

EFFECTIVE USE OF THE FDA PRE-SUBMISSION PROCESS: AN INDUSTRY VIEWPOINT

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Agenda

- Pre-Submission Timing
- Business Drivers
- Pre-Sub Best Practices
- Taking Advantage of the Pre-Submission Process
- Case Studies

Pre-Submission Timing

- Not too early and not too late
 - You need sufficient information about your product to inform the response, with enough time to plan your submission strategy and studies
- FDA generally recommends one pre-sub per product. Additional questions and follow up information may be managed under the same Q-sub.
- Non-trivial follow up may require a supplement
- Pre-sub discussions typically occur early in product development during planning stages
- Pre-sub decisions will drive design considerations and performance testing

Presubmission Timing

Package sent to FDA*	Day 0
Acknowledgement by FDA	Day 3-5
Request Accepted	Day 14-19
Proposed Dates	Day 18-20
Meeting with FDA	Day 74-76

* For content see FDA Pre-Submission Guidance

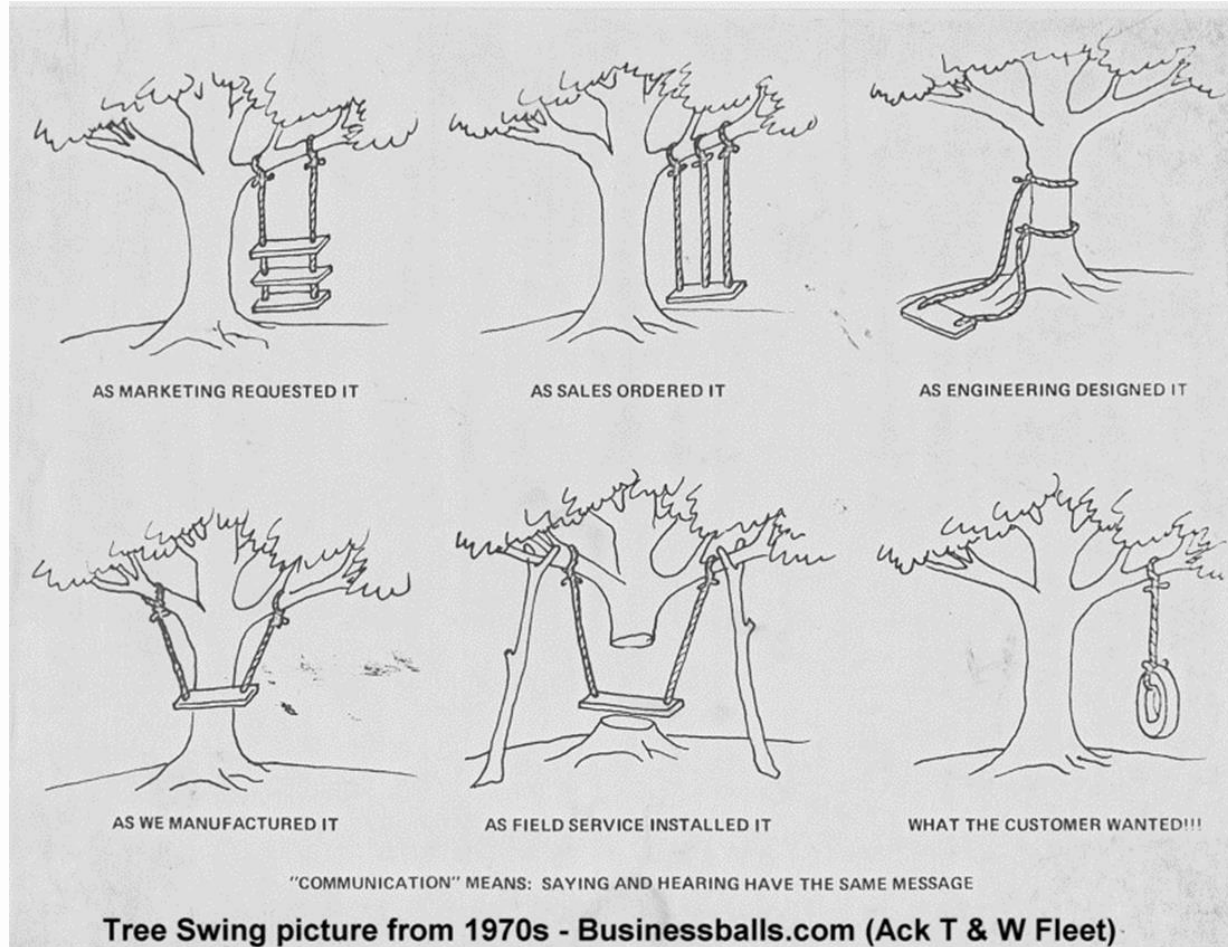
Business Drivers

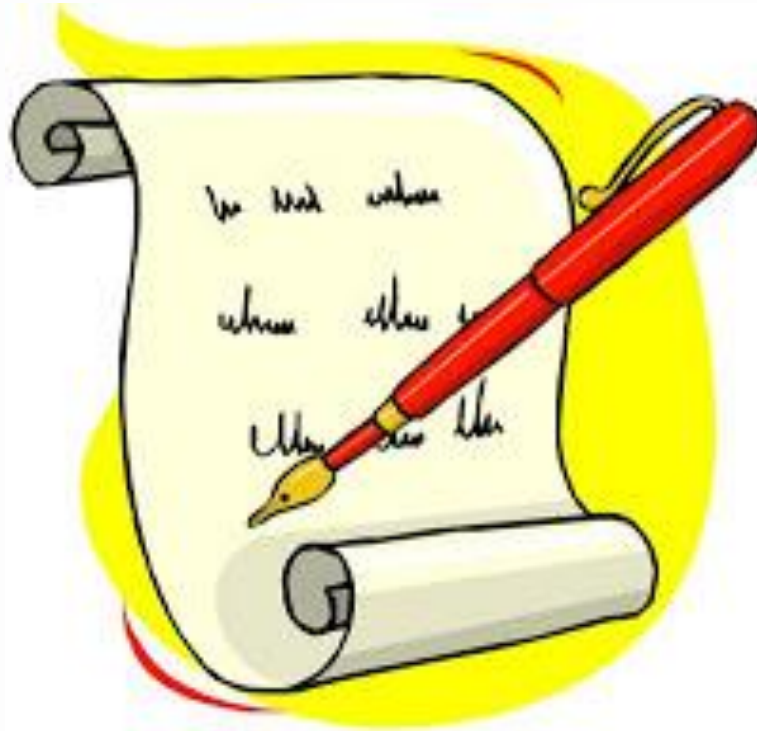
- Time to market
- Understanding potential regulatory pathways can inform decisions about market strategies
- Better control of development cost
- Reduce re-design and re-testing cycles with input from FDA on performance test plans
- Clarify questions in advance of FDA review of the pre-market submission; reduce uncertainty
- Submission contents clearly defined to reduce risk of NSE/ not approvable decisions or delays

Pre-submission Best Practices

- Clearly define your objectives. Helps to keep the project team and FDA focused.
- Determine key questions that you need answered. Put the specific question in the form of a statement - what you would propose and why. Ask if FDA agrees.
- Make sure the device description has sufficient detail; use diagrams, photos, quick reference guide (to demonstrate simple to use, if applicable)
- Take time to work on the intended use/ indications for use statement before sending to FDA. Make sure it is clear and well considered.
- Decide if you want an in-person meeting, conference call or written response.

What is your Device?





Keep in mind most of your communication with FDA will be the written word.

Taking Advantage of the Pre-Sub Process

- One time free advice
- FDA provides written responses to questions of your choosing.
- The FDA meeting is limited to 1h. Plan your time carefully.
- Prepare an agenda with assigned speakers.
- Coach your team on what to say, and what not to say.
- Recommend attendees – your team and FDA
 - Consider statistician, clinician, academic expert
- Assign someone to take meeting minutes.
- Refer to FDA guidance for required content and eCopy.

Taking Advantage of the Pre-sub Process

Reasons for a Pre-sub – Regulatory Strategy

- 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? Would changes in technology or medical practice dictate the need for additional clinical data?
- Are there multiple potential regulatory approaches that need clarification as your company considers product design and market needs?
- Are you considering bundling multiple devices in your submission?

Taking Advantage of the Pre-sub Process

Reasons for a Pre-sub – Intended Use

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

Taking Advantage of the Pre-sub 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?
- Is there special controls guidance that applies to your device?
- Can CLSI standards be used as written or will FDA require some modifications in methods?
- Confirm applicability of older guidance
- Do deviations from guidance noted in summaries for similar products apply to your device?
- Do you have questions about the software and cybersecurity guidance documents?

Taking Advantage of the Pre-sub Process

Reasons for a Pre-sub – Performance testing

- Does the analytical validation plan support the clinical application for your device?
- Seek feedback on the clinical study design: specimen type(s), sample numbers, patient population(s), statistical analysis.
- Is method comparison sufficient, or will FDA require additional clinical data?
- CLIA waiver considerations – dual submission
- Do you plan to use sites outside the U.S.?

Industry Experience

Case Study #1

- Device company submitted a pre-sub to determine appropriate classification for a novel cardiac marker.
- Company proposed de novo pathway finding only predicates with a diagnostic intended use. New marker is intended for monitoring.
- Through discussion with FDA, an appropriate existing regulatory classification regulation was identified which allows for a traditional 510k pathway, avoiding the more lengthy de novo process.
- FDA is requiring clinical data for the new device as a straight forward method comparison would not provide sufficient assurance of safety and efficacy.

Industry Experience

Case Study #2

- Sponsor submitted pre-submission on a new analyzer with 5 new reagent assays.
- Initial feedback was sought on bundling, predicate options, and performance study plans.
- FDA accepted bundling and provided some helpful suggestions on predicates options.
- FDA feedback on analytical performance plans, clinical protocols (method comparison, reference range, reproducibility) was key to timely design of studies.
- A supplement was filed to seek input and clarification on use of the Replacement Reagent/ Instrument Family guidance for a next gen analyzer.

A word cloud featuring the phrase "THANK YOU" in large red letters at the center. Surrounding it are various expressions of gratitude in multiple languages, including English, Spanish, French, German, Italian, and several indigenous languages. The words are arranged in a circular pattern, with some appearing in larger fonts than others. The background is white, and the overall design is clean and modern.

THANK YOU

WELALIN

SPASIBO

MAAKE

MULTUMESC

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ASANTE

KIITOS

VINAKA

ARIGATO

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MATONDO

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