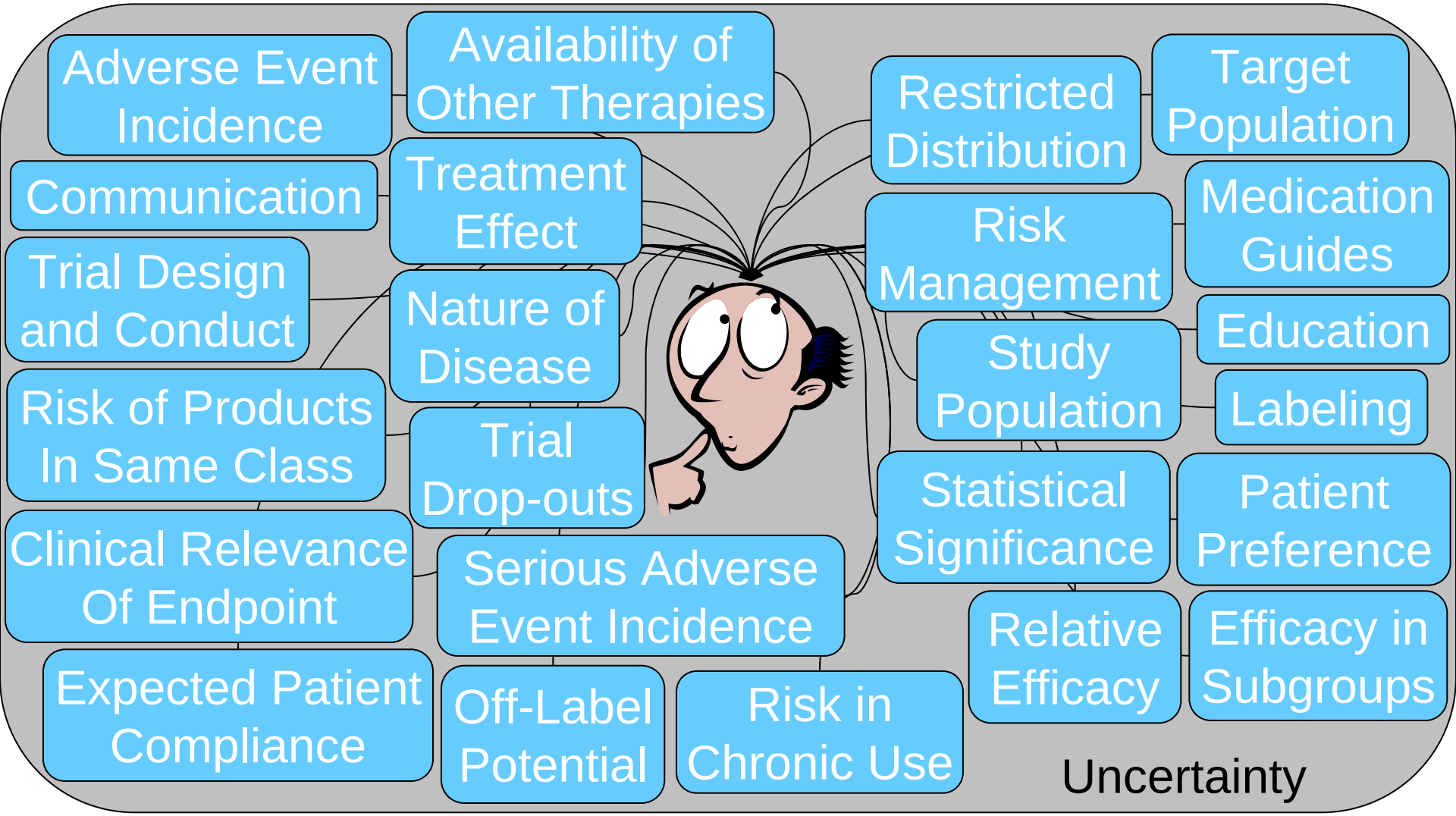
A United States Regulator's Perspective on Risk-Benefit Considerations

John Jenkins, M.D.
Director, Office of New Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
April 23, 2010

Benefit/Risk Assessments

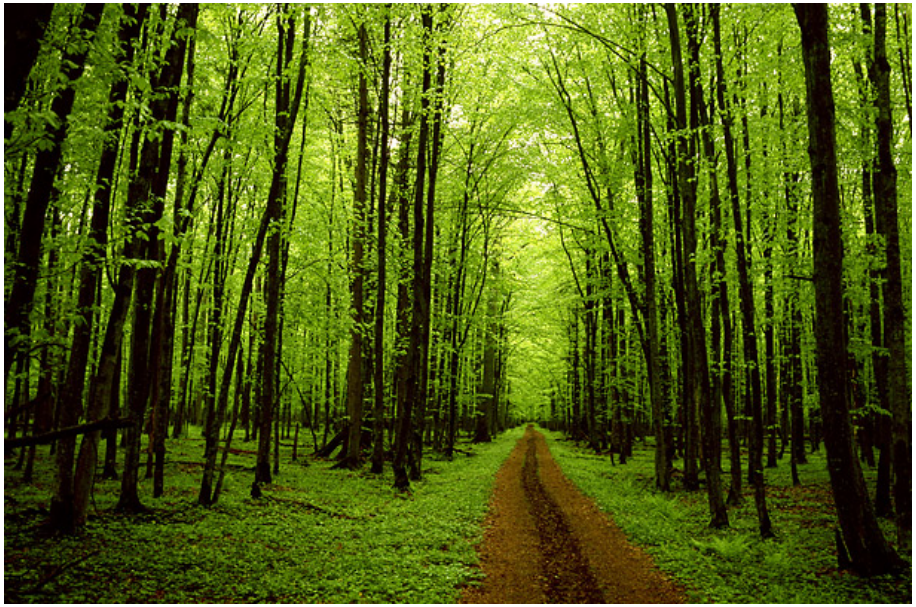
- Assessment of B/R is a qualitative approach that is grounded in quantification of various data elements
  - Benefits – Efficacy endpoints from controlled clinical trials
  - Risks – Harms reported in clinical trials and other sources (e.g., spontaneous adverse event reports)
- Evaluation of B/R is dynamic
  - Knowledge of benefits and risks evolves over product life-cycle
- Decisions on B/R require judgment on the part of the regulator and are influenced by:
  - Statutory/regulatory standards
  - Societal expectations
  - Personal values and perspectives

What's On The Regulator's Mind?



What Might Help a Regulator?

…a framework that moves them from here:



What Might Help a Regulator?

…to here:

Desirable Properties

- Simple and user-friendly
- Address critical issues
- Capture expert views faithfully
- Represent transparently
- Compatible with quantitative analysis of clinical benefit and safety information
- Facilitate communications (internal and external)
- Broadly applicable

Potential Qualitative Framework

Consideration	Favorable Benefit-Risk	Non-Contributory	Unfavorable Benefit-Risk
Severity of Condition			
Unmet Medical Need			
Clinical Benefit			
Risk			
Risk Management			

Framework Attributes

- Simple, not simplistic, design based on mental model approach
- Supports sound expert judgment, not a replacement for it
- Indentifies and respects areas of expert disagreement
- It tells the story:
  - What is the problem?
  - What other potential solutions exist?
  - What is the benefit of proposed solution?
  - What am I worried about?
  - What can I do to mitigate/monitor those concerns?

Value of Framework

- Provides a high-level snapshot – the “big picture” – of the issues relevant to the regulatory decision
- Provides concise bottom-line description of the evidence on each topic and the B-R implications
- Supports more structured discussions of the range of issues involved in B-R assessments
- Could improve predictability and consistency through a standardized structure
- Could function as a living document, able to be updated based on new information

Judgment and B/R

- Science provides data to inform our analyses of B/R, it does not provide the answers – judgment is required
- Regulators make judgments on B/R at the population level
- Doctors and patients must translate the population B/R information to make judgments on an individual patient level

Choice and B/R

- What is the value of having additional choices for treatment of a specific condition?
  - U.S. statutory standard does **not** require that a new therapeutic be superior to available choices, only that it be safe and effective for the intended use
  - This standard implicitly values choices and frames regulatory decision-making

Choice and B/R

- Who should be making the choices on what products are available to doctors and patients
  - Our system requires that regulators decide on what products are approved
  - Our system also assumes that prescribers and patients have a role in decision-making
  - Where to set that balance is influenced by many factors and significantly impact judgments made by regulators both pre-approval and postmarketing

Summary

- Regulatory R/B decision-making is a qualitative science grounded in quantitative data
- Judgment is required in making regulatory R/B decisions and those judgments are influenced by many factors, both extrinsic and intrinsic
- Clearly outlining the available data and how decisions (judgments) were made can improve transparency of the decision-making process

Acknowledgements:

– Patrick Frey, MPP
– Joyce Korvick, M.D.