

A risk perspective on Roger Cooke's
“Uncertainty Quantification ...”

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Workshop on Uncertainty Modeling
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Uncertainty, Uncertainty in Context, and Uncertainty with Specifications I

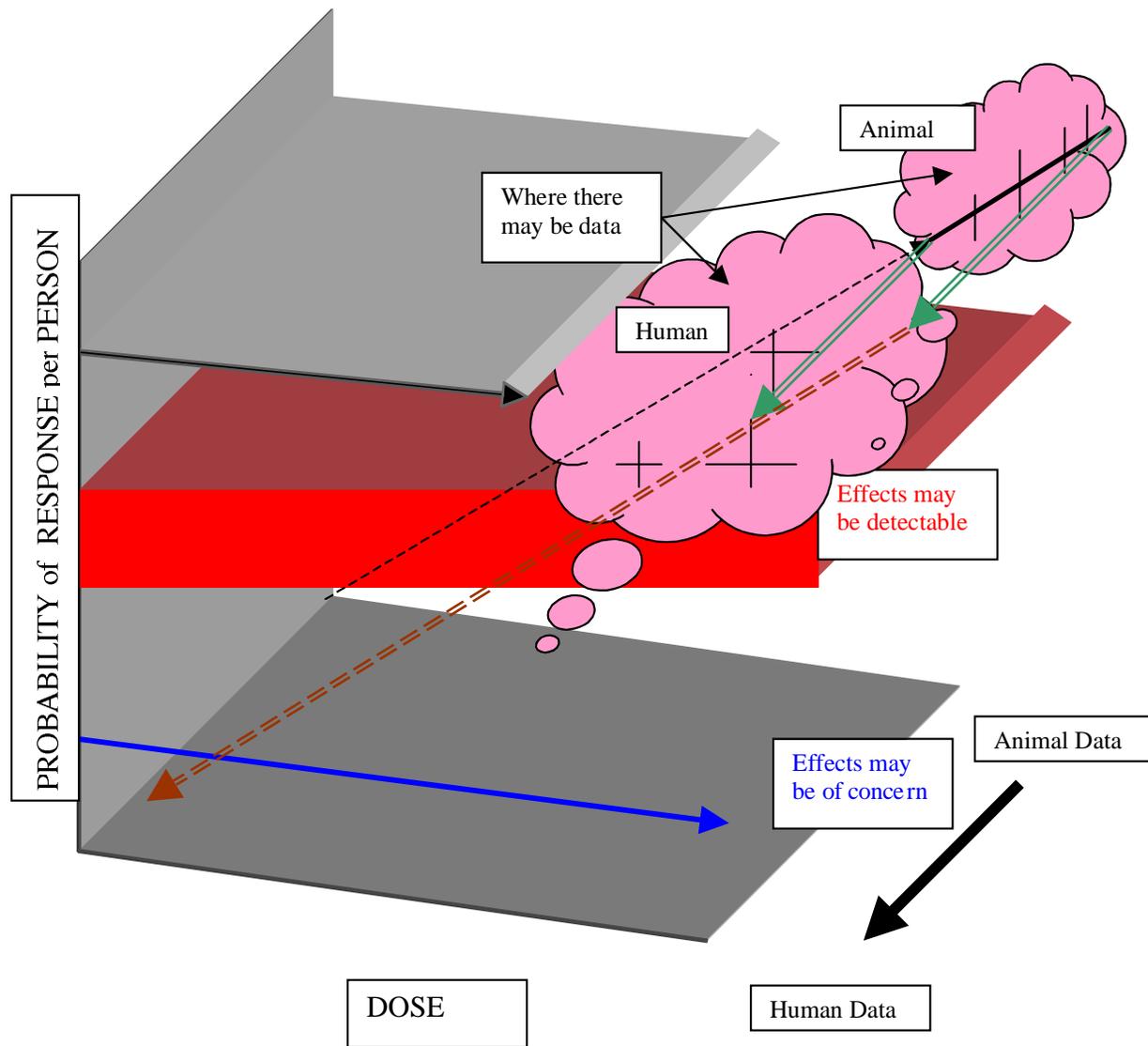
- **Regulatory Context**
 - Concern is with uncertainty in (extrapolated) risks at relevant (low) doses
 - Need clarity/transparency/defendability of risk and uncertainty estimates
 - Need to be responsible, neither too fearful or too complacent

Uncertainty, Uncertainty in Context, and Uncertainty with Specifications II

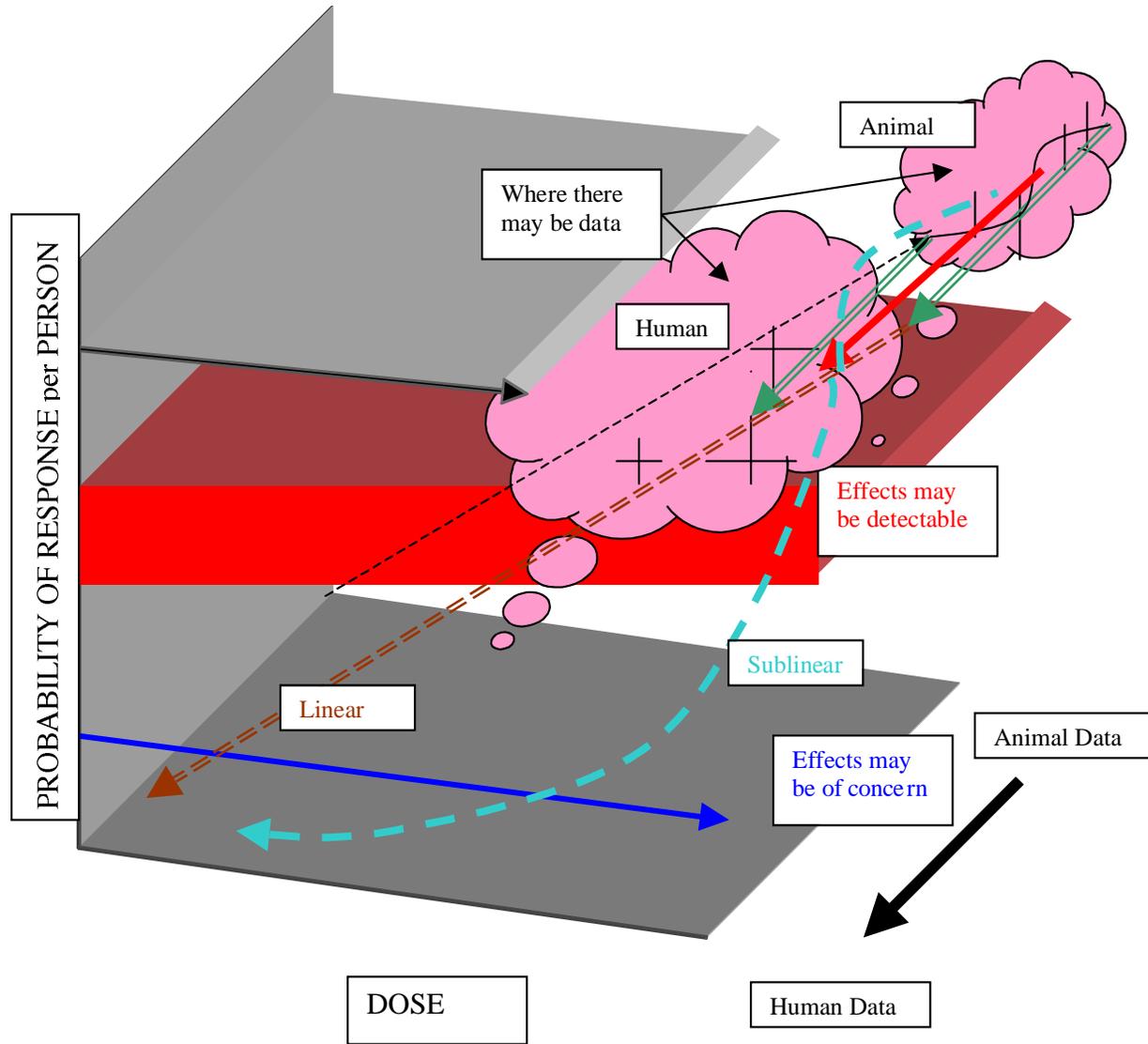
- Risk Analytic Context
 - Support regulators/clients/intervenors
 - Good methods which are transparent and address relevant (low dose) risks
 - Vigilance concerning new phenonema, potential problems, and misconceptions
 - Generate new and relevant knowledge - including moderating between toxicologists and statisticians

Themes from Cooke's Paper

- Starting point: specification of “observable uncertainty”
- Key observation: “Observable uncertainty” not the same as what is generated by “Statistics as usual”
- 2nd key observation: Probability inversion provides a method for fitting D/R reflecting “observable uncertainty”



Extrapolations



Extrapolations - Continued

Some lurking issues

- Regarding the “tent poles”
 - Is “observational uncertainty” informative for extrapolation?
 - We should note that certain other “observational uncertainties” e.g. detection in the assays are not simply binomial
 - How informative is the “isotonic” restriction? - the relationship with background is critical here
- Not much attention was paid to the presented questions about combining data - can these methods help?
- More generally, choices of D/R relationships affect what quantities are important for extrapolation and what uncertainties matter

Questions posed from a risk/regulatory perspective: each has “unanswered” uncertainty

- Is there an effect?
- What is a favored D/R model
 - How good is the evidence for it?
 - What are plausible alternative choices? And their relationship to the evidence
- What are human risks at relevant (low dose) exposures?
- What is the role of background?
- What is the full package of information that we bring to bear on these questions?
- Can toxicologists and statisticians communicate better?