Expanded Access Programs for Drugs and Biologics

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Expanded Access

• Today broad access to information about unapproved experimental new drugs still in development
• Strong desire by patients, families, and their physicians to have access to those drugs without knowledge of the safety or effectiveness of those drugs when faced with desperation or life threatening situations
• Tension between this desire and sponsors ability to provide the drug and the development needs for the entire patient community to determine if the drug is safe and effective
• EAP should be the Option of Last Resort
  – Approved drugs first; Clinical Trials second; then EAP
Barriers to Expanded Access

• Patient and Physician Knowledge of process
  – Regulatory
  – Sponsor

• Sponsor concerns
  – Cost, Manufacturing and drug supply
  – Concern that EA might adversely affect clinical development and the regulatory progress

• IRB process, cost, and knowledge
Do adverse event data from EA really have a negative regulatory effect?

• Adverse events not unexpected in these patients, often related to underlying disease
  – FDA reviewers experienced in discerning adverse events relationships
  – Four decades of experience with only rare examples

• Expedited AE reporting: no special requirements occurring under expanded access INDs
  – Requirement is to report serious unexpected suspected adverse reactions only, not all adverse events or even deaths
  – defined to mean “there is evidence to suggest a causal relationship between the drug and adverse event...”
Could EAPs Negatively Impair Development?

Reporting adverse effects and clinical hold

• A clinical Hold is an order to delay or suspend a proposed clinical investigation or to suspend an ongoing investigation.
• No new subjects may be recruited to the study and placed on the investigational drug; patients already in the study should be taken off therapy involving the investigational drug unless specifically permitted by FDA in the interest of patient safety – includes expanded access programs.
• When human subjects are or would be exposed to an unreasonable and significant risk of illness or injury.
Reporting Adverse Effects and clinical hold

• FDA analyzed its tracking system to determine how often safety findings in an expanded access IND lead to interruption and/or termination of a drug development program (a clinical hold of a commercial developer’s IND)
• Looked at 10 years, from 2005 – 2015
• Found 2 instances, involving death of patients shortly after administration
• Preliminary Data: 10,597 commercial INDs with an active status
  – 8,936 expanded access INDs submitted referencing 368 unique commercial INDs
  – 665 expanded access protocols submitted by sponsors to their commercial INDs
  – The incidence of a commercial drug development program being place on hold was 2 out of 1033 or 0.2%
Does FDA review add value to the process?

- FDA grants over 99% of submissions requesting expanded access, these number about 1000 per year.

- Review of these approvals demonstrates that FDA requests changes to protect the patient in about 11%
  - (not a rubber stamp but an important safeguard in the process)
Navigating a Complex Landscape

• Patient and physician frustration with a complex process
• It takes a village: physician, sponsor, regulator, IRB,
• Knowledge of how to navigate through the process often lacking
  – who to contact both at the sponsor level, regulatory level, or IRB level
• FDA and other stakeholders have considered the need for a clearinghouse of such information on the process and contacts and education and support.
• Establish a Navigator and sought a partner with which to do this
• Much previous thought as to the shape and nature of such a Navigator
• Sought Public Opinion together with RUF
The Navigator

- Public Private Partnership with RUF
- Provide a central clearinghouse for information on expanded access
  - Education: EA processes, potential resources for healthcare providers without IRB access, inform healthcare providers about their responsibilities
  - Navigate: maintain a database of sponsor policies, procedures, and contacts for EA
  - Track: utilization of the navigator
  - Emergencies would still go straight to FDA