms and shapes and this category includes, for example, quantum dots, fullerenes, nanotubes and nanowires (Maynard and Aitken, 2007). There are four subcategories of systems with nanoparticles, depending on the environment around the nanoparticles:

- subcategory IIIa has nanoparticles bound to the surface of another solid structure;

([3]) It is important to note that this is not a universally accepted definition and that, as with the term nanotechnology, a number of different definitions as to what constitutes a nanomaterial exists. The articulation by the European Commission of their recommendation for a definition is discussed in detail in Section 22.5 of this chapter.

- subcategory IIIb consists of systems where nanoparticles are suspended in a liquid;
- subcategory IIIc is nanoparticles suspended in solids;
- subcategory IIId consists of airborne nanoparticles.

Most health and environmental impact concerns have been raised over nanoparticles that fall into subcategories IIIc and IIId (see, for example, SCENIHR, 2009; RCEP, 2008; Madl and Pinkerton, 2009). A major benefit of the proposed categorisation framework is that it provides a tool for dividing nanosystems into identifiable parts, thereby facilitating evaluations of, for example, relevant exposure routes or analysis of effect studies according to relevance to the material tested.

22.2 Development of nanotechnology and nanomaterials

The development of nanotechnology has been rapid when assessed by a number of metrics, including government funding and number of research publications and industrial patents (see, for example, Chen and Roco, 2009; Youtie et al., 2008; Sylvester and Bowman, 2011). Early nanotechnology development was driven by advances in materials science and scientific breakthroughs such as the discovery of fullerenes, quantum dots and carbon nanotubes (Iijima, 1991) along with innovations that allowed nanostructures to be visualised, such as the invention of the scanning tunnelling microscope and the atomic force microscope (Kroto et al., 1986; Iijima, 1991; Binning et al., 1982 and 1986).

One of the key turning points in science and technology policy in relation to nanotechnology was the establishment of the National Nanotechnology Initiative (NNI) by the United States of America (USA) Government in 2000, along with significant increases in research and development (R&D) funding for nanotechnology-related research (Igami and Okazaki, 2007). Since then, most developed and many emerging economies have launched national initiatives or prioritise research in nanotechnology (Roco, 2011). Although somewhat speculative in nature, Lux Research (2008) estimated that in 2008 alone global nanotechnology R&D investment was around USD 18.2 billion, representing USD 8.4 billion from governments, USD 8.6 billion from corporate sources and USD 1.2 billion from venture capital investors. Government funding of academic research has lead to a significant increase in the number of scientific research publications in nanotechnology (Linkov et al., 2009). Scientific activities sparked by government funding have had a crucial role in nanotechnology-related knowledge creation and technology transfer, although there is often some time lag before scientific knowledge is diffused into useful inventions and applications (Igami and Okazaki, 2007).

22.3 Current production and application of nanotechnology and nanomaterials

According to the Nanotechnology Company Database, there are now about 2 000 nanotechnology-focused companies around the world; the majority of these are based in the US (estimates suggest 1 100), and 670 have their headquarters within the European Union (Nanowerk, 2010). These companies range from multinationals to small and medium-size companies and university spin-offs. They span a wide range of sectors and applications including energy, analysis, textiles, anti-microbial wound dressings, paints and coatings, fuel catalysts and additives, lubricants, cosmetics and food packaging (Chaundry et al., 2006; Hodge et al., 2010).

Till now, the emerging nature of the technology has ensured that much of the public and private sector attention has been on R&D activities. However, one could argue that nanotechnology is entering in a new era in which both the number of products containing nanomaterials and the sophistication of these nanomaterials have increased spectacularly. Mundane products will soon, it would appear, be superseded by a range of innovative nanotechnology-based products.

In 2006, the Project for Emerging Nanotechnologies (PEN) at the Woodrow Wilson International Center for Scholars launched an online inventory of consumer products that are reported to include nanomaterials (the Consumer Products Inventory). At the time of its launch in March 2006, the global inventory contained 212 different products available for purchase. This number increased to 580 products in 2007, and in March 2011 the inventory contained 1 317 products from about 30 countries (PEN, 2011). These products fall into a number of different categories including health and fitness, home and garden, and electronics and computers. More than half (738) were considered to be health and fitness-related and included products as diverse as hair straighteners, sporting equipment and cosmetics. The primary material in many of the products was nanoscale silver (PEN, 2011). The

Woodrow Wilson Consumer Products Inventory contains information such as product name, company, manufacturer or supplier, country of origin, and a short product description. However, it does not contain information about how many units of a given product are produced and sold or the mass/volume of nanomaterial in each product. Such information is only available if the producers themselves make it available, which occurs rarely. It is therefore not surprising that the public, and even the relevant regulators themselves, have limited knowledge about the current production volumes of nanomaterials. Moreover, the veracity of the available information must be considered, given its scattered and incomplete nature.

Publicly available information on commercially produced engineered nanomaterials is at best patchy. For example, in 2001, the global production of carbon-based nanomaterials was estimated to be around several hundred tonnes per year; by 2003 global production of nanotubes alone was estimated to be about 900 tonnes (Kleiner and Hogan, 2003). Frontier Carbon Corp, a Japanese-based company, produces more than 40 tonnes of C60 per annum, mainly for use in a range of goods including sporting goods, batteries, lubricants and polymer additives (Fujitani et al., 2008). The consulting firm Cientifica (2006) has estimated that in 2006 the global annual production of nanotubes and fibres was 65 tonnes, giving it a commercial value of about EUR 144 million. Cientifica (2006) has suggested that the value of nanotubes and fibres will exceed EUR 3 billion by 2010, representing an annual growth rate of well over 60 %. The veracity of these claims is still to be tested. Even though information about the production of carbon-based nanomaterials is scarce, more is known, or at least guessed at, about such materials than about many other nanomaterials such as quantum dots, nano-metals and materials with nanostructured surfaces.

22.4 Signs of early warnings

Concerns have been raised about the potential risks of nanotechnology and nanomaterials almost since the emergence of nanotechnology (Drexler, 1986), and historical analogies have been made with both ambient ultrafine particles and asbestos (RS and RAE, 2004; Seaton et al., 2009; Mullins, 2010). Ambient ultrafine particles, which can come from multiple sources, are defined as airborne nanoscale particles, including particles incidentally produced such as those in diesel exhaust and incinerator stacks. Ultrafine particles are typically considered to be smaller than 0.1 micron (i.e. < 100 nm). Research on ultrafine particles has found an increased morbidity and mortality from cardiovascular and pulmonary diseases inversely correlated with size i.e. the smaller the particles, the more dangerous (Oberdorster et al., 2005a; Pope and Dockery, 2006). Since nanomaterials are in the same size range as ultrafine particles, concerns have been raised on whether nanomaterials could have the same hazardous properties as ultrafine particles.

Much of the research performed on ultrafine particles in the 1990s now feeds into what we know about the potential risk of nanomaterials and lays the foundation for many of the current scientific research hypotheses in the field of nano(eco) toxicology (Oberdorster et al., 2007). One of the most important hypotheses is that the hazard properties of nanoparticles might be related to inherent physico-chemical properties different from those traditionally used for industrial chemicals, e.g. particle size, shape, crystal structure, surface area, surface chemistry and surface charge. As early as 1990 Oberdorster et al. (1990) and Ferin et al (1990) reported that ultrafine titanium dioxide (TiO_2) and aluminium oxide (Al_2O_3) of 30 and 20 nm, respectively, induced a very striking inflammatory reaction in the lung of rats compared to larger particles of 250 and 500 nm. Two years later Oberdorster et al. (1992) reported that the crystallinity of TiO_2 nanoparticles influenced their toxicity and that surface area was a better descriptor than mass for the adverse effects observed in rats. Donaldson et al. (2002) have since observed a similar correlation for carbon black, when studying the ability of nano and micron particles to cause inflammatory effects in rats. Warheit et al. (2006) and Sayes et al. (2007), however, did not observe any correlation with surface area when evaluating biological response in rats after exposure to nano-sized TiO_2, SiO_2 and other particles.

One study has found a statistically significant increase in malignant lung tumours in rats following chronic inhalation of nano-sized TiO_2 (Heinrich et al., 1995) and, on the basis of this study, NIOSH (2011) has determined that ultrafine TiO_2 should be considered a potential occupational carcinogen. NIOSH further concluded that TiO_2 is not a direct-acting carcinogen, but acts through a secondary genotoxicity mechanism that is not specific to TiO_2 but primarily related to particle size and surface area and surface area was found to be the critical metric for occupational inhalation exposure to TiO_2.

Visual similarities between carbon nanotubes (CNTs) and asbestos fibres have led to others raising

concerns about them having the same hazardous properties (Huczko et al., 2001; Warheit, 2009). In 2004 Lam et al. (2004) published a study in which they exposed mice to a number of single-walled CNTs of different purity and found that all nanotubes induced dose-dependent granulomas and interstitial inflammation in the lungs. The results presented by Lam and co-workers were supported by observations by Warheit et al. (2004) who also observed pulmonary granulomas in rats after exposure to single-walled CNT soot. However, in contrast to Lam et al., the effects observed by Warheit et al. (2004) were not dose-dependent. Absence of pulmonary biomarkers suggests a potentially new mechanism of pulmonary toxicity and induced injury (Warheit et al., 2004). More recently, Poland et al. (2008) compared the toxicity of four kinds of multi-walled carbon nanotubes (MWCNTs) of various diameters, lengths, shape and chemical composition by exposing the mesothelial lining of the body cavity of three mice to 50 mg MWCNT for 24 hours or 7 days. This method was used as a surrogate for the mesothelial lining of the chest cavity. They found that long MWCNTs produced length dependent inflammation, foreign body giant cells and granulomas that were qualitatively and quantitatively similar to the foreign body inflammatory response caused by long asbestos. Only the long MWCNTs caused significant increase in polymorphonuclear leukocytes or protein exudation. The short MWCNTs failed to cause any significant inflammation at 1 day or giant cell formation at 7 days. The finding that the length of CNTs affects their biological activity is supported by findings by Takagi et al. (2008) and Muller et al. (2009). Poland et al. (2008) also found that water-soluble components of MWCNTs did not produce significant inflammatory effects 24 hours after injection, which rules out the concern that residue metals were the cause of the observed effects, an association that other researchers had previously hypothesised on the basis of *in vitro* studies (Shvedova et al., 2005; Kagan et al., 2006).

Most studies of CNTs have used intra-tracheal or intra-peritoneal administration. Intra-tracheal and intra-peritoneal instillation bypasses upper respiratory tract defences and does not deposit particles evenly in the lung in a manner similar to inhalation. This has historically led to the biological relevance of such studies being questioned (Oiser et al., 1997). Recently, however, a number of nose-only inhalation studies on CNTs have been published in peer-reviewed journals by industry (BASF, Nanocyl and Bayer) that support previous findings such as Ellinger-Ziegelbauer and Pauluhn (2009), Ma-Hock et al. (2009) and Pauluhn (2010). For example, in a 90-day nose-only inhalation toxicity study of MWCNTs, Ma-Hock et al. (2009) found that the incidence and severity of granulomatous inflammation of the lung and the lung-draining lymph nodes were concentration-dependent, something which has previously been demonstrated for intra-tracheally instilled single-walled carbon nanotubes (SWCNTs) (Lam et al., 2004) and MWCNTs (Muller et al., 2005). Interestingly, exposure via inhalation revealed inflammation in the nasal cavity, larynx and trachea, where the particles are deposited during inhalation, as well as alveolar lipoproteinosis. This had not been observed using intra-tracheal or intra-peritoneal administration (Ma-Hock et al., 2009).

In addition to CNTs, substantial concerns have been raised over the use of nanometre-scale silver particles, or nanosilver, especially in regard to its widespread prevalence in everyday consumer products. Nanosilver is reportedly one of the most widely used nanomaterials in consumer products today (PEN, 2011), and the antibacterial properties of nanosilver have been exploited in a very diverse set of products and applications. These include dietary supplements, personal-care products, powdered colours, varnish, textile, paper, interior and exterior paints, printing colours, water and air purification, polymer-based products and foils for antibacterial protection such as washing machines, kitchenware and food storage (PEN, 2011). The scale of use is currently unknown as there are no labelling requirements for nanoproducts, and the concentrations used are also unknown for most of the products on the market (Boxall et al., 2008).

Many applications involving nanosilver involve direct exposure of the substance to humans. This has raised concern about the potential human health effect of the material. The potential health and environmental impacts of nanosilver have been subject to many reviews (Luoma, 2008; Aitken et al., 2009; Wijnhoven et al., 2009; Pronk et al., 2009; Stone et al., 2010, Christensen et al., 2010; Mikkelsen et al., 2011). The toxicity of silver metal is generally considered to be relatively low (Wijnhoven et al., 2009). At very high concentrations, repeated ingestion or inhalation of colloidal silver has been found to lead to deposition of silver metal/silver sulphide particles in the skin, eye and other organs, leading to blue or bluish-grey discolouration of the skin. Although cosmetically undesirable and irreversible, the condition — known as argyria — is not life threatening. It has been shown that silver from nanoparticles can enter the body via oral and inhalation routes and that silver is absorbed and distributed to target organs such as the liver, olfactory bulb, lungs, skin, brain, kidneys

and testes (Sung et al., 2008 and 2009; Kim et al., 2008). The form in which the silver is transmitted through and accumulated within the body is however unclear, i.e. whether it is present as particles, ions or complexes (Mikkelsen et al., 2011). Nanosilver has been associated with inflammation as well as slight liver damage in mice after oral exposure (Cha et al., 2008; Kim et al., 2008). Prolonged exposure to nanosilver particles via inhalation has been found to produce an inflammatory response in the lungs of rats, as well as inducing alterations in lung function (Sung et al., 2008).

A number of *in vitro* studies have found that the toxicity of nanosilver is mediated by an increase in the production of reactive oxygen species, stimulating inflammation and subsequent cell death. The relevance of this is unclear and subject to scientific investigation (Stone et al., 2010; Christensen et al., 2010; Mikkelsen et al., 2011). In an extensive review of risk assessments of nanosilver, Wijnhoven et al. (2009) concluded that the number of well-controlled studies on the potential toxicities of nanosilver as well as current knowledge of the kinetics of nanosilver is too limited to provide a proper foundation for human risk assessment.

With regard to environmental organisms, concerns have been raised by the expected increased emissions and toxicity of nanoscale materials compared to bulk forms of the same material. In this respect, silver nanoparticles may serve as an example since the substance is being used in an increasing number of consumer products because of its antibacterial properties. Silver is known to be ecotoxic. However the toxicity is highly dependent on the form and speciation of the metal. In the registration of silver under REACH (Registration, Evaluation and Authorisation of CHemicals) (Regulation (EC) No 1907/2006), predicted no-effect concentrations (PNECs) are reported as 0.04 μg/L (micrograms per litre) (freshwater), 0.86 mg/L (marine water) and 0.025 mg/L (sewage treatment plants) (ECHA, 2011). Toxicity tests using silver nanoparticles also reveal very-low-effect concentrations. For freshwater algae EC50-values as low as 4 μg/L have been found, and values far below 1 mg/L have been reported for crustaceans (Navarro et al., 2008; Griffitt et al., 2008). EC50 is the maximum concentration that induces a response halfway. Inhibition of nitrifying bacteria can occur at concentrations below 1 mg/L (Hu, 2010) and the function of wastewater treatment plants may therefore be affected by the presence of silver nanoparticles. For ionic silver it is known that the speciation in aqueous media determines bioavailability and toxicity. This is likely also to be the case for elemental silver nanoparticles, but the influence of speciation on uptake, depuration and toxicity has yet to be studied in depth. The environmental concentrations resulting from the use of nanosilver in consumer products are at present uncertain, although a number of different estimates have been made (e.g. Mueller and Nowack, 2008; Gottschalk et al., 2010). Where silver nanoparticles are incorporated in textiles, they can be released during washing (Benn et al., 2010). Resulting environmental concentrations in the low ng/L range have been proposed by Gottschalk et al. (2010). It remains uncertain whether silver nanoparticles are more toxic than their bulk counterpart or ionic silver, since the effects can in many cases be ascribed to the ionic form of silver (Ag+). Some studies have documented a more pronounced effect associated with nanosilver (e.g. Navarro et al., 2008), but the data so far are not conclusive.

After reviewing the current level of scientific knowledge of nanosilver, Aitken et al. (2009) stated that there is:

> …indicative evidence of the harm of silver nanoparticles at low concentrations on aquatic invertebrates, which suggests that the environmental release of silver nanoparticles will be detrimental for the environment and that any industry/institute using silver nanoparticles should consider taking the necessary steps to reduce or eliminate the potential exposure of the environment to these nanoparticles.

The authors further stated that there is insufficient evidence to make a risk assessment feasible for nanosilver. They did however go on to state … there is sufficient evidence to suggest that silver nanoparticles may be harmful to the environment and therefore the use of the precautionary principle should be considered in this case (Aitken et al., 2009).

Although preliminary, these studies on the nanoforms of TiO_2 and silver as well as carbon nanotubes are indicative of wider concerns that materials intentionally designed and engineered at the nanoscale to exhibit novel properties may also pose emergent risks. They therefore arguably trigger indicators of early warnings regarding the potential impacts of engineered nanomaterials, and as a consequence have led to increased attention and funding on various aspects of nanotechnological health and environmental risks (Hankin et al., 2011; Aitken et al., 2011; National Academy of Sciences, 2012).

22.5 Current (lack of nano-specific) regulation for nanomaterials

Whereas there has been some government funding of environmental, health and safety research into the potential adverse effect of nanotechnology and nanomaterials, there has been limited action from regulatory decision-makers towards changing existing technology-neutral regulation to take the unique properties of these materials into account. This is not surprising given the current state of scientific understanding of nanomaterial hazards and risks. Nor is this lag in regulatory response unique to nanotechnologies. As observed by Ludlow et al. (2009), the emergence of a new technology is, for example, likely to be perceived as a period of under-regulation in which the development of a specific regulatory response will occur subsequent to an initial period of research and development (R&D) and commercialisation. It must also be remembered that the regulatory frameworks under which nanomaterials currently fall are in any case not perfect, with many current regimes outdated and needing to be overhauled. Such recasts were needed prior to the commercialisation of nanotechnology and in many respects nanomaterials highlight many of the deficiencies that have existed for some time.

In an effort to elicit information regarding the types of nanomaterials being produced and imported into their jurisdictions, some governments, for example in the United Kingdom, USA and Australia, have implemented voluntary reporting schemes for nanomaterials (see, for example, DEFRA, 2006a and 2006b; US EPA, 2007; Weiss, 2005; NICNAS, 2008). Voluntary in nature, and somewhat onerous in operation, the schemes can be described as at best underwhelming. In the United Kingdom, for example, the Department for Environment, Food and Rural Affairs (DEFRA) received a total of 13 submissions over the life of the programme (2 years). The US scheme, which ended in 2009, fared a little better with the Environmental Protection Agency (EPA) receiving submissions from a total of 31 organisations (DEFRA, 2008; Hansen, 2009; Maynard and Rejeski, 2009). Given the lack of buy-in from stakeholders, it is not surprising that other jurisdictions, including France and California, have focused their efforts on mandatory nanomaterial reporting schemes.

Nanomaterials which are defined as chemical substances are regulated by the EPA under the Toxic Substances Control Act (TSCA) (US EPA, 2009a; Breggin et al., 2009). Pursuant to the TSCA, chemical substances are typically regulated on the basis of their Chemical Abstract Service (CAS) number; this system differentiates chemicals on the basis of their novel molecular structure and not their size. Silver, for example, is an existing chemical under the TSCA with its own unique CAS number. The TSCA Inventory is not able to differentiate nanosilver from bulk silver under the current framework, as the nanoscale and bulk versions of the substances both have the same CAS number. This approach ignores evidence that size and shape often lead to nanomaterials behaving in substantially different ways from their bulk counterparts. In the case of nano-silver, this failure to trigger regulatory oversight for the nanoscale substance has already raised considerable debate among various stakeholders, including those within the scientific community, due to its increasingly widespread use in consumer products (see, for example, Chen and Schluesener, 2008; Wijnhoven et al., 2009).

It is important, however, to note that the approach adopted under the TSCA is not unique, with chemical substances traditionally regulated on the basis of being existing or new based on their CAS number in most jurisdictions. At this stage, the majority of nanoscale substances are considered to be existing chemical substances under these frameworks.

One approach that the EPA has implemented in order to gather additional data on existing chemicals manufactured at the nansocale is through the use of its significant new use rule (SNUR). As explained by Widmer and Maili (2010), Section 5(a)(2) of the TSCA provides the EPA with the regulatory authority to request addition information on existing chemicals for the purpose of regulatory review where the proposed use of the chemical has significantly changed since it was initially reviewed. This regulatory tool has so far been employed for several types of nanomaterials, including single-walled and multi-walled CNTs. The EPA has proposed a more encompassing SNUR that would require companies that intend to manufacture, import or process new nanoscale materials based on chemical substances listed on the TSCA Inventory to submit a significant new use notice (SNUN) to the EPA at least 90 days in advance (Matus et al., 2011).

Even if a nanomaterial has a novel molecular structure, the US EPA must show that it may pose an unreasonable risk of significant exposure before manufacturers are required to undertake environmental, health and safety testing. These are just the data the agency needs to determine whether the substance poses an unreasonable risk — a classic regulatory paradox. Nonetheless, the EPA has proposed a data collection rule that would require the submission of certain existing data

on nanomaterials, including production volume, methods of manufacture and processing, exposure and release information, and available health and safety data. Despite these limitations and some recent moves towards reform of the TSCA, actual amendments have yet to be implemented (Davies, 2006 and 2009; US EPA, 2009b; Breggin et al., 2009). A December 2011, EPA Office of the Inspector General report (EPA OIG, 2011) found several limitations in the EPAs evaluation and management of engineered nanomaterials, including:

- Program offices do not have a formal process to coordinate the dissemination and utilisation of the potentially mandated information;
- EPA is not communicating an overall message to external stakeholders regarding policy changes and the risks of nanomaterials;
- EPA proposes to regulate nanomaterials as chemicals and its success in managing nanomaterials will be linked to the existing limitations of those applicable statutes;
- EPAs management of nanomaterials is limited by lack of risk information and reliance on industry-submitted data.

The Office of the Inspector General concluded that:

> 'these issues present significant barriers to effective nanomaterial management when combined with existing resource challenges. If EPA does not improve its internal processes and develop a clear and consistent stakeholder communication process, the Agency will not be able to assure that it is effectively managing nanomaterial risks.'

The EUs approach towards ensuring adequate protection of human health and the environment also relies heavily on chemical legislation, in particular the REACH Regulation, which was adopted by the Council and Parliament in 2006 and has been implemented progressively within the EU since 2007 (EP and CEU, 2006). As articulated in Article 1 of REACH, the purpose of the scheme is to ensure a high level of protection of human health and the environment. To fulfil this overarching objective, the regulation has expressly incorporated the precautionary principle into its text and sets out a no data, no market requirement under Article 5. Pursuant to this Article, REACH prohibits the manufacture or sale of any substance in the EU that has not been registered with the European Chemical Agency in accordance with the regulation. In this respect, REACH applies uniformly to existing and new chemicals, thus overcoming some of the difficulties associated with systems analogous to the TSCA.

As with the US system, however, REACH relies on the CAS identification system for the registration of chemical substances. One of the limitations of REACH yet to be addressed is related to whether a nano-equivalent of a substance with different physico-chemical and (eco)toxicological properties from the bulk substance would be considered as the same or different from the bulk substance under REACH. The regulation requires that a registration dossier be submitted to the European Chemical Agency containing information about manufacture and uses, classification and labelling, and guidance for safe use. If a nanomaterial is considered to be different from its bulk equivalent, hazard information has to be generated for this registration dossier if more than 1 tonne/year is produced. On the other hand, if the nanomaterial is considered to be the same as a registered bulk material, the appropriateness of the hazard information data submitted in the registration dossier is open to discussion (Chaundry et al., 2006; Breggin et al., 2009; Milieu and RPA, 2009). To date, the only amendment has been to annul the exemption status of carbon and graphite under REACH (CEC, 2008a; Breggin et al., 2009; Milieu and RPA, 2009).

It has recently been reported that companies have set up two different data-gathering groups on carbon nanotubes — one group of companies considers them as new substances while the other, including global chemical producing companies such as Arkema and Bayer, consider them as bulk graphite (Milmo, 2009). This example shows that whether nanomaterials are to be considered new or not is not just a theoretical question, but a source of confusion among regulated parties. Clearer guidance is expected on the issue from the European Commission as a result of the review of REACH in 2012.

If nanomaterials are considered to be different from their bulk counterpart, and if they are produced or imported in quantities of more than 10 tonnes, companies have to complete a chemical safety assessment. Companies are urged to use existing guidelines, however both the Commission of the European Communities (CEC, 2008a) and SCENIHR (2007) and others have pointed out that current test guidelines that support REACH are based on conventional methodologies for assessing chemical risks and may not be appropriate for assessing risks associated with nanomaterials. This means that,

although manufacturers and importers might be required to provide a chemical safety assessment, they cannot rely on the toxicological profile of the equivalent bulk material and cannot use existing test and risk assessment guidelines since these might not provide any meaningful results or be practically applicable, because of the limitations of conventional methods (Hansen, 2009; Milmo, 2009).

Pursuant to the text of the regulation, REACH is to be reviewed in 2012. It is generally expected that the revisions will include provisions related to nanomaterials. This is not surprising given the last-minute attempts to specifically include nanomaterials in the text of REACH during the second reading speech in 2006 (Bowman and van Calster, 2007). However, how REACH can be modified to expressly regulate nanomaterials — and the extent thereof — is still up for debate among politicians, regulators and stakeholders in the EU.

Expressly differentiating nanomaterials from their bulk equivalents in legislation is not new to the European Parliament and Council, as highlighted by the recent recast of the regulatory regime for cosmetics. While this recast was not initiated in response to the increasing use of nanomaterials in cosmetic products — but rather to increase transparency and streamline human safety requirements — considerable debate centred on the issue of nanomaterials (Bowman et al., 2010).

The Cosmetic Regulation, adopted in 2009, requires that all cosmetics that contain nanomaterials — which are defined as an insoluble or bio-persistent and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm (Article 2(k)) — be labelled. This will be done by placing the word nano in brackets after the nanoscale ingredient (Article 19(1)(g)) and will come into effect in 2012. As observed by Bowman et al. (2010), the regulation does not set a minimum threshold for this labelling requirement, which suggests that the mere presence of any nanoparticles in the cosmetic will be enough to trigger this requirement.

In addition to the labelling requirements, producers will have to provide a safety assessment of the nanomaterial used (European Parliament, 2009). The regulation also requires the European Commission to create a publicly available catalogue of all nanomaterials used in cosmetic products placed on the market … and the reasonably foreseeable exposure conditions (Article 16(10)(a)). Titanium dioxide, zinc oxide and lipid-based nanocapsules are examples of materials used in cosmetics such as sunscreens and moisturisers, while it has been reported that fullerenes have been used in a small number of facial creams (PEN, 2011).

Although the recast of the Cosmetic Regulation could be interpreted as a successful political effort to address the potential risk and transparency concerns relating to the use of nanomaterials in such consumer products, recent controversies surrounding the recast of the EU Novel Foods Regulation is evidence of the challenges that lie ahead for implementing future nano-specific revisions to existing legislation such as REACH. In regard to the EU Novel Foods Regulation, the European Parliament and the Council of the European Union recently failed to reach an agreement about changes to the instrument that would have ensured that the regulation includes foods modified by new production processes such as nanotechnology.

In its current form, the EU Novel Foods Regulation requires pre-market approval of all new food ingredients and products as well as safety assessments by European Food Safety Authorities on the composition, nutritional value, metabolism, intended use and level of microbiological and chemical contaminants. Studies on the toxicology, allergenicity and details of the manufacturing process may also be considered. Had the proposed revisions been adopted, such information relating to nanomaterials might have assisted in addressing current concerns surrounding their use in such applications in relation to nanoparticles (CEC, 2008b; Chaudhry et al., 2012).

The failure of the political parties to reach a compromise in regard to the Novel Foods Regulation should act as a warning sign of what to expect in regard to the likely negotiations around revisions to REACH, in which the stakes appear to be significantly higher for many parties. There is, we would argue, the potential for nanomaterials to be overlooked in the 2012 REACH revision discussion, with attention focusing instead on the myriad of other issues in play, including increasing dossier quality, limiting registration bureaucracy and lessening the impact of the regulation on small to medium enterprises.

Many of these issues are so controversial that the EU Commission is trying to downplay expectations for the 2012 REACH revision, arguing that no fundamental overhaul should be expected (EurActiv, 2011). In regard to nanomaterials, such efforts to maintain the status quo are worrying given the rapidly increasing evidence of risks as well as the swift growth of production and commercialisation

of nanomaterials and products. Such political statements are further worrying given the fact that the next formal REACH revision with relevance for nanomaterials is not scheduled before 2019 (EP and CEU, 2006). Substantial time is being wasted and effective regulation of nanomaterials is being pushed even further into the future although it is clear that immediate revisions are needed to address the most obvious and short-term limitations of the current legislative framework.

Against this background of legislative reform and associated debates, a number of other policy-related activities have occurred within the EU that have the potential to impact on the longer-term regulatory approach in relation to nanomaterials. For example, in 2009 the European Parliaments Environment Committee adopted a report on regulation of nanomaterials in general which calls for application of the no data, no market principle (as already incorporated in REACH) until safety assessments can be made (Schylter, 2009). While the fate of the proposal to implement this principle is unclear, it would appear to put additional pressure on the European Commission and the Council to address the potential risks of nanomaterials in the short to medium term.

Of arguably greater significance is the October 2011 recommendation of a definition of the term nanomaterial by the European Commission specifically for legislative, policy and research purposes. As set out in the Official Journal of the European Union (2011), a nanomaterial means:

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

This definition differs considerably from the one in the Cosmetic Regulation (as articulated above) and was mooted in relation to the recast of the Novel Foods Regulation. It is therefore not surprising that this recommendation for a definition has not been without considerable controversy and global debate. According to Maynard (2011), the Commissions push for a one size fits all policy-based definition has the potential to sideline the science and may fail to capture what is important for addressing risk. Others within the scientific community have similarly expressed concern about the fact that the definition fails to take into account the key physico-chemical characteristics associated with potential risks (see, for example, ChemSec, 2011). In response to such criticisms, Hermann Stamm of the European Commission Joint Research Centre Institute for Health and Consumer Protection has contended …such a definition is urgently needed, especially for particulate nanomaterials. The aim should be to identify a general class of materials for attention — whether they are benign or hazardous (Stamm, 2011). It would seem that both camps have valid points; it is important that the crafting of such a definition does not act as a barrier to the effective regulation of nanomaterials.

The fact that existing legislation may have serious shortcomings when it comes to effectively regulating nanomaterials is not a new revelation. Government and independent reviews of the current regulatory frameworks and their applicability to nanotechnologies have now been published (see, for example, Chaudhry et al., 2006; Ludlow et al., 2007; European Commission, 2008). While the reports have varied in scope, method and the instruments that they have sought to evaluate, each has concluded that nanomaterials are currently captured under the existing regimes. However, the failure of such instruments to differentiate between nano-based products and their conventional counterparts has raised a number of concerns regarding the ongoing effectiveness of these regimes. A number of cross-cutting issues that appear to be common to most jurisdictions have now been examined through these reviews. The main areas of concern include that, as discussed above, the regimes do not differentiate between novel and known substances for the purposes of triggering regulatory oversight; that requirements for regulators to undertake safety evaluations on novel substances are triggered by mass or volume thresholds that are not tailored to the current production volumes of nanoscale materials; the lack of trust in the appropriateness of conventional risk assessment protocols and technical guidelines; and that risk thresholds and exposure limits established with existing methodologies are questionable (Ludlow et al., 2007; Baun et al., 2009).

In most countries, nanomaterials are still being treated within existing regulatory frameworks, under which the nanomaterials have inherited

the scope and features of the previous analogous regime (Stokes and Bowman, 2012). At this stage of development and commercialisation, countries such as the US, Australia, China and India, as well as the Organisation for Economic Co-operation and Development (OECD) and the EU, are proposing to treat nanomaterials primarily in the same manner as their conventional chemical counterparts (CEC, 2008; US EPA, 2007 and 2009b; OECD, 2009a and 2009b). In doing so, they have opted to retain the regulatory status quo despite the growing body of literature that suggests that some nanomaterials may cause harm to human and/or environmental health. This approach is not surprising given the current knowledge deficits in the evolving state of the scientific art and a general lack of express reliance on the precautionary principle in most jurisdictions.

Australia is one country that has explicitly moved to differentiate the requirements for some new industrial nanoscale chemicals. Recent administrative changes to its National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (which may be considered analogous to the TSCA), which came into effect in January 2011, have sought to remove several of the low-volume/low-concentrate exemptions that usually apply to new industrial chemicals (NICNAS, 2010). While minor and incremental in nature, such a shift is indicative of how some countries may attempt to tweak their regulatory frameworks in the first instance rather than move towards more wholesale changes.

A number of features related to engineered nanomaterials indicate that the identification of hazards may deviate from what is known about regular chemicals. While our current approach to toxicity-driven risk is based on the paradigm attributed to Parcelsus, that it is the dose that makes the poison, and most extrapolations from toxicity tests assume that there is a correlation between mass and toxicity, this may not hold true for engineered nanoparticles (Baun and Hansen, 2008). As pointed out in a number of studies, other properties such as surface area and surface chemistry may be better indicators of the toxicity of some nanoparticles. This raises the question of how to determine the relevant exposure concentrations in laboratory studies and in occupational and environmental settings. In response to this concern, SCENIHR has stated that amendments have to be made to the existing technical guideline for risk assessment of chemicals since: due to the physico-chemical properties of nanoparticles, their behaviour and their potential adverse effects are not solely dependent on exposure in terms of the mass concentration … (SCENIHR, 2007).

Another issue that makes engineered nanomaterials, especially nanoparticles, different from conventional industrial chemicals is their ability to agglomerate (form clusters of weakly bound particles) or aggregate (form clusters of strongly bound particles) into stable particles. Aggregated particles are generally considered to be less prone to biological uptake, however it is not correct to assume that they are inherently safe. While the aggregation and agglomeration behaviour of engineered nanoparticles is only partly understood, it is known that their formation is concentration-dependent and that smaller aggregates/agglomerates may be formed at lower initial concentrations. If toxicity is inversely associated with aggregation/agglomeration size, our traditional understanding of concentration-response relationships may have to be altered for nanoparticles since higher concentrations may not necessarily result in higher toxicity. Furthermore, it is not known whether larger benign agglomerates may be broken down after inhalation or ingestion, resulting in smaller, and perhaps less benign, agglomerates or single particles. For these reasons the statement that lower exposure equals lower effects should be seriously scrutinised before it can be considered valid for engineered nanoparticles (Baun and Hansen, 2008; Baun et al., 2009).

In environmental hazard identification it is not only the toxicity, but also the degradability and potential for bioaccumulation that are used as parameters to identify chemical compounds that are environmentally hazardous. Very few studies have addressed these two parameters for engineered nanomaterials (Stone et al., 2010; Mikkelsen et al., 2011) and, as described above, serious concerns have been raised about whether the knowledge built up for regular chemicals can be transferred to nanoparticles. This led the SCENIHR (2007) to conclude that: The criteria used for persistence, bioaccumulation and toxicity (PBT) assessment applied for substances in soluble form should be assessed for applicability to nanoparticles.

Finally, in order to take the unique properties of any type of nanoparticles into consideration, it has often been argued that risk assessments of nanoparticles need to be completed on a case-by-case basis (see for example, SCENIHR, 2007 and 2009; Stone et al., 2010). Past experiences with case-by-case risk assessment of regular chemicals indicates that such an approach can be very time- and resource-intensive even with well-defined data demands and hence one has to wonder whether this is the most appropriate approach when it comes to risk assessment of nanoparticles. The

situation for these is further complicated by the fact that the hazard characteristics will be linked not only to the chemical identity but also to a number of other characteristics and their combinations. For example, it has been claimed that there are up to 50 000 potential combinations of single-walled carbon nanotubes (SWCNTs), depending on their structural type, length, surface coating, manufacturing processes and purification method (Schmidt, 2007). Each of these 50 000 SWCNTs may have different chemical, physical and biological properties that determine their overall hazard. Although not all of them are expected to be of commercial relevance, there are many kinds of nanoparticles, such as fullerenes, quantum dots, and metal and metal oxide nanoparticles, which imply a great complexity in performing case-by-case risk assessments for nanoparticles.

22.6 Late lessons from early warnings for nanotechnology

A comparison between the EEA recommendations made in 2001 and the current situation for nanotechnology shows that stakeholders are doing some things right, but we are still in danger of repeating old, and potentially costly, mistakes. In this section we briefly discuss the current development of regulation and environmental, health and safety research in view of the late lessons from early warnings learned by the EEA in 2001.

22.6.1 Lessons 1–3: heed the 'warnings'

According to *Late lessons from early warning* Volume 1. 'No matter how sophisticated knowledge is, it will always be subject to some degree of ignorance (i.e. 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' (EEA, 2001).

Perhaps more than any preceding technology, the early development of nanotechnology has been characterised by discussions of potential risks and the need for regulatory reform (Grieger et al., 2009; Fiedler and Reynolds, 1994). Such discussions have always been an integral part of the government-led National Nanotechnology Initiative (NNI) in the US, for example, while in the EU the landmark report published by the Royal Society & Royal Academy of Engineering (RS and RAE) in 2004 emphasised the need to address uncertainties regarding the risks of nanomaterials (RS and RAE, 2004). Levi-Faur and Comhanester (2007) have observed that unlike other cases where the discussion of the associated risks has followed the development of new technologies, the discussion on the proper regulatory framework for the governance of nanotechnology risks is accompanying the development of the technology and the associated products themselves. While hard government action may still be limited, we have however seen the emergence of a number of nano-specific self-regulatory activities within industry, including codes of conduct, guidance documents and risk assessment/management frameworks (Bowman and Hodge, 2009; Meili and Widmer, 2010). Voluntary in nature, they sit within the shadow of formal regulatory obligations and do not seek to usurp legislative requirements.

Currently, most economies investing in nanotechnology season discussions about future directions in research with questions concerning potential risks and how to manage them. Yet despite some moves (for example, the funding of early investigations into environmental, health and safety risks) to respond to ignorance and uncertainty rather than simply discuss them, coordinated action seems slow to emerge. The EEA report recommends looking out for warning signs such as materials that are novel, bio-persistent, readily dispersed or bioaccumulative, and/or materials that lead to irreversible action (such as mesothelioma caused by the inhalation of asbestiform fibres).

These warning signs are clearly relevant to many nanomaterials, some of which have novel properties, may be capable of being incorporated in highly diverse products, may be transported to places in the human body in new ways, such as across the blood, brain or placental barriers, and may be designed to be persistent. Too little is known at this early stage of the technologys development trajectory to predict the environmental fate of many nanomaterials, and appropriate documentation of environmental dispersion through monitoring is not expected in the short term (SCENIHR, 2007). The extent to which specific nanomaterials are bioaccumulative or lead to irreversible impact is largely unknown, but the current state of knowledge suggest that the potential exists for such behaviour under some circumstances (Moore, 2006; Stone et al., 2011; Mikkelsen et al., 2011) (see Box 22.1 on how EEAs warning signs apply to C60 and CNTs).

The global response to these warning signs may be described, at least in our view, as patchy at best, with governments being slow, and sometimes complacent, regarding the need to gather essential data, for example on production, use patterns and the effectiveness of current types of personal protection

equipment (see Section 22.5 on the current regulation of nanomaterials). Saying this, it is important to acknowledge that efforts to date have been better than those seen in response to the emergence of earlier technologies, but they are still far from ideal.

A number of reports have made specific recommendations on developing responsive research strategies (see for instance Oberdorster et al., 2005b; Maynard et al., 2006; Tsuji et al., 2006; SCENIHR, 2006; National Academy of Sciences, 2012). For example Maynard et al. (2006) called for:

- the development of strategic programmes that enable relevant risk-focused research, within the next 12 months;
- the development of instruments to assess exposure to engineered nanomaterials, within the next 3–10 years;
- the development of robust systems for evaluating the health and environmental impact of engineered nanomaterials over their entire life, within the next 5 years;
- the development and validation of methods to evaluate the toxicity of engineered nanomaterials, within the next 5–15 years;
- the development of models for predicting the potential impact of engineered nanomaterials on the environment and human health, within the next 10 years.

Calls for research 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 published by the NNI (2008). However, there are still critical gaps in our knowledge that need to be addressed in EHS research programmes. These include, but are not limited to, epidemiological investigation of exposed populations; the behaviour and impact of ingested nanomaterials; investigation of the fate, behaviour and (eco)toxicity of nanomaterials throughout the life cycle; and interactions between nanomaterials and environmental matrices such as natural organic matter and sediments and other pollutants already present in the environment (Maynard 2006; Baun et al., 2008; Grieger et al., 2009; National Academy of Sciences, 2012).

Research strategies that target recognised areas of uncertainty (including the applicability of current testing procedures and equipment, how to assess human and environmental effects, and how to do exposure assessments and characterisation of nanomaterials) should be relatively easy to develop, as the critical questions to be addressed are generally agreed (Maynard et al., 2006; Grieger et al., 2009). But the EEA report highlights the dangers of entirely missing important areas because the right questions have not been identified, leading to blind spots in our understanding. The report cites the widespread use of anti-microbials as growth promoters in food animals, methyl tert-butyl ether (MTBE) and tributyltin as three examples where conventional thinking led to inappropriate assumptions and a lack of recognition of broader issues. At present it is not clear whether the recognition of ignorance in the field of nanomaterial-related EHS risks is sufficient to avoid blind spots, or whether the novel properties of nanomaterials inherently will generate blind spots because of their novelty (see Box 22.1).

22.6.2 Lessons 4 and 11: reduce obstacles to action

Even when research throws up useful information, it may be ignored and overlooked through what the EEA authors call institutional ignorance. They cite cases where regulators have 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, environmental sciences and law to understand nanomaterial properties and risks (Karn et al., 2003). 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. It is critical to set aside resources to create an infrastructure that gets people working together across disciplines (Lynch, 2006).

Interdisciplinary obstacles also affect regulatory oversight in decision-making (EEA, 2001). In a discussion on how nanomaterials were covered under the TSCA, the US EPA appeared 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 (US EPA, 2007). 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 (SCENIHR, 2007).

Box 22.1 EEA's warning signs applied to fullerenes and carbon nanotubes

To acknowledge and respond to ignorance, i.e. potential risks that you do not know (EEA, 2001), seems almost impossible when it comes to a rapidly emerging technology such as nanotechnology. In cases of ignorance, the EEA recommends being proactive, alert and humble about the state of the scientific evidence indicating harm as well as looking for warning signs such as novelty, persistence, ready dispersion, bioaccumulation, leading to potentially irreversible action. These lessons bear an uncanny resemblance to many of the concerns now being raised about various forms of nanomaterials such as the two types of nanoparticles: C60-fullerenes and carbon nanotubes (CNTs).

No single exhaustive taxonomy exists for novel materials and, as noted by the Royal Commission on Environmental Pollution (RCEP, 2008), it is unlikely that one is possible or even necessarily desirable. That said, one could argue that nanomaterials are novel by definition in the sense that many of the definitions of nanotechnology require either novel applications, whatever they might be, and/or that nanomaterials exhibit novel properties compared to bulk materials (see for example the definitions cited earlier in the chapter). In the following, C60 and CNT will be used as illustrative examples of nanomaterials that are novel in their use pattern and properties.

At present, very few studies have addressed the degradability of engineered C60 and CNT, but, because of their structure, they are expected to be persistent in the environment. Both C60 and CNT are often seen as anthropogenic, however they may also be formed in forest fires or volcanic eruptions. Although the sources of naturally occurring carbon-containing nanoparticles are different from the engineered ones, the particles are, from a chemical point of view, identical, and geological studies have shown that both C60 and CNT may be very resistant to degradation. Thus, Becker et al. (1994) observed C60 in 1.85 billion year-old shock-produced breccias of the Sudbury impact structure in Ontario, Canada and C60 has also been found in a 70 million-year-old fossil dinosaur eggshell from Xixia, China (Zhenxia et al., 1998). CNT and fullerenes have been extracted from 10 000-year-old ice-core melt samples (Murr et al., 2004).

Whether C60 and CNT are readily dispersed depends on a number of factors such as the environmental compartment considered (e.g. air, water, soil). Little is known about the fate and transport of C60 and CNT in air and soil, but under laboratory conditions hydrophobic nanoparticles such as C60 and CNT have been found to aggregate rapidly (Fortner et al., 2005; Baun et al., 2008). As a result of sedimentation, they may therefore not be readily dispersed after emission to the aquatic environment. However, the dispersivity of nanomaterials can be altered, for example by changing the surface chemistry, and hydroxylated C60, for example, is much more soluble in water (Sayes et al., 2004). What happens in the environment, and how interaction with natural substances (e.g. humic substances) and water-living organisms influence dispersion, are however unclear (Roberts et al., 2007; Hansen et al., 2009).

The potential bioaccumulation of nanomaterials is believed to depend on a combination of the specific properties of the nanomaterial (such as biodegradability, lipophilicity, aqueous solubility) that influence overall bioavailability. For example carbon nanotubes are known to be non-biodegradable, insoluble in water and lipophilic, which indicates that carbon nanotubes have a potential to bioaccumulate. However, there is a profound lack of studies addressing the issue of bioaccumulation of engineered nanomaterials (RCEP, 2008).

Because of the lack of scientific research, it is currently almost impossible to say whether or not the production and use of nanomaterials could lead to potentially irreversible action. Some studies have indicated that some CNTs might be able to cause effects that would be classified as irreversible (e.g. Poland et al., 2009; Smith et al., 2007). Widespread production and use of C60 and CNT will inevitably lead to the release of these materials into the environment, and hence an irreversible action, as they would be practically impossible to locate and recover after release (Hansen et al., 2009).

22.6.3 Lessons 5 and 8: stay in the real world

The EEA panel assertion from 2001 (EEA, 2001) 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 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 (Weiss, 2006).

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 or incorporated in solid matrices (like PCBs) will eventually end up in the environment. Moreover, there is evidence that the R&D 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. A study by Powell (2007) found that many scientists who are developing new nanotechnologies do not think that nanotechnologies pose new or substantial risks and that concerns about risks are based on invalid science (Powell 2007). This is a mistake in our view, and there is plenty of historical evidence to support this view in the first EEA report *Late lessons from early warnings* (EEA, 2001), including the sorry tale of asbestos. Clearly, applied researchers and 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 the regulatory appraisal process, although such knowledge of course needs as much critical appraisal as specialist knowledge.

Nanotechnology is complex, and it can be argued that non-experts have little to contribute to its safe development and use currently. But non-specialists intimately involved with a technology can bring unique insight to the table since they may have some of the clearest ideas about what is important, what has the potential to work and what may not (Gavelin et al., 2007).

22.6.4 Lessons 6 and 9: consider wider issues

Concerns have often been raised that speculation on risks overshadows real benefits, or that an unbalanced promotion of possible benefits will prevent potential risks from being critically scrutinised.

Nanotechnology is in such a position (Maynard et al., 2011). Pros include economic benefits, improved materials, reduced use of resources and new medical treatments (RS and RAE, 2004; Roco and Bainbridge, 2005), while cons mainly revolve around worker health, consumer exposure and environmental impacts. Comparisons have also been made between ultrafine particles in the atmosphere — which are known to cause health problems — and specific types of nanoparticles (RS and RAE, 2004, Oberdorster et al., 2005b; Maynard et al., 2006).

It is generally difficult 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 (Maynard et al., 2011).

If proclaimed pros do not materialise 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 may be 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 in 2001 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 prevent 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, industries and scientists promoting it. But so far the deliberate engagement of citizens and the public in risk-related decisions on nanotechnology has been very limited.

22.6.5 Lesson 7: evaluate alternative solutions

This lesson may simply be summarised by saying, dont become so enamoured by a new technology, that you are blinded to alternative solutions. Past lessons have shown there is a tendency for proponents to justify heavy investment in a new technology by promoting its application to every conceivable problem, with the result that alternatives are insufficiently scrutinised, and the most appropriate solution not always selected.

While 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 the need to find the best solution to a given problem, rather than to squeeze a solution out of the latest technology. This means that, in some cases, while nanotechnology **could** be used, it may be questionable whether it **should**. In the context of such discussions, assessment of alternatives can be used to provide helpful guidance in case of doubt as it provides a structured approach to examining a wide range of alternatives (e.g. technologies, processes, social changes) to potentially hazardous activities (Rossi et al., 2006).

Alternatives assessment is normally a six-step process that includes:

1) identification of target(s) for action;

2) characterisation and prioritisation of end uses;

3) identification of alternatives;

4) evaluation and comparison of alternatives;

5) selection of preferred alternative(s); and

6) review of selected alternative.

The scope of any alternatives assessment should be broad enough to examine the service and function that it requires as opposed to just examining, for example, the opportunities of substituting a hazardous chemical with a less hazardous one. In the case of nanomaterials this means that alternatives need not simply be nanomaterials, but may include the process or administrative changes that reduce the need for the materials in the first place (Rossi et al., 2006; Linkov et al., 2009). While alternatives assessment is generally applied to existing technologies and problems, the thinking about alternatives can be applied at the design phase, which did not occur in the case of nanotechnology.

22.6.6 Lesson 10: maintain 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. For example according to the EEA panel one factor in the slow UK response to BSE was that the governmental regulatory body was responsible first to the industry and only second to consumers. In many countries, the organisations responsible for overseeing the development of nanotechnologies through R&D are the very ones that address health and environmental issues.

In 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 nanotechnologys implications' (Denison, 2007a).

Concerns that such a conflict of interest could jeopardise effective environmental, health and safety research were most recently articulated by the US National Academies of Science in a research strategy for environmental, health and safety aspects of engineered nanomaterials:

> 'There is a concern that the dual and potentially conflicting roles of the NNI — developing and promoting nanotechnology and its applications while identifying and mitigating risks that arise from such applications — impede implementation and evaluation of the EHS risk research…To implement the research strategy effectively, a clear separation of management and budgetary authority and accountability is needed between the functions of developing and promoting applications of nanotechnology and of understanding and assessing potential health and environmental implications. Such a separation is needed to ensure that progress in implementing an effective nanotechnology-related EHS research strategy is not hampered' (National Academy of Sciences, 2012).

While 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 over 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.

22.6.7 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 (EEA, 2001). 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.

Twenty years have elapsed since first indications of nanomaterial harm were published (Ferin et al., 1990; Oberdorster et al., 1990), and in the intervening time an increasing body of literature has been developed on how nanomaterials interact with cells, mammals and aquatic organisms (Hansen et al., 2007; Stone et al., 2010). Yet many governments still call for more information as a substitute for action; there are indications that understanding and managing the risks of engineered nanomaterials are being paralysed by analysis. While it is clear that more scientific information is needed, 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 may therefore be 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 because of their intrinsic properties or use or exposure characteristics. For example, Maynard et al. (2011) have proposed principles of emergent risk, plausibility and impact to identify materials of high concern. Further, a thorough consideration of health and safety implications at the design phase of a nanomaterial, including consideration of possible safer production methods and alternatives to the material, will facilitate decisions as economic interests are not fully entrenched at that point.

22.7 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 all emerging technologies, many of the lessons are directly relevant to nanotechnology today. Yet the picture is not as bleak as it might be. Table 22.1 provides a qualitative analysis of 10 main EU Member State national and multilateral scientific reports that have provided input to the EU regulatory and political decision-makers on nanomaterials over the course of the last decade. For each of the late lessons from the first volume of this publication (EEA, 2001) we have provided an assessment of whether the lessons there have been mentioned in passing (+), have been substantially discussed and/or analysed (++), or whether a strategy to address a given lesson has been suggested (+++). Blanks means that no noticed was taken of these lessons.

While progress in developing sustainable nanotechnologies has been slow, the qualitative analysis above indicates that policy makers and relevant stakeholders seem to have learnt at least some of the lessons: they are asking more critical questions early on about health and environmental fate and effects; developing collaborations that cross disciplines, departments and international boundaries; beginning the process of targeting research to develop relevant knowledge; engaging stakeholders; and asking whether existing oversight mechanisms are fit for purpose.

But are we doing enough? The second half of Table 22.1 provides a qualitative analysis of the main EU regulatory actions taken over the course of the last decade in response to the twelve lessons.

The Cosmetic and the Biocides regulations acknowledge that there is a high level of scientific uncertainty regarding the risks of nanomaterials. They require industry to submit data and information about physical/chemical characteristics and the exposure and toxicological profile of a given nanomaterial, thereby providing some elements of a strategy toward long-term environmental and health monitoring to help identify and reduce scientific blind spots. The burden of providing health and safety data being placed on industry also helps to overcome the problem of paralysis by analysis since companies are in theory not able to market their products without proper data and information about risks. To some extent, regulatory independence is also ensured in the Cosmetic and the Biocides regulations in the sense that the scientific

Table 22.1 Late lessons learned, as indicated in 10 EU Member State nanomaterials reports

Lessons (EEA, 2001)	Royal S& RAE (2004)	DG Sanco (2004)	Chaundry et al. (2006)	IRGB (2006)	SCENIHR (2007)	RCEP (2008)	CEC (2008)	Stone et al. (2009)	RIVM (2009)	Aitken et al. (2009)	SCENIHR (2009)	Cosmetic Regulation	Biocides Regulation	Food Additives Regulation	RoHS * and WEEE **
Acknowledge and respond to ignorance, uncertainty and risk in technology appraisal	++	++	++	++	++	++	+	++	++	++	++	++	++	+	+
Provide long-term environmental and health monitoring and research into early warnings	++	++		++	+	++	+	++	+		++	++	++	+	+
Identify and work to reduce scientific blind spots and knowledge gaps	++	+		+	++	++	+	+			++	++	++	+	+
Identify and reduce interdisciplinary obstacles to learning	++			+	+	+									
Account for real-world conditions in regulatory appraisal		+										+	+		+
Systematically scrutinise claimed benefits and risks	+	+		+		+							++		
Ensure use of lay knowledge, as well as specialist expertise	++	+		++											
Evaluate alternative options for meeting needs, and promote robust, diverse and adaptable technologies															
Account fully for the assumptions and values of different social groups	++	+		++		+									
Maintain regulatory independence of interested parties while retaining an inclusive approach to information and opinion gathering	+											++			
Identify and reduce institutional obstacles to learning and action	++			+		+									
Avoid paralysis by analysis by acting to reduce potential harm when there are reasonable grounds for concern	+	+		+	++	+						+	+	+	+

Note: A empty cell indicates no notice taken
+ mentioned in passing; ++ substantially discussed and/or analysed; +++ strategy suggested/implemented
* Restriction of Hazardous Substances Directive; ** Waste Electrical and Electronic Equipment Directive.

committees such as the European Commissions Scientific Committee on Consumer Safety and the European Food Safety Agency that are responsible for evaluating the health and safety data and the information provided by industry are independent from the regulatory agencies that promote the use of nanomaterials in those same products. However, these agencies have recently come under attack for not being independent from industry interests (Muilerman and Tweedale, 2011).

In the light of the 14 case studies in the first volume (EEA, 2001), the question here seems not to be whether we have learnt the lessons, but whether we are applying them effectively enough to prevent nanotechnology becoming yet another future case study on how not to introduce a new technology. Despite a good start, it seems that we have become distracted by the way that nanotechnology is being overseen by the very government organisations that promote it; research strategies are not leading to clear answers to critical questions; collaboration continues to be hampered by disciplinary and institutional barriers; and stakeholders are not being fully engaged, or not being engaged early enough. In part this is attributable to bureaucratic inertia, although comments from some quarters, such as risk research jeopardises innovation or regulation is bad for business, only cloud the waters when clarity of thought and action are needed.

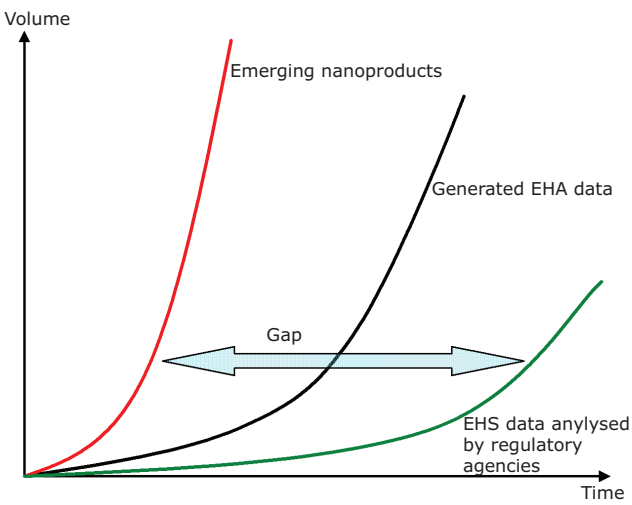
If we are to realise the commercial and social benefits of nanotechnology without leaving a legacy of harm, and to prevent nanotechnology from becoming a lesson in what not to do for future generations, perhaps it is time to go back to the classroom and re-learn these late lessons from early warnings.

22.8 Precautionary strategies for nanomaterials

Linkov et al. (2009) have pointed out that there seems to be a substantial time lag between the emergence of products containing nanomaterials, the generation of EHS data and their subsequent use by regulatory agencies (see Figure 22.2).

They argue that this results from these agencies having limited resources and that it will take time for regulatory agencies to adjust risk assessment procedures so that they are applicable to nanomaterials. The precise extent of the time lag is unclear, but there is historical evidence indicating that it will not be less than two decades. In 1977, Lawless and his team analysed 45 episodes of public alarm or strong concern over various technologies including reproduction and genetics, food and medicine, and environmental problems. A common theme identified by Lawless was that social institutions grapple with the problem for varying amounts of time while papers on effects increase in the technical literature. On average, this delay is one or two decades (Lawless, 1977). Volume 1 of this publication (EEA, 2001) found that the time gap between the first report of harm and effective regulatory action was decades, and in some cases, even over a century. Although the cases analysed by the EEA and Lawless may not reflect all emerging technologies, they do represent plausible worst-case scenarios. Given that the shelf life of specific new nanotechnology products is likely to be short because of continuous technology improvements, Linkov et al. (2009) argue that the approaches to regulating these materials should be adjusted to the evolving nature of the field. The question however is how this should be done.

Figure 22.2 Schematic representation of the emergence of nanotechnology products in comparison with generated EHS data



Source: Reprinted with permission from Linkov, I. et al., 2009.

RCEP (2008) has pointed out that existing regulatory approaches cannot be relied on to detect and manage problems before a novel technology such as nanomaterials has become ubiquitous. Although, this observation is rather bleak and discouraging, several precautionary strategies have nevertheless been suggested over the past decade. Some have focused on providing recommendations on how to adapt existing legislation, for example Chaundry et al., 2006; Fuhr et al., 2007; Franco et al., 2007; Ludlow et al., 2007 and Breggin et al., 2009. Specific recommendations include clarification of key terms and definitions of nanotechnology and material properties; ensuring the relevance of the scope and objectives of existing legislation; clear definition of thresholds relevant to nanomaterials; and risk assessment of nanomaterials prior to or after release into the environment.

Others have focused on providing recommendations on how to adapt existing risk assessment methods and risk management procedures such as the nano-risk framework jointly developed by the American non-governmental organisation Environmental Defense and the DuPont Corporation (ED and DuPont, 2007). This framework describes a process for ensuring the responsible development of nanoscale materials, and is designed to be used iteratively at different stages of development including basic R&D, prototyping, pilot testing, test marketing, and finally when new information becomes available. The suggested framework consists of six distinct steps:

- develop the nanomaterial and its intended uses;
- develop nanomaterial hazard and exposure profiles along the full life cycle;
- evaluate information generated to assess the probability of nanomaterial risks;
- evaluate risk management options and recommend a course of action;
- decide alongside key stakeholders whether to continue R&D and production;

- update and re-execute the risk evaluation regularly and share appropriate information with relevant stakeholders (ED and DuPont, 2007).

A third series of recommendations from various stakeholders and experts, for example the International Council on Risk Governance (2007) and RCEP (2009), have a much broader focus and have provided recommendations on issues more relevant to the governance of emerging technologies and innovation. In addition to a wide range of recommendations focused on restructuring risk research and regulation of chemicals and emerging technologies, RCEP (2009) has called for the development of flexible and resilient forms of adaptive management to allow us to handle such difficult situations and emergent technologies while recognising the high degree of ignorance and uncertainty and the time it will take to address these. According to RCEP (2009), key elements of such a framework should be structured around modification and extension of the existing regulatory framework as a matter of urgency, and development of an early warning system including robust arrangements for monitoring complemented (and informed) by the full range of perspectives on innovation.

Similarly, ICRG (2006, 2007) has suggested an integrated analytic framework for risk governance, consisting of pre-assessment, risk appraisal, and judgment of tolerability and acceptability, with risk management and communication as integrated elements that provide connectivity between the other elements. Application of the framework to nanotechnologies has led to a number of recommendations that fall into five categories: improve the knowledge base; strengthen risk management structures and processes; promote stakeholder communication and participation; ensure social benefits and acceptance; and collaboration between stakeholders and nations.

Recently, the German Advisory Council on the Environment for the German Government has called for a multifaceted strategy that includes intensification of risk research, promotion of social dialogue, development of a single piece of nano-specific legislation based on the precautionary principle, establishment of a labelling and product register, and a reform of the current chemical, product and environmental legislation (SRU German Advisory Council for the Environment, 2011).

In many ways, these recommendations echo those made by the Royal Society and Royal Academy of Engineering in 2004 in areas such as health, safety and environmental impacts; regulatory, social and ethical issues; stakeholder and public dialogue; and ensuring the responsible development of nanotechnologies. Key recommendations include:

- Research into possible adverse health, safety and environmental impacts of nanomaterials, which the RS and RAE (2004) argue should be an integral part of the innovation and design process of products including nanomaterials.

- Avoidance of the release of manufactured nanoparticles and nanotubes into the environment as far as possible.

- Regulatory authorities to consider whether existing regulations are appropriate to protect humans and the environment and inclusion of future applications of nanotechnologies in their horizon-scanning programmes to ensure timely identification of any regulatory gaps.

- Consideration of whether ethical and social implications of advanced technologies (such as nanotechnologies) should form part of the formal training of all research students and staff working in these areas.

- Comprehensive qualitative work involving members of the general public as well as members of interested sections of society, and government funding of public dialogue around the development of nanotechnologies.

- Establishment of a group that brings together representatives of a wide range of stakeholders to look at new and emerging technologies and identify, at the earliest possible stage, areas where potential health, safety, environmental, social, ethical and regulatory issues may arise and advise on how these might be addressed.

While a regulatory, stakeholder engagement and R&D strategy are critical elements of a precautionary approach to nanomaterials, one must not forget the critical role of design in ensuring that technology development occurs in parallel with technology assessment. Nanotechnology development has occurred in the absence of clear design rules for chemists and materials developers on how to integrate health, safety and environmental concerns into the design of nanomaterials. This is not surprising given that most chemists and materials designers are not trained to recognise these issues. The emerging area of green nanotechnology offers promise for the future. For this type of focus on preventive design to occur, we will need a cultural transition: that chemists and materials developers

are educated on health, safety and environment; that environment, health and safety become quality concerns in the development of new materials, equal to economic and performance considerations; that research on the sustainability of materials is funded at levels significant enough to identify early warnings; and that regulatory systems provide incentives for safer and sustainable materials.

When it comes to addressing R&D gaps, specific legislative gaps, limitations in current risk assessment and risk management approaches as well as risk governance of nanotechnologies and other emerging technologies, a common denominator of all of these recommendations is that many of them are not or have yet to be successfully implemented by political decision-makers. As a result, there remains a developmental environment that hinders the adoption of precautionary yet socially and economically responsive strategies in the field of nanotechnology. If left unresolved, this has the potential to hamper our ability as a society to ensure the responsible development of nanotechnologies.

Table 22.2 Early warnings and actions

1974	Taniguchi first uses the term nanotechnology referring to the ability to engineer materials precisely at the nanometre (nm) level
1981	Scanning tunnelling microscope developed
1985	Atomic force microscope developed
1985	Fullerenes discovered at Rice University
1986	Drexler raises concern about potential risks of nanotechnology
1991	Iijima discovers carbon nanotubes
1992	Surface area found to be a better descriptor than mass for the adverse effects observed in rats exposed to TiO_2
2000	National Nanotechnology Initiative (NNI) established by the US Government
2003	Making analogies with ultrafine particles and asbestos, the Royal Society and Royal Academy of Engineering in the UK calls for more research and for avoidance of the release of manufactured nanoparticles and nanotubes into the environment
2004	Single-walled carbon nanotubes of different purity found to induced dose-dependent granulomas and interstitial inflammation in the lungs of mice
2006	Project for Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars launches online consumer nanoproduct inventory totalling 212 products
2006	2 year voluntary reporting program set up in the United Kingdom by DEFRA
2007	Publication of Nano-risk framework jointly developed by the American non-governmental organisation Environmental Defense and the DuPont Corporation
2007	Voluntary reporting program set up in the US by the US EPA
2008	Long multi-walled carbon nanotubes are found to produce adverse effects qualitatively and quantitatively similar those caused by long asbestos
2009	Voluntary reporting program end in the US receiving only 31 submissions
2009	Cosmetic Regulation in Europe adopted that requires labelling and safety assessment of nanomaterials
2009	European Parliaments Environment Committee call for application of the no data, no market principle in regard to regulation of nanomaterials
2011	Australia explicitly moves to differentiate the requirements for some new industrial nanoscale chemicals in its National Industrial Chemicals Notification and Assessment Scheme
2011	NIOSH (2011) has determined that ultrafine TiO_2 should be considered a potential occupational carcinogen
2011	European Commission publishes proposal of a definition of nanomaterials

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