RCR Forum

The Environmental Implications of Biotechnology

Daniel A. Vallero, Ph.D.
Duke University, Pratt School of Engineering

October 27, 2009

1

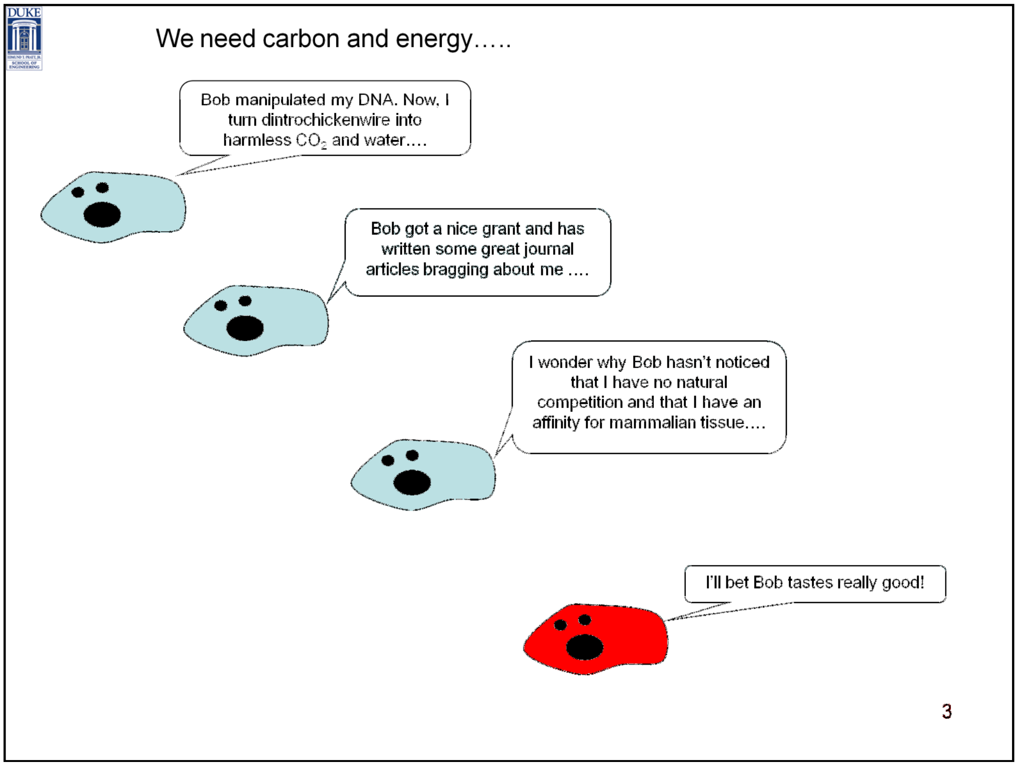
Duke University's Responsible Conduct of Research Program is led by the Graduate School. The major components of the program are a day long orientation training for incoming PhD students, department and center-level ethics training tailored to specific research and forums on specific topics. Graduate students must participate in a defined number of forums to receive graduate credit, which is part of the PhD requirements at Duke. The Pratt School of Engineering collaborates with the Graduate School.

No matter your research, likely to encounter biotechnology….

Red	Medical
Yellow	Food Biotechnology
Green	Agriculture
Blue	Aquatic
White	Gene-based industry
Grey	Fermentation
Brown	Arid
Gold	Nanotechnology/Bioinformatics
Purple	Intellectual
Dark	Bioterrorism/Warfare

2

This particular RCR forum addresses biotechnology and its many research mandates. It draws heavily from D.A. Vallero (2010). *Environmental Biotechnology: A Biosystems Approach.* Elsevier Academic Press. ISBN-10: 012375089X; ISBN-13: 978-0123750891.



A bit of humor, based on the so-called "Gray Goo Syndrome" first articulated by Sir Martin Rees (2003). *Our Final Hour: A Scientist's Warning: How Terror, Error, and Environmental Disaster Threaten Humankind's Future In This Century--On Earth and Beyond*. Basic Books. ISBN-10: 0465068626

ISBN-13: 978-0465068623. Rees presents an unlikely worst case scenario, in which well-intentioned scientists unleash genetically engineered "superpathogens" that can ultimately turn the entire globe into goo as a result of out of control bacterial metabolism (e.g. shutting off normal homeostasis)…

This is an interesting teaching device: Try a thought experiment related to our own research. What is the worst possible outcome that could result from the most unfortunate confluence of events? What if someone wanted to take your newly found knowledge and deliberately misuse it (i.e. dual use)?

L’Acide Case Study

1. Read first 2 pages.
2. Skim the attachment… (Select salient material, depending on your area of expertise).
3. Break into groups (by color of your handout).
4. Discuss the facts first.
5. Share opinions on responsible actions.
6. Find way to reach consensus (not necessarily unanimity).
7. “Hire” a spokesperson.
8. Be ready to share details with the whole group (particularly the ones you brought up in the breakout).

4

This case creates hidden agendas to illustrate how perspectives can help to determine the acceptability of an engineering project. See the four different cases. Do not let the readers know that their case is different from the others.

“Hold paramount…”

- Engineers must “hold paramount the safety, health and welfare of the public.”
- Characterizes the need for not only protecting public health and the environment, but to be guardians for sustaining these protections.
- But, ***how*** do we do this….?

5

This is the first canon of every engineering code of ethics. Our principal client is the “public.” In this way, we differ from physicians (patient), attorneys (justice system) and most other professionals.

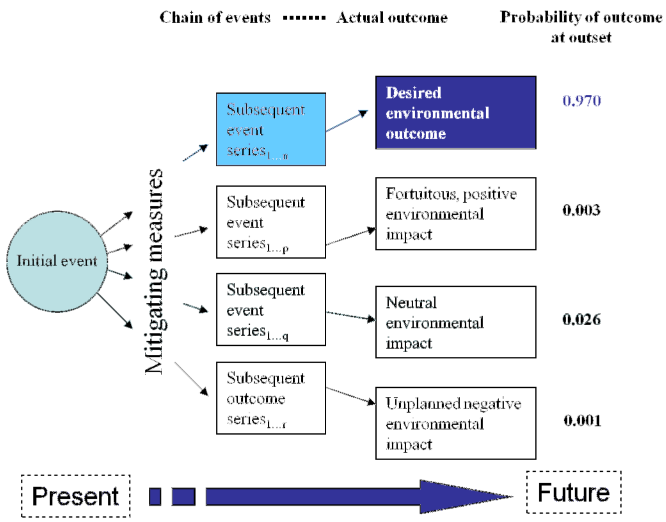
Contaminant Cleanup Feasibility

1. Protect human health and environment
2. Comply with applicable regs
3. Provide long-term effectiveness & permanence
4. Reduce toxicity, mobility or volume (treatment)
5. Provide short-term effectiveness
6. Consider ease of implementation
7. Consider cost
8. Gain State's acceptance
9. Gain community's acceptance

6

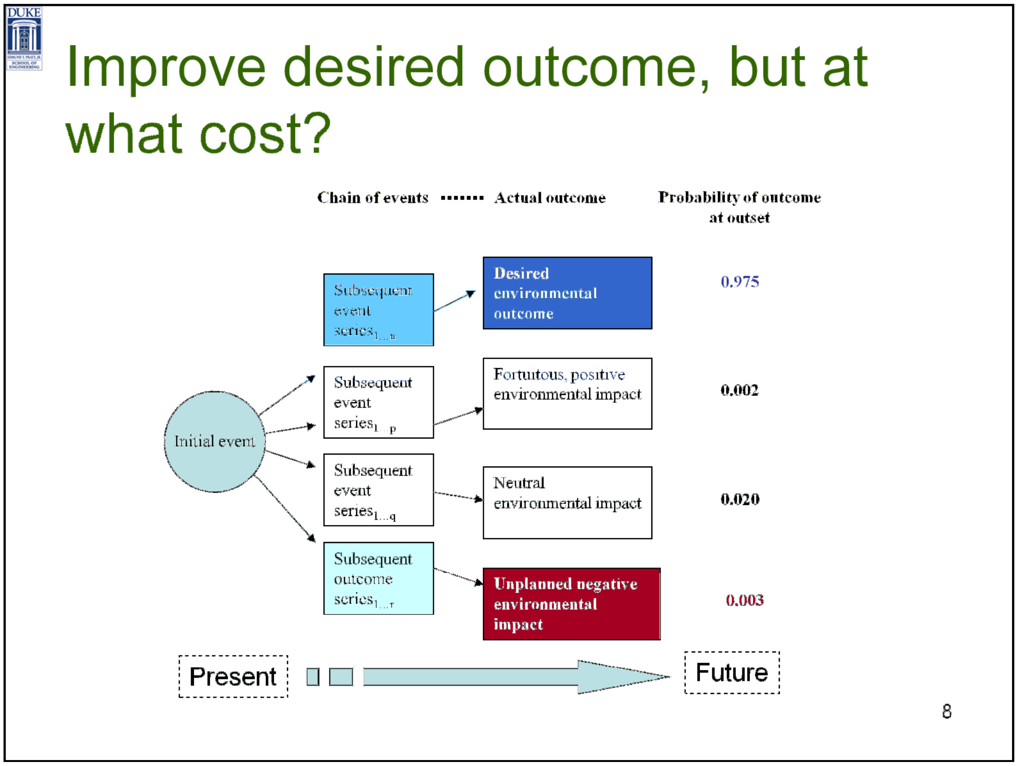
This list is a compilation of the steps taken by state and federal environmental agencies to remediate sites. It is provided here as a benchmark for the L'Acide case. How well does the case adhere to these nine standards?

Chaos

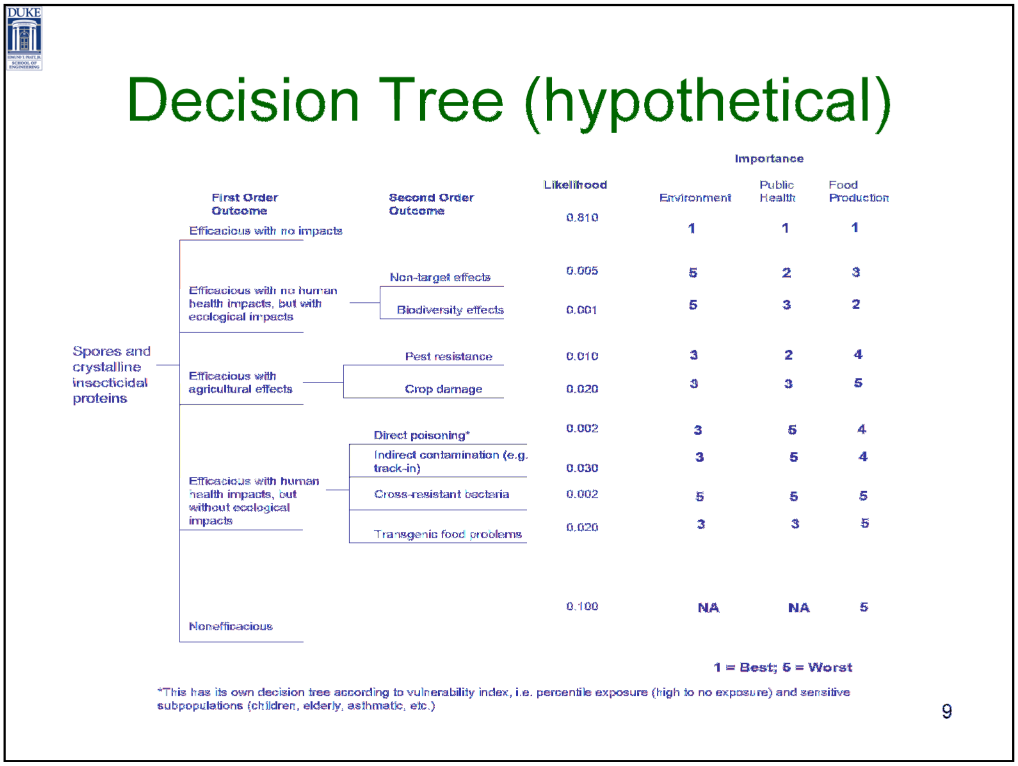


7

Environmental engineers must be aware that the outcomes of their designs and actions are uncertain; i.e. the desired outcome is never a sure thing. The best we can do is control the initial and boundary conditions to some level of satisfaction. In fact, even good projects have a potential (albeit very small likelihood) for harm. This is a function of contingent probabilities (often almost impossible to quantify) of events that lead to different outcomes.



Here is a case where we improved the likelihood of our desired outcome, but also increased the likelihood of a negative outcome….



In this hypothetical example, the decision tree shows competition among values (environmental, health and food). All three are desirable, but at what threshold is something good for food yet a “no go” because of potential impacts on health? This is a common debate concerning genetically modified organisms (GMOs).

European classes of risks posed genetically modified microorganisms

Hazard Level	Description of Microbial Hazard
Least	Never identified as causative agents of disease in humans and that offer any threat to the environment.
Hazardous when contained, low human risk	May cause disease in human and which might, therefore, offer a hazard to laboratory workers. They are unlikely to spread in the environment. Prophylactics are available and treatment is effective.
Severe when contained, moderate human risk	Severe threat to the health of laboratory workers, but a comparatively small risk to the population at large. Prophylactics are available and treatment is effective.
High human population risk	Severe illness in humans and serious hazard to laboratory workers and to people at large. In general, effective prophylactics are not available and no effective treatment is known.
Greatest ecological and human population risk	Most severe threat to the environment, beyond humans. May lead to heavy economic losses. Includes several classes, Epl, Ep2, Ep3 (see Table 1.2 for descriptions) to accommodate plant pathogens.

10

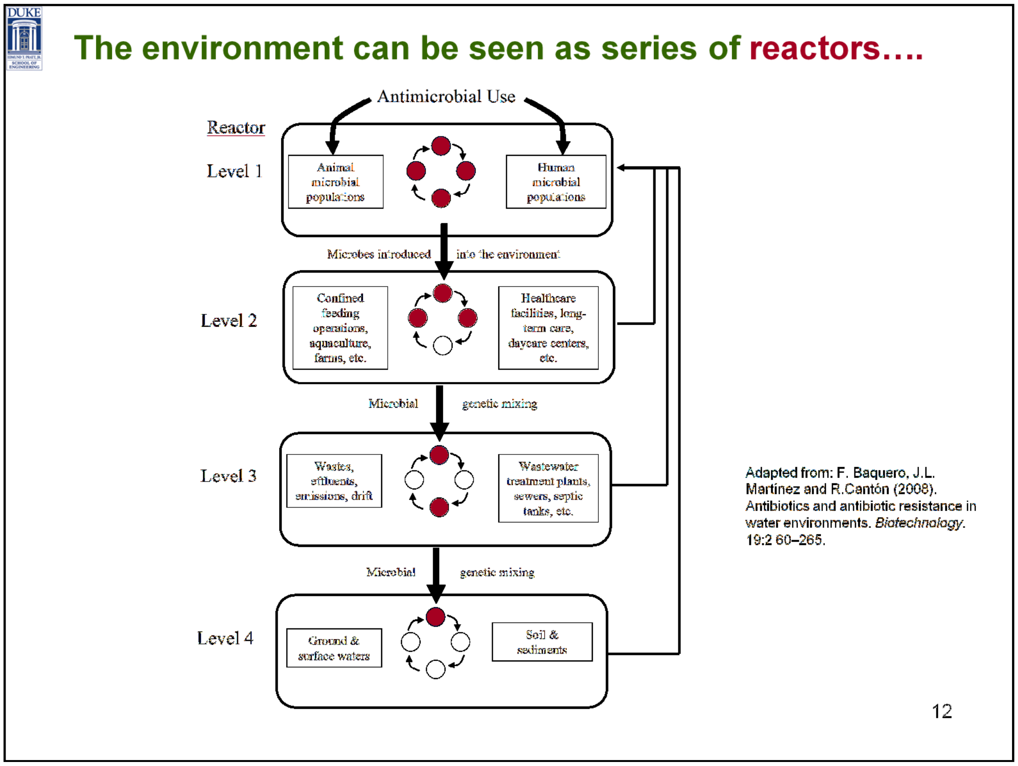
Europe has been a leader in GMO precautionary viewpoints. Here is the EU's hazard system. It is possible that even if a microbe is in the green category, with increased information or due to adaptive changes, it could move toward greater risks. *E. coli* is an example. The question for scientists is that given the uncertainties associated with recombinant DNA insertion and other areas of genetic modification, could we be introducing expression of traits other than those we have targeted; e.g. could allergenicity of plants be increased as we insert genes to improve production? Or, could the newly introduced strains gain competitive advantages over indigenous , unmodified strains, which adversely affects biodiversity, predator-prey relationships, food chains or productivity in adjacent ecosystems?

European classes of microbes causing diseases in plants.

Biotechnology Class	Description of Microbes in Class
Ep 1.	May cause diseases in plants but have only local significance. They may be mentioned in a list of pathogens for the individual countries concerned. Very often they are endemic plant pathogens and do not require any special physical containment. However, it may be advisable to employ good microbiological techniques
Ep 2.	Known to cause outbreaks of disease in crops as well as in ornamental plants. These pathogens are subject to regulations for species listed by authorities in the country concerned
Ep 3.	Mentioned in quarantine lists. Importation and handling are generally forbidden. The regulatory authorities must be consulted by prospective users

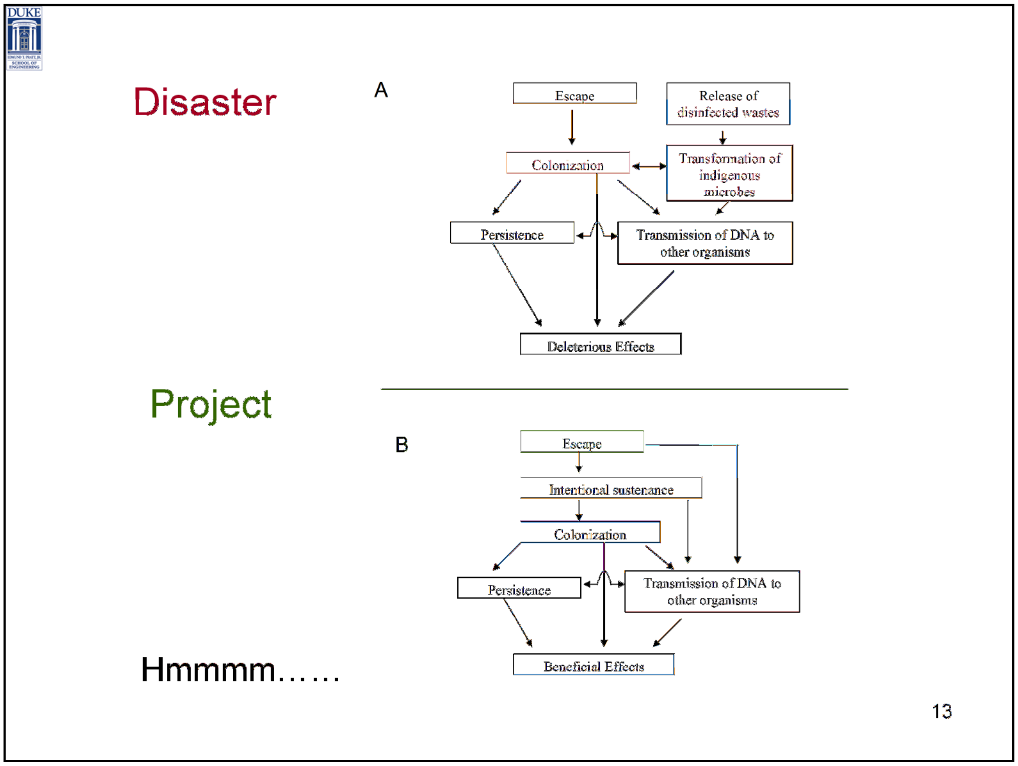
11

This is another European classification related to plant pathogenesis. Thus, the same microbe could have different levels of concern depending on the receptor (e.g. humans versus plants).



This is a modification of Baquero et al. conception of how microbial populations can grow, adapt and transform in the environment. In the lower level reactors (1 and 2), human and animal microbial populations (filled circles) mix with environmental microbial populations (clear circles), which increases genetic variation, allowing new resistance mechanism in the microbial populations, whereupon these new strains, with the potential for greater resistance, are re-introduced to the human and animal environments (feedback arrows). Therefore, even if the human populations have not yet used an antibiotic, if a similar form is used in animals, the genetic adaptations may allow for resistant strains of bacteria to find their way into human populations, rendering a new antibiotic less efficacious.

Such “reactors” provide lessons on the chaos discussed in earlier slides.



This slide illustrates that the flow of events and outcomes between an undesirable effect and a desirable effect can be quite similar. For example, an accidental release of a genetically modified bacterium from research is highly regulated (e.g. in the U.S., the National Institutes of Health has strict confinement rules for microbes undergoing research), but very similar strains may be intentionally applied to "non-research" projects, such as environmental cleanup.

What lessons can be or need to be learned from these similarities?

Perception is crucial

- Which line is longer?

The Müller-Lyer Illusion.

14

The following slides illustrate the illusion that the top line appears longer.

Perception is crucial

- Which line is longer?

The Müller-Lyer Illusion.

15

But….

Perception is crucial

- Which line is longer?

The Müller-Lyer Illusion.

16

As we learn more…

Perception is crucial

- Which line is longer?

The Müller-Lyer Illusion.

17

We find…

Perception is crucial

- Which line is longer?

The Müller-Lyer Illusion.

18

… that the difference…

Perception is crucial

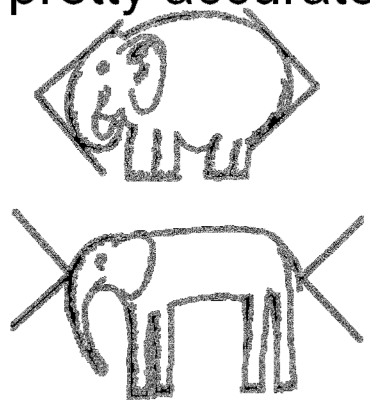
- Which line is longer?

The Müller-Lyer Illusion.

19

… does not, in fact, exist.

But sometimes, perception is pretty accurate….



Source: *Pardon,* ca. 1970.

20

… but all generalizations are bad (including the generalization that all generalizations are bad)…

Think about that……

Problem of valuation of environmental resource

- Always a problem with non-monetized valuation
- E.g. what is the value of a life?
- Dilemma of gross domestic product for eco-resources
- Rethinking value (beyond willingness to pay)

21

One of the vexing problems in environmental decision making is how to place a value of resources. Monetized value is the easiest, e.g. benefit-cost ratios.

Environmental Ethics

What is valued?

Humans exclusively

↓

All cognitive entities

↓

All sentient entities

↓

All biotic entities

↓

All material entities

↓

All entities and ecological phenomenon (abiotic and biotic, plus other values, richness, abundance, diversity sustainability)

22

The first step in environmental ethics is to decide what is valued and what value system is being used….

Environmental Ethics

What is valued?	Ethical View
Humans exclusively	Anthropocentric
↓	
All cognitive entities	
↓	
All sentient entities	
↓	
All biotic entities	
↓	
All material entities	
↓	
All entities and ecological phenomenon (abiotic and biotic, plus other values, richness, abundance, diversity sustainability)	

23

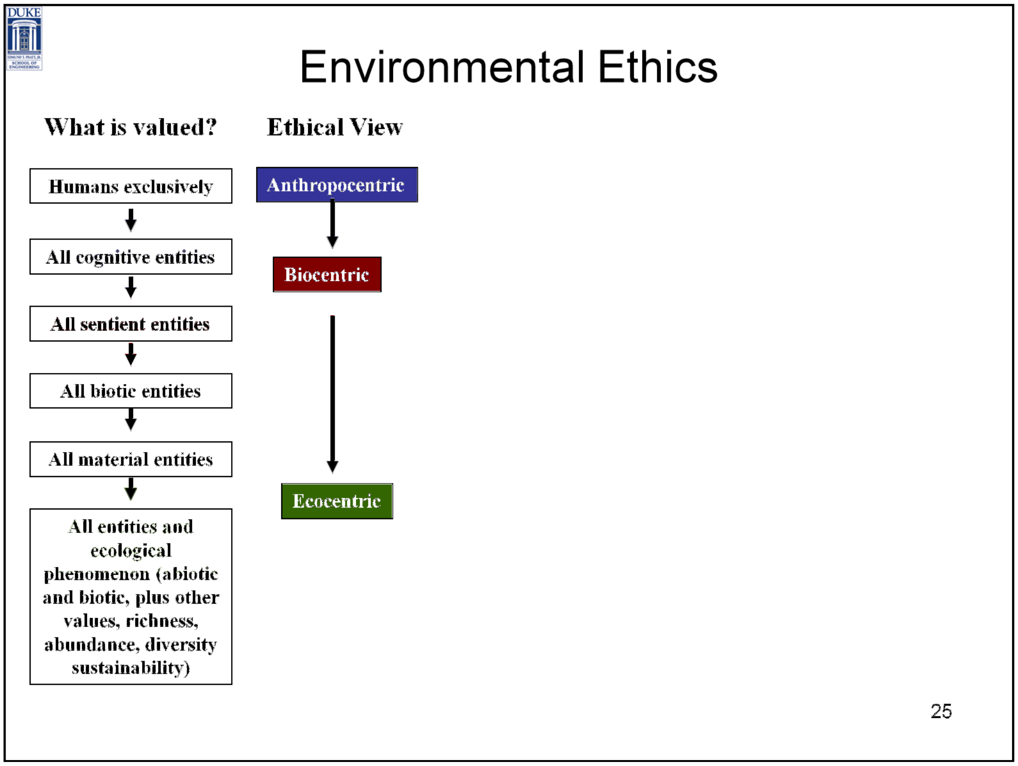
Human-oriented?

Environmental Ethics

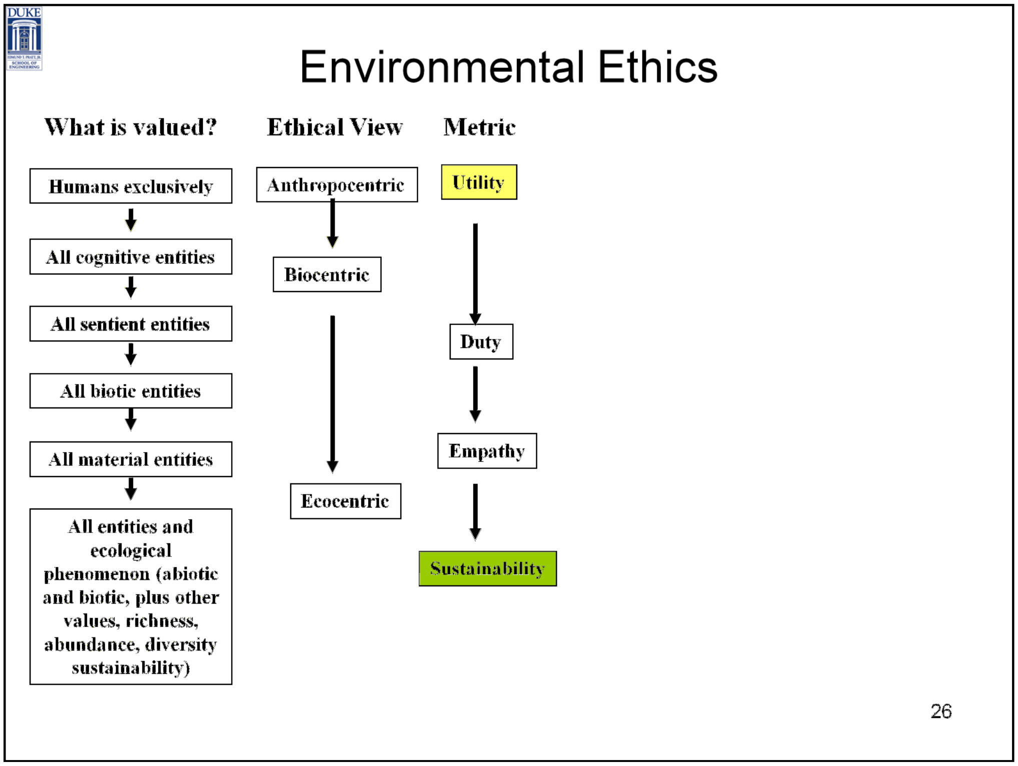
What is valued?	Ethical View
Humans exclusively	**Anthropocentric**
↓	↓
All cognitive entities	**Biocentric**
↓	
All sentient entities	
↓	
All biotic entities	
↓	
All material entities	
↓	
All entities and ecological phenomenon (abiotic and biotic, plus other values, richness, abundance, diversity sustainability)	

24

Organism-oriented?



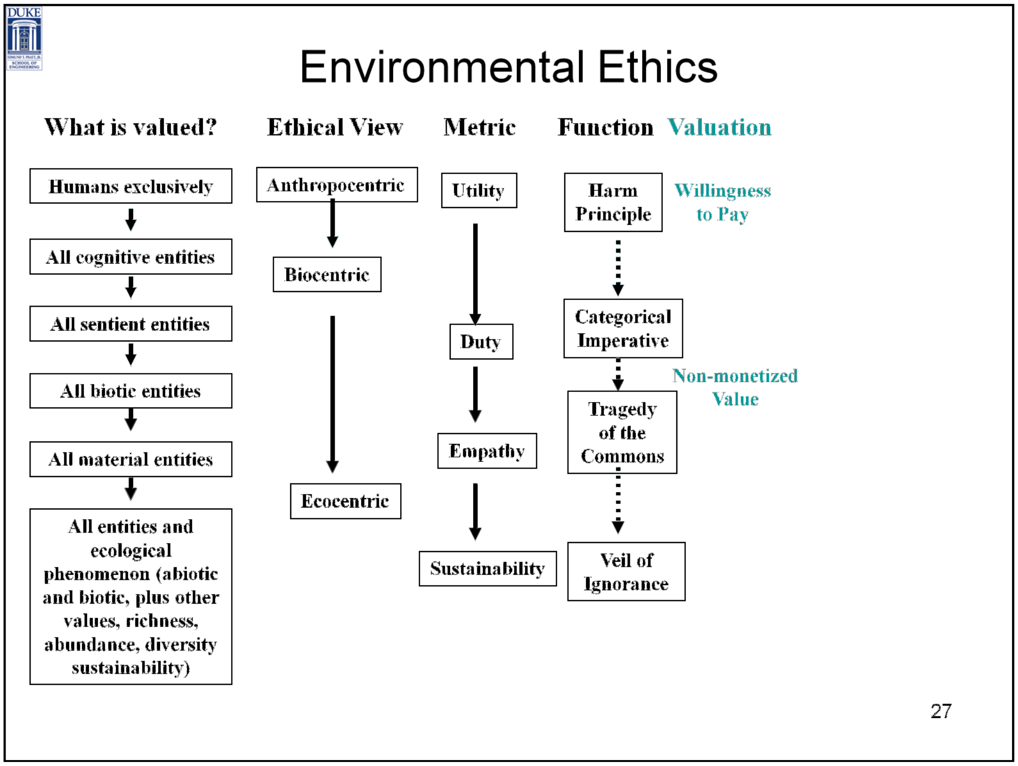
Or, ecosystem-oriented?



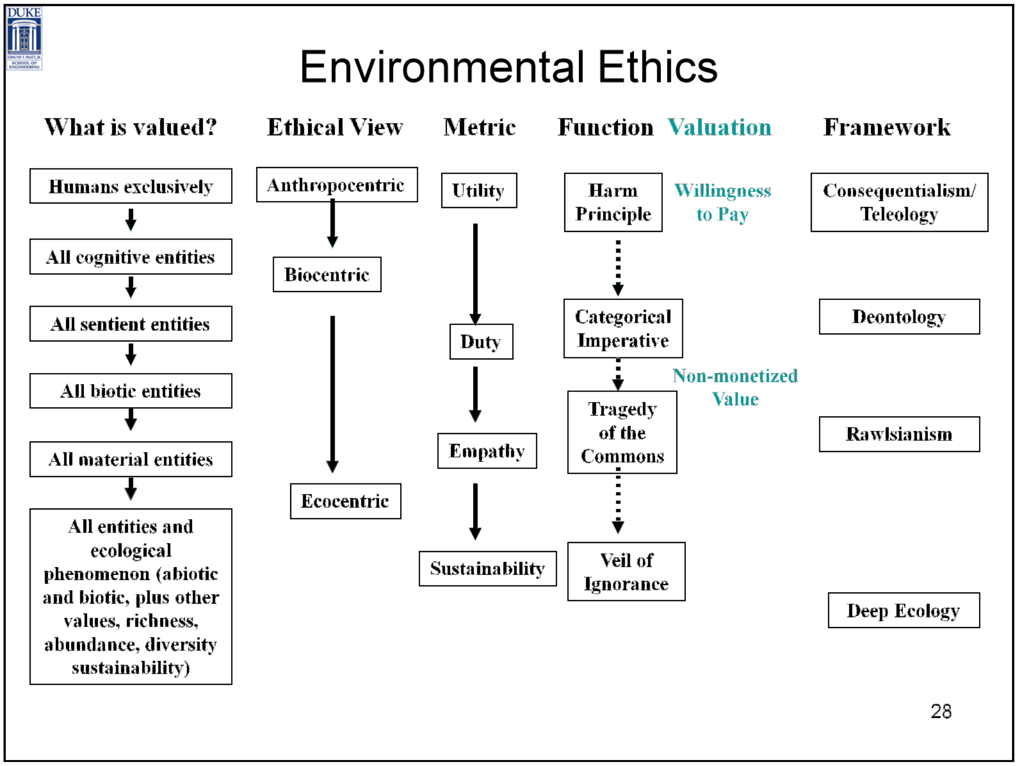
Often, if humans are the exclusive concern, then utility (use of the resource) is the metric. However, such a utilitarian view may not be supportable when the metric is something other than the “greatest good for greatest number….”

Empathy is a very useful metric, whether just for humans or for other sentient animals.

Sustainability tracks with a systems (e.g. life cycle perspective).



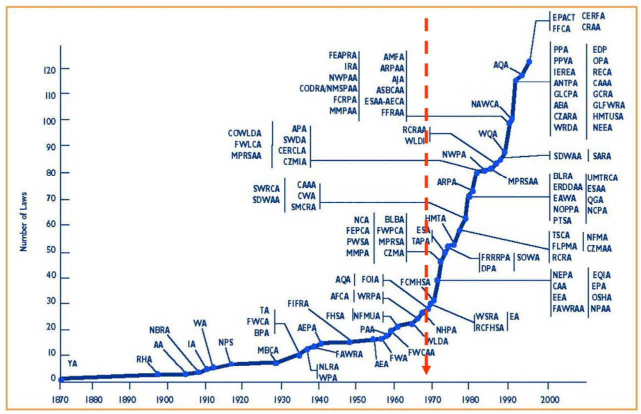
Each of the systems has a commensurate function or credo.



The danger of deep ecology is that it can be used to diminish value of individuals (the person) compared to some “systematic” value. People should never be used as objects.

Environmental Legislation

Sea change
•Sources
•Ambient



(From D. Allen & D. Shonnard, *Green Engineering*, Prentice-Hall, 2002)

29

This slide indicates the exponential growth of environmental legislation over the past few decades. These laws apply to all media, e.g. air, water, soil…

Factors increasing perceived risk:

(after Covello, 1992)

1. Possible Severely Negative or Catastrophic Outcome
2. Unfamiliarity with Situation and Potential Risks
3. Inability to Explain Processes and Mechanism
4. Little Certainty in the Science and Engineering
5. Perception of Personal Control
6. Involuntary Exposures to Risks
7. Risk to Children and Sensitive Groups
8. Long-term Exposures, Latency Periods, Chronic Risk
9. Possible Transgenerational Exposures and Risks
10. Uncertainty about Potential Victims

30

These factors were drawn from the nuclear power industry -- V. Covello (1992). Risk comparisons and risk communications. In *Communicating Risk to the Public*. R.E. Kasperson and P. Stallen (Eds.). Kluwer, New York, NY.

… and the risk is perceived to increase even more when …

- Greater “dread”
  - Major problem for nuclear power industry
- Mistrust of corporate or governmental partners
  - Guilt by association
- Negative media attention
- A history of accidents and failures at this site or in similar situations
- Benefits are not clear
- Mistakes are irreversible
  - Global climate change, for example

So, then what is risk, really?

- Definition: Probability of harm or loss
- Part of our everyday lives
  - Different for each of us
  - Basis for decision-making
- But is it *quantifiable*?

32

Risk is a very common term, but what does it really mean and how does it apply to ethical decision making.

… depends on how you ask but,…

- **Yes it is quantifiable:**
  - ✓**Risk = *f*(Hazard x Exposure)**
- **A probability, a fraction**
- **Part of our everyday lives**
  - **Different for each of us**
  - **Basis for decision-making**

33

Risk Assessment Defined:

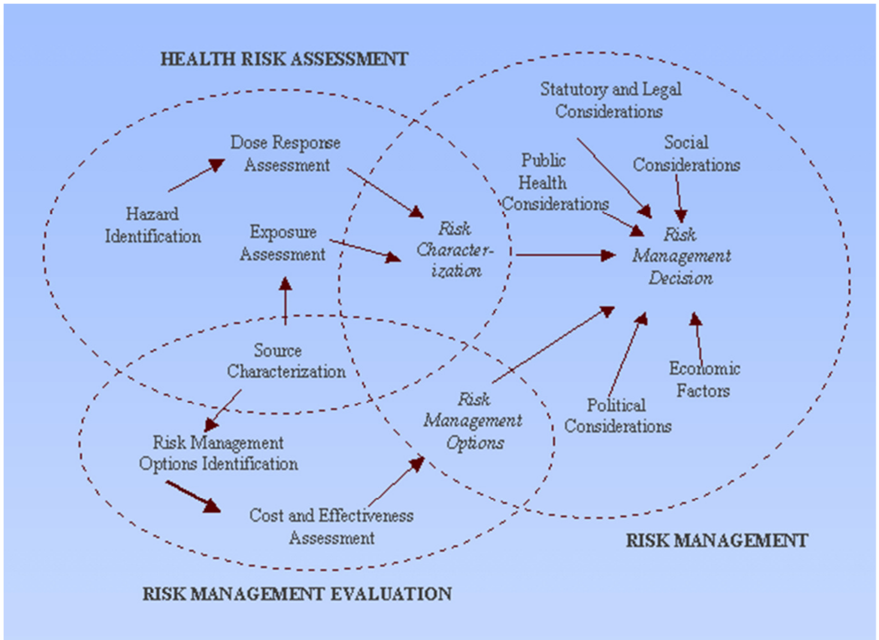
Risk assessment is a process where information is analyzed to determine if an environmental hazard might cause harm to exposed persons and ecosystems.

Paraphrased from the "**Risk Assessment in the Federal Government"** (National Research Council, 1983)

34

This has actually become the standard, but is slowly changing (e.g. the National Academy of Engineering recently released its *Science and Decisions…).*

Risk assessment…



35

Here is a risk assessment paradigm used in U.S. environmental regulatory agencies.

Different Processes at Work: Not everyone thinks like you do….*

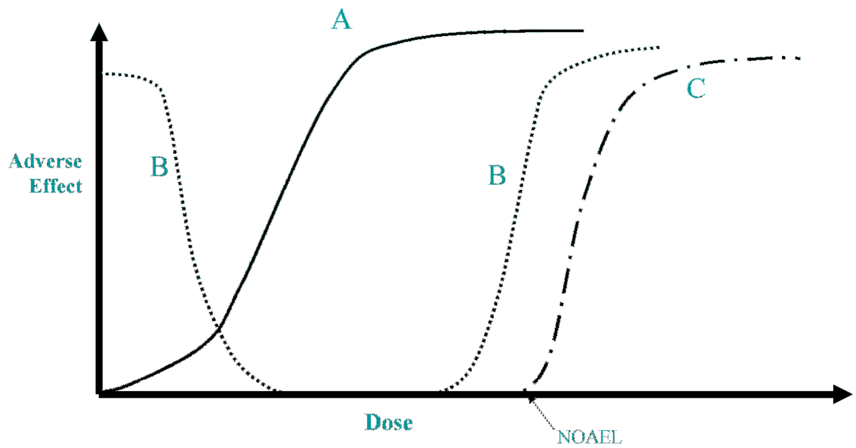
Analytical Phase	Risk Assessment Processes	Risk Perception Processes
Identifying risk	Physical, chemical, and biological monitoring and measuring of the event	Personal awareness
	Deductive reasoning	Intuition
	Statistical inference	
Estimating risk	Magnitude, frequency and duration calculations	Personal experience
	Cost estimation and damage assessment	Intangible losses and non-monetized valuation
	Economic costs	
Evaluating risk	Cost/benefit analysis	Personality factors
	Community policy analysis	Individual action

*Adapted from K. Smith, 1992

36

Most people do not think like scientists and engineers. And even within the scientific community, there is much diversity in how to assess risks (e.g. social scientists versus engineers; environmental engineers versus mechanical engineers)

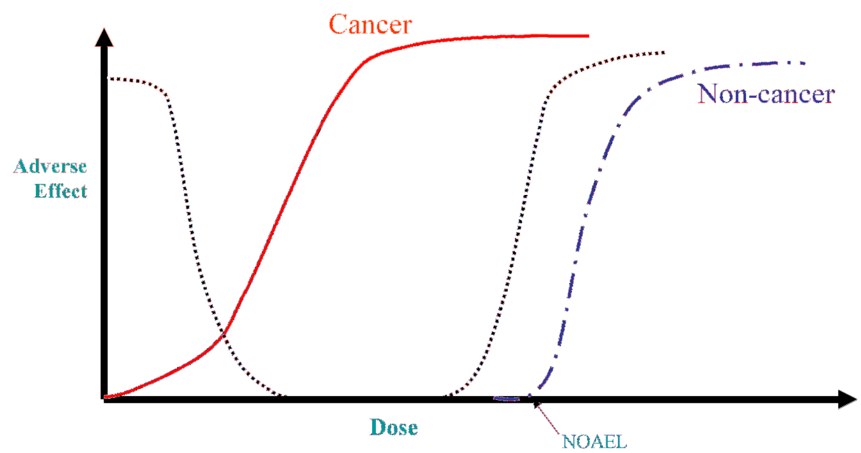
Dose-Response:
A Way to Define a Hazard



37

Quantifying risk depends on a biological gradient (taken from pharmacology).

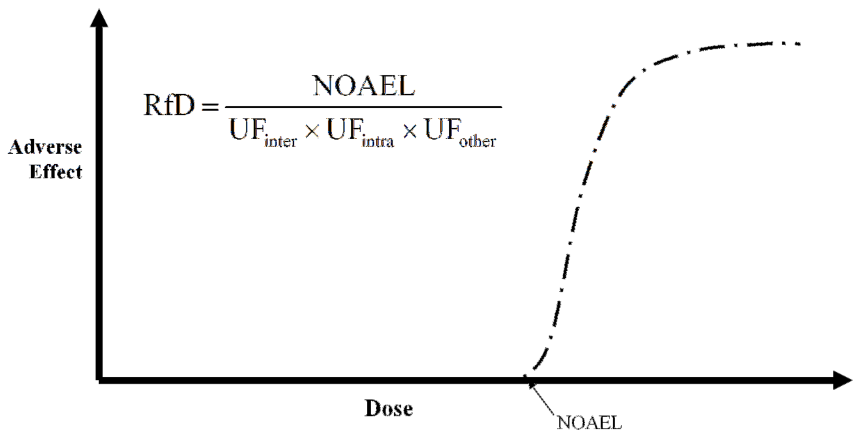
Dose-Response: No threshold for cancer



38

Harm can be a social phenomenon (at least, its existence is determined through a social lens). In this case, the curve for cancer is forced through zero dose. Thus, one molecule can cause cancer (unlikely, but that is a policy).

Dose-Response: Safety in Reference Dose

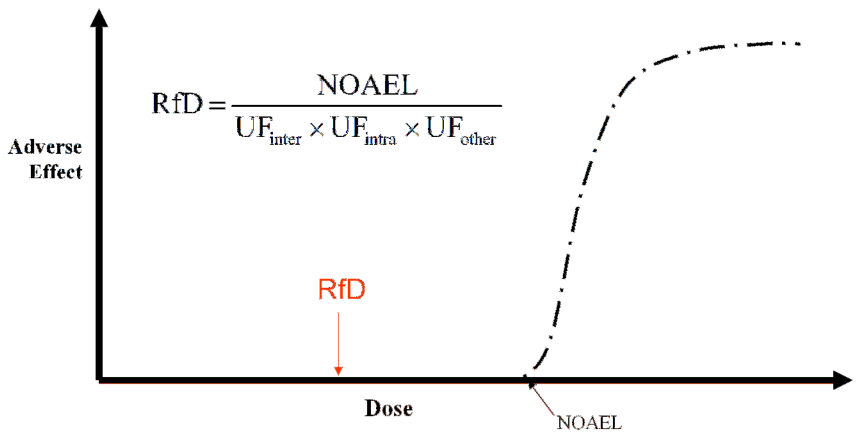


$$RfD = \frac{NOAEL}{UF_{inter} \times UF_{intra} \times UF_{other}}$$

39

RfD is the environmental safety factor, but only applies to non-carcinogens. The "no observable adverse effect level" (NOAEL) is usually derived from animal studies. Note that uncertainty can come from the research – e.g. the inter- and intra-species uncertainty factors. UF_{inter} factors in the differences in sensitivity of the test animals and humans, whereas UF_{intra} represents the differences in sensitivity for certain groups of humans (e.g. children, immunocompromised, elderly). Other uncertainties (UF_{other}) may result from different study designs or the data, e.g. if a NOAEL is not established, then the threshold may be estimated from the lowest observed adverse effect level (LOAEL).

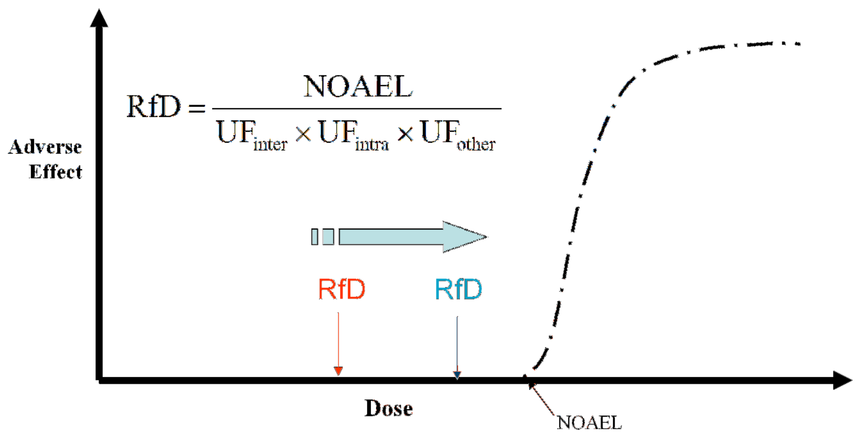
Dose-Response: Safety in Reference Dose



40

The RfD is designed to provide a margin of safety (note that uncertainty factors are included in the denominator so increasing uncertainty means a lower acceptable concentrations. With much uncertainty, the RfD approaches 0. An RfD of zero means there is no safe dose.

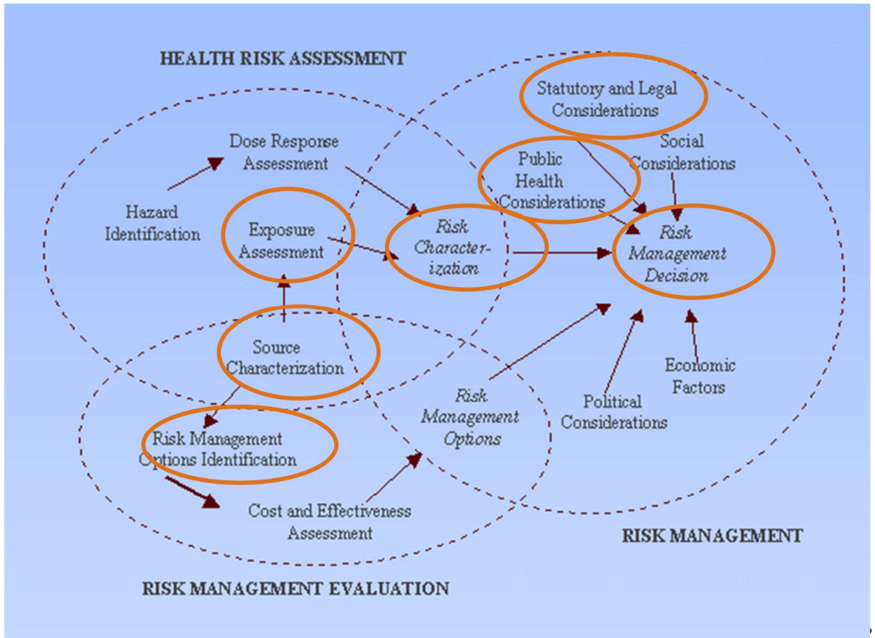
Improved Certainty from Better Measurements



41

Sometimes, improved and greater amounts of data show that RfD has been too protective.

Exposure …



The dose-response and RfD are inherent to the hazard (e.g. toxicity). The other half of the risk equation is exposure. The highlighted areas show where engineers can reduce exposures, thus help to manage risks.

Calculating Exposures: Amount of Hazard Reaching Us

$$E = \int_{t=t_1}^{t=t_2} C(t)\,dt$$

Where,

E **= personal exposure during time period from t_1 to t_2**

C(t) = concentration at interface, at t.

43

There is not a complete consensus, and many disagree with this equation of exposure, but it does indicate that exposure is a function of time. In this instance, exposure is integration of the concentration of a substance with respect to time. So, the longer one is exposed and the higher the dose, the greater the exposure.

Exposure bridges the physical and social sciences

Chemistry & Physics

$$E = \int_{t=t_1}^{t=t_2} C(t)\, dt$$

Psychology & Sociology

Where,

E = personal exposure during time period from t_1 to t_2

$C(t)$ = concentration at interface, at t.

44

This equation is also a convenient way to show that engineers may have to leave their traditional comfort zones to address risk. Most engineers are less comfortable with the social sciences, but estimating exposures means knowing where people are, how long they spend in these locations and maybe even why they do so (e.g. most of the time, people stay indoors – but this varies by season, by age and other demographics and even by culture). Also, general rules can be dangerous. For example, applying potential exposures from mean U.S. household activities, such as cleaning, may be completely inapplicable to maquiladora communities on the U.S.-Mexican border. In this instance, the floors were swept frequently, but they are sometimes only dirt floors. So, the "cleaning" would actually increase exposure to soil-laden contaminants.

Discussion Questions

- What principles of research ethics are conflicting in this example?
- Is there more information you need to help you resolve this conflict?
- How should this conflict be resolved?

45

Back to the L'Acide case: Does any of this risk information change the answers that each group suggested after reading the cases?

It's a matter of trust….

- This is a commodity that can be lost easily but regained with much difficulty….
- Numerous examples of loss of trust in sciences….

46

<u>Bottom line</u>: The currency of engineering is trust; trust from the public, trust from the client, and trust in ourselves.

An 6-step approach to ethical decision making (from Resnik)

1. State or define the problem/issue
2. Gather information
3. Delineate options.
4. Apply different values, rules, principles, regulations to the different options.
5. Resolve conflicts among values, rules, etc.
6. Make a decision and act

47

David Resnik of the National Institute of Environmental Health Sciences shared these steps with Duke in a keynote at our RCR orientation (August 2008 and August 2009). A key point is that not making a decision is indeed a decision and not acting is an act! So, a fact-based, moral decision is preferred. This follows the logical instrument, the syllogism:

- Fact-based premise
- Fact-value premise (link between facts and moral imperatives)
- Evaluative premise
- Moral conclusion

A few final words…

- Do you agree with the risk paradigm?
- Should it be evidence based?
- How about the precautionary principle?

48

The precautionary principle is more widely applied in Europe's regulatory community than in the U.S. It states that if the potential for widespread, irreversible negative consequences can result, then such an action should be prohibited (e.g. a drug, chemical should be kept off the market). This can be good, but can also present opportunity costs, such as not approving a drug that may be efficacious in treating diseases, e.g. cancer drugs.

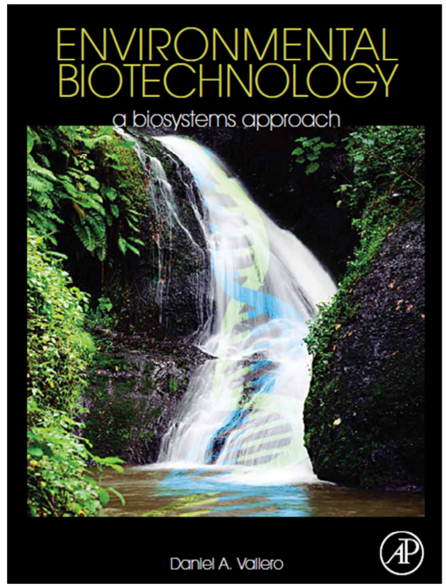
The Greek is roughly translated as "skill of character."

The Latin is roughly translated as "let the client trust."

All engineering codes of ethics include requirements of both character ("hold paramount the safety, health and welfare of the public) and competence (e.g. conduct within one's own area of expertise and be a faithful agent).

If you have questions, contact me….

- dav1@duke.edu
- 919-541-3306



50

If you would like to adapt this presentation or the cases, please contact:

Daniel A. Vallero, Ph.D.
Adjunct Professor of Engineering Ethics
Pratt School of Engineering
Duke University

Phone: 919-660-5200
Fax: 919-660-5219
Website: http://www.cee.duke.edu/faculty/vallero/index.php