

A background image showing a cluster of orange, round pills in the upper left corner, with one pill in sharp focus in the lower right corner. The pills are set against a white background with a blue curved border at the top.

Development of a Benefit-Risk Framework

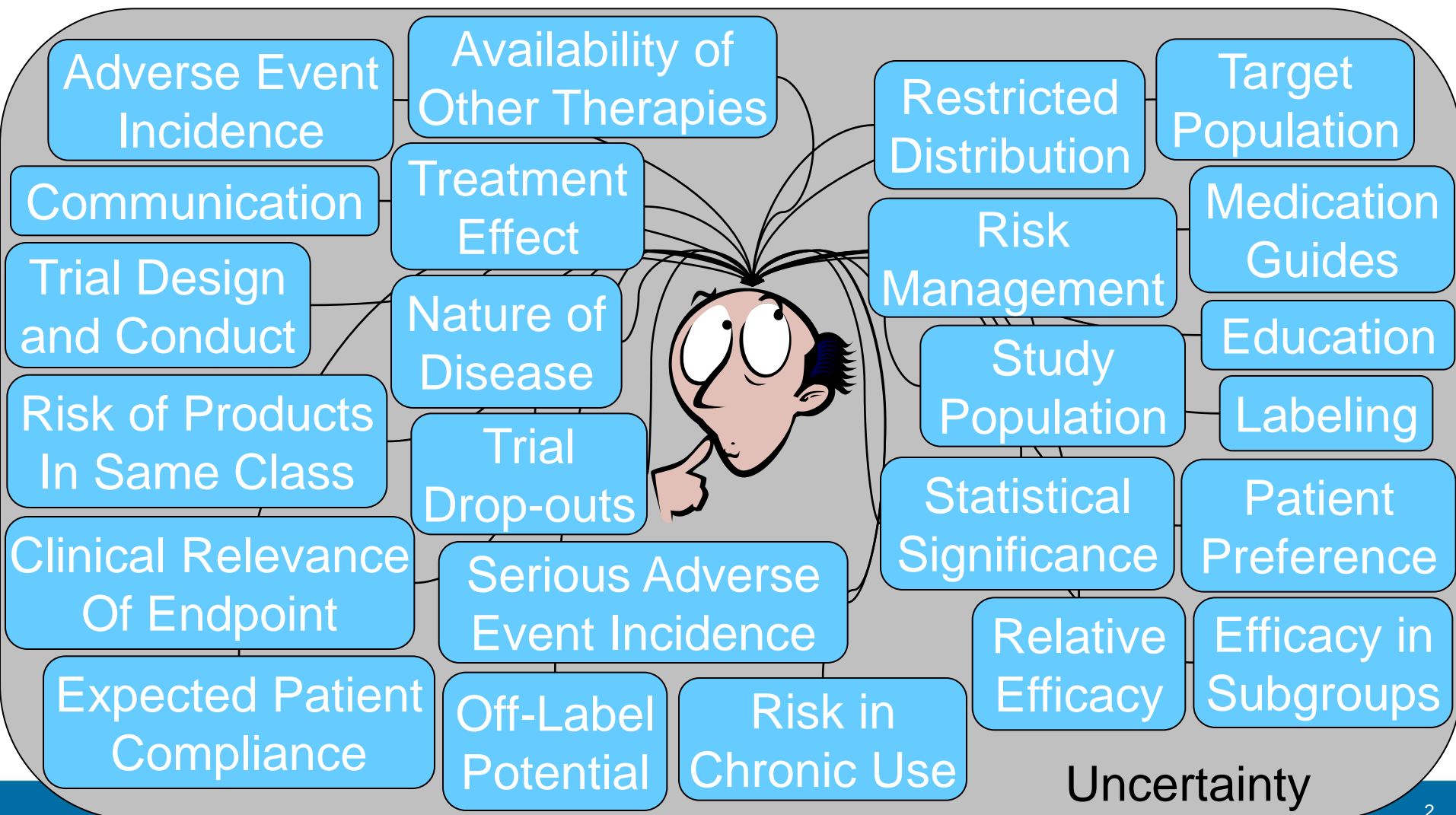
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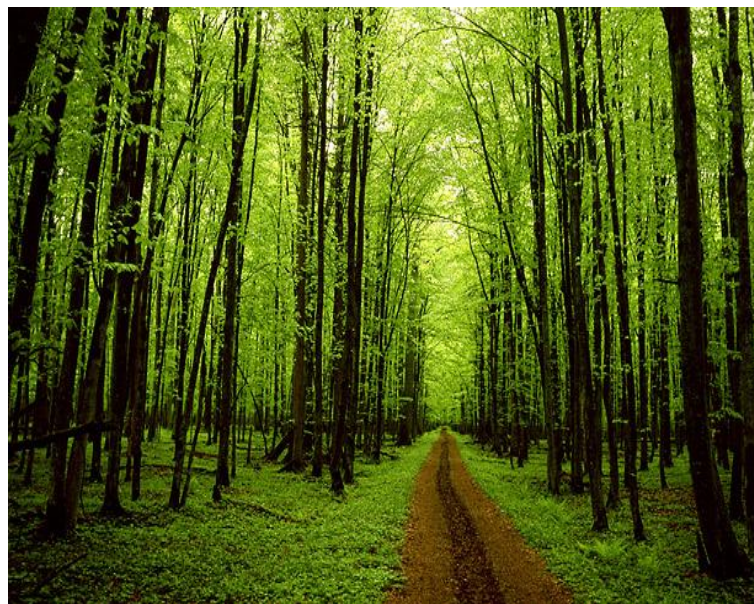
April 13, 2011

What's On The Regulator's Mind?



What Might Help a Regulator?

...a framework that moves them from here:



...to here:



Key Design Principles of a Framework

- Addresses critical B-R considerations, including range of opinion
- Captures expert views faithfully and represent transparently
- Recognizes that B-R assessment is qualitative approach grounded in quantification of certain data
- Consistent with a review team's existing processes
- Recognizes dynamic nature of B-R assessment over the life cycle
- Facilitate communications (internal and external)
- Broadly applicable to the range of regulatory decisions

What was the strategy in developing a framework?

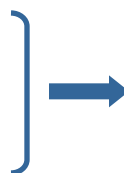
- Use case studies of past regulatory decisions to “tease out” the range of Bs and Rs considered
- Case studies were considered to be more challenging from a B-R perspective
- Develop an analytical framework that can serve as a template for the full range of FDA’s B-R decisions
- Overall process and development guided senior management in CDER

What we've done so far...

- **Develop and test conceptual framework**
 - Individual interview process
 - 6 case studies of prior regulatory actions
- **Additional road-testing and fine-tuning**
 - Focus group process
 - 2 case studies
 - Framework revised as a result (more later)
- **Piloting revised framework**
 - Now beginning to integrate framework in ongoing reviews

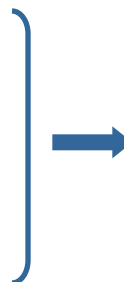
Five “Buckets” of B-R Considerations

- Analysis of Condition
- Unmet Medical Need



Provides regulators with the clinical context for weighing benefits and risks

- Clinical Benefit
- Risk
- Risk Management



Incorporates expert judgments based on evaluation of the efficacy and safety data and the expected impact of efforts to reduce and further characterize risks

Within each bucket, there are two kinds of summary...

- **Evidence and Uncertainties**
 - What you know (facts)
 - What you don't know (uncertainties and underlying assumptions)
- **Conclusions and Reasons**
 - Integration of the facts and uncertainties
 - Drawing conclusions within each key consideration

B-R Framework

Consideration	Evidence and Uncertainties	Conclusions and Reasons
Analysis of Condition	Summary of evidence:	Conclusions (implications for decision):
Unmet Medical Need	Summary of evidence:	Conclusions (implications for decision):
Clinical Benefit	Summary of evidence:	Conclusions (implications for decision):
Risk	Summary of evidence:	Conclusions (implications for decision):
Risk Management	Summary of evidence:	Conclusions (implications for decision):

Some Attributes of the B-R Framework

- Intuitive design based on mental model approach
- Supports, does not replace, sound expert judgment
- Identifies 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
- Ensures a balanced approach in consideration of benefits and risks
- Potential to improve predictability and consistency of decision-making through a standardized structure
- Clearly outlining the available data and articulating the thinking and judgment behind regulatory decisions can improve transparency of the decision-making process