Omics and the Precautionary Principle

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May 28, 2008

Disclosure of My Biases

- I am an American
- Lawyer
- Who is a strong proponent of the "rule of law":
  - "the establishment and fair enforcement of an ordered set of rules to guide human conduct in a transparent, consistent, and predictable manner"

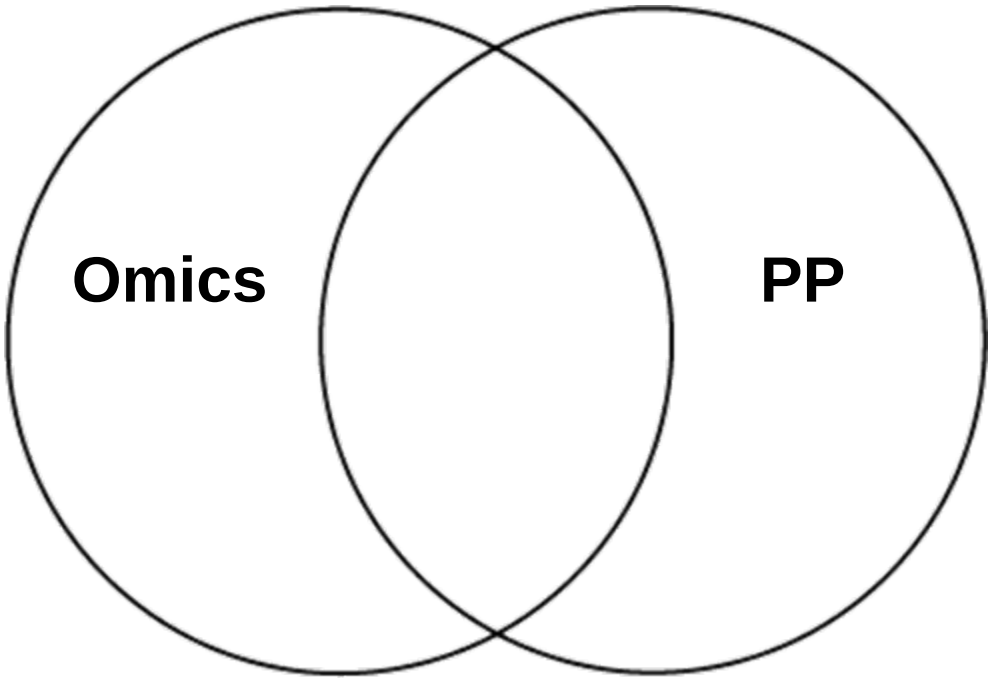
RF and Omics

- As we have seen at this workshop, high throughput toxicogenomic approaches can provide new data on potential health effects of RF:
  - More sensitive, earlier biomarkers of toxicity?
  - Insight on toxicological pathways/ mechanisms?
  - Existence and mode of action of individual hypersenitivity to RF?

RF and the PP

- UK Independent Expert Group on Mobile Phones ("Stewart Report")
  - recommended "precautionary approach" (e.g., restrictions on use by children)
- Some countries (e.g., Switzerland, Italy, Belgium) have reduced allowable exposure levels based on PP
- Concerns/litigation over mobile base stations near schools in UK and elsewhere in which PP plays central role
- WHO (2000) – issued position paper arguing against application of PP to EMF/RF

RF: Intersection of Omics and PP



Intersection creates challenges for both Omics and the Precautionary Principle

Challenge to Omics from the Precautionary Principle

- Omics will produce many findings of unknown significance
  1. some findings likely innocuous
  2. some findings likely represent real risk
  - Problem: often can't distinguish (1) v. (2)
- PP *might* require treating many or all findings of uncertain significance as (2) (i.e., real risk)
  - Omics then may result in over-regulation of many products, creating potential for backlash and resistance to omics

Challenge to Precautionary Principle from Omics

- PP construed to err on side of safety and (sometimes?) treat uncertain results as evidence of real risk until disproved
- Omics likely to generate some uncertain results for virtually any product tested
  - Strict version of PP may thus require restrictions (bans?) on all such products, discrediting the PP
  - To avoid such absurd results, PP must be moderated in some principled and yet-to-be defined way

Precautionary Principle: Key Elements

- Underlying concepts:
  - Better safe than sorry
  - Prevent harm before it occurs
  - Absence of evidence is not evidence of absence
- Put burden of proof on proponent of technology/ product

Examples of Overlooked Risks (False Negatives)

- Products once thought safe:
  - asbestos
  - chlorofluorocarbons (CFCs)
  - leaded gasoline
  - MTBE
  - DES
  - beef/mad cow disease
- But also consider:
  - saccharin
  - Bendectin
  - Swine flu
  - recombinant DNA
  - silicone breast implants
  - “ice minus” bacteria
  - MMR vaccine
  - coffee!
  - chocolate!!

The Proliferation of the Precautionary Principle

- Incorporated into more than 60 international environmental treaties
- Included in 1992 Maastricht amendments to European Treaty
- Incorporated into national laws of many countries (e.g., most EU nations, Australia, Canada)
- Being applied as binding law by some courts (e.g., Australia, New Zealand, India, Brazil)
- Recently adopted by some U.S. cities (San Francisco, Seattle)

Problem 1: No Standard Version of the Precautionary Principle

- There is no standard text of the precautionary principle
- Treaties, regulators, and courts apply “the” precautionary principle without specifying which version they are using
- Over 50 different formulations have been collected; subtle differences in wording have significant policy consequences

Dimensions of Precautionary Principle

Threat Dimension	*Uncertainty Dimension*	*Action Dimension*	*Command Dimension*
potentially dangerous actions	in some way uncertain	action to protect the environment	is mandatory
possible risks	unusually short on scientific understanding	measures to prevent environmental degradation	should be taken
identified risk	scientific evidence is not conclusive	limit, regulate or prevent	is required
non-negligible harm	some cause and effect relationships are not fully established scientifically	regulatory action/regulatory inaction	is a premium on
activity raising threats to the environment or human health	strong scientific evidence on causal relationships or the extent of the damage is missing	regulatory measures	is justified
in some way non-negligible environmental risks being run by not regulating	lack of scientific proof of cause and effect	cautious and conservative approach to human interventions	may be required
significant risks of damage to the environment	lack of scientific certainty on the cause and effect relationships	precautionary measures	not acting is not justified
threats of serious or irreversible damage	lack of full scientific certainty	precautionary action to limit the use of potentially dangerous materials or the spread of potentially dangerous pollutants	may be justified
human interventions in environmental sectors that are unusually susceptible to significant injury, especially irreversible injury	before full scientific proof is established	cost-effective measures to prevent environmental degradation	[uncertainty] shall not be used as an argument for postponement
	before a causal link has been established by absolutely clear scientific evidence		[the Government] will be prepared to act if the balances of likely costs and benefits justifies it

Source: Sandin 1999

Rio Declaration (1992) (weak version?)

- “Where there are threats of serious and irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.”

Wingspread Statement (1999) (strong version?)

- “When an activity raises threats of harms to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically.”

World Charter for Nature (1982) (absolute version?)

- “Where potential adverse effects are not fully understood, the activities should not proceed.”
- See also Greenpeace position:
  - “Do not emit a substance unless you have proof it will not do harm to the environment”

Problem 2: Ambiguity of the Precautionary Principle

- For any given version of the PP:
  - How substantial must the potential risk be?
    - Serious and/or irreversible? Or any risk?
  - What level of risk is acceptable?
  - What early indications of potential hazard needed to trigger precaution?
  - How much data must proponent produce to demonstrate “safe”?
  - How are costs and risk-risk tradeoffs factored in?

What Precautionary Actions Required?

- Ban?
- Moratorium?
- Partial ban (specific uses)
  - e.g., children/cell phones
- Product design requirements
  - e.g., limits on power
- Labeling?
- Public education?
- More research?

What is the Precautionary Principle?

- Decision rule?
- Binding legal requirement?
- Ethical principle?
- General guidance?
- General philosophical approach?

EU Commission Communication (2000)

- Sought to provide more guidance on PP:
  - Proportionality
  - Nondiscrimination
  - Consistency
  - Risk management tool
  - Based on risk assessment
  - Need cost-benefit balancing
  - Provisional
- But:
  - many questions not answered
  - many PP proponents vehemently disagreed

The Precautionary Principle: Intentionally Ambiguous?

- "Paradoxically, we conclude that the application of precaution will remain politically potent so long as it continues to be tantalizing ill-defined and imperfectly translatable into codes of conduct, while capturing the emotions of misgiving and guilt. … [I]t is neither a well-defined nor a stable concept. Rather, it is has become the repository for a jumble of adventurous beliefs that challenge the status quo of political power, ideology, and environmental rights." Jordan & O'Riordan (1999)

Some Examples of Arbitrary Applications of PP?

- Netherlands and Norway banned Kellogg's Corn Flakes
- France banned “Red Bull” caffeinated beverages
- Denmark banned Ocean Spray Cranberry drinks
- EU Directive on worker exposure to physical agents (electromagnetic fields) that will restrict MRI use
- Support for EU subsidization of coal-mining industry
- Zambia rejection of US food aid that may genetically-modified corn

Problem 3: Precautionary Paradox

- Many technologies present both potential health & environmental benefits and risks
  - It is unclear whether the PP would prohibit or require such technologies
  - PP might suggest that the PP is itself not prudent
- Application of PP may increase rather than decrease public anxiety about a technology (Wiedemann & Schutz, 2005)
- Political sustainability if too many “false positives”
  - “cry wolf” problem

The "precautionary principle", properly applied, forbids the precautionary principle.

Michael Crichton in *State of Fear*, 2004

Courtesy of Chris Portier

Absolute Version of the PP and Genomics

- No product allowed unless proven save
- Irrelevant to RF?
  - Not possible to “prove” safety with or without genomic data?
    - How would a manufacturer prove safety?
      - Complete safety (impossible)?
      - defined test battery?
- Omics may be nail in coffin for absolute PP
  - may not be politically, economically or legally sustainable

Traditional Toxicological Response to Omics (Weak version of PP?)

- Recognize some precaution necessary
- Balances need for precaution with danger of over-protectiveness
- Two possible approaches:
  - Phenotypic anchoring
  - Weight of evidence

U.S. National Academy of Sciences (2007)

- "[A] critical issue in the regulatory application of toxicogenomics will be determining whether and when a change constitutes an adverse effect. Many changes in gene expression, protein levels, and metabolite profiles will be adaptive responses to a stimulus that are not representative or predictive of a toxic response. Other toxicogenomic changes may be strongly indicative of a toxic response. Therefore, it will be important to distinguish true biomarkers of toxicity from reversible or adaptive responses and to do so in a way that is transparent, predictable, and consistent for the affected entities …. ***At least initially, phenotypic anchoring of toxicogenomic changes to well-established toxicologic end points will likely be necessary to identify toxicologically significant markers."***

  - NRC, Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment, p. 187

EPA Interim Policy on Genomics (June 2002)

- Genomic data can be used “to explore the possible link between exposure, mechanism(s) of action, and adverse effects” of toxic substances
- May also be useful to EPA “in setting priorities, in ranking of chemicals for further testing, and in supporting possible regulatory actions.”
- “EPA will consider genomics information on a case-by-case basis.”
- Genomic data *alone* are “insufficient as a basis for decisions” at present time

“Strong” Version of the PP and Omics

- This version requires precautionary action beyond that appropriate under traditional toxicological response
- Ambiguities of PP really impact hard here

Example of Strong Version: Environmental Defense Fund

- “tying the interpretation of toxicogenomics testing so strictly to traditional toxicity tests would keep this promise from being realized because information gained could be no more comprehensive than current test methods. Such scientific shackling of toxicogenomics approaches must be prevented if the new technologies are going to provide their maximal benefits.”
  - John Balbus, EHP 113:818-822 (2005)

Strong version of PP and Omics

Tox Data	Omic Data	Action
Positive	Irrelevant	Precaut. action
Equivocal	Positive	Precaut. action?
	Equivocal	?
	Negative	Do nothing
Negative	Positive	Precaut. action?
	Equivocal	Do nothing?
	Negative	Do nothing

Conclusion (1)

- Intersection of Omics and PP in context of RF presents two converging challenges:
  - Challenge to Omics – how to deal with data of uncertain significance that balances precaution vs. over-reaction
  - Challenge to PP – how to implement “precautionary principle” without making PP either irrelevant or absurd

Conclusion (2)

- Precaution is an appropriate and essential element of policy response to uncertain risks
- Must be balance between Type I and Type II errors
- Must move beyond slogan of “precautionary principle” to develop transparent, predictable, and coherent guidelines for implementing PP
  - PP may be too vague at this time to provide meaningful role in applying omic data
  - PP may be refractory to further specification

Conclusion (3)

- *There is always an easy solution to every human problem -- neat, plausible, and wrong.*

  - H. L. Mencken (1880-1956)