Effective Use of the FDA Pre-Submission Process: An Industry View

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Pre-Submission Timing

- The time for a pre-submission is not too early and not too late
- You need to have sufficient information about your product to inform the responses to your questions, but enough time to plan your studies and submission strategy
- FDA generally recommends one pre-Submission per product/system but additional questions and follow up information can be managed under the same Q-sub depending on complexity
- Generally Pre-Submission discussions are conducted during the product definition and project planning stages of development
- Pre-Submission decisions will drive design considerations and performance testing

Pre-Submission Business Drivers

- Time to Market
  - Understanding potential regulatory pathways can inform decisions about market strategies
  - Market leadership in key product areas can be established through different regulatory pathways (for example: incrementally)
- Minimize Costs of Development
  - Proactive planning of lengthy development cycles
  - Clarify open questions in advance to reduce uncertainty during product review
  - Informed decisions on validation criteria and product performance expectations to reduce re-design and re-testing cycles
  - Clear definition of submission contents to reduce risk of NSE/not approvable decisions, or delays

Pre-Submission Development Process

- Define your objectives
- Determine key questions that you need answered
- Consider possible responses to your questions and put the questions in the form of statement of what you would propose and why, then ask if FDA agrees
- Assemble enough information in your pre-Submission to give FDA the background necessary to make informed assessments/decisions
- Consider whether a demo or video of operation of your device would be helpful in the context of your questions
- Decide if you want an in-person meeting or a conference call
- You will receive a written response to your questions in advance, which may be sufficient

Taking Advantage of the Pre-Submission Process

- One time free advice
- Written responses to questions of your choosing
- Assemble the proposed labeling and proposed study plans
- Submit a clear well considered intended use
- Recommend attendees for the discussion: both yours and FDA staff
- Propose potential dates for a call or meeting
- Submit your request 75 days prior to the meeting or call
- Submit eCopies per FDA guidance
- Response that your pre-sub is accepted within 14 days

Taking Advantage of the Pre-Submission Process
Reasons for a Pre-sub – Regulatory Strategy

- Are there opportunities for bundling? Gain agreement in advance
- Is the technology new or complex such that FDA will have concerns that could change the classification? data requirements? submission content?
- Are the data requirements consistent with similar cleared or approved devices? Or would changes in technology or medical practice dictate the need for additional data requirements
- Are there multiple potential regulatory approaches that need clarification as your company considers product design and market needs.

Taking Advantage of the Pre-Submission Process
Reasons for a Pre-sub – Intended Use

- Are there anticipated issues with your intended use versus the classification regulation?
- Does FDA anticipate new public health issues or safety concerns for this device or type of device that would impact your intended use?
- Can the intended use be general or will FDA require specific populations or settings to be described?
- What are the pros and cons of beginning with a narrow intended use and expanding as data become available?

Taking Advantage of the Pre-Submission Process
Reasons for a Pre-sub – Guidance and Standards

- Is there new guidance for products of this type or new requirements not yet captured in guidance?
- Can guidance for other devices be extrapolated to apply to your device?
- Can CLSI standards be used as a “base” or do they need to be strictly followed as written?
- Does longstanding guidance (potentially dated) still apply?
- Do deviations from guidance seen in other submissions for similar products apply to this device?

Taking Advantage of the Pre-Submission Process

Reasons for a Pre-sub – Clinical trials/studies or performance characteristic testing

- Will FDA provide feedback on the clinical study design, sample numbers, patient population or statistical analysis method?
- Are there CLIA Complexity issues, waiver trial designs to discuss?
- Do you anticipate trials outside the US, confirm that FDA will be comfortable with the trial locations.
- Will analytical validation planned be sufficient to support the clinical application?

Industry Examples/Recent Experience
Case #1

- Device company submitted a pre-Sub to determine if studies for 510(k) and CLIA waiver could be combined
- FDA encouraged sponsor to pursue sequential 510(k) (POC) and CLIA waiver applications to reduce submission risk
- After further consideration the sponsor found no commercial value for their product without CLIA waiver
- Through discussion with FDA were able to define study designs that meet both sponsor and FDA criteria and to combine in a dual 510(k) CLIA waiver submission
- Discussion was detailed to include study locations, operator qualifications, protocols
- FDA provided valuable detailed advice and suggestions on study designs proposed by the sponsor
- Company is very satisfied with the process

Industry Examples/Recent Experience
Case #2

- Sponsor submitted a pre-sub for proposed use of an LDT as a CoDx for cancer therapy
- Initial feedback was sought on use of an LDT, use of a retrospective analysis design for phase 3 studies
- Confirmed acceptability of an LDT with appropriate PMA approval concurrent with NDA for the therapeutic
- Also sought feedback on proposed study designs, protocols, sample types and projected numbers, statistical calculations which had originally been designed to satisfy OUS requirements. Detailed information was provided by the sponsor
- FDA provided helpful feedback and advice on study designs
- Sponsor is revising study designs, protocols for follow up review by FDA
- Sponsor found FDA feedback helpful, identifying potential issues before testing was completed