

“Big-Ticket” Considerations When Working With FDA

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Dealing With FDA's Regulatory Oversight

- The basic requirements of FDA regulation are in the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act
- To navigate this regulatory pathway requires not only an understanding and appreciation of applicable statutory and regulatory requirements, but also entails an understanding of basic policies, sometimes unwritten, that drive decision-making at FDA

Dealing With FDA's Regulatory Oversight

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- Key areas:
 - ✓ product development and marketing authorization strategies
 - ✓ e.g., human clinical trials, premarket approval applications, manufacturing controls
 - ✓ product exclusivity
 - ✓ e.g., Hatch-Waxman, pediatric, orphan drugs
 - ✓ product safety and effectiveness standards

Dealing With FDA's Regulatory Oversight

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- ✓ product quality assurance
 - commonly referred to as current Good Manufacturing Practices (GMPs)
- ✓ product advertising and promotion controls
- ✓ postmarket surveillance

Common Mistakes Early Stage Life Sciences Companies Make With FDA

- Underestimating the skepticism that FDA brings to product review
- Failure to appreciate that the data requirements to establish the safety and effectiveness of a product are significant
- Failure to recognize expense and time commitments

Common Mistakes Early Stage Life Sciences Companies Make With FDA

(cont'd)

- Misconception that all beneficial products are approved for marketing
- Misconception that FDA will act as a consultant and always acts objectively and reasonably
- Misconception that FDA will give smaller companies a regulatory “pass,” because of size or limited resources

Some Words About Clinical Trials

- By knowing the concerns and potential pitfalls in advance, a company can proactively plan, rather than reacting
- Accept the fact that a central focus of human clinical investigations is the protection of human subjects
 - ▮ ensure that your protocol will generate the necessary clinical endpoints, but also will minimize the number of patients exposed to the risks of such trials

Some Words About Clinical Trials

(cont'd)

- Key concerns for FDA investigators, who inspect sponsors, investigators and clinical sites, include data integrity, subject protection and the proper conduct of studies according to the protocol
 - ▮ accurate
 - ▮ real-time
 - ▮ compliant

Some Words About Clinical Trials

(cont'd)

- FDA investigators look negatively at trials with:
 - ☐ study imbalances
 - e.g., numbers don't add up or patients not treated the same
 - ☐ many dropouts
 - ☐ study changes
 - ☐ protocol violations
 - ☐ hidden problems

Red-Flag

Compliance-Related Issues

- Changes in clinical studies require proper authorization and should be made through protocol amendments
 - ▮ keep FDA updated and be careful about unilateral actions
- Recognize that device accountability can be more of an issue than drug accountability
 - ▮ for example, implants
 - ▮ account for all the devices

Red-Flag Compliance-Related Issues

(cont'd)

- Unreported device adverse events are a major issue, in part, because the device regulations are not as clear as the drug regulations on the question of what constitutes an adverse event

Due Diligence Considerations

- Due diligence of potential investigator
 - ▮ is the doctor qualified to conduct a clinical trial?
 - ▮ has the doctor previously performed studies in the U.S. for other companies?
 - ▮ is the doctor familiar with FDA rules governing clinical trials and willing to comply with their requirements?
 - ▮ has the doctor/investigator been debarred or disqualified by the government?
 - ▮ are you comfortable with sub-investigators?

The Clinical Study Agreement

- The contract with a potential investigator should ensure FDA regulatory compliance and protect the company/sponsor
 - ▮ IND/IDE responsibilities clearly described
 - ▮ informed consent and IRB review obligations identified
 - ▮ audits of investigator permitted
 - ▮ requirement to notify sponsor of FDA or other government inspection of clinical site, and agreement that sponsor is allowed to provide input on any resulting responses to FDA

The Clinical Study Agreement

(cont'd)

- ▣ certification of no disqualification/debarment
- ▣ indemnification for investigator's non-compliance or negligence
- ▣ publication opportunities/intellectual property rights identified and resolved in advance
- ▣ confidentiality issues

The Clinical Study Agreement

(cont'd)

- Non-compliance can lead to FDA action
 - ▮ clinical hold
 - ▮ refusal to accept data to support marketing applications
 - ▮ loss of credibility
 - ▮ enforcement actions, such as a Warning Letter
 - ▮ other delays and more questions

Parting Words

- Remember bureaucracy and formal rules apply
- Your company's timeline and priorities are not necessarily the government's
- Document decisions
- Plan for the worst – Murphy was an optimist

