8 REACH and the precautionary principle: costs and benefits of proposed EU chemical legislation

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Introduction

In October 2003, the European Commission adopted a proposal for a new and revolutionary chemical regulation known as 'REACH' (Registration, Evaluation, and Authorization of Chemical Substances). REACH is one of the most important EU legislative initiatives in recent years.

The proposed regulation would replace over 40 existing directives and regulations, and would implement the proposals set out in the Commission's White Paper on the Strategy for a Future Chemicals policy (COM(2001)88), involving a major overhaul and expansion of the EU's chemical legislation.

The draft regulation is a response to demands by European environmental NGOs and green political parties.[1] They have argued that existing chemicals, which constitute 99 per cent of the total volume of chemicals used in Europe, create unknown risks to human health and the environment.[2] European Commissioner Margo Wallstrom calls this 'an unacceptable knowledge gap' and laments that 'we are unwittingly testing chemicals on both living humans and animals'.[3] The Commissioner also faults the present current chemicals regulatory system because government assessments have been slow and because it does not encourage innovation. Her proposed solution to these problems is the REACH regime.[4]

The REACH regime is viewed as the way to achieve a 'toxic free' society or, to the extent that such a society is unachievable, it would at least create a society which optimally reduces risks arising from chemicals. REACH seems to have been inspired by Rachel Carson's book *Silent Spring* which blamed synthetic chemicals for what was perceived as an increasingly unhealthy, unsafe and unnatural world.[5] It also reflects a deep belief in the kind of technocratic social engineering endorsed by the Club of Rome in its report *The Limits to Growth*.[6]

More than 40 years later, these philosophies still appear to be influential. To establish a 'toxic-free' society, the draft regulation would create an unprecedented level of government control over the manufacture and use of chemicals as substances, in preparations, or in so-called 'articles', i.e. all products that are not substances or preparations. The REACH regime is intended (a) to close the alleged 'knowledge gap' with regard to existing chemicals (i.e. those that were on the market as of 1981 and are listed in the European Inventory of Existing Chemical Substances) (EINECS), and (b) to control environmental and health risks arising from chemicals in products ranging from carcinogens to endocrine disruption (i.e. hormonal effects) which are said to be caused by phthalates used as softeners in PVC plastics. In designing the new system, the responsible Commissioners have been guided by the precautionary and substitution principles.

Unfortunately, as discussed further below, these principles do not provide any reliable guidance for developing a sound chemical risk control system.

In an eight week internet consultation on a draft of the proposed regulation in 2003, the Commission invited comments on the 'workability of the system' – not on the basic principles on which the regime is based, which are deemed to be beyond dispute. The Commission asserts that 'it is widely accepted that existing legislation needs to be improved in order to meet public

concern in Europe about the potential impact of chemicals on health and the environment'.

This, however, is a *non sequitur*. Even if there was agreement that the chemical law regime needs to be improved, that would not establish REACH necessarily as the preferred option.

Moreover there is a close relation between a system's theoretical foundations and its workability. A system that is based on flawed concepts is likely to be 'unworkable' in terms of public policy.

This chapter challenges the assumption that the REACH regime would in fact reduce chemical risks. As explained below, even if it were workable (which it is not) there are grounds to believe that REACH would actually increase risks. In addition, where REACH would reduce some risks, it would do so at exorbitant cost while simultaneously creating new risks or increasing other risks. Alternative regulatory regimes could achieve better risk reduction at much lower cost.

Though various international treaties address chemical risks,[7] and there are several additional initiatives underway,[8] the Commission did not attempt to coordinate its proposal with these existing and proposed international instruments. Rather, the Commission believes that the REACH approach should become the new international standard. In light of the fact that the international initiatives are much more targeted and limited than REACH, it is doubtful whether REACH will be endorsed broadly by the international community. However, this argument may be quite convenient when the Commission is called on to justify the draft regulation. It should also be noted that the Commission has embarked on other initiatives to address chemicals, including a policy initiative called SCALE (Science-Based, focusing on Children, raising Awareness, and relying on Legislation and Evaluation) known in Brussels' corridors as 'Super-REACH'.

This chapter discusses the background to the REACH proposal, and analyses key features of the REACH regime.[9] [10] It argues that 'chemo-phobia' is the main motivation behind REACH and criticises the undue emphasis of REACH on synthetic – as opposed to natural – chemicals. It analyses the government's endorsement of dose/effect models that may not be representative for low level exposures. The chapter also evaluates REACH's precautionary approach, and identifies the fundamental flaws of precautionary chemical regulation. Finally, it summarises fundamental problems with the draft REACH regime and outlines an alternative regulatory approach which would achieve superior risk reduction at much lower cost.

Ex ante regulation of chemicals, of course, is not generally objectionable.[11] For instance, it may be appropriate to regulate chemicals which pose an immediate threat to humans and the environment. However, that does not justify regulation of all chemicals. It also may be appropriate to require pre-marketing testing of certain categories of chemicals known to present significant risks. This is not sufficient justification for a regulation which requires the generation of massive amounts of data on all chemicals. Where such disproportionate regulation is combined with a precautionary approach, as in the REACH proposal, the consequences can be serious.

Background and objectives

Based on a review of the existing European Community (EC) chemical legislation, the Commission concludes that this legislation does not provide 'a high level of protection' as the Treaty requires. A major problem identified by the review was 'the general lack of knowledge about the properties and the uses of existing substances' (the 'knowledge gap'). Existing substances, which include all chemicals listed in EINECS and which are reported to amount to some 90 per cent or more of the total volume of all substances on the market, are not subject to testing to determine their properties.

In the Commission's opinion the exemption of existing substances is a problem, because of all new substances which are subject to testing about 70 per cent have been found to be dangerous. Note that in itself the 70 per cent figure (assuming it is correct) is meaningless. It may simply reflect the fact that the current testing

and classification systems are indiscriminate and include many 'false-positives' (substances that are found dangerous but are not in fact dangerous). In addition, the Commission believes that REACH is necessary because the risk assessment process conducted by member states to evaluate the properties of existing substances is slow, inefficient and ineffective.

Ironically, the Commission's justification for the proposed REACH regime will depend heavily on Member State agencies. In the Commission's view, paradoxically, government failure is invoked to justify more – rather than less – government. This vicious circle may well lead to governmental failure on an ever grander scale.[12]

At first impression, REACH would appear to be an overreaction to a limited problem. To the extent that lack of knowledge about risks associated with existing chemical substances is an issue, improving the current risk assessment regime would appear to be the preferred solution. Yet the responsible Commissioners want to do much more than solve the problem of existing substances. They use the 'knowledge gap' as a pretext for creating the most comprehensive and bureaucratic system of government chemical control that would exist anywhere in the world.[13] And because chemicals are used in virtually all production processes and products, the system would give government agencies a level of control over the whole economy which they could hitherto only dream of.

The stated objectives of the new regime, as spelled out in the White Paper, would be as follows:

a protection of human health and the environment
b maintenance and enhancement of the competitiveness of the EU chemical industry
c prevention of fragmentation of the internal market
d increased transparency
e integration with international efforts
f promotion of non-animal testing
g conformity with EU international obligations under the World Trade Organisation (WTO).

The Commission states that the 'new REACH system should put Europe well in advance of most other countries in terms of the health and safety guarantees provided by manufacturers and importers of chemicals'. However, the Commission provides little or no explanation for how the new regime will actually help to achieve these objectives. Its analysis of the problem and the solution reflects an idealistic concept of the effects of legislative and regulatory interventions in light of how government agencies in fact operate.

For instance, how will REACH help to resolve issues such as endocrine disruption, if that truly is an issue?[14] The testing and information required under REACH would not seem to be suitable for detecting such risks. On the contrary, REACH may well increase the 'knowledge gap' because it relies on a highly standardised *in vivo* testing regime and fixed toxicological endpoints which do not necessarily generate the data required for risk reduction.[15] Under REACH a massive amount of data on chemicals would be generated, but much of it would be irrelevant to risk reduction.

It is no surprise that the proposed regime intends to promote sustainable development. To achieve sustainable development objectives, 'care has been taken to design the requirements in such a way [that] the required balance between the three pillars of sustainable development will be assured'. Specifically, the new regime would deliver significant improvements to health and the environment 'by bringing within the scope of the authorization system all substances of high concern, by ensuring that non-confidential data is made available to the public and to downstream users, and by encouraging the development of safer chemicals'.

As a related matter, it would also 'encourage research and innovation'. The Commission's theory of 'research and innovation' is basically that government-imposed chemical bans and restrictions will force industry to (a) develop other chemicals, which (b) will be safer and more environmentally friendly.

Both assumptions, however, are exactly that: assumptions. Moreover, they are highly questionable assumptions. The net result of the REACH system could be *fewer* chemicals than would otherwise

exist, and substitute chemicals may well have more, rather than less, health and environmental impact. The REACH regime will hamper innovation by limiting the number ('base') of chemicals available for development of new products through 'trial-and-error'. It does so not only by increasing the cost of developing new chemicals, but also by restricting uses of chemicals.

The second assumption that substitute chemicals will be safer and more environment-friendly also reflects wishful thinking rather than analysis. As discussed below, REACH's emphasis on hazard and risk reduction with little regard for exposure, and its undervaluation of benefits associated with chemicals may well result in too much information on relatively insignificant risks and not enough information on relatively significant risks. This would translate into insufficient measures to reduce significant risks and would thus result in increased net risk.

More generally, by shifting resources away from useful and beneficial activities – such as targeted testing of specific chemicals which provide cause for concern – to excessive informational and other requirements, REACH will make society less safe.

The draft regime reflects the precautionary and substitution principles. As the Commission puts it, 'the precautionary principle will continue to guide the approach in implementation of necessary measures'. Consequently, chemical restrictions or bans may be imposed even where scientific studies are ambiguous, and producers and importers will be required to establish the safety of their products. Substitution of chemical products is contemplated in the authorisation process when 'greener' or 'safer' alternatives exist, although the draft regulation cryptically adds that their existence is not alone sufficient grounds to refuse authorisation.

Key features of the REACH regime

The main feature of the proposed REACH regime is the creation of a single, comprehensive, over-arching, unified system of bureaucratic oversight over all existing and new substances during all stages of their entire lifecycle, including design and production, industrial and consumer use and disposal.

The requirements which apply to a specific substance, including the testing requirements, would depend primarily on volumes of chemicals produced or imported, but the Commission adds that the requirements 'may be tailored based on intrinsic properties and conditions of use'. The exemptions are limited and often partial, so many substances (pharmaceuticals, food additives, cosmetics, etc.) will be subject to both the new chemical regime and to product-specific legislation. Even intermediates are covered with some exemptions, though they rarely cause any adverse effects.[16] Substances subject to registration may be imported or manufactured only after a waiting period of 60 days following registration, unless the authorities indicate otherwise or a specific restriction applies irrespective of whether the substances pose any risk.

The REACH system would apply not only to substances marketed as substances or in preparations, as with the current EC chemical legislation, but also to substances in any finished product even if the chemical components of these products rarely result in adverse effects.

As such the new regime raises major issues, including trade barrier issues, with respect to goods that are imported into the EC. The Commission does not address these issues, but boldly asserts that the REACH system puts 'EU and non-EU producers of chemicals on an equal footing'[17] and the new requirements 'are the minimum necessary to ensure that health and safety objectives established can be achieved, every effort having been made to reduce the costs and burdens of the system'.

Does a system which requires notification or reporting of any chemical in a product in excess of a low threshold, irrespective of risk or exposure, indeed reflect an effort to reduce costs and burdens? These provisions clearly raise issues under international trade law and could spark a trade war.

The REACH system would involve three elements: registration, evaluation and authorisation. The current EC chemical regime

requires pre-market testing and notification for 'new' chemicals,[18] but does not impose pre-market authorisation.[19] The proposed system requires registration for all substances, both new and existing, subject to limited exceptions.[20] Registration files would have to include:

a summaries of all existing available test data and other available information, as well as
b a description of uses[21] and related exposure scenarios
c a so-called 'chemical safety report' which must identify all risks that could arise during a substance's lifecycle (substances in volumes of less than ten tonnes per year would not be subject to this requirement) and
d proposed risk-reduction measures.

This information would be fed into a central database run by the European Chemicals Agency, to be established under the regulation. Substances could not be manufactured or imported unless they had been properly registered; any uses would have to be reported to the agency.

These requirements are overly broad in a number of respects. First, they apply to all substances, without regard to risk or exposure. There would appear to be no justification for imposing this regime on substances and uses that are generally recognised as safe, or where there is no plausible exposure scenario. Even known carcinogens pose no threat to human health where humans are not exposed or are exposed at extremely low levels. Further, summaries of all available data and information must be submitted. This is inappropriate – for instance submission of speculative, unsound or otherwise doubtful data would not be sensible.

The proposed regime would apply four volume thresholds for purposes of testing and registration – 1 tonne, 10 tons, 100 tonnes and 1,000 tonnes, all per year and per manufacturer. At each volume threshold, additional test data would be required, as detailed in the draft Annexes attached to the regulation. Below the one-tonne threshold, no registration would be required. At regular tonnage levels above one tonne, additional data on issues such as long-term and chronic effects would be required.

Testing is not necessarily required with respect to each registration. To minimise animal testing, registrants can use other information available to them, including 'studies from other countries, previous animal testing, in vitro data, epidemiological studies, etc'. In addition, to minimise duplicate testing the regulation provides for compulsory 'data sharing' arrangements.

Furthermore, the authorities *may* (but are not required to) allow derogations from the standard testing regime where 'testing does not appear to be scientifically necessary', 'is not technically possible' or it is not necessary 'based on the exposure scenarios'. A transitional period of 11 years would be allowed to phase in the programme for the large number of existing substances. Again, these requirements are purely volume-based and not related to any hazard, risk or exposure. The discretionary derogations do not provide much comfort in this regard.

Evaluation of the registered information would be required for all substances which exceed a production volume of 100 tonnes (this is approximately 5,000 substances, corresponding to 15 per cent of the substances subject to registration). National authorities must also evaluate proposals for testing, determine whether they comply with the pertinent rules, and order registrants to carry out testing. They may aggregate the volumes of different registrants and require that the registrants submit additional information based on aggregated volumes.

In addition, at any tonnage level, national authorities may evaluate a substance on a priority basis and require additional information or testing if, as the Commission proposes, they have 'concerns about the potential risks posed by the substances or the quality of the registration dossier'. The draft regulation, however, stipulates that any such decision must be 'justified by a change of circumstances or acquired knowledge'. Draft evaluation decisions will be circulated to the European Agency and other national

authorities; if amendments are proposed the final decision will be made by a Member State committee. Although the regulation prevents simultaneous evaluations by multiple national authorities, it permits consecutive evaluations and testing orders. The regulation effectively grants broad discretion to more or less sophisticated Member State authorities, with no right for the Agency to correct erroneous decisions to evaluate a substance or require testing, thus adding to the uncertainty created by the new regime.

Full pre-market authorisation would be required for substances with certain hazardous properties.[22] These substances include carcinogenic, mutagenic or repro-toxic (CMR) substances, categories 1 and 2 under the current chemicals legislation; persistent bio-accumulative and toxic (PBT) substances; and very persistent and very bio-accumulative (vPvB) substances.[23]

In addition, authorisation would be required for substances such as endocrine disruptors, which the authorities determine give rise to 'an equivalent level of concern'. Substances subject to authorisation, as listed in an Annex to the regulation, may not be used unless the use of the substance is exempt or has been specifically authorised. Generic exemptions from authorisation apply to certain regulated substances such as plant protection products, food additives and medicines, and to certain research and development uses which do not exceed one tonne per year.

All other substances are subject to an individualised authorisation process, and there would be two types. Authorisations to market specific products[24] are granted by the Commission, while non-marketing applications (e.g. uses in a production process) would be handled by the Member State authorities. An authorisation will be given if the 'the risk … from the use of the substance arising from the intrinsic properties … is adequately controlled'. Even if the risk is not 'adequately controlled', authorisation may be granted if 'socio-economic benefits outweigh the risk to human health and/or the environment'.

As noted above, substitution must be considered but the existence of 'greener' or 'safer' alternatives is not, alone, a sufficient reason to refuse authorisation. Authorisations are specific to the applicant – thus there is no procedure to grant generic authorisation for certain specific applications or if certain general conditions to prevent exposure are met. This feature renders this process unduly restrictive. Moreover, it is unclear why the Commission proposes both an authorisation process and a restrictions procedure; the latter is discussed below.

The draft regulation also imposes specific restrictions on the manufacture, marketing and use of certain dangerous substances and preparations, including bans or restrictions with respect to substances in articles. The restrictions that exist pursuant to the Marketing and Use Directive 76/769/ EEC (OJ L262/201) would continue under the new regime, and would be set forth in an annex to the regulation. In addition, the regulation provides a procedure to introduce new restrictions and amend current restrictions, regardless of whether a chemical is subject to registration.

When a chemical poses an 'unacceptable risk' which 'needs to be addressed on a Community-wide basis', the relevant Annex must be amended pursuant to a centralised EU regulatory procedure. The regulation provides no further definition of the term 'unacceptable risk', thus granting broad discretion to the authorities. No cost/benefit analysis as foreseen in the authorisation process and required by the EU Treaty[25] is required here. To streamline the regulation, the authorisation and restrictions procedure should be merged into one procedure, based on sound risk assessment and cost/benefit analysis, pursuant to which general use conditions can be imposed with respect to certain dangerous substances in certain dangerous applications.

In connection with registration, as noted above, an obligation on chemical manufacturers, importers and in some instances, users to assess the risks arising from the manufacture, import or use of chemicals in volumes which exceed ten tonnes a year. The topics to be covered by the assessment are:

i human health hazard assessment, which is aimed at

determining the classification and labelling of a substance and a 'Derived No Effect Level', or DNEL

ii human health hazard assessment of physiochemical properties

iii environmental hazard assessment, including identification of the 'Predicted No Effect Concentration', or PNEC, for each environmental medium

iv PBT and PvP assessment;

v exposure assessment, if the substance is found to be dangerous, including risk management measures, during all relevant parts of the substance's life cycle, taking into account possible degradation, transformation, or reaction processes, and

vi risk characterization for each exposure scenario, both for human populations and environmental media.

Detailed procedures for conducting the assessment are laid out in the annexes. The assessment should address, among other things, the manufacturer's or importer's use and all 'identified uses', and consider all stages of the lifecycle of the substance, including the waste phase. It should be 'based on a comparison of the potential adverse effects of a substance with the known and reasonable foreseeable exposure of man and/or the environment to that substance'.

When the manufacturer carries out the assessment, as a first step it must consider 'all relevant available information, including the information in the technical dossier (which is part of the registration dossier), and 'other available information'. Testing is required, in principle, if there is insufficient data.

However, if 'risk management procedures which are necessary to control a well-characterized risk may also be sufficient to control other potential risks', it may not be necessary to generate the missing information. If, on the other hand, a manufacturer or importer believes that further information is required, he must submit a reasoned proposal for a testing strategy to the national authorities.

The REACH regime does not limit chemical assessment obligations to known hazardous substances which pose known risks in certain applications. Rather, it employs a 'shot-gun' remedy and imposes these obligations on all substances and uses,[26] in case there is a dangerous chemical or application amongst them. Reflecting the precautionary principle, the REACH regime also opens the door to a new kind of science, known as 'precautionary science'.

By assessing the safety of chemicals, setting a 'derived no effect level' and assessing environmental hazards, REACH requires that 'if there are several studies addressing the same effect, then normally the study or studies giving rise to the highest concern shall be used'. This preference for the most alarming studies, apparently without regard to both relative and absolute data quality, distorts the scientific process and creates incentives for scientists locked into the dogma of the environmental movement to generate 'studies' giving rise to 'high concerns'.

This upwards bias introduced through the proposed regime does not promote a process which generates objective and balanced data. The scientific community will be confronted systematically with the 'politics of risk regulation', a subject from which most true scientists would prefer to avoid.

Chemo-phobia: 'chemicals cause everything bad'

The brief analysis of the draft REACH regime presented above results in the following 'big picture' – the regime would greatly expand the scope of the EC's current chemical legislation and transform it from a regime predominantly[27] focused on occupational protection into an overarching consumer protection, product safety, environmental protection and occupational health regime. It would extend the EC law's scope from chemical substances as such, to products containing chemicals. It would require both laboratory testing and risk assessment, and would introduce use-specific registrations and authorizations. It would apply to both new substances and substances already on the market (to which a transition regime applies).[28] Government authorities would be in a position to exercise

significant control over the manufacture and use of chemicals from 'cradle to grave'.

As such, the new regime would have significant implications not only for chemical producers but also for all chemical users and the general public. Thus, subject to limited exceptions, REACH would expand government control to cover *all* chemicals in *all* uses. The Commission hopes to make the situation workable by first tackling *only* the 30,000 'most dangerous' and most heavily used chemicals, and phasing the work over 11 years, allowing most chemicals to continue in use until the government decides otherwise. Given the fact that everything we use is made of chemicals, government registration, evaluation and/or authorisation of *all* uses of *all* significant chemicals prior to use is a formula for potential government control over our entire system of production.

The apparent mission of the REACH draftsmen is to respond to public concern about chemicals. It is probably true that due to a number of factors, including the way the news media covers chemical issues and government responses to these issues, the public is confused about chemicals, their benefits and risks. Indeed, public 'chemo-phobia' may be widespread in Europe.

Yet the scope and intrusiveness of the REACH regime suggest a move to exploit the public's unfounded fears. In the name of health and environmental protection, REACH proponents may be attempting to create the utopian 'toxic free' society. Given the broad discretion granted to government agencies which will have the authority to decide for all of us which chemicals (and thus which products) we want and which chemicals we should avoid, this system should raise red flags from a 'checks and balances' viewpoint.

The proposed approach is questionable in at least two respects. First, it assumes that an objective standard exists to make these decisions. The reality is that individuals in society prefer different chemicals which have different risks and different benefits. The selection of chemicals is a subjective process that proceeds in the marketplace.

Secondly, the Commission's draft reflects a utopian vision of how regulatory agencies operate, especially when exercising broad discretion.[29] It reflects an unjustified belief in the salutary effects of government's interventions on behalf of society. The Commission believes that through the REACH system we will be relieved of the risks with which industry has unduly burdened society. The reality will more closely reflect the kind of society that Beck foresaw, where the process of risk regulation becomes heavily politicised.[30] This process will have little to do with objective, science-based decision-making.

Instead it will be a system which, in the Commission's own words, will respond well to 'public concern in Europe about the potential impact of chemicals on health and the environment'.[31] That public concern may be based on misperception, misinformation or even anti-industrial or anti-market ideologies is not an issue which seems to concern the REACH draftsmen.[32] On the contrary, it may serve them well since it creates opportunities for the expansion of government and its powers.

Natural and synthetic chemicals

The proposed REACH regime regulates only chemicals brought under human control, e.g. those which are used in production or are present in products, for obvious reasons. Moreover, it exempts 'substances occurring in nature if they are not chemically modified'. The combined result of these provisions is that the regime focuses mainly on synthetic, as opposed to natural, chemicals.

As the Commission believes, is there reason to be concerned about the health and environmental effects of synthetic chemicals? Are synthetic chemicals, for instance, significant causes of diseases such as cancer? If so, what individual categories of chemicals are of concern? Again, the Commission fails to put the issue in perspective.

The question whether synthetic chemicals need to be regulated on such a broad scale and as intrusively as REACH – in the context of the total human exposure to chemicals both from natural and anthropogenic sources – remains unanswered.

This is not a purely academic problem. Rather the undue focus on

synthetic chemicals is bound to result in a misallocation of resources, which may make society less, rather than more, safe. Contrary to conventional wisdom, 99.9 per cent of all chemicals to which we are exposed (mainly through food) are of natural origin. Of all dietary pesticides we consume, for instance, 99.99 per cent are of a natural origin. This amounts to a daily intake of roughly 1,500 mg of natural pesticides and their breakdown products. Human exposure to synthetic pesticide residues amounts to about 0.09 mg per day.[33]

Even though only a small proportion of natural pesticides which have been tested for carcinogenicity, 37 of the 71 tested are rodent carcinogens. Naturally occurring pesticides which are proven rodent carcinogens are ubiquitous in fruits, vegetables, herbs and spices. In a single cup of coffee, the natural chemicals which are *known* rodent carcinogens are about equal in weight to one year's worth of synthetic pesticide residues which are rodent carcinogens, even though only 3 per cent of natural chemicals in roasted coffee have been adequately tested for carcinogenicity.[34] Despite these levels of exposure to carcinogens, we still drink coffee.

Toxicological profiles of food stuffs tend be complex, and so is the human body's response to carcinogens. There is much to pathogenesis that we do not understand well, but it is clear that consumption of food and cancer are closely related. Natural substances in food are estimated to be responsible for about 30 to 70 per cent of all human cancers.[35] The specific natural carcinogenic compounds are manifold and only limited knowledge is available. (See Table 2: "Carcinogenicity Status of Natural Pesticides Tested in Rodents", page 27).

Given that the EU does not, or at least not to any significant extent, regulate these *known* potentially carcinogenic chemicals, how does it justify the regulation of chemicals which are not known to pose risks?

It is in theory conceivable that synthetic chemicals are riskier than natural chemicals, despite the fact that the amounts of synthetic chemicals to which humans are exposed are dwarfed by the amounts of natural chemicals to which they are exposed, for example in food. However, given the large number of different chemicals to which human beings are exposed, this hypothesis is extremely implausible. Human beings do not have a specific defence mechanism against each potentially harmful chemical. Rather, they are endowed with more general defence mechanisms. This can be explained from an evolutionary standpoint. Unlike chemical-specific defence systems, a general defence mechanism allows a human being to change his or her diet without being the victim of increased cancer risks.

Despite the fact that exposure of humans to natural chemicals dwarfs the exposure to synthetic chemicals, public policy has focused heavily on protecting the general public specifically from synthetic toxic chemicals, particularly carcinogens. There is no inherent reason why natural chemicals cannot be regulated in the same way as synthetic chemicals.

Unfortunately regulators have no clue by what mechanism of action and at what exposure levels a toxic substance may harm individuals. To be on the safe side, regulatory toxicology assumes that even tiny doses can cause injury. Risk aversion and the precautionary approach have produced regulation which imposes complete bans on toxic chemicals (so-called 'zero-tolerance') or, where that is unattainable, requires exposure to be reduced to the lowest possible level (e.g. analytical limits of detection levels).

According to precautionary regulatory philosophy, the scientific impossibility of arriving at an acceptable daily intake or exposure level – whether due to lack of data, as in the case of chloramphenicol (an antibiotic banned for veterinary purposes, but still used in hospitals to treat, e.g., ophthalmic infections) or for any other reason – translates into over-simplifications, such as 'dangerous at any dose' or 'no dose-no cancer'. There is reason to believe, as discussed below, that this precautionary approach may in fact increase not reduce risks.

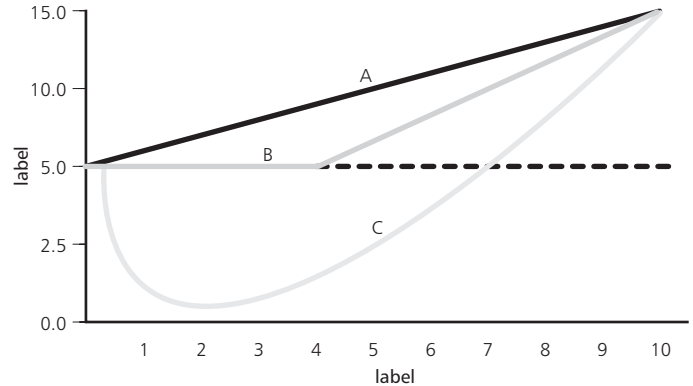
Dose/effect models

Traditionally, two models for determining dose-response relationships have been used in the toxicological assessment and regulation of chemicals. A threshold model (depicted in Figure 5 as B) is used in the assessment of risks for non-carcinogens, and a linear non-threshold (LNT) model (depicted in Figure 5 as A) is used to extrapolate risks from high doses to very low doses in the case of suspected genotoxic carcinogens. For instance, the risks associated with low-level exposure to chloramphenicol are derived from the LNT model.

These traditional models cannot, of course, claim to exhaust the possible shapes of dose-response curves. Recently, Calabrese and Baldwin argued that neither the threshold model nor the non-threshold linear model accurately describe most dose-response curves. They argue that the most common curve is U-shaped (depicted in Figure 5 as C), and hence both models currently in use, and in particular the LNT model, provide unreliable estimates of low-dose risk.[36]

The phenomenon reflected in this U-shaped curve is also known as 'hormesis' – moderate stimulation of response at low doses and an inhibitory response at higher doses.[37] In Figure 5, tumours per animal are depicted on the y-axis and the corresponding dose on the x-axis.[38] The animal control group (not exposed to the carcinogen) is depicted by the black horizontal dotted line at the 5-level on the y-axis. The hormesis model C predicts a lower number of tumours than the control group when exposure levels of the carcinogen are below 7.[39] This hormesis concept is inconsistent with the LNT model currently used to estimate cancer risks,[40] and suggests not only that there are thresholds, but also that low level exposure is in a sense 'beneficial', i.e. that low-level exposure within the U-shaped part of model C will increase fitness of the exposed organisms. Hormesis can be explained as an adaptive response of an organism to toxicological perturbations. If the hormesis theory provides an accurate model of the real world, low doses of toxic and carcinogenic agents may well reduce, rather than increase (as the conventional models predict) the incidence of adverse effects.

Figure 5 **Three toxicological dose-response models**



The hormesis theory requires that we redefine the concepts of 'pollution' and 'contamination'.[41] It challenges the premise that 'pollutants' are unmitigated 'evils'. It challenges modern environmentalism which is built in large part on the moral dichotomies of good versus evil, clean versus dirty, natural versus unnatural.[42]

Consequently, hormesis also challenges the very premises of the precautionary REACH approach: chemicals are neither bad nor good in a toxicological sense, but they are both, depending on exposure levels and adaptive responses from exposed organisms including human beings. In light of the hormesis theory the European Union should revisit the conventional precautionary models implicit in the REACH regime. If the hormesis model is a more accurate description of dose-effect relations in the world, the REACH regime would appear not to be precautionary but conversely could potentially increase risks.

Fundamental flaws of precautionary chemical regulation

Clearly the LNT model is consistent with the precautionary principle. The preference for this model however, reflects a strong availability bias.[43] With a long and established tradition in toxicology, the LNT model is intuitive to regulators whereas other models are not (or are to a much lesser extent). Moreover the LNT model is attractive from a government control perspective, as it allows government to exercise 'complete' control over synthetically produced chemicals, whether or not they create any risks at a particular exposure level.

The availability heuristic is not the only problem with the precautionary approach. In addition, it also neglects the probability of adverse effects (the so-called 'probability neglect').[44] The precautionary approach of chemical regulation as reflected in REACH focuses on outcomes of exposure in human beings – e.g. cancer – but neglects the probability of this outcome.

Probabilities should of course play a major role in regulatory decision-making because they determine the magnitude of a problem and thus inform risk-reduction decisions. By underplaying the importance of probabilities, REACH will result in cost-ineffective decisions and, indirectly (through misallocation of resources) will contribute to increased risk. Indeed the neglect of probability may well lead to the probability of neglect (of other issues).

Further, the REACH regime creates a risk of system neglect and a 'free rider' dilemma. When a problem is fully analysed in all its theoretical and empirical aspects, it is often difficult to assess the effects and consequences of legal interventions.[45]

The precautionary principle has an appearance of providing guidance and being workable only because an arbitrarily selected limited subset of relevant effects is considered. All other effects are not on the precautionary 'radar screen' (so-called 'system neglect'). Key aspects of system neglect are risk/risk and risk/cost trade-offs.

For instance the REACH regime virtually ignores the trade-off between environmental risks (e.g. those thought to be associated with brominated flame retardants) and human safety risks (e.g. increased fire safety risks resulting from restrictions on brominated flame retardants). Nor does it deal adequately with the trade-off between perceived exposure risks for citizens, and burdens imposed on scientific and industrial activities which are created by regulatory interventions intended to curb those risks.[46]

Further, the REACH approach will probably reinforce the public's 'chemo-phobia' and misperceptions of chemicals' risks and benefits.[47] Through REACH the European Union adds to the confusion since the public, with the help of government, may well view the regime as a prerequisite for a safe and healthy environment.[48]

From a risk communication viewpoint, REACH is defective.[49] In 1981, chemicals did not feature on the list of major threats to public health.[50] This has not changed in the last 20 years.[51] The Commission has not clearly demonstrated that chemicals should now be added to the list. The precautionary REACH approach encourages people to think that with the government's help a 'safe' toxic free environment is attainable. A toxic-free environment, however, does not exist. Perhaps counter-intuitively, such an environment would probably not be safe since it might expose us to greater risks.

Moreover environmental protection and safety are not the only things we have to worry about. REACH oversimplifies the world and thereby misleads people and misguides regulatory action. With the REACH programme, synthetic chemicals are indicted as major threats to human health and the environment, which they are not.

The precautionary culture, of which the precautionary principle is one part, entails the view that regulators and other decision-makers have a duty to predict and prevent all damage, irrespective of cost and reality. By disregarding scarcity of resources, the precautionary culture misleads people to believe that risks can indeed be eliminated through government regulation.[52] This culture also espouses the idea that scientific and industrial entrepreneurs should be required to prove that their activities will not cause harm, which is also an implicit part of the REACH programme.

However, proving a negative is logically impossible.[53] The bulk of

the costs of these precautionary regimes is invisible to the public; costs are borne by private parties not by government agencies. Although REACH's proponents pretend to assess costs and benefits, much of the private costs are in fact disregarded. The REACH regime would thus allow the government to gain political benefit from a bureaucratic regime allegedly intended to reduce risks, for which private parties pay. This political benefit will accrue if the EU is able to persuade the public that the alleged risks from synthetic chemicals are effectively controlled on a European level through REACH.[54]

This is a form of deception that does not promote the public good. As political philosopher Aaron Wildavsky describes it:[55]

> *'The precautionary principle is a marvellous piece of rhetoric. It places the speaker on the side of the citizen – I am acting for your health – and portrays opponents of the contemplated ban or regulation as indifferent or hostile to the public's health.* The rhetoric works in part because it assumes what actually should be proven, namely, that the health effects of the actions in view will be superior to the alternative. And this comparison is made favourable in the only possible way – by assuming also that there are no health detriments from the proposed regulation. *The rhetoric seems to present a choice between health and money or even suggests health with no loss whatsoever, for a tangential presumption is that "industry will find a better and a cheaper as well as safe way". Something* (health) *is gained with nothing lost* (no adverse health effects from the bans or regulations)'.

Further, in an international world, the REACH programme may simply relocate, rather than reduce, risks. Activities that REACH will unduly restrict or ban will probably be conducted in jurisdictions with more reasonable regulatory regimes. Where this is the case, REACH effectively espouses a NIMBY ("not in my back yard") attitude. This is not an argument against efficient and reasonable regulation of chemical risk. But where regulation is based on the precautionary approach, the NIMBY argument deserves serious consideration as it may suggest that the proposed regulation is inefficient or unreasonable.

Finally, implicit in the precautionary REACH system is the view that potential public health risks owing to low level exposure to synthetic chemicals are to be averted at all cost.[56] Cost-benefit analysis is rejected by those who adhere to 'precaution' because it compares the costs borne by some with the benefits accrued to others.

There is no denying that distributional issues (who is exposed to risk? who pays for risk reduction?) play a role in risk regulation. The precautionary approach however, is an inadequate response to this problem.[57] We have better options.

An alternative regulatory approach

The draftsmen of the REACH programme approached the problem from exactly the wrong direction. They focused on chemicals *per se* as the problem, whereas they should have focused on adverse effects. They focused on what we do not know, whereas they should have focused on what we know. In essence, they reasoned as follows:

1 The government does not have sufficient information on all chemicals, because not all chemicals are subject to testing and notification.
2 In some uses, some chemicals cause environmental or health damage, which the government could avoid if it had sufficient information.
3 Therefore, the government should require full information on all chemicals in all uses so that all damage can be avoided.

This reasoning is flawed because it assumes that generating massive amounts of information, quite apart from the exorbitant cost, will allow the government effectively to reduce overall risks

associated with chemicals, thus preventing damage. Much of the data, information and documents generated under REACH, including data on substances known to be non-dangerous and on 'intrinsic properties' (hazards, as opposed to risks), will be irrelevant to risk reduction.

Compared to alternative regulatory approaches, this approach is bound to result in higher overall risk levels and more damage because it does not sufficiently direct scarce resources to the most serious risks. To the extent that REACH prioritises, it does so primarily to phase in the comprehensive programme for existing chemicals. In addition, the system as designed grossly overestimates the ability of government to act on the massive volumes of information submitted to it. REACH's emphasis on synthetic as opposed to natural chemicals, and its endorsement of conventional toxicological models to determine dose-effect relations, exacerbates the inherent flaws in the proposed regime.

The misallocation of risk-reduction resources required by REACH would be unprecedented in history. Unfortunately if REACH becomes law Europeans will face much higher risk levels than is necessary. In the United States – which has not adopted any regime which comes even close to the REACH programme – research on the cost-effectiveness of risk regulation has confirmed the dramatic public health consequences of such misallocation.

One estimate suggests that the United States could prevent 60,000 deaths a year by redirecting the same monetary resources to more cost-effective programmes.[58] Tengs et al. showed that the median environmental policies concerned with environmental toxin control are 150 times *less effective* per life-year saved than the median medical programme.[59] If the US experience is representative, the REACH regime may well create countervailing risks which are many times higher than those it controls.

The economic cost of chemical risk regulation, up to a point, may reduce risk, but once we are over that point, it will in any event (even if it does not more or less directly increase risk) increase risk indirectly by making us poorer. Since poverty is negatively correlated with health, average lifespan and environmental conditions, the massive administrative cost of the REACH regime will lead to a Europe with worse public health and environmental conditions.[60]

The European Union should avoid the pitfalls of unbounded commitments to regulate chemical risks. Indeed, risk regulation is a critically important issue in need of fundamental evaluation.[61]

The analysis presented in this chapter shows the way to a cost-effective chemical risk-reduction programme. This programme focuses first on known adverse effects, their incidence and magnitude. It focuses on exposure to the chemicals, whether natural or synthetic, which cause these adverse effects. The risks identified are then prioritised. A plausible strategy for setting priorities involves ranking risks on the basis of the nature of the risk (carcinogenesis, etc.) and typical human exposure levels, possibly using some reliable quantification tool to facilitate ranking. Resources will then be allocated on a priority basis to those risks which rank highest in terms of estimated total adverse impact.

Exposure-ranking, instead of production-volume ranking, is a critical difference from the draft REACH regime. It implies a shift in regulatory target from the *source* to the *object* in need of protection. As the *source* of risk (i.e. chemical products in the case of REACH) does not necessarily reach the vulnerable *object* (i.e. human beings and/or the environment), for instance, due to *path* characteristics, an exposure-oriented approach will be more effective than a source-oriented approach such as REACH.

Proponents of REACH might argue that the information necessary to establish such a ranking does not exist because there is no data on many chemicals. This could be a problem in some cases, but it should not be exaggerated as is illustrated by the discussion above on exposure to natural chemicals through food. There is much information available on serious adverse effects in respect of which government has not taken adequate action.

The criticism shows that an exposure-oriented approach should be supplemented by a targeted research programme. For a suspect chemical, research on causal mechanisms of carcinogenesis (for

example) is required to assess possible human risk[62] (see the Human Exposure-Rodent Potency database[63]). An exposure-oriented approach is far more effective than a regulatory policy focusing on synthetic chemicals and volumes as potential risk sources, since neither is indicative of exposure and adverse effects. As part of such a programme a targeted, step-by-step programme for testing chemicals and identifying chemical risk could be considered.

Once risks have been ranked on the basis of exposure and overall adverse impact, possible risk-reduction measures should be evaluated. To ensure the cost-effectiveness of the programme, such evaluation should involve marginal cost-benefit analysis. Thus, resources will be concentrated on known serious risks that can be significantly reduced at relatively low cost.

Assessing hazards and intrinsic physico-chemical properties will often not be necessary, because there is no relevant exposure. Despite its many flaws, one could argue that the proposed REACH regime would also have certain benefits. For instance, under REACH's testing and registration requirements, authorities might be able to identify at an early stage a possible adverse effect of a particular chemical. That effect may not be detected, at least not early on, under an exposure-oriented regime. While this may be a benefit of REACH, it is achieved at very high cost in terms of overall risk and exposure levels, direct expenses associated with implementing REACH, and indirect costs resulting from 'de-selection', poorer product quality and performance, substitution effects, and the like.

Any proposal to overhaul the EU chemical legislation should be: (a) based on sound scientific analysis, not anecdotal evidence; (b) subject to broad, open consultation and public comment, not restricted to aspects of 'workability'; and (c) subject to rigorous, comparative cost-benefit analysis, not a limited compliance cost assessment. In this process, the European Union should consider alternative regulatory approaches, such as the exposure-oriented approach outlined in this article.

The REACH team should be sent back to the drawing board. It should not be charged with designing a comprehensive regulatory regime which in principle encompasses all chemicals and all uses. Instead, its task should be to design a system that will achieve a cost-effective reduction of overall chemical risks. If the European Union is serious about risk reduction, it owes this obligation to the people of Europe.

Notes

1 Commission officials have argued that the REACH regime is necessary because Europe, unlike the United States, does not have a civil liability system that generates sufficient incentives to produce safe and environment-friendly chemicals. Not surprisingly, they did not provide any theoretical and empirical arguments to back up this proposition. They have also claimed that REACH is merely an implementation of the international commitment confirmed in Johannesburg 'to sound management of chemicals throughout their life cycle and of hazardous wastes for sustainable development and for the protection of human health and the environment, *inter alia*, aiming to achieve by 2020 that chemicals are used and produced in ways that lead to the minimization of significant adverse effects on human health and the environment, using transparent science-based risk assessment procedures and science-based risk management procedures, taking into account the precautionary approach, as set out in Principle 15 of the Rio Declaration on Environment and Development': Johannesburg World Summit on Sustainable Development, Plan of Implementation (4 September 2002), para. 22. Even if REACH were an appropriate way to implement this commitment, there are numerous alternatives that would achieve these objectives.

2 The five key demands of European environmental groups and green political parties are: (a) a full right to know, including what chemicals are present in products; (b) a deadline by which all chemicals on the market must have had their safety assessed; (c) the phasing-out of persistent or bioaccumulative chemicals; (d) the replacement of less safe chemicals with safer alternatives; (e) a commitment to stop all releases of hazardous substances to the environment by 2020. REACH meets most of their demands.

3 European Voice Conference (2003).

4 As discussed in the subsequent text, REACH's justification creates a paradox: government failure calls for more government action.

5 Carson (2003).

6 Hanekamp et al (2003).

7 The Stockholm Convention on persistent organic pollutants (POPs) is the most recent addition.

8 Such as the 'SAICHEM' (Strategic Approach to International Management of Chemical Substances) initiative.

9 We discuss both the White Paper and the proposed regulation except where the proposed regulation deviates from the White Paper. Thus, when we criticize the White Paper, our criticism is also directed at the proposed regulation.

10 We do not cover all aspects of the REACH regime. Issues such as forced data sharing, compulsory payments for data and disclosure of confidential business information are not discussed here. Further, we do not analyse important legal issues such as decentralisation of authority, procedures, legal uncertainty, and rights to due process and judicial review.

11 Handling chemical risk only through the liability system may not result in adequate incentives where there are problems of information, causal indeterminacy, or long latency periods.

12 Bergkamp (2003).

13 The US TSCA (Toxic Substances Control Act) regime and the Japanese legislation, even after the recent amendments, are not nearly as intrusive as REACH.

14 Safe (1995); SH Safe (1997); Safe (2000).

15 Ames et al (1996); Gold et al (1992).

16 'Old' polymers will be exempt from registration until further notice.

17 To the extent that the REACH regime imposes disproportionate cost on, or eliminates a competitive disadvantage of, importers, it raises serious issues under WTO law.

18 'New' chemicals are those that do not appear on the list of chemicals reported to be on the market as of 18 September 1981, the so-called EINECS list.

19 Product-specific legislation, of course, may require premarketing authorization. Examples are pharmaceutical and pesticide legislation.

20 According to the Commission, registration of basic information would be required for approximately 30,000 substances, including all existing and new substances exceeding a production or import volume in the EC of one ton per year per manufacturer. The Commission estimates that 80 per cent of the substances, i.e. all low volume chemicals (less than 100 tonnes per year), would require only registration.

21 The registrant would be required to include all uses identified to it by downstream users.

22 The number of substances subject to authorisation is estimated at 1,400 (five per cent of the substances subject to registration).

23 Definitions are set forth in Annex XII of the regulation.

24 Placing on the market is broadly defined to include 'supplying or making available, whether in turn for payment or free of charge'.

25 Article 174(3) of the EU Treaty requires that the European Union, 'in preparing its policy on the environment, shall take account of: (i) available scientific and technical data; (ii) environmental conditions in various regions of the Community; (iii) the potential benefits and costs of action or lack of action; (iv) the economic and social development of the Community as a whole and the balanced development of its regions'.

26 Given the complexity of these procedures, chemical safety assessment can be carried out only by experts. Other than large chemical companies, regulated entities cannot afford to hire staff with the expertise necessary to meet these requirements. How would one explain to a company which has used chemicals safely for many years that it now has to make substantial investments in producing chemical safety assessments only to provide evidence to the authorities that the chemicals can be used safely? How can the Government expect dry cleaners, automobile service centres, photo shops, hairdressers and restaurant owners, who may well be using multiple chemicals, to meet these requirements?

27 Some elements of the EC's current chemical legislation are aimed at consumer or environmental protection. The Dangerous Substances Directive 76/464/EEC (OJ L129/23) and Dangerous Preparations Directive 88/379/EEC (OJ L187/14), for instance, impose labelling requirements with respect to consumer products and provide for an eco-toxicity label. The Marketing and Use Directive restricts the use of certain dangerous substances in certain consumer products.

28 These are the so-called 'phase in substances'.

29 Hollander (1998).

30 Beck (1986).

31 From a sociological viewpoint, government programmes like REACH can be regarded as designed to exploit the public's fear. They create dependency on government and a vicious cycle of government intervention pursuant to a mechanism along the following lines: (a) pressure groups identify risk; (b) research is conducted; (c) science cannot exclude risk; (d) pressure groups demand government action; (e) government takes action; and (f) the public becomes concerned and fear is reinforced, producing fertile soil for additional risk regulation. This mechanism creates asymmetric incentives for government: much blame for not intervening if hindsight determines a risk, but no blame for unnecessary, counter-productive or inefficient regulation. The result is too much government intervention, too early, too often. Furedi (1997).

32 Flynn et al (2001).

33 Ames and Gold (1997).

34 Ames et al (1990).

35 Doll and Peto (1981).
36 Calabrese and Baldwin (2003a); Calabrese and Baldwin (2003b).
37 Luckey (1991).
38 Calabrese and Baldwin (2003a).
39 See Biological Effects of Low Level Exposure (BELLE) website at www.belleonline.com.
40 Indeed, the advocates of the hormesis U-shaped model (Calabrese and Baldwin 2003a) challenge the regulators' choice for the LNT model on scientific grounds:

> 'The *a priori* criteria we developed to assess whether experiments displayed evidence of hormesis based on study design, magnitude of the stimulatory response, statistical significance of the stimulatory response and reproducibility of findings, revealed up to 5,000 examples of hormetic responses independent of chemical class/physical agent, biological model and endpoint measured. Low levels of agents such as cadmium, dioxin, saccharin, various polycyclic aromatic hydrocarbons, X-rays and various gamma-ray sources reduce tumours in some species. Low doses of X-rays enhance life span in male and female mice and guinea pigs; ethanol and acetaldehyde enhance longevity in fruit flies; multiple stressor agents extend longevity in nematodes; numerous toxic substances (for example, cadmium and lead) enhance growth in various plant species. Low or modest consumption of ethanol reduces total mortality in humans, while increasing it at higher levels of consumption. The hormesis concept is thus highly generalisable and far-reaching'.

41 See Cross (2001); see also www.belleonline.com/n2v92.html; and Wiener (2001); see also http://www.belleonline.com/n13v92.html .
42 Douglas and Wildavsky (1982).
43 Sunstein (2002); Kahneman (1982).
44 Sunstein (2000).
45 Dorner (1996).
46 Graham and Wiener (1995).
47 Flynn et al (2001).
48 Sapolsky (1990).
49 See Renn (1998).
50 Doll and Peto (1981).
51 Ames and Gold (2000).
52 Pieterman and Hanekamp (2002).
53 Bergkamp (2003).
54 Sapolsky (1990).
55 Wildavsky (1997)
56 Pieterman and Hanekamp (2002).
57 Bergkamp (2003).
58 Teng and Graham (1996).
59 The actual difference is likely to be greater, because cancer risk estimates for toxin-control programmes are worst-case, hypothetical estimates, and there may be no risk at all at low dose exposure levels (Gold *et al*. 1992).
60 Sunstein (2000).
61 Hahn (1996).
62 Carcinogenic Potency Project; see also Gold et al (2002).
63 Carcinogenic Potency Project, *ibid.*

Sources

Ames, B. N., Profet, M. and Gold, L. S. (1990). "Dietary pesticides (99.99% all natural)". *Proceedings of the National Academy of Sciences* 87, p. 7777.

Ames, B. N., Gold, L. S. and Shigenaga, M. K. (1996). "Cancer prevention, rodent high-dose cancer tests and risk assessment". (1996) *Risk Analysis* 16, p.613.

Ames, B. N. and Gold, L. S. (1997). "Environmental Pollution, Pesticides, and the Prevention of Cancer: Misconceptions". *FASEB Journal* 11, p. 1041.

Ames, B. N. and Gold, L. S. (2000). "Paracelsus to parascience: the environmental cancer distraction". *Mutation Research* 447, p.3.

Beck, U. (1986). *Risikogesellschaft: Auf dem Weg in eine andere Moderne.* Suhrkamp.

Bergkamp, L. (2003). *European Community Law for the New Economy.* Antwerp: Intersentia.

Carcinogenic Potency Project. Available at http://potency.berkeley.edu/

Carson, R. (2003). *Silent Spring* Boston, Houghton Mifflin Company (2002) (first published 1962).

Calabrese, E. J. and Baldwin, L. A. (2003a). "Toxicology Rethinks its Central Belief. Hormesis Demands a Repraisal of the Way Risks are Assessed" *Nature* 421, p.691.

Calabrese, E. J. and Baldwin, L. A. (2003b). 'Hormesis: the dose-response revolution' *Annual Review of Pharmacology and Toxicology* 43, p. *175.*

Cross, F. B. (2001). "Legal Implications of Hormesis" *Humans & Experimental Toxicology* 20(3), p.156.

Doll, R. and Peto, R. (1981). "The causes of cancer: Quantitative estimates of avoidable risks of cancer in the United States today". *Journal of the National Cancer Institute* 66, p. 1192.

Dorner, D. *The Logic of Failure* (Perseus Books, 1996).

Douglas, M. and Wildavsky, A. (1982). *Risk and Culture. An Essay on the Selection of Technological and Environmental Dangers.* Berkeley, University of California Press.

European Voice Conference (2003). 'Beyond REACH', Brussels, 31 March and 1 April.

Flynn, J., Slovic, P., Kunreuther, H. (2001). *Risk, Media and Stigma. Understanding Public Challenges to Modern Science and Technology.* London: Earthscan.

Furedi, F. (1997). *Culture of Fear: Risk-Taking and the Morality of Low Expectations.* Continuum.

Graham, J. D. and Wiener, J. D. (1995) Eds. *Risk vs. Risk. Tradeoffs in Protecting Health and the Environment.* Cambridge, Massachusetts, USA: Harvard University Press.

Gold, L. S., Slone, T. H., Stern, B. R., Manley, N. B., Ames, B. N. (1992). "Rodent carcinogens: setting priorities". *Science* 258, pp.261–65.

Gold, L. S., Slone, T. H., Manley, N. B. and Ames, B. N. (2002)., *Misconceptions about the Causes of Cancer* (Vancouver, The Fraser Institute); available at http://potency.berkeley.edu/text/Gold_Misconceptions.pdf.

Hahn, R. W. Ed. (1996). *Risks, Costs and Lives Saved. Getting Better Results from Regulation*. Oxford University Press.

Hanekamp, J. C., Vera-Navas, G. and Verstegen, S. W. (2003). "The historical roots of precautionary thinking: The cultural ecological critique and 'The Limits to Growth'" *Journal of Risk Research*; submitted for publication.

Hollander, P. (1998). *Political Pilgrims: Western Intellectuals in Search of the Good Society*. New Brunswick: Transaction Publishers.

Kahneman, D., Slovic, P. and Tversky, A. Eds. (1982). *Judgement under uncertainty: Heuristics and biases.* Cambridge: Cambridge University Press.

Luckey, T. D. (1991). *Radiation Hormesis.* Boca Raton, CRC Press.

Pieterman, R. and Hanekamp, J. C. (2002). *The Cautious Society? An Essay on the Rise of the Precautionary Culture.* Zoetermeer, Heidelberg Appeal Netherlands.

Renn, O. (1998). "Implications of the hormesis hypothesis for risk perception and communication" *Human & Environmental Toxicology 17, p.431.*

Safe, S. H. (1995). "Environmental and dietary estrogens and human health: is there a problem?" *Environmental Health Perspectives* 103, p346.

Safe, S. H (1997). "Is there an association between exposure to environmental estrogens and breast cancer?" *Environmental Health Perspectives* 105(3), p 675.

Safe, S. H. (2000). "Endocrine disruptors and human health – Is there a problem? An update" *Environmental Health Perspectives* 108, p. *487.*

Sapolsky, H. (1990) The Politics of Risk, *Daedalus* 119–4, 83–96.

Sunstein, C. S. (2002). “Beyond the Precautionary Principle”. John M Olin Law & Economics Working Paper No. 149 (2nd series). University of Chicago Law School.
Sunstein, C. S. (2000). *Risk and Reason. Safety, Law and the Environment.* Cambridge: Cambridge University Press.
Teng, T. O., Graham, J. D. (1996) “*The Opportunity Cost Of* Haphazard Social Investments in Life-Saving” in Hahn RW, Ed. *Risks, Costs, and Lives Saved: Getting Better Results from Regulation. New York:* Oxford University Press. pp. 167–182.
Wiener, J. B. (2001). “Hormesis and the Radical Moderation of Law” (2001) *Human & Experimental Toxicology* 20(3), p. 162.
Wildavsky, A. (1997). *But is it true? A Citizen’s Guide to Environmental Health and Safety Issues*. Cambridge, Massachusetts, USA: Harvard University Press.