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FDA/IVD Industry Roundtable

Achieving Regulatory Success in Today's Changing Environment; Suggestions for the IVD Industry

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IVD Initiatives and Directions

- FDA is in the midst of significant reevaluation of regulatory review processes, especially for medical devices
  - CDRH Office of Compliance in October 2009 emphasized the need to address regulatory non-compliance more quickly and aggressively
  - CDRH hosted a February 2010 Public Meeting addressing “Incorporation of New Science Into Regulatory Decisionmaking” where the 510(k) review process was closely scrutinized
  - OIVD met publicly with stakeholders on July 19 and 20, 2010 to address a risk-based application for oversight of Laboratory Developed Tests

IVD Initiatives and Directions

Dr. Gutierrez, upon taking the OIVD Director's position in July 2009, expressed numerous regulatory pathway concerns:

- "flaws in the 510(k) premarket notification program in that "substantial equivalence" allows a test maker to show its test is similar to an already cleared device in lieu of a more extensive safety and efficacy review
- A process that "invites unwanted variability among test makers
- Use of labeling terms, such as "sensitivity" (rate of true positives) and "specificity" (rate of true negatives) even when the terms "don't really describe what manufacturers actually proved to us"

Goals and Objectives

- FDA's stated regulatory goals include:
  - Flexibility – by developing "new regulatory frameworks" that address new products
  - Collaboration – by working with academia and industry "to identify knowledge gaps and fill them; identify confidence deficits and address them"
  - Openness – by being "more transparent and endeavor[ing] to help the public understand the rationale and reasoning behind the decisions we make which have such far-reaching impacts on public health."
- Overarching goals of the agency today continue to be guiding the approval process to ensure "a future that provides safer and more effective therapies"

Impact

- Each of these new areas of focus lessen predictability of the regulatory requirements and may lengthen the premarket review process
- The pendulum appears to have swung back toward a zero risk mentality in all phases of premarket and postmarket review
- Whether communicating with FDA at the presubmission phase, or responding to a compliance concerns, keep the agency's goals and needs in focus

The Role of the IVD Roundtable

- In July 1995, FDA and the IVD Industry began these roundtable meetings to “improve communications between FDA and our colleagues in the in vitro diagnostic industry” and to “explore new ways of communicating before regulatory problems become a barrier between us, and communicating in a helpful way rather than the adversarial atmosphere we know too well”

  Letter from Ken Shelin to IVD Industry participants 7/5/95.

The Role of the IVD Roundtable

- Concerns and assumptions identified in 1995, surprisingly, still sound familiar today
  - FDA believed that industry
    - Saw the agency as an adversary
    - Viewed FDA as impeding progress, and
    - Created an uneven playing field
  - Industry believed FDA sees industry as
    - Purely profit oriented
    - Manipulative, and
    - Acting based on hidden agendas
- Fora (such as this Roundtable), however, provide effective avenues for correcting these misimpressions and fostering the clearance/approval and marketing of safe and effective IVDs

Keys to working well with FDA

- Be Honest
  - Pre-IDE and IDE meetings
    - Describe products and their intended uses accurately and fully
    - Present clearly what you know, what you believe, and how you intend to conduct preclinical and clinical testing to better characterize the IVD you hope to market
    - Know your proposed intended use/indications for use. Don't theorize about possible, future uses other than to let FDA know you will be back for additional discussions at a later date
    - If FDA has new concerns, listen and suggest following-up after analyzing the issues – avoid knee-jerk responses
  - During the review process
    - "Least Burdensome" is in the eye of the beholder. Be prepared to push back (if necessary) based on facts and data, rather than emotion
  - Postmarket
    - Review events for reportability as MDRs (Part 803) or as biological adverse events
    - Include health hazard and risk information when alerting FDA to corrections and removals

Keys to working well with FDA

- Be Cooperative
  - Don’t assume you know better than the reviewer
  - Listen carefully to OIVD’s requests
  - If a request is unclear, get clarification before complaining, but don’t be afraid to ask for the rationale and reasoning behind the decisions
  - Be willing to communicate, but don’t insist on over communication – time is a precious commodity
  - Meet deadlines for requested information or communicate early when additional time is needed

Keys to working well with FDA

- Be Knowledgeable
  - Look at relevant precedent
  - Identify differences or “new science,” and think about how this may impact your product’s regulatory pathway, risk/benefit profile, or data requirements
  - If you are asking the agency to extrapolate into a new area, understand how this impacts the regulatory pathway and be prepared to explain both how and why your preferred approach is appropriate
- Be Responsible
  - When new information becomes available (even unexpected information), let FDA know
- Be Intelligent
  - Review correspondence and communication for accuracy
  - Ensure that submissions are clear, internally consistent, and complete

Dealing With FDA's Zero Risk Mentality

- Companies need to provide sound physical, chemical, and biological evidence supporting their positions
- Well-designed, controlled, and executed preclinical studies are required
- Superb and clear presentation of the data is a must
- Even then, understand that FDA may continue to request additional data

Conclusion

- In working with FDA
  - Open and honest communication must be your foundation
  - Knowledge of all FDA requirements is critical
  - The pendulum of regulation swings back and forth through various cycles, but ultimately sound data, clear communication, common sense, and cooperative regulation typically wins the day

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