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AGG Webinar

Challenges And Opportunities When Communicating With The Food And Drug Administration

Presented by Alan Minsk, Food and Drug Practice Chair and Partner

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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 *(cont'd)*

- FDA's regulations and guidance are not always black and white and can, at times, be broad and sometimes vague
- Key areas:
  - ✓ product development and marketing authorization strategies
    - e.g., good laboratory practices, good clinical practices, human clinical trials, premarket approval applications, manufacturing controls
  - ✓ product exclusivity
    - e.g., Hatch-Waxman, pediatric, orphan drugs

Dealing With FDA's Regulatory Oversight *(cont'd)*

- ✓ product safety and effectiveness standards
- ✓ product quality assurance
  - ➢ commonly referred to as current Good Manufacturing Practices (GMPs) or Quality System Regulations (QSRs)
- ✓ product advertising and promotion controls
- ✓ postmarket surveillance

Common Mistakes Early Stage Life Sciences Companies Make With FDA

- Underestimating the critical review 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*)

- Failure to listen and be receptive to suggestions, recommendations and constructive criticism from FDA and outside consultants
  - ✓ don't discount or ignore FDA's concerns
  - ✓ good ideas can always be made better and more focused

Common Mistakes Early Stage Life Sciences Companies Make With FDA (*cont'd*)

- Failure to understand how FDA will regulate <u>your</u> product
  - ✓ drugs (<u>e.g.</u>, OTC v. Rx, full NDA, hybrid 505(b)(2) NDA, ANDA)
  - ✓ food (<u>e.g.</u>, dietary supplement, traditional food, medical foods)
  - ✓ biologics and biosimilars (<u>e.g.</u>, vaccines, serums)
  - ✓ cosmetics
  - ✓ devices (see next slide)
  - ✓ combination products

Common Mistakes Early Stage Life Sciences Companies Make With FDA *(cont'd)*

- Misconception that FDA knows everything
  - ✓ you might have to educate FDA about your product
  - ✓ FDA has a number of new personnel
- Misconception that FDA doesn't know more or have experience with your type of product
  - ✓ FDA has access to data from other many other sources, and it has seen much from other similar products
  - ✓ FDA has many qualified, experienced people
  - ✓ FDA may be doing you a favor with its questioning

 9 not if, but how.®

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
- Misconception that FDA will give smaller companies a regulatory "pass," because of size or limited resources
- Misconception that FDA will meet its deadlines or communicate effectively
- Misconception that FDA will admit it is wrong

 10 not if, but how.®

Communications in the Clinical Trial Stage

- Be a healthy skeptic – the Beautiful Baby Syndrome
  - ✓ by knowing the potential regulatory and safety concerns of your product in advance, a company can proactively plan, rather than react
    - risk minimization and risk management
  - ✓ listen carefully to FDA, even if it sounds like the information provided is odd

Communications in the Clinical Trial Stage *(cont'd)*

- ✓ get inside FDA's head and do your homework
  - review what FDA has required of other similar products, e.g., precedents
  - evaluate what were the safety issues those products faced and how resolved
  - shy away from "novelty" and "revolutionary" marketing claims
  - engage consultants who are familiar with your review FDA division

Communications in the Clinical Trial Stage *(cont'd)*

- Accept the fact that a central focus of human clinical investigations is the protection of human subjects
- Poor communications with clinical investigators can result in poor outcomes with FDA

Communications in the Clinical Trial Stage *(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

Meeting with FDA About Your Study

- By reviewing FDA requirements, guidelines, precedents, knowing your review division, and recognizing likely FDA expectations, you can try to control your message and push your priorities
  - ✓ FDA might want to use your product as a learning opportunity for its staff
  - ✓ FDA might have a preconceived misperception about your product, based on its experience with other products
- Share with FDA how you plan to use any foreign data to support the marketing application

Meeting with FDA About Your Study *(cont'd)*

- Have a game plan
  - ✓ know the difference between an agency requirement versus a guideline or request (and when a request is essentially a requirement)
    - ➢ and understand why FDA is asking, so you can respond effectively
  - ✓ know when and how to push back
    - ➢ pick battles carefully and keep emotion out of it
    - ➢ consult with advisors
      - ❑ be open and honest with outside advisors so they can provide the best counsel

Meeting with FDA About Your Study *(cont'd)*

- ✓ show preparedness and familiarity with regulatory process, your product, and similar products
  - credibility is key
  - may be able to rely on existing data to avoid reinventing the wheel
- ✓ another avenue to downsizing or eliminating additional trials is to examine existing data
  - it may be possible to find answers within the sponsor's own data, another sponsor's data or the published literature
  - utilizing the full potential of data that have already been collected might help to drive down costs and negate the need for additional clinical subjects

Meeting with FDA About Your Study *(cont'd)*

- While it might be tempting to simply agree with FDA at every stage, such as a proposed study design, it might not be in your best interest
- But, be willing to listen and be open to criticism and suggestions, as FDA ultimately runs the show
- In the end, you want to have a clear understanding of FDA's expectations and, as much as possible, agency buy-in

Response Game Plan

- Form a Response Team
- Review FDA enforcement correspondence for accuracy, clarity, completeness, and foundation
- Submit a timely written response
- In cases where you disagree with the investigator, provide a complete explanation in support of the company's position

Response Game Plan *(cont'd)*

- Respond quickly to agency requests, state company position clearly and implement corrective action
- Check ego at door – arrogance is a major turnoff and is counterproductive
- Issue information to important constituents as soon as possible

Response Game Plan *(cont'd)*

- Document decisions, but keep it simple, stupid
- Give yourself credit for what you have done
  - ✓ e.g., training, documentation
- But don't give yourself too much credit
  - ✓ no one likes a braggart and the enforcement action indicates your company is not perfect
- See the big picture – read between the lines

Response Game Plan *(cont'd)*

- Have proactive timelines for corrective action that are credible and achievable and keep commitments to FDA
  - ✓ don't promise what you can't deliver
  - ✓ if you promise something, you'd better deliver
  - ✓ give yourself some flexibility with standard operating procedures and deadlines, so long as compliance is met
  - ✓ haste can make waste

Response Game Plan *(cont'd)*

- Consider requesting a meeting with FDA District Office
- Determine whether it is useful to bring the matter to FDA headquarters
- Prepare for follow-up inspection, especially if a Warning Letter has been received
- Convey commitment to compliance
  - ✓ consider what resources and commitments will be involved if you sign a consent decree

When Communications With FDA Seem to Break Down

- Seek clarification and understand the issues
  - ✓ read between the lines
  - ✓ have a neutral advisor review and offer suggestions for next steps and resolution
- Consider use of Ombudsman, appeals process, and external resources

How to Enhance Your Relationship With FDA

A. You should understand and adhere to acceptable conventions when communicating with FDA

- A relationship with FDA is not unlike other relationships
- Be sensitive to internal dynamics of FDA
- Respect FDA representatives as peers
- Be understanding of FDA's priorities and resource limitations
  - ✓ expect the unexpected - - Murphy was an optimist
- Be cognizant of the appropriate regulatory pathway
- Frank discussion and openness with FDA is important

How to Enhance Your Relationship With FDA *(cont'd)*

- Do not waste FDA's time
  - ✓ look at precedents / past FDA decisions
  - ✓ do not make FDA think too hard
  - ✓ pre-empt and anticipate FDA questions
- Honor the chain of command
- Minimize unproductive venting
  - ✓ have a rhyme and reason for points of disagreement and be prepared to distinguish your product from other products, if this a point of contention

How to Enhance Your Relationship With FDA *(cont'd)*

B. Rules for negotiating

- Put yourself in FDA's position
- Listen carefully to FDA, even if it sounds like the question asked or information requested seems odd
- Have a plan of action and backup plan
- Do not play hardball, but do not be too soft
- Ask questions to understand the "big picture"
- Be responsive/flexible
- Follow through on commitments

How to Enhance Your Relationship With FDA *(cont'd)*

- Must gain trust of FDA and show you are familiar with the rules, agency expectations, and sound scientific principles
- Even if you and FDA disagree, but there is mutual respect and trust, you will get farther with FDA
- FDA can be open-minded to good, scientific arguments, particularly if there is a significant public health benefit
- Create a high level of confidence in the company's abilities
  - ✓ credibility is key
  - ✓ provide clinical data, as applicable (FDA is expecting such data more frequently)
  - ✓ check your assumption and know your weaknesses
    - □ be a healthy skeptic and avoid the Beautiful Baby Syndrome
    - □ look at FDA's responses and actions on similar products (precedents)

How to Enhance Your Relationship With FDA *(cont'd)*

C. Minimizing Surprises

- Establish a reasonable timetable for regulatory approval
- Assign sufficient resources to do the job
- Hire the right advisors/consultants
- Consider singles and playing base to base or aim for the homerun

How to Enhance Your Relationship With FDA *(cont'd)*

D. How to deal with setbacks

- Define the points of disagreement
- Have you met the regulatory requirements?
- Is science on your side?
- What are your strongest and weakest points?
- Have you made your points effectively?
- Is FDA facing other pressures that affect your marketing application?
- Is there common ground?
- Do you have a back-up plan that meets your company needs but also satisfies FDA's interests and concerns?
  - ✓ get FDA out of any box it might find itself

How to Enhance Your Relationship With FDA *(cont'd*

E. Tactics that can backfire

- Evasion
- Dishonesty
- Unrealistic expectations
- Submitting poorly organized or sloppy documents
- Failing to maintain operational quality

Thank you for attending

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