BiQ Quarterly Newsletter - March 2022 Boulder iQ and Boulder Sterilization

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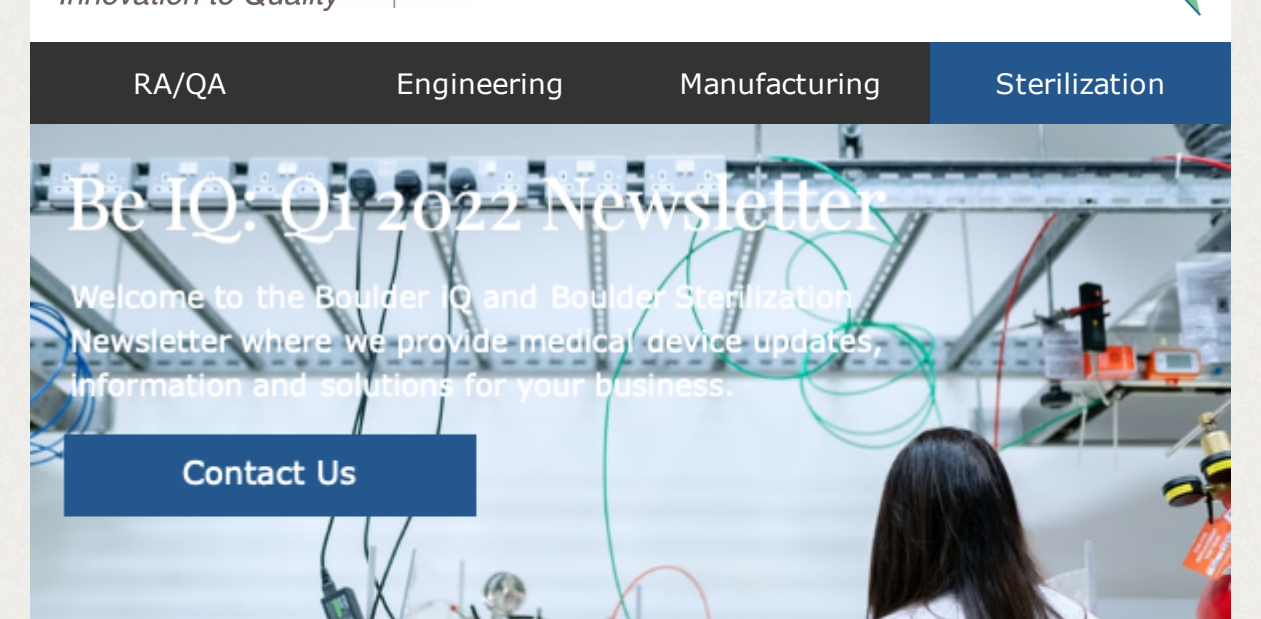


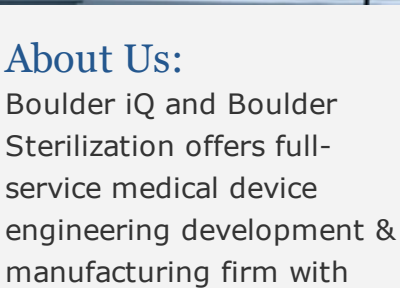
Be IQ: Q1 2022 Newsletter

Welcome to the Boulder iQ and Boulder Sterilization Newsletter where we provide medical device updates, information and solutions for your business.

Contact Us

About Us:

Boulder iQ and Boulder Sterilization offers full-service medical device engineering development & manufacturing firm with regulatory affairs, clean room assembly and on-site EO sterilization. Boulder iQ and Boulder Sterilization focus on the most efficient processes for the best possible "time to market."



Medical Device Packaging Labels 101

Check out our article from MedDeviceOnline. Here, we discuss how to get your medical device packaging done correctly the first time.

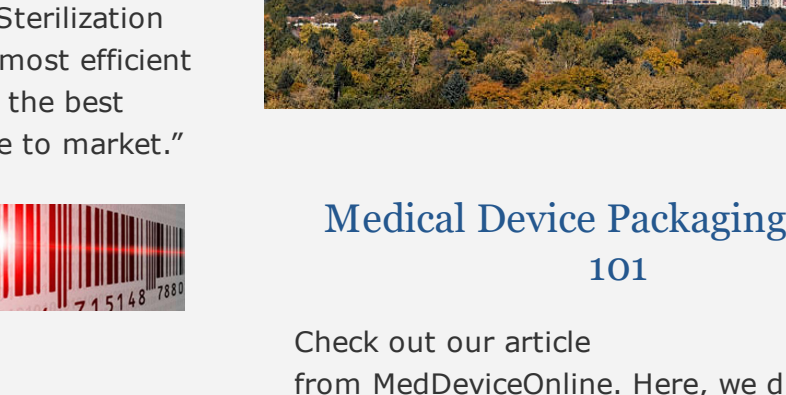
Read more

In this Issue

We take a look at a variety of topics: Unpacking Contracts: Fixed-Bid vs Time and Materials, Animal Study Mishaps, and FDA Q-Sub Meetings.

From The Desk of Peggy

Unpacking Contracts: Fixed-Bid or Time and Materials



Peggy Fasano, COO, Boulder iQ and Boulder Sterilization

We have many clients who come in asking if we do fixed-bid or time and materials (T&M) for our proposals. Now the simple "consulting" answer is that it depends. Fixed bid and T&M have a time and place where they work best. Fixed-bid contracts are exactly like they sound, the price is fixed. This provides easy budgeting for the client and works well for projects that have a well-defined process with little uncertainty. When there are projects that are more evolutionary and have more unknowns, not having any room for flexibility can be challenging for both the consulting team and the client. With a fixed-bid contract, I have seen projects where the quality of the work product was subpar because the consulting team underbid and struggled to break even on the contract. To de-risk this happening, consulting companies typically pad the fixed bid to provide a buffer for any unforeseen risks that may happen in more nebulous projects. Here at Boulder iQ, we have some projects that are fixed-bid since they follow a standard process and rarely have unknown factors. These projects include our sterilization validations, writing 510(k)s, and implementing Quality Management Systems.

For more enigmatic projects, we typically propose time and materials. In this form, the client pays for the exact cost of the work based on an hourly labor rate and any material costs. These projects will still follow a plan and a scope with estimated deadlines, but there is more flexibility to change or adapt the scope of the project as more information presents itself. With T&M, the client has full transparency of the service they are getting and understand exactly what they are paying. Status updates are even more important in this category, so the consulting team and client are aligned with the steps and goals of the project. An issue clients face with T&M is the final cost of the project is unknown and could potentially change significantly, which can be hard for budgeting.

Here at Boulder iQ, we typically provide an estimate for the T&M project and stay within a percentage of this project. If there are large scope changes that will significantly change the cost, that is a conversation that is had as soon as possible. Scope creep can be very easy in T&M projects, so it is important to always keep the objective of the project in mind. We have worked with startups that tend to start adding more features once the development process has started for a product. We take it as part of our job to remind the clients of their goal, which is typically to have a minimum viable product out on the market as efficiently as possible. That type of conversation usually ends in features or add-ons being pushed to the second generation of the product once the company is post-revenue.

In conclusion, there are times when a fixed-bid contract is best and times when a T&M contract is best. When you are evaluating a project, think about flexibility, risks, unknowns, quality, and budgeting and how you would weigh each of these before deciding which is the better method.

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Animal Study Mishaps
How to Prevent Mistakes

By Peggy Fasano, Chief Operating Officer, Boulder iQ and Boulder Sterilization

Introduction:

Animal studies are an important aspect of any medical device product development program. Animal studies provide data and evidence needed for development and regulatory submission. It can illustrate the performance and efficacy of the device in a live biological system. The study can also provide evidence on the safety of the device, demonstrate proof of principle early in the product development process and show the living being's response to the product. It also can be a major investor milestone.

There are two types of animal studies: Good Laboratory Practice (GLP) and Non-Good Laboratory Practice (Non-GLP). GLP animal study follows 21 CFR Part 58 standards thereby these animal studies must follow the approved protocol exactly. The protocol will be developed in collaboration between the lab, quality, and the client. Any protocol deviations will be recorded and inspected by a quality team. All equipment needs to be qualified and calibrated. Due to the complexity of these studies, they are more expensive. Animal studies can also be "Non-GLP". These studies do not need to follow 21 CFR part 28 standards. The protocol can be changed during the execution and can be more experimental. Typically, teams start with several non-GLP studies before conducting a GLP study. Any data needed for a regulatory submission must be done in a GLP study.

Animal studies follow a specific process. A protocol needs to be developed including determining the type of animal to be used, how to emulate the situation needed for the device, the number of devices needed to test, and the number of animal subjects. The study needs to be scheduled with a lab and the correct personnel will need to be coordinated to be on site including the lab technicians, anesthesiologists, surgeon, engineers etc. The equipment and product that is needed for the animal study needs to be thoroughly tested by the client and shipped to the lab. The study will be conducted, data and pictures will be collected. A report will be written following the study summarizing the results.

There are different stages of the product development process that can be conducted for an animal study. The most common stages are at the beginning of the product development during the initial concept generation as well as at the end of product development during the verification and validation stage. Testing early in development is helpful to perfect the performance of the product and initial safety. The animal study testing in the verification and validation stage will show the safety and efficiency of the product.

Animal studies can be critical for finalizing the product development stages and submitting for market clearance with a regulatory body. Animal studies can be tricky to successfully conduct and execute, being it can be hard to recover from a mistake. These studies are not only expensive but also difficult to reschedule. There are plenty of mishaps that can occur during an animal study but most importantly, ways to avoid them.

Animal Study Mishaps:

An example animal study mishap happened during a GLP animal study with pigs. The product was being tested on three pigs in one day, which was an extremely tight timeline. A saline drip was required to be turned on at a specific rate and during specific times. The specific rate was supposed to be 3 mL/min; however, halfway through the second animal subject, it was discovered that the rate was at 3mL/hour not per minute. Being extremely diligent to double and triple check every setting can help to mitigate mishaps like this. Also assigning multiple people to conduct the final checks would be beneficial to the success of the study. Due to the discovery of the incorrect flow rate, additional testing needed to be done on the subject in an attempt to get enough data so the GLP study could remain valid. It resulted in the study needing additional review and approval from the quality team as well as the Institutional Animal Care and Use Committee. This resulted in the testing duration of the study increasing by an additional 3 hours as well as pushing the physical limits of the test subject.

Things happen. In an instant, something can occur that provides insight into the product being tested, or into the procedure or protocol but then the event is over. In testing a new form of endoscope, a flash was seen briefly on the display screen. Fortunately, a multi-view video recording was in process. Such multi-view capability combines a view of the operator (i.e., the doctor), the operating site of the patient, the fluoroscope screen and vital signs monitor simultaneously in one video recording. Note that the cameras and video mixing equipment to accomplish this is not very expensive, and the potential to capture, analyze and correct problems based on the recordings is extremely valuable. In this case the attempted articulation of the endoscope tip while in a particular part of the animal anatomy had placed too much stress on the control wire and snapped a fiber-optic illumination conduit. The design was adjusted to prevent this possibility in future product builds.

Mishap Prevention:

So how do you avoid these mishaps that can complicate and/or end an animal study early? The simple answer is preparation, precision and diligence. Let's dive a little deeper.

Preparation:

When preparing for the animal study, it is essential to plan to test equipment and your device beforehand as well as have extra product in case a failure occurs. For one animal study that was conducted, we brought 10 products for an early-stage product development animal study where only one was needed, and all 10 were used.

In addition to more product, create data sheets beforehand of all manual data that needs to be collected during the animal study. This requires great attention to detail and thoroughness to determine all these data points prior to starting the study. This will keep the team organized, ensure all data is collected and ideally minimize errors from occurring.

Along with the lab staff, plan on bringing at least 2-3 staff members to ensure the animal study goes smoothly. A study manager should be the lead to ensure the protocol steps are conducted correctly, and that all data and details are collected. An engineering team member should mainly be responsible for the data collection. And a third team member, engineer or quality, should be there for any support where needed. Now obviously, if the product is complicated or the animal study is complicated, more people may be needed during the animal study.

Lastly, if possible, having an in-person meeting with the animal lab team prior to the study can help to ensure everyone is on the same page. The same goes for setting up and checking all the equipment the prior evening to prepare for a smooth study. We have found this helpful with complicated studies where many people are needed to participate in the study.

Diligence:

During the animal study, plan on videotaping the entire animal study so tape can be reviewed if needed, especially if timing is important in the study. The videotaping should be on the animal and a data acquisition system (if used), or any other critical equipment needed using a multi-view video mixer as described in the example above.

In addition, it is important to double, and triple check every piece of equipment, equipment settings, product setup and settings throughout the entire study. Being diligent and continuously checking set points and data points can prevent and catch mistakes early.

Conclusion:

Animal studies are critical for product development and must be conducted with great attention to detail and significant preparation. Performance of product and proof of concept can be proven and later illustrate the safety of the product. Animal studies can be difficult to perform flawlessly but not impossible. Mishaps happen, so it is recommended that several non-GLP animal studies should be conducted prior to a GLP study. Mishaps can be reduced through preparation, diligence during the animal study, recording the data through data sheets, data acquisition systems and videotaping. Animal studies are expensive and hard to reschedule, so it's important to be as prepared as possible in advance. Reviewing, rehearsing, and being fully prepared can make the difference between a failed or successful animal study.

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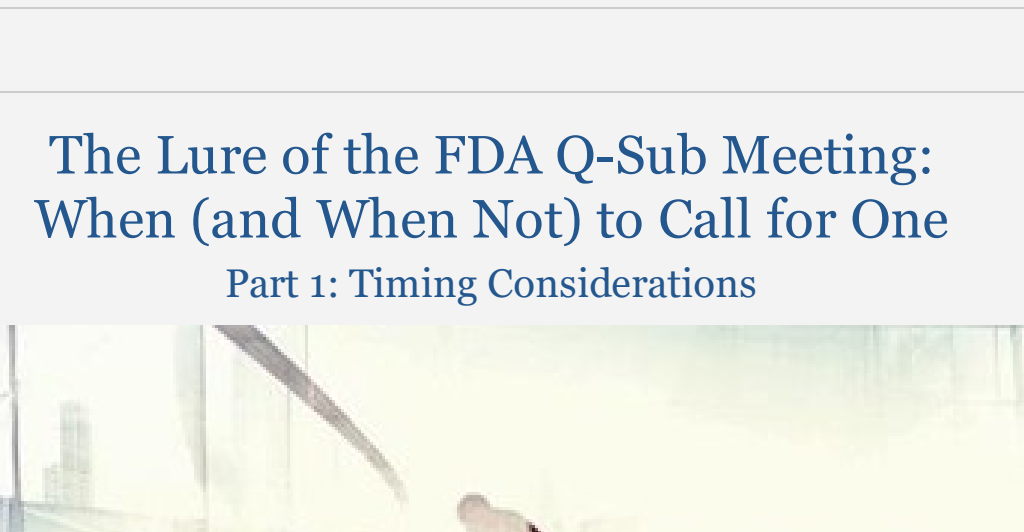
The Lure of the FDA Q-Sub Meeting: When (and When Not) to Call for One
Part 1: Timing Considerations



The Lure of the FDA Q-Sub Meeting: When (and When Not) to Call for One - Part 1

Ah. The Q-Sub. The FDA loves Q-Sub meetings, manufacturers love to get FDA input and they're free. What's the issue?

There is no issue – when product developers use the program well. That entails knowing when to call for a Q-Sub meeting, and knowing how to utilize the program to speed the development process and time to market.

Also known as the Pre-Submission Program, or Q-Sub for short, the FDA's Pre-Submission Program gives manufacturers of medical device and in vitro diagnostic devices a way to get feedback on the regulatory process and requirements for their devices. The Q-Sub program began with the Pre-IDE feedback system of the mid-1990s. The FDA then launched the Pre-Submission Program and expanded PreIDE communications in 2013. In 2019, the FDA broadened the scope of the Q-Sub process further.

Timing considerations for a Q-sub meeting

One of the most commonly asked questions and most frequently discussed topics in the development process is about when to do a Q-Sub meeting. Do it too early, and a manufacturer will not have enough information to get truly helpful answers from the FDA. Do it too late, and the manufacturer could face serious setbacks in getting a product to market, because they've learned they'll need to make key adjustments in the development process.

Consider calling for a Q-Sub meeting when:

- You know you will need specific information on your product classification before you complete your regulatory submission for any Class I, II or III device.

FDA input can be especially useful for devices that incorporate new technologies, or that are "first of a kind" devices. You may gain valuable information to tweak your development process and to streamline the regulatory submission process. In fact, the FDA actively encourages device manufacturers to use the Q-Sub process because doing so helps the final submission's overall quality. However, Q-Sub meeting information is not binding, and should never be confused with a 513(g), which is a binding decision on a product classification code.

- You have well-thought-out, specific questions.

Because the FDA welcomes Q-Subs, they like to know what is going on in device development, and because Q-Sub meetings are free, developers sometimes want to jump in with a barrage of questions. Particularly if the questions are ones the manufacturer could answer itself, this becomes a grand waste of time. It also sends the message to the FDA that the device developer has not been thorough in its preparation and organization.

Remember that the FDA maintains all materials presented for and at the meeting in a company file. They will refer to that file in any other communications or submissions, so it's important to be clear, consistent and professional in any Q-Sub meeting.

- You are ready, willing and able to dedicate time and effort to proper preparation.

Preparing for a Q-Sub meeting is time-consuming and challenging. Here at Boulder iQ, we will typically take 20-60 hours over two to three months to assemble, organize and present the right background information and questions for an effective, valuable Q-Sub meeting.

First, the FDA needs the right kind and amount of background on a company and a product to provide good, comprehensive responses to questions. As passionate as a developer may be about its product, it is important to avoid weighing down the FDA with information. Providing too much can be confusing. The result is inability to answer questions and referrals to a myriad of documents that may or may not be helpful.

Then, the company needs to develop good, on-topic questions. While every situation is unique, it is usually best to ask no more than four very well-thought-out questions. Asking questions that are too general simply wastes time. Types of questions that fall under this category might be along the lines of:

- What kind of testing do we need to do?
- What's the reimbursement code?
- Is my device a 510(k) device?
- What materials should we use?

On the other hand, if the company asked the following types of questions, chances are extremely high that responses would be on target, helpful – and let the company quickly adjust as necessary to meet its roadmap.

- We think that the technology we are using means that our device will fall into a (specified) code for the following reasons. Does the FDA agree? If not, please comment.
- We think that we will need to perform (x, y, z) testing for the following reasons. Does the FDA agree? If not, please comment.

The Phase 0 question

In terms of exact timeframes, some developers are anxious to take advantage of the Q-Sub program and request a meeting early on during Phase 0, before the design control process starts. Whether or not that's a smart idea depends on the company and situation. Usually, one of two scenarios prevails.

One is where the developer has had a professional regulatory expert plan a strong regulatory route to market. In that case, the company may not need a Q-Sub at all – during Phase 0 or later. The other scenario is one in which the manufacturer has enough unknowns and questions to really need FDA input on its product classification code and/or what standards or guidance documents to follow. In that case, a Phase 0 Q-Sub may make sense.

For example, take a company developing a device that is similar to existing devices in function but is using different internal technology. They may have specific, legitimate questions on whether the device falls under the standard device category or a different one for the technology it's using. Here, a Phase 0 Q-Sub could be very helpful. The information the company could learn in the meeting could significantly impact its design control process and everything else down the line.

If you are thinking about requesting a Phase 0 Q-Sub, also consider that all material you submit and present during the meeting will go into a reference file the FDA maintains on your company. If you have a Phase 0 Q-Sub and then pivot significantly in design – which happens frequently in device development – it may confuse the FDA when it comes time for regulatory submission or even a second Q-Sub meeting.

Because many design changes can take place early on, it may be advantageous to wait until you complete Phase 1, design input, to request a Q-Sub meeting. Then you should be able to provide the FDA with the product requirements document, regulatory strategy and instructions for use. With that information, the FDA should be able to confidently and comprehensively respond to questions.

In our next newsletter, Part 2 of "The Lure of the FDA Q-Sub Meeting: When (and When Not) to Call for One" will cover strategic considerations for multiple Q-Sub meetings, how to structure and plan out the meeting, and choice of meeting spokesperson.

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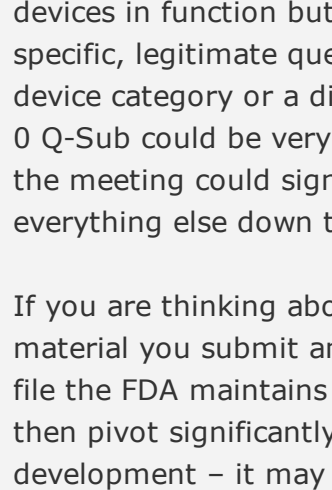

Making Deciscions...

Making deciscions keeps getting more complicated and can be hard to navigate, we at Boulder iQ are here to help collect data, weigh factors, and make choices easier.

Peggy Fasano, COO of Boulder iQ

Contact us	Opening hours	Practice Areas
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