Pre-Submission Guidance Review with Q&A

AMDM Pre-Submissions Workshop
April 2018

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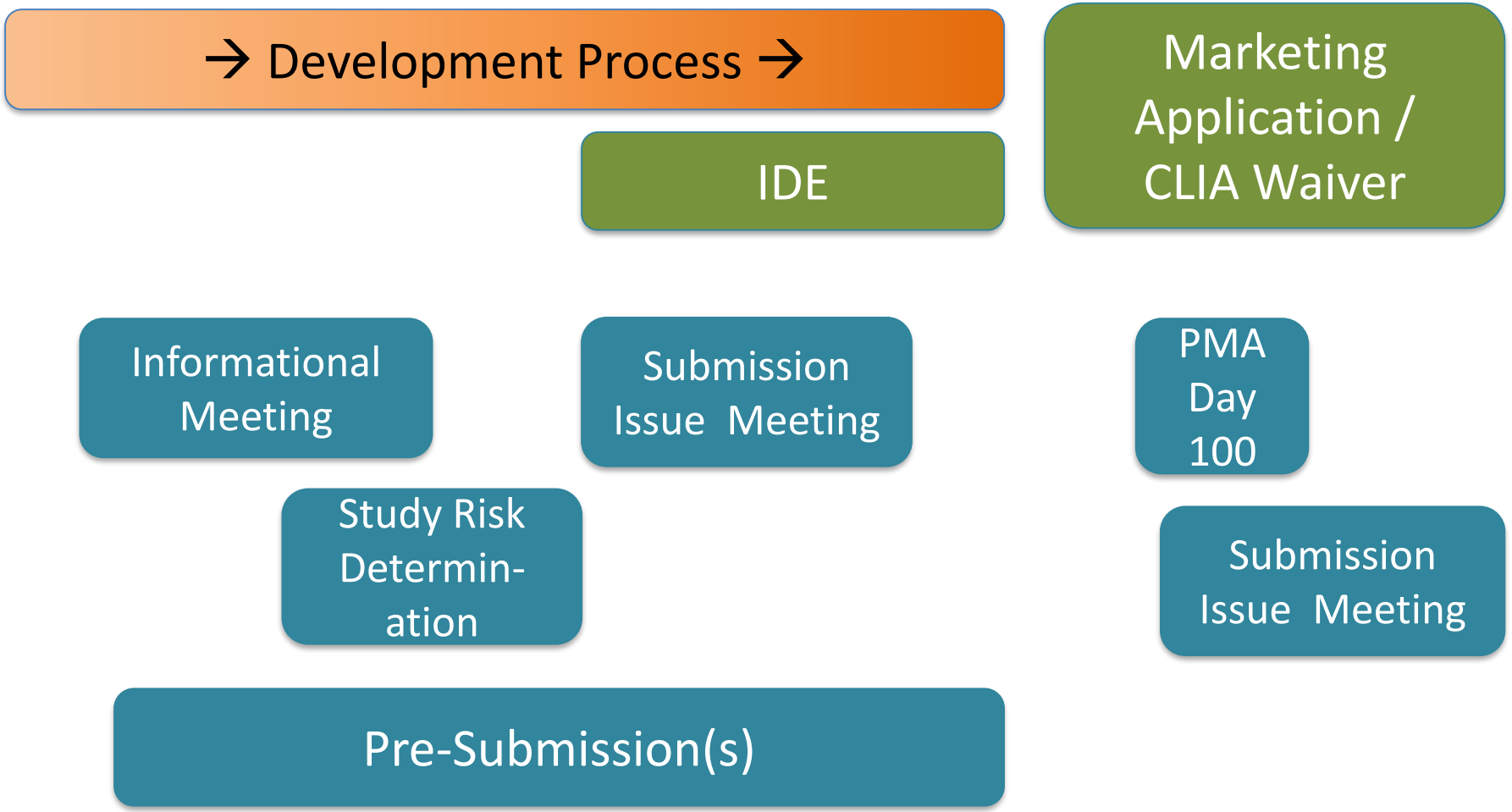
Orienting to the World of Q-Subs

- What and When
- Risk and Uncertainty
- So you want to submit a Q-Sub
  - Homework
  - Starting Well
  - Milestones
  - Nomenclature
  - Follow Up

Q-Subs cover many different submitter requests

- Informational Meetings (Info)
- Study Risk Determinations (SRDs)
- Pre-Submissions (Pre-Subs)
- Submission Issue Meetings (SIMs)
- PMA Day 100 Meetings (PMA 100)
- Breakthrough Device Designation Requests

Q-Subs are Appropriate at Different Device Development Stages



Informational Meetings can Introduce Novel Devices to FDA

- Don’t expect formal FDA feedback
- You want to introduce
  - A novel device
  - A novel mode of action
- An opportunity for informal Q & A

What Regs Apply to your Study

- Submit a **Study Risk Determination**
- Is the Study:
  - **Exempt** from most IDE Regulations?
  - **Non-Significant Risk**?
  - **Significant Risk**?

- See Elaine Katrivanos's IDE slides for more details on these

Pre-Submissions have Broad Applicability

- Future submission can be a
  - PMA,
  - 510(k),
  - De Novo,
  - CLIA Waiver or
  - IDE
- Submit ***before*** you submit your marketing application, IDE, or CLIA Waiver

Use Pre-Subs When You Are Uncertain

- How does FDA respond to your key concerns?
- Is FDA thinking about the issues differently?
- Meet and familiarize relevant FDA staff with your device

Uncertainty is Best Addressed Early

- Course corrections are less expensive when made early
- More opportunity to work towards win-win approaches

Submission Issue Meetings are for Hold Letters and IDE Letters

- When:
  - Your marketing application or CLIA Waiver has received a deficiency letter
  - Or you have an IDE letter

Submission Issue Meetings are for Hold Letters and IDE Letters

- Hold letter or IDE
- **You want to review your planned approach to the deficiencies with FDA**

Submission Issue Meetings are for Hold Letters and IDE Letters

- HOLD or IDE letter
- You want to review your planned approach to the deficiencies with FDA
- **Not needed for a simple clarification question**
  - Call or email the Lead Reviewer

Submission Issue Meetings are for Hold Letters and IDE Letters

- HOLD or IDE letter
- You want to review your planned approach to the deficiencies with FDA
- Not a simple clarification question
- **Not a 'pre-review' of your response**
  - Intent is to chart a path
  - Not to review the entire response

Submission Issue Meetings can be Quick

- Our goal is to turn these around in 21 days
- New protocols or other complex proposals will take longer
- The sooner you submit your Submission Issue Meeting request, the more likely you are to receive prompt feedback

PMA Day 100 Meetings May not be Your Best Choice

- Day 100 meetings should happen by day 100
  - Guidance Issued prior to MDUFMA

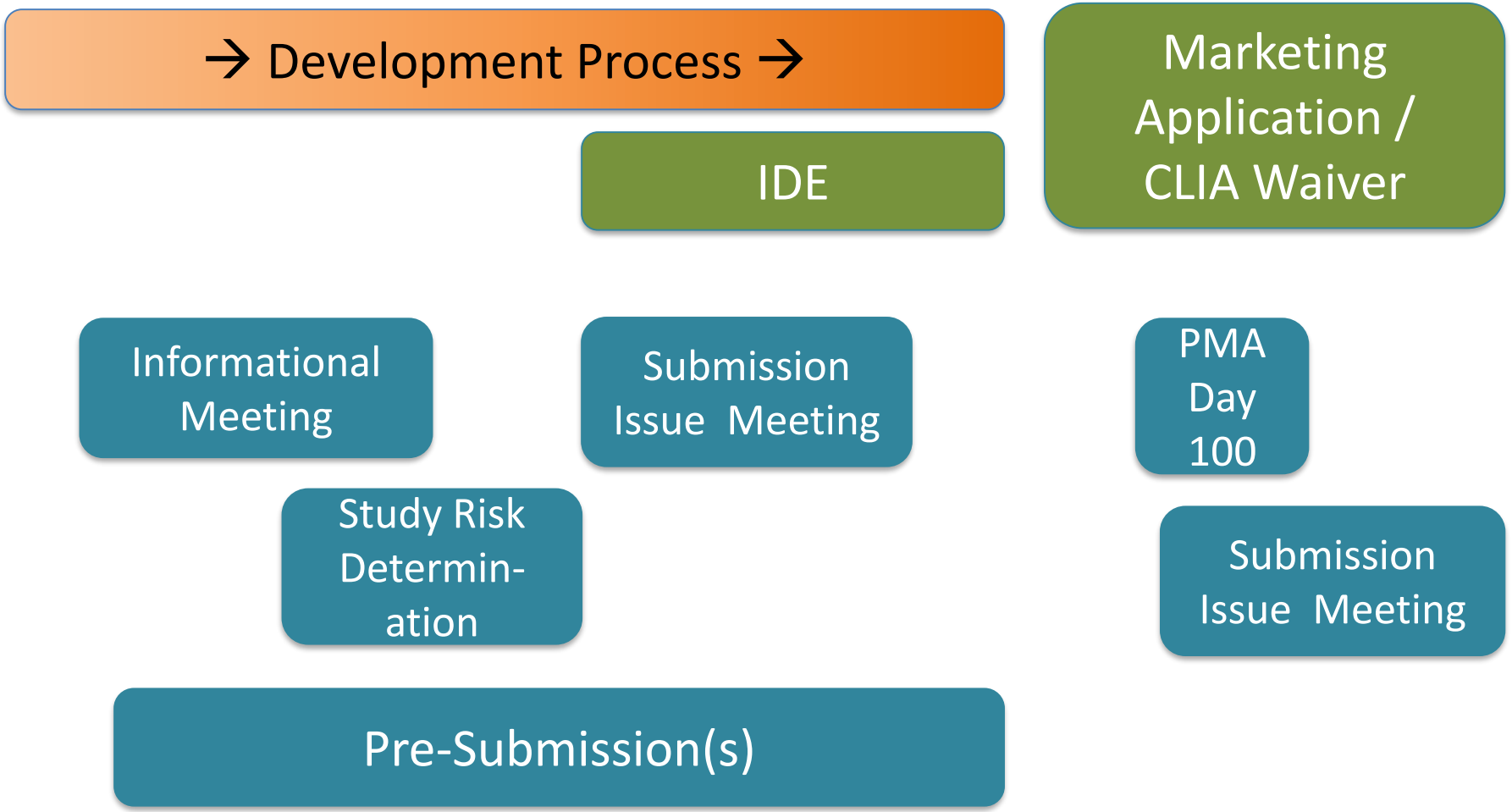
PMA Day 100 Meetings May not be Your Best Choice

- Day 100 meetings should happen by day 100
- Day 90 – MDUFA goal for Major Deficiencies
  - Leaves < 10 days for you to review deficiencies prior to meeting

PMA Day 100 Meetings May not be Your Best Choice

- Day 100 meetings should happen by day 100
- Day 90 – MDUFA goal for Major Deficiencies
- **Submission Issue Meeting may be a better option**

Q-Subs are Appropriate at Different Device Development Stages



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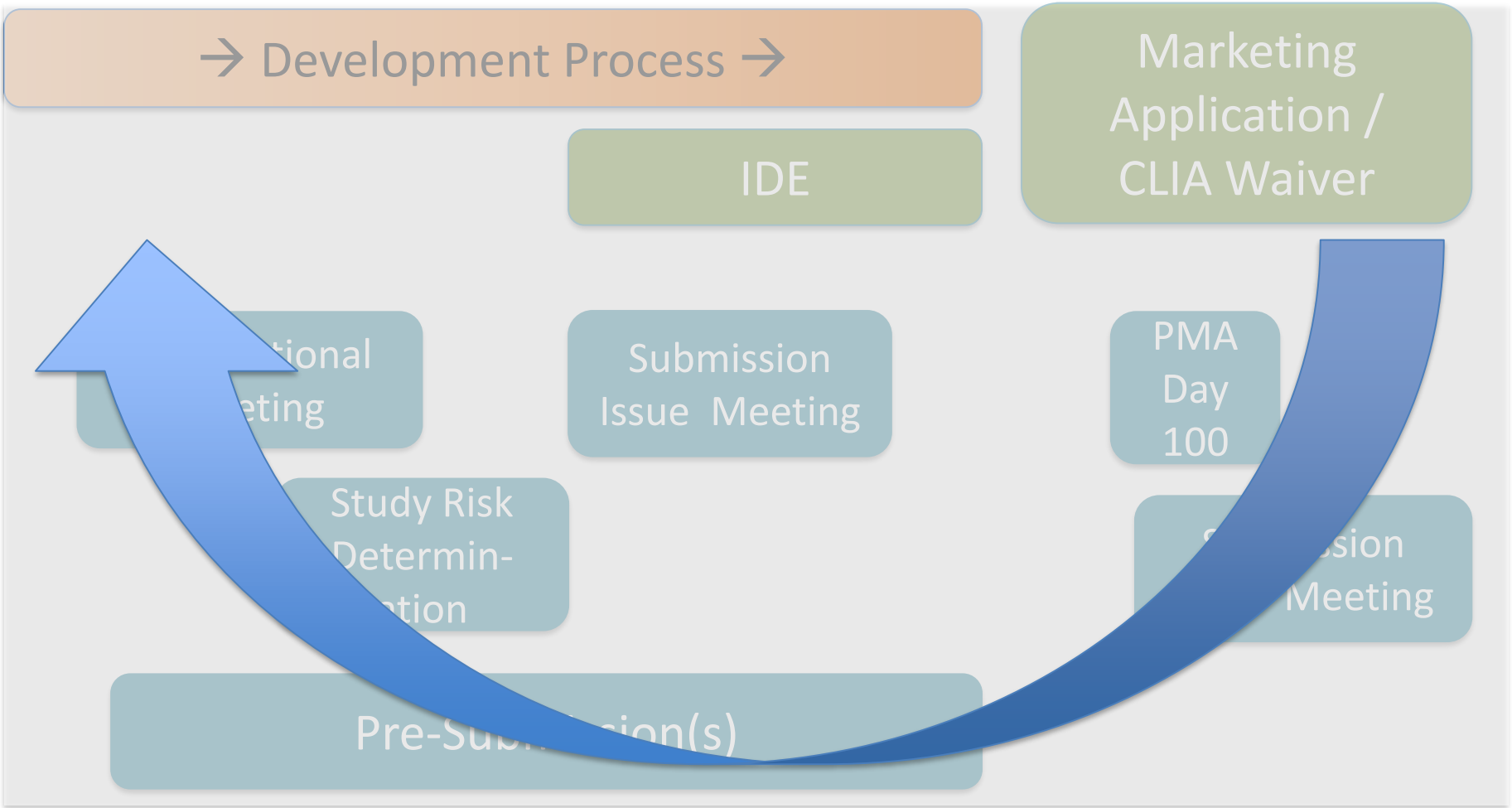


So You Want to Submit a Q-Sub…

Review the Info FDA has for You before Submitting a Q-Sub

- **The Pre-Submission Guidance**
  - *Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with FDA Staff*
    - Revision issued September 29, 2017

    http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf
- **eCopy Program**
  - The page contains links to Guidance, video, FAQ, and tools, including a validation module https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/ucm370879.htm
- **Optional form 3514**
  - Be clear about what you're submitting, who you are, and whom we should contact – optional because a good cover letter can have all this
  - https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM080872.pdf

Write a Clear Cover Letter

- What type of Q-Sub do you want?
- If Pre-Sub
  - **All Pre-Subs get written feedback**
  - Do you want a meeting as well?
  - If a meeting, propose three specific meeting dates

Write a Clear Cover Letter

- What type of Q-Sub do you want?
- If Pre-Sub
  - All Pre-Subs get written feedback
  - Do you want a meeting as well?
  - If a meeting, propose three specific meeting dates
  - **Easier to schedule a meeting at the beginning, then cancel**
  - **Dates around days 60-75 are more likely to be feasible**

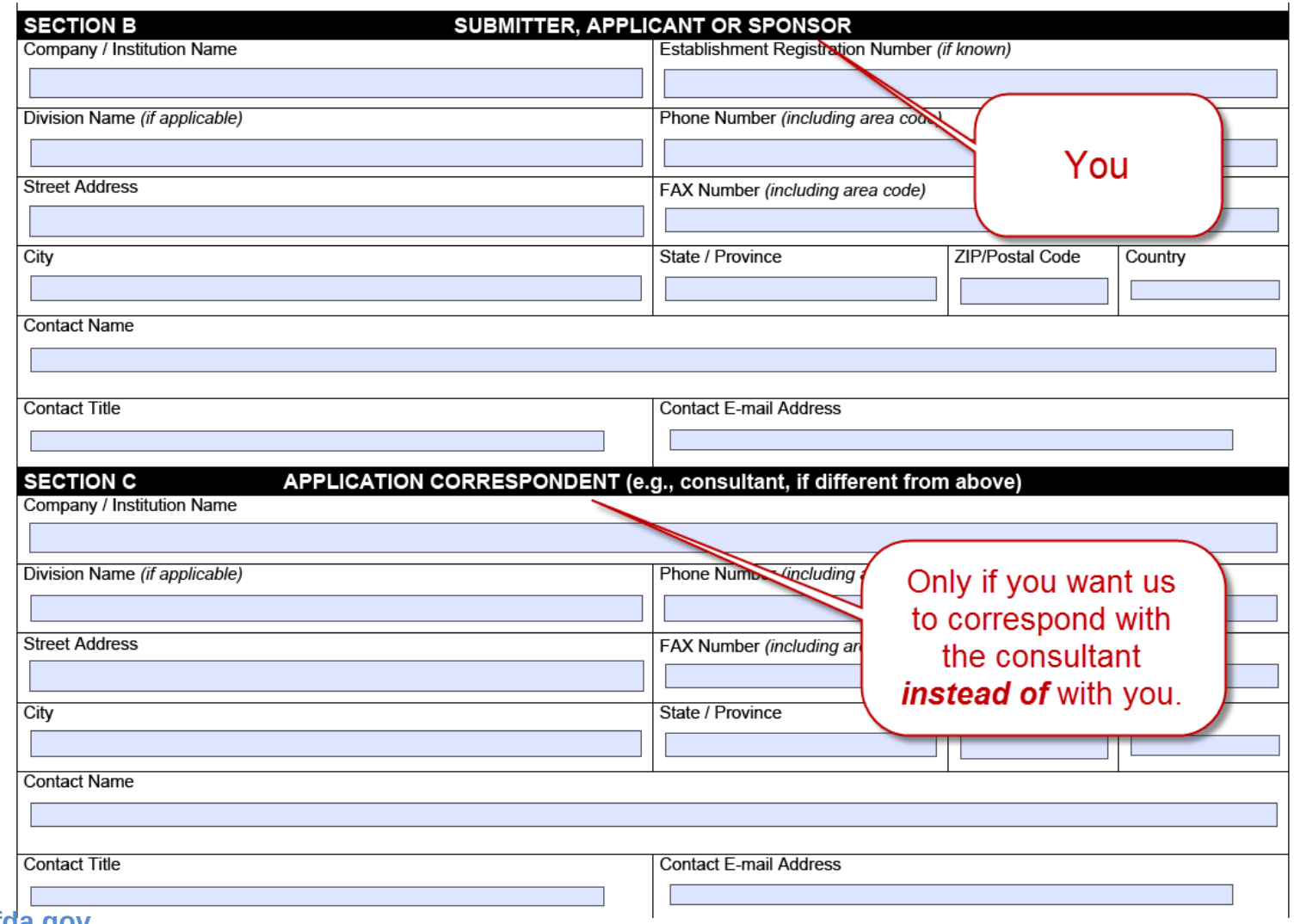
Write a Clear Cover Letter

- What type of Q-Sub do you want?
- If Pre-Sub, meeting?
- **Have you had a previous Q-Sub?**
  - **Provide Q-Sub Number**
  - Same device and intended use

Write a Clear Cover Letter

- What type of Q-Sub do you want?
- If Pre-Sub, meeting?
- Previous Q-Sub?
- **With whom should we correspond?**

3514 – Be Clear about with Whom We Correspond



SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name	Establishment Registration Number *(if known)*		
Division Name *(if applicable)*	Phone Number *(including area code)*		
Street Address	FAX Number *(including area code)*		
City	State / Province	ZIP/Postal Code	Country
Contact Name			
Contact Title	Contact E-mail Address		

You

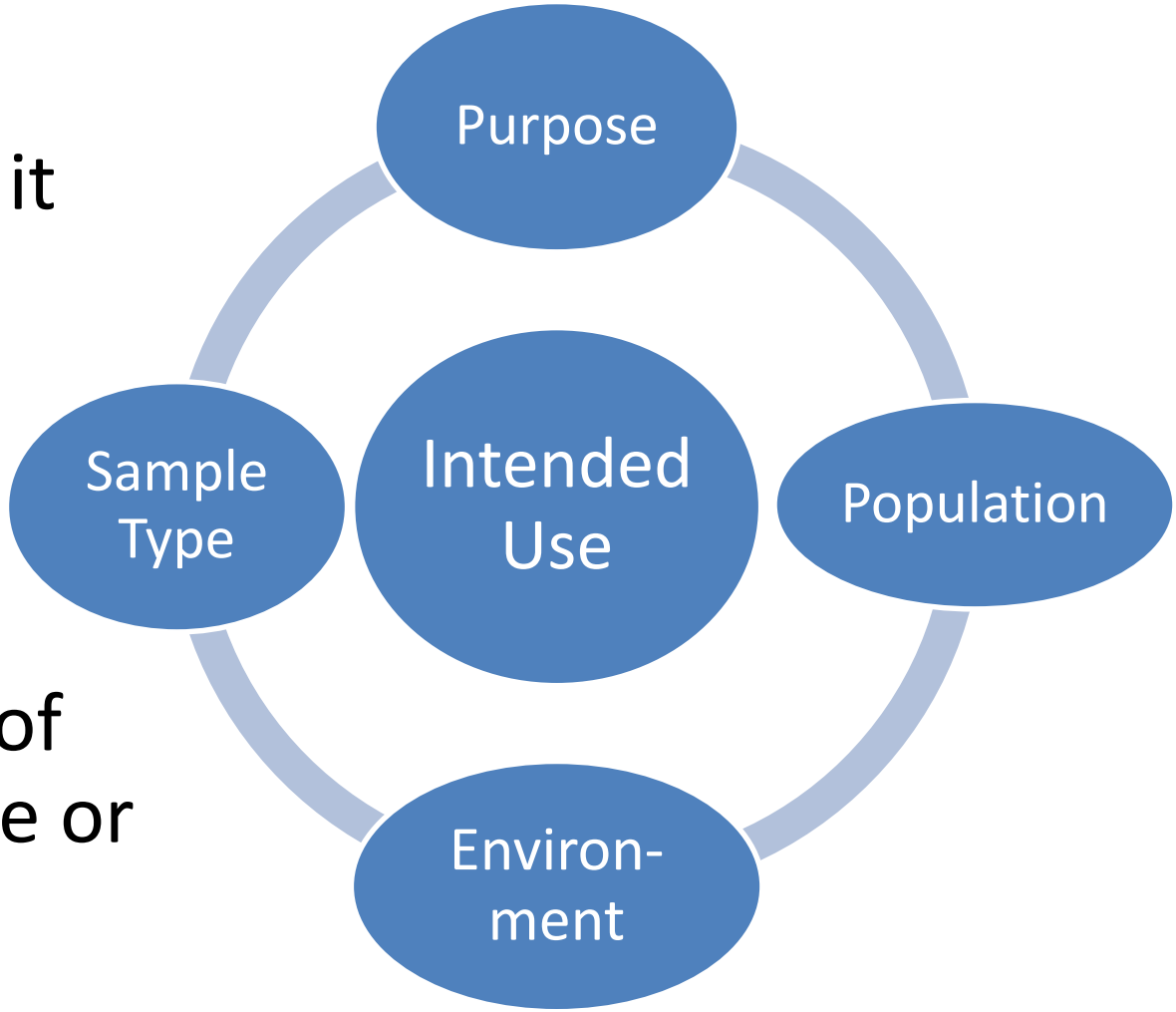
SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name			
Division Name *(if applicable)*	Phone Number *(including area code)*		
Street Address	FAX Number *(including area code)*		
City	State / Province		
Contact Name			
Contact Title	Contact E-mail Address		

Only if you want us to correspond with the consultant ***instead of*** with you.

Describe Your Device in Detail

- How does it work?
- Examples of Clinical Use or Impact?



Ask Specific Questions

- Focus on your current need
- Specific questions lead to specific answers
- Vague or broad questions force us to interpret your need

Pre-Sub Written Feedback Milestones

- Day 15: Acceptance Review
- Day 70: Written Feedback

Pre-Sub Meeting Milestones

Timeline	Action
Day 15	Acceptance If accepted, email states whether meeting agreed to or provides 2 alternative dates
Day 30	Meeting date agreed to or escalation to management
5 days Before Meeting (or Day 70 if earlier)	Written Feedback
Meeting	Meet unless you cancelled Q-Sub Closed
Meeting plus 15 Days	Your deadline for submitting meeting minutes

Decide how best to use the Meeting

- Once you have our feedback, it's OK to cancel the meeting
- You should provide an agenda 2 days before the meeting
  - Focus on the feedback or questions that you want to clarify

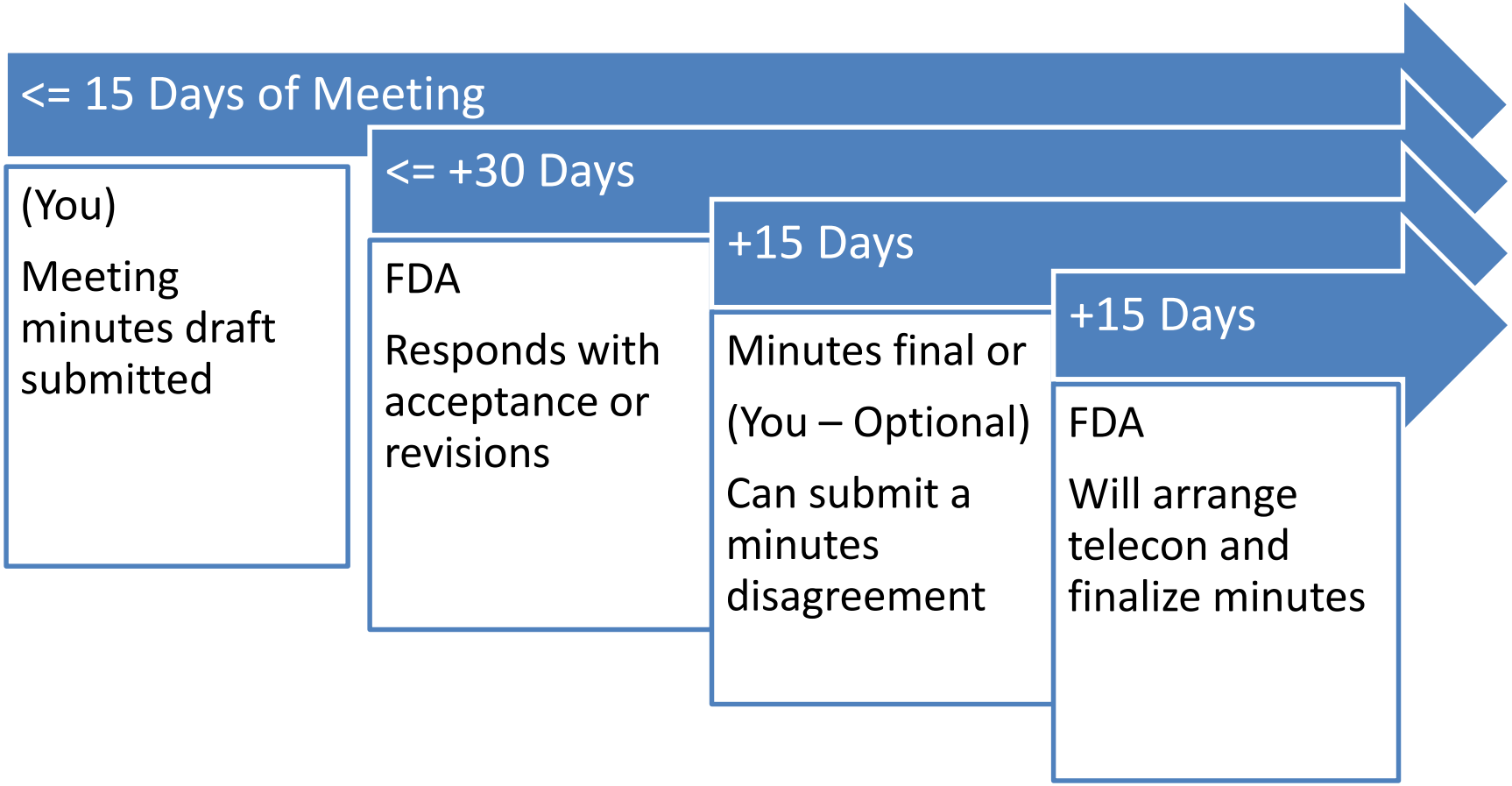
The Sponsor is Responsible for the First Draft of Meeting Minutes

- Within 15 days of the meeting, you should submit these formally as a Q-Sub amendment
  - Clearly state that these are meeting minutes in your cover letter
  - Include the Q-Sub number under which you had the meeting

The Sponsor is Responsible for the First Draft of Meeting Minutes

- Within 15 days of the meeting, you should submit these formally as a Q-Sub amendment
- Minutes should reflect a **summary of the discussion** and key points during the meeting
  - Do not include follow up questions; these should be a new supplement (more on this later)

You Draft Minutes; FDA Finalizes



Q-Submission Nomenclature – Amendments and Supplements

- ***Amendments*** contain additional information about an existing request for feedback, for example:
  - Slides
  - Agenda updates
  - Meeting minutes
  - Meeting minutes disagreements
  - Change of Submitter/Correspondent
- ***Supplements*** contain new requests for feedback on the same device/indication
  - Can be any kind of Q-Sub

Address our Feedback

- When you submit your next submission…
- If you didn't follow our advice, say why

Top Ideas I Hope You Take Away…

- Much more knowledgeable about the different types of Q-Subs and when they might help you
- Pre-Subs are about reducing uncertainty
- Preparation and focus are key to getting the most out of the process
- Write clear cover letters

Questions?

Pre-Sub Questions can Narrow Your Uncertainty

- Analytical Studies
  - Does FDA agree with the proposal for use of contrived samples in analytical studies described in Section X?
  - Does FDA agree with the proposal for incorporating additional sites in place of a day to day component in the precision study?
  - Are the proposed study designs for demonstrating precision and accuracy adequate to support use of the assay in the Phase 3 clinical study?
- Clinical Studies
  - As described, the clinical study will recruit patients at multiple sites in the EU and the US. Are the EU sites for this study acceptable?
- Predicate device
  - Do you have concerns with the proposed predicate device described?
- *Caution*:
  - A pre-sub is not a dry run for a marketing application or IDE

Successful Pre-Sub Meetings take Planning and Focus

- Provide FDA sufficient information to get a complete picture of your device and intended use
- Focus the meeting on what you want to get out of it
  - Not the time for the company history or its management
  - Allow 2/3 of the time for discussion, so your presentation should be about 1/3 of the time
- Bring a dedicated attendee to take notes
- Summarize action items at the close of the meeting; ask for clarification if needed

FDA Provides the Final Meeting Minutes

- Within 30 days of receiving your minutes, we'll either
  - Email you that your meeting minutes were accepted as-is
  - Email you a revised set of minutes
- If you disagree with our revisions, you have 15 days to submit a "minutes disagreement"
  - Clearly state that this is a "minutes disagreement" in your cover letter
  - Include the Q-Sub number under which you had the meeting
  - FDA will arrange a teleconference to discuss the minutes
  - After the telecon, FDA will revise the minutes if needed to reflect the resolution or will note that the parties agree to disagree
- The minutes will then be final

Avoid Common Omissions when You Submit Your Pre-Sub

- Your cover letter should make clear that you are submitting a **pre-submission** and want either a **meeting** (telecon or face-to-face) or **written feedback**
  - Meeting requests get written feedback a few days prior to the meeting
  - Meeting requests should include 3 or more potential dates
  - If this is a follow up to a previous Pre-Sub, include the number of that Pre-Sub
- Describe your device and what it does
  - Describe the physical, chemical, and/or biological principles
  - Describe the software and other device components
  - You may have been working on it for years, but we only have what you tell us
- Provide your current indications for use or the clinical use of your devices
  - For example, the analyte(s) and disease condition monitored, diagnosed, or screened
- Your study design(s) and protocol(s)
- The specific questions you want FDA to answer relevant to your planned marketing application

Breakthrough Devices - General

- General:
  - See EAP Program Web page: https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/ucm441467.htm
  - Our EAP Guidance was issued prior to 21st Century Cures
  - 21st Century Cures expanded the program and renamed it "Breakthrough Devices" (Sec. 515B of the Food, Drug and Cosmetic Act)
  - We are in the process of catching up:
    - We issued draft Breakthrough Device Guidance last October.
    - Draft guidance is not for implementation, so don't rely on those features yet.

Breakthrough Devices – Designation Requests

- Devices subject to premarket approval applications (PMAs), premarket notification (510[k]) or requests for De Novo designation are eligible for Breakthrough designation if the following criteria are met:

1. Provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions; AND
2. The device meets at least one of the following criteria:
   a) Represent breakthrough technologies;
   b) No approved or cleared alternatives exist;
   c) Offer clinically meaningful advantages over existing approved or cleared alternatives including the potential, when compared to existing approved alternatives, to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients' ability to manage their own care (such as through self-directed personal assistance), or establish long-term clinical efficiencies; or
   d) The availability of which is in the best interest of patients.