Chemicals & Complexity: towards transparent, consistent, & precautionary evaluations of controversial evidence

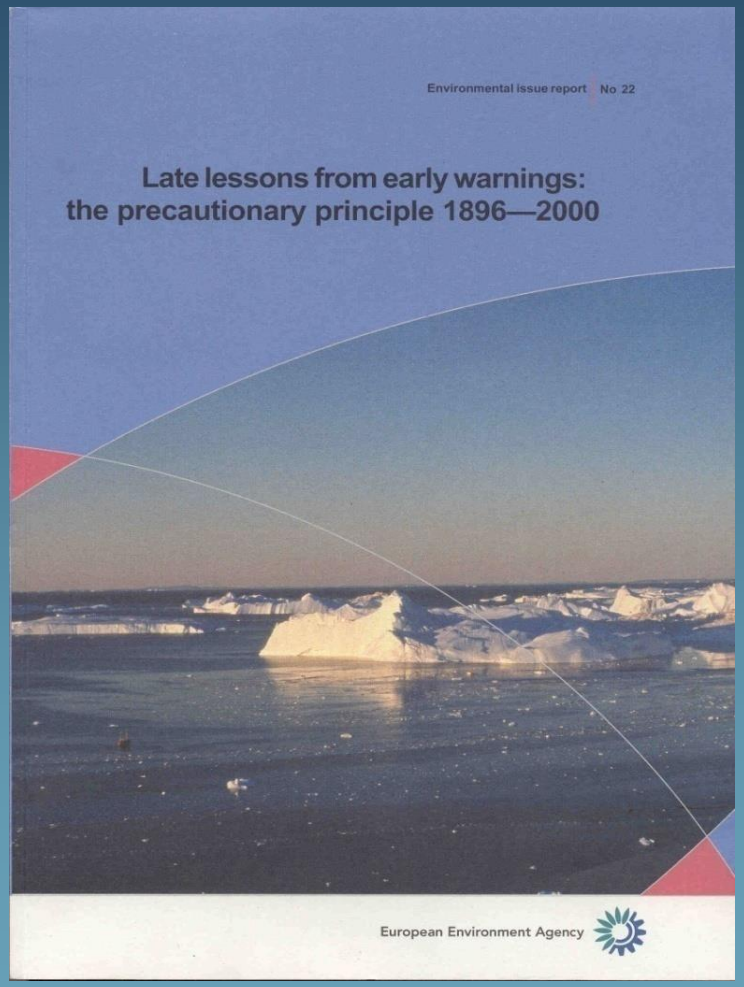
David Gee, Ex Senior Adviser, Science, Policy, Emerging Issues, European Environment Agency, Copenhagen.

Agenda for the Session

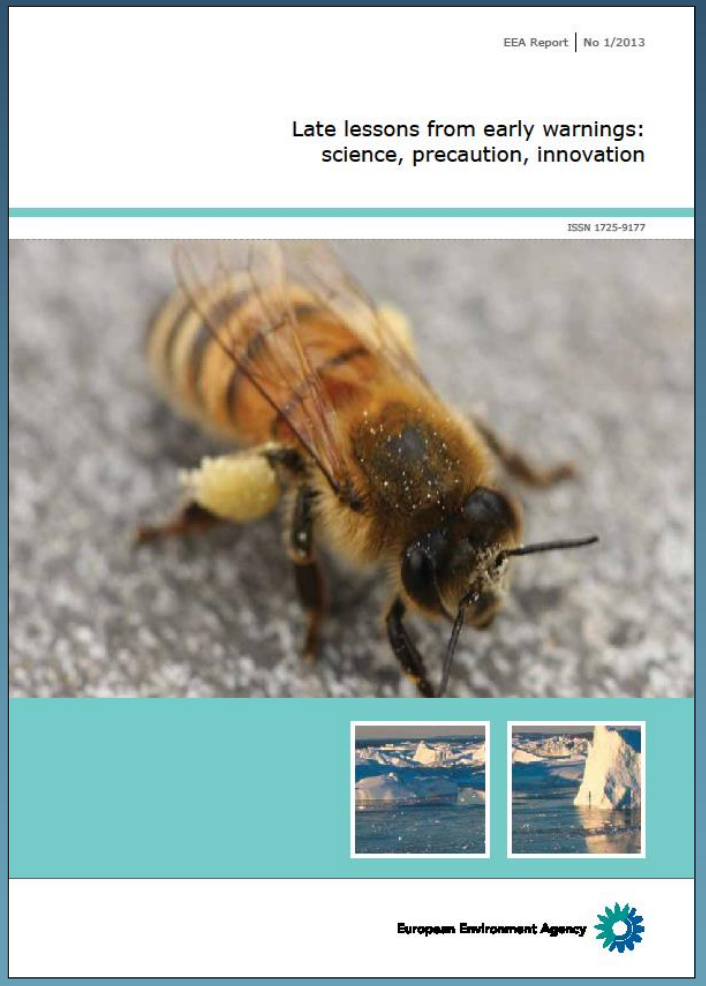
- Introductory remarks
- Some “Late Lessons from Early Warning” about chemicals: PCBs CFCs Neonicotinoids/Bees DES,BPA
- Some sources of divergent evaluations of the “same” evidence David Gee
- A critique of EFSA’s evaluation of the evidence on BPA Paul Whaley
- Discussion
- Implications for ENSSER?

Homo Sapiens (tragicus?) as slow learners
Two volumes

2001



2013



European Environment Agency

34 case studies

'Environmental chemicals'

- **Beryllium**
- PCBs
- CFCs
- TBT antifoulants
- **Mercury**
- **Environmental Tobacco**
- **Perchlorethylene**
- **Booster biocides**
- **DBCP**
- **DDT**
- **Vinyl chloride**
- **Bisphenol A**

Ecosystems

- **Ecosystems resilience**
- Great Lakes pollution
- Fish stock collapse
- Acid rain
- **Bee decline, France**
- **Invasive alien species**
- **Floods**
- **Climate change**

Transport fuel additives

- Benzene
- MBTE
- **Lead**

'Micro technologies'

- **Nano**
- **GMOs**

Animal feed additives

- BSE, 'mad cow disease'
- Beef hormones
- Antibiotics

- Asbestos

Pharmaceuticals

- **Contraceptive pill**
- DES

Radiations

- X-rays
- **Mobile phones**
- **Nuclear accidents**

European Environment Agency

“Acknowledge complexity, variability, uncertainty”

- “the causal links between stressors and harm are more **complex** than was previously thought”
- “much harm from cancers and climate change to decline in bees and in children’s IQ decline is caused by **co-causal factors acting independently or together**”
- **“Timing of exposure** can determine “the poison”
- **“Low dose effects** can be greater than high doses” (radiations, BPA)
- **“Varying susceptibilities** from age, sex, immune state, stress, genes, epigentics… “
- **“there are continuums from “effects” to “adverse” effects..”**
- **“But sometimes Thresholds & tipping points…”**
- **“Systems level effects are** not predictable from individual cells/organisms eg bee colonies;
- More **transparency about uncertainties** in risk assessments.

CFCs and “global experimentation”

“..neither governments nor multinational companies have a mandate for global experiments..

*CFCs provide a stark warning..**all too often technology outstrips the science needed to assess the risks..***

Policymakers must learn to recognise when ignorance has been replaced by understanding, however rudimentary”

Joe Farman, Halocarbons and the ozone hole, Late Lessons, 2001.

CFCs: Is “one molecule along” chemical innovation wise?

“more money is now needed to phase out HCFCs..

It would surely have been better to stimulate more radical changes in technology from the outset..

..focused on prudent long term goals of halocarbon-free and energy efficient technologies”

Halocarbons & the ozone layer, Joe Farman, Late Lessons, 2001, p 81.

Incremental or more radical chemistry?

- CFCs had a global warming potential of about 10,000..
- HCVCs and HFCs have a GWP of around 1400..
- The new HFOs have 4!

"We chemists tend to look for the next molecule or tweek along…perhaps more radical approaches should be adopted"

Ole John Nielsen, Professor, Atmospheric Chemistry , Copenhagen University, Nov 18th ,2013.

Chemicals: from Products to Services.

UNIDO has launched a global programme that promotes the application of **chemical leasing** in industry in 10 developing countries.

The hydrocarbon solvent supplier supervises the application of the solvent in the process of cleaning equipment at General Motors Egypt and receives payment per vehicle produced instead of solvents sold and the supplier takes back the solvent waste for recycling.

Solvent consumption is reduced from 1.5 L to 0.85 L per vehicle.

Something light

Cornered

by Mike Baldwin

"What's important is that we learn from what we must never admit happened."

Monsanto…and PCBs….internal view….1969

“the problem involves the US, Canada, and parts of Europe..evidence of contamination has been shown in remote parts of the world..

but stopping PCB production is not an option: ***it would cause profit to cease and liability to soar because we would be admitting guilt by our actions”.***

Monsanto: internal Pollution Abatement Plan,1969

Costs of Inaction-PCBs-and relevance to costs of REACH

- **15b euros over 1971-2018** for costs of PCB soil/site remediation only ; excludes health/ecosystem damage.(Swedish estimate)
- **Costs of REACH-2-4b euro over 10 years**
- If REACH prevents 1 “PCB” disaster over the next decades will have paid for itself..
- this is likely because there are > 30k untested *existing* substances; and
- 75% of c 2k *new* substances are classified as “hazardous”

Some Lessons of PCBs

- **Persistence, bio-accumulation and large spatial range** ensures widespread and enduring contamination long after a ban.
- **Action on early liver damage effects in workers** in 1930s could have stimulated research and lower exposures
- *"The non application of the **precautionary principle** has left a legacy the total effects and costs of which can only be guessed at"*

Koppe & Keys, Late Lessons ,2001.

And Exposures expand over time…..

- Asbestos/DBCP/Be **producers, users, bystanders** eg insulators, plantation workers, passive smokers
- **Domestic:** asbestos mesothelioma deaths from washing overalls;children of asbestos workers, smokers
- **Environmental:** near asbestos & lead mines and factories; teachers from asbestos; DBCP in water; passive smokers
- **Consumers:** BPA
- **Next generations:** Asbestos, radiations, Mercury at Minamata, DES, climate changes
- **non target species:** Goucho & Bees; Polar bears & fish from PCBs,Hg; oysters from TBT; fish from the Pill

Some insights from the Honey Bees and Pesticides case study

“Seed dressing systemic insecticides and honeybees”, Maxim L. & van der Sluijs,J., Late Lessons from Early Warnings, EEA 2013.

Flawed Risk Assessments for neonicotinoid pesticides and Bees

- Wrong risk regime: ie for **sprayed not sytemic** pesticides.
- **"Low" exposures** to bees assumed to be safe.
- Acute effects on bees only cf **sub-lethal, chronic** and **colony level effects.**
- **Neglect of systemic effects within hives cf bees**
- **Inadequate evaluation of multi-causality and complexity.**
- No/little **representation of beekeepers** & relevant academic researchers
- Independent critiques of RAs need **data access & transparent evaluations:** but these not available

the search for the single cause..of all impacts.. in all regions !?

"The Risk Assessment ***does not allow us to demonstrate*** *that maize seed dressing with Gaucho can be* ***solely*** *responsible, at* ***national*** *level, for* ***all colony losses, behavioural troubles, honey bee mortalities, or general decline in honey production"***

French Commission for Toxic Products , 2002: see "Seed dressing systemic insecticides and honeybees", Maxim L. & van der Sluijs,J., Late Lessons from Early Warnings, EEA 2013.

or embrace multi-causality….

"Gaucho…is of concern (on maize) as ***one*** *of the* ***explanatory elements for the weakening of the bee populations observed*** *despite the ban of Gaucho in sunflowers."*

Multifactor study of the Honeybee Colonies Decline, French Scientific & Technical Committee, 2003, see Late Lessons, Bees chapter

Some Implications of Multi-causality

Causal complexity increases…therefore…

..a "**sufficiency of evidence" for action on "a plausible association"** needs to decrease..

..with less weight on statistical significance.. and more weight on **statistical power & confidence limits**

..& embrace complexity

"These findings suggest the ***existence of epigenomic cultures in honey bee colonies as superorganisms****..*

…generating context-dependent molecular flexibility in the brain..

.. the highly dynamic nature of this process orchestrates ***the complex interplay between social stimuli and the genome*** *and ultimately determines workers' behavioural outcomes".*

"DNA methylation changes elicited by social stimuli in the brains of worker honey bee" Lockett, R. Kucharski and R. Maleszka Genes, Brain and Behavior (2012) 11: 235–242

Regulatory Science does not keep pace with technological innovation…

"the new generation of neonicotinoids was first marketed in France in 1993, and new methods for assessing their new risks for honeybees are still not in regulatory use today!" (2014)

Laura Maxim, co-author of the Bees chapter

DES Update 2013

- “Impacts of prenatal exposure far greater than in 2000.
- Adenocarcinoma of vagina and cervix; reproductive effects; increased risks of breast cancer.
- Increased risks of TDS in **sons**
- Early elevation of birth defects in male & female **grandchildren**”

Swan ,Late Lessons , 2013.

the Nature of Harm expands over time….

- **Asbestos**: 1929 asbestosis; 1954 lung cancer; 1959 mesothelioma, 2012 throat & other cancers
- **Tobacco**: 1951 lung cancer; 2012 many cancers, foetal harm; heart disease
- **PCBs**: 1960s bird reproduction;2012s neurological harm in children; soil contamination
- **Lead**: 1979 brain damage in children; 2012 heart disease in adults
- **Minamata:** 1950 brain damage & neurological; 1960s birth defects 1990s childrens IQ & behavioural
- **DES**: 1970 vaginal cancer; 1980s reproductive problems; 2012 breast cancer

And harm is caused at lower & lower levels of exposure…

- Asbestos
- Lead
- PCBs
- Mercury
- TBT
- Radiations
- BPA….etc

….often with, eventually, no known threshold…

eg Lead (EFSA, 2012).

DES Conclusions.

- "The tragic DES "experiment" provides important lessons for todays synthetic oestrogens eg of **BPA** …now 10 billion pounds in use..and studies to identify effects only now being conducted"
- Extreme caution should be taken before exposing pregnant women to endocrine disruptors
- "No evidence of harm is not evidence of no harm"
- Pharmaceutical industry: no long term pre-market tests; ignored; aggressively promoted DES after known toxic effects and inefficacy.
- Failure of regulatory agencies to act quickly on emerging evidence-until harm serious demonstrated

Research: how much to develop products and protect people/environments?

EU Public Research 1994-2013	"Products"	"Protection"
Nanotechnology (2002-2013)	5 billion	112 million **(2%)**
Biotechnology(1994-2013)	7.5billion	273 million **(4%)**
Information Communications Technology/EMF(2007-2013)	19 billion	18 million **(0.09%)**

“Scientific Inertia” in chemicals Research

- An analysis of 78 environmental and health journals 1899-2009 revealed a focus on:
- PCBs, sulphur dioxide, benzene, asbestos, TBT, MBTE and the pharmaceutical agent DES.
- Of the nearly 15,000 articles published on these substances some 40% had been published since 2000.

See chapter on Precautionary Science, Grandjean, Late Lessons ,2013.

Inertia…….

- **There were 15,000 articles published between 2000-2009 on lead, mercury and DDT alone.**
- **Only 352 articles researched 8 of the emerging, large production chemicals identified as priorities by the US EPA, eg 1,3-Dichlorobenzene.**
- **There were no articles on five other priority chemicals.**

Some explanations for "scientific inertia":

- the traditional scientific requirement for high levels of proof;
- the need to publish quickly using familiar intellectual & technological resources;
- and the conservative approach of many reviewers and research funders.

See chapter on Precautionary Science, Grandjean, Late Lessons ,2013.

“Adequate and anticipatory research on the potential hazards of emerging technologies: a case of myopia and inertia?”

Steffen vos Hansen & David Gee

Journal of Epidemiology & Community Health, June 2014

“BPA: Contested science ,divergent safety evaluations”, Late Lessons, 2013.

- 1989 –2012 Sonnenschein et al; Vandenberg- U shaped dose/response curves
- 1992 BPA added to list of “endocrine disruptors”
- 1993 Krishnan et al- accidental discovery of BPA leaching
- 1997 Colrangle & Roy- breast tissue proliferation; & more potent than expected.
- 2008 Palanza et al-irreversible developmental effects in animals
- 2008/2011 NTP/NIEHS multiple modes of action.
- 2009 Edinton & Ritte- BPA toxic concentrations higher in children than adults
- 2001-2011 50 studies showing potentially adverse effects below “safe limit” of 50ug/kg/bw
- 2002/2011 8 divergent BPA Risk assessments reviewed

Gies A & Soto A, Late Lessons, 2013

BPA Chapter Conclusions

- Toxicity: “expectations based on inappropriate assumptions”
- “Good Laboratory Practice (GLP/OECD) not necessarily good science” (Myers et al 2009).
- “Manufacturing of Doubt”; Funding bias; conflicts of interest in science & regulatory advice (see also Tobacco chapter)
- New independent RAs needed with relevant scientific expertise
- Precautionary action needed.
- More independent science needed (Holland 2012)

“Manufacturing Scientific Doubt”

“Doubt is our product since it is the best means of competing with the ‘body of fact’ that exists in the mind of the general public.”

From an executive at Brown & Williamson, Tobacco Company, 1969.

See EEA chapters on Beryllium,tobacco, leaded petrol, climate change etc. And Michaels 2009: Oreskes,2010 on manufacturing doubt.

Different Conclusions from "Same" Knowledge Evaluated

Classification of TCE risk assessment reports in 1995/6
(from Ruden 2002)

- - - Negative	+ - - Positive animal	+ - + Positive aninal, negative human, plausible risk	+ + + Positive animal & human, plausible risk
1996 ACGIH	1996 HSIA, Online, Industry	1996 OECD/EU UK, Int.Org.	1995 IARC
			1996 Deutsche Forschungsgemeinschaft, DFG, Germany
			1996 MAK Germany Occ. Agency

Science & Judgements …….

"When different risk assessors..reach different conclusions..they do so because they are adopting different Risk Assessment Policies (RAPs) rather than because some committees provide more or less scientific answers than others"

"data and documents do not interpret themselves: interpretation often involves judgements and assumptions"

JRC/IPTS Report on "RAPs: Differences across Food Jurisdications"(2008p10)

EEA Workshop Conclusion on "Sources of Divergent Evaluations". 2008

A. Institutional/Cultural factors eg RAC mandate & membership

B Knowledges accepted for review

C Weights given to knowledges reviewed

D "Rules" by which knowledges assessed become evidence asserted.

F Approaches to evaluating Uncertainties, Understandings, Confidences, & Likelihoods about the knowledge base and cause/effect links; and

G "Rules" for conclusions about Strengths of Evidence (for different Risk Management options) and Strengths/nature of recommendations

On Selecting the RA Committee: BSE

"Really, the key is the setting up of the Committee: who is on it and the nature of the investigations" (MAFF official, BSE transcript, 1998, 29 June,p79-81)

"the opposition to the involvement of the Public Health Laboratory Service in BSE policy was anxiety that this would be tantamount to admitting the possibility of a human health risk".

- (Welsh Chief MO,Phillips BSE Inquiry,2000, V 11. para 4.28)

(See BSE chapter in « Late Lessons from Early Warnings:the Precautionary Principle 1898-2000 », EEA, 2001.

Some Biases in Research & Risk Assessment

- **Funding bias**: See the Vatican and its seeking of scientists who would contradict Galileo. See histories of Asbestos, Lead, some Pharma, Tobacco, BPA, & Mobile phones..where source of funding strongly predicts nature of the results
- **Intellectual bias** *ie commitment to a paradigm; authored previous evaluation/RA; "beware group think" (IPCC, 2010)*
- **Methodological biases** towards false negatives
- **Reporting & Publication biases**

See chapters on Precautionary Science & on Precaution, Late Lessons ,2013

Some Intellectual Interests/Commitments of Scientists

- From different scientific disciplines eg toxicology v endocrinology; engineers and doctors
- Prior beliefs
- Paradigms preferred
- Prejudices and Passions
- Biases preferred

(See « Rivals: Conflict as the Fuel of Science », M. White, Vintage, 2002, for Newton v Leibnitz, etc)

Intellectual Bias: the Beef Hormones case at WTO

"The European Communities alleges that "**that Drs. Boisseau and Boobis,**..as "co-authors" of the JECFA reports, "cannot be considered to be independent and impartial in these circumstances, because this would amount to asking them to review and criticise reports that are their own doing".

Upheld at WTO Appellate Body

Source: p27, para 65 World Trade Organization, WT/DS320/AB/R, "United States-Continued Suspension of Obligations in the EC-Hormones Dispute", (16 October 2008)

Methodological Biases: Environmental Health Sciences and Their Main Directions of Error

SCIENTIFIC STUDIES	SOME METHODOLOGICAL FEATURES	MAIN[1] DIRECTIONS OF ERROR:
Experimental	•High doses	**False positive**
Studies	•Short (in biological terms) range of doses	False negative
(Animal)	•Low genetic variability	False negative
	•Few exposures to mixtures	False negative
	•Few Foetal-lifetime exposures	False negative
	•High fertility strains	False negative (Developmental/reproductive endpoints)

[1] Some features can go either way (e.g.inapproriate controls) but most of the features mainly err in the direction shown in the table

(Gee, Bailar, Grandjean,2004, Gee 2008, Grandjean,2013, Gee,2014)

Observational Studies (Wildlife & Humans)	•Confounders	**False positive/negative**
	•Inappropriate controls	**False positive/negative**
	•Non-differential exposure misclassification	False negative
	•Insensitive outcome measures	False negative
	•Inadequate follow-up	False negative
	•Lost cases	False negative
	•Simple models that do not reflect complexity	False negative
	•Multi-causality	False negative
Both	•Publication bias towards positives	**False positive**
	•Reporting bias	False negative
Experimental And Observational Studies	•Scientific cultural pressure to avoid false positives	False negative
	•Low statistical power (e.g. From small studies)	False negative
	•5 % probability level to minimise chances of false positives	False negative
	•Funding bias	False negative

Qualitative expression of Uncertainty In 100 EU SC Opinions (Hardy/Hart ,2007)

EU Committee	Any term for "Uncertainty" from Table 16	"Uncertain" or "uncertainty"	
	In concluding section	In concluding section	Anywhere in opinion
SCCNFP	20%	0%	5%
SCCP	52%	0%	29%
SCENIHR	80%	80%	80%
SCHER	63%	26%	53%
SCMPMD	73%	18%	55%
SCTEE	83%	38%	79%

The PP: Two roles?

- As a **trigger for debates on future innovation pathways** in a water, energy and resource-constrained world (eg France , GMOs ,1997-2005

- As a **legal and moral justification for more timely actions** on early warnings about potential hazards.

EEA working definition of the Precautionary Principle

"The PP provides justification for public policy actions in situations of ***scientific complexity, uncertainty and ignorance,*** where there may be a need to act in order to avoid, or reduce, potentially serious or irreversible ***threats*** to health or the environment, using ***appropriate strengths of scientific evidence*****,** and taking into account the likely ***pros and cons*** of proportionate actions and inactions".

Some Strengths of Scientific Evidence….

- **Beyond all reasonable doubt** (scientific causality & criminal law)
- **Reasonable certainty** (Int.Panel Climate Change , 2007)
- **Balance of probabilities/evidence** (IPCC,2001; civil law)
- **Strong possibility** (IARC on ELF ,2002; on RF 2011)
- **Reasonable grounds for concern**(EU Communication on PP)
- **Scientific suspicion of risk** (Swedish Chemicals Law,1975)
- **"Pertinent information"** (WTO SPS justifying member state actions to protect health

  ……which are appropriate for different purposes, depending mainly on the costs of being wrong in acting/not acting

More Precaution with EDCs is needed because ..

- Complexity & multi-causality delays “sufficient” knowledge of harm...
- ..requiring exposure reductions on “low” strengths of evidence
- fast technological change overtakes..
- ..the slow increase in scientific knowledge
- Plausible evidence of delayed & serious impacts is available
- lessons from the past tragedies with EDCs eg DES,TBT, DBCP.

Barriers to Precautionary Action: Science

- Unrealistic **assumptions** about “safety”
- Authoritative but unsupported **assertions** of safety
- **Inadequate research** (“inertia”, low hazard/products ratio)
- Failure to acknowledge **scientific uncertainties & ignorance**
- **Complexity** permits multiple interpretations & “manufacture of doubt”
- **Conservative science**: methodological, intellectual, funding, reporting biases towards “safety”

Barriers to Precautionary Action:Policy

- Inadequate/conflicting risk assessments
- Market failures ie costs of harm externalised onto society
- Corporate incentives & power; “manufactured doubt”; control of research (leaded petrol, GMOs)
- Regulatory capture
- Short termism
- **“Losers” mobilise**, “gainers” do not
- “Willfull Blindness”

Need for greater public engagement

- In hazard/risk/options/alternative assessments

- In applying the PP via “acceptable” levels of protection for health & environments and
- in choosing appropriate strengths of evidence for action
- In **choosing strategic innovation pathways** to 2050 on energy, agriculture (GMOs chapter)& consumer product chemicals.

Thank you

geedavid90@gmail.com