Boulder iQ
Innovation to Quality

Boulder Sterilization

RA/QA | Engineering | Manufacturing | Sterilization

About Us:

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

From the Desk of Founder: Jim Kasic

Dear Colleague:
2020 was quite a year! Everyone was impacted by the pandemic and associated economic challenges. At Boulder iQ we were affected as well, but 2020 turned out to be a significant year of growth for us in the services we are able to offer our clients...

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We take a look at a variety of topics from RA/QA to Phase Gate Engineering to Sterilization and the launch of our new accelerator.

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From the Desk of Founder Jim Kasic (cont.)

...After almost 10 years at our previous location in a multi-company facility, we purchased our own building, allowing us to install much larger and more diverse equipment and capabilities.

- We now have over 2000 square feet of clean room manufacturing area
- We have a new quick-turnaround ethylene oxide sterilization center, the only one between California and the East Coast
- We established the Boulder Medical Device Accelerator (see www.bouldermda.com) to help nurture select start-up and emerging companies

- We significantly upgraded our Regulatory Affairs department, adding Dr. Mike Andrews as leader of the team with his extensive background overall, nationally and internationally, plus his experience as a medical device review executive with the FDA

We're in position to grow dramatically in 2021. We will be doubling our sterilization capabilities (again), while maintaining our best-in-the-industry 4-day turnaround for EO sterilization runs. We have final assembly and packaging capabilities to support placing product into sterilization, and our engineering team is ready to design or help you design your products from concept to production release. Plus, as noted at the top of this newsletter, the EU Medical Device Regulations go into effect this year as well and Boulder iQ has a step-by-step, efficient approach to evaluate your readiness and help you get there!

If you're not familiar with Boulder iQ I invite you to contact us so we can show you what we can do for your company. If you're a virtual company just getting started, we can provide full support services including design, qualification, manufacturing, regulatory clearance and release. If you're a well-established company, we can provide design and qualification assistance and unparalleled speed in performing your ethylene oxide sterilization runs for various test purposes. If you've had regulatory issues such as form 483 observations or a Regulatory Letter, we're here to help, if you need to address the new EU Medical Device Regulations, we have highly efficient programs to help you achieve compliance.

Take a look and we believe you'll want Boulder iQ to become your trusted medical device partner. We will be honored to support you!
My best wishes for a safe and prosperous 2021 to you all!

Sincerely,
Jim Kasic
Founder and Chairman

2021

The Regulatory Scene

The EU Medical Device Regulation: Post Market Surveillance

By Mike Andrews, PhD, Boulder iQ

The EU Medical Devices Regulation (MDR) goes into effect on May 21st. The MDR takes more of a life-cycle approach than the Medical Devices Directive (MDD), which focused on the pre-approval stage of medical device manufacturing. One area which shows significantly increased emphasis over the MDD is Post-market Surveillance.

The word "safety" appears 40 times in the MDD and 248 times in the MDR. The term Post-market Surveillance only appears twice in the MDD, it appears 57 times in the MDR. Certain activities which were undefined in the MDD are fully detailed in the MDR.

For example, the MDD did not define Post-market Surveillance (PMS). However, it did refer to post-market surveillance as *"an undertaking by the manufacturer to institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase, including the provisions referred to in Annex X."* The first of the provisions in Annex X is that the *"clinical evaluation and its documentation be actively updated with the data obtained from the post-market surveillance."* The second provision is that Post-market Surveillance must include Post-market Clinical Follow-up (PMCF) unless not doing so could be justified. No details are provided in the MDD as to what constitutes a PMCF. The PCMF Plan is mentioned only once in the MDD and it too is not detailed.

The MDR filled in a number of gaps in the MDD by providing detail on the requirements for PMS and PMCF. The MDR provides a definition of Post-market Surveillance. It is defined as *"all activities carried out by manufacturers in cooperation with other economic operators to institute and keep up to date a systematic procedure to proactively collect and review experience gained from devices they place on the market, make available on the market or put into service for the purpose of identifying any need to immediately apply any*

necessary corrective or preventive actions."

There are two critical phrases in the PMS definition. The first is "*systematic procedure.*" Thus, a Post-market Surveillance Plan is required. And the findings of the post-market surveillance are to be reported. The reporting takes the form of one of two new documents, i.e., the PMS Report for Class I devices and the Periodic Safety Update Report (PSUR) for Class IIa, IIb, and III devices.

The second critical phrase is "*proactively collect.*" it is not sufficient to merely rely upon complaints that are received as a measure of how your device is performing in the field. You must go out and collect, in some fashion, the full field experience with your device.
The MDR specifies that the data collected by the PMS system is to be used to:

- update the benefit-risk determination and to improve risk management;
- update the design and manufacturing information, instructions for use, and labelling;
- update the clinical evaluation;
- update the summary of safety and clinical performance;
- identify the need for preventive, corrective or field safety corrective action;
- identify options to improve the usability, performance, and safety of the device;
- when relevant, to contribute to the post-market surveillance of other devices; and
- to detect and report trends

The MDR does not include a definition of PMCF. However, it does describe PMCF as a "*continuous process*" in which a manufacturer "shall proactively collect and evaluate clinical data from the use in or on humans of a device which bears CE marking and is placed on the market or put into service within its intended purpose' with the "aim of confirming the safety and performance throughout the expected lifetime of the device, of ensuring the continued acceptability of identified risks and of detecting emerging risks on the basis of factual evidence." The purpose of a PMCF is to:

- confirm the safety and performance of the device throughout its expected lifetime,
- identify previously unknown side-effects and monitor those side-effects and contraindications,
- identify and analyze new risks,
- ensure that the benefit-risk ratio is acceptable, and

- identify possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct.

The MDR details the requirements for the PMS Plan and for the PMCF Plan. The PMS Plan should address the collection and use of the following information:

- serious incidents, including information from PSURs, and field safety corrective actions;
- non-serious incidents and data on any undesirable side-effects;
- trend reporting;
- relevant specialist or technical literature, databases and/or registers;
- feedback and complaints from users, distributors, and importers; and
- publicly available information about similar medical devices.

The PMS Plan should include:

1. a proactive and systematic process to collect the information referred to above. The process should allow a correct characterization of the performance of the devices and should also allow a comparison to be made between the device and similar products available on the market;
2. effective and appropriate methods and processes to assess the collected data;
3. indicators and threshold values that may be used to reassess the risk/benefit analysis and risk management;
4. effective and appropriate methods and tools to investigate complaints and analyze market-related experience collected in the field;
5. methods and protocols to manage the incidents subject to trend reporting, including the methods and protocols to be used to establish a statistically significant increase in the frequency or severity of incidents as well as the observation period;
6. methods and protocols for communication with competent authorities, notified bodies, economic operators and users;
7. reference to procedures with respect to a Post-market Surveillance System and a Post-market Surveillance Report;
8. systematic procedures to identify and initiate appropriate measures including corrective actions;
   effective tools to trace and identify devices for which corrective actions might be necessary;
9. a PMCF plan or a justification as to why a PMCF is not applicable; and
10. the PSUR or the PMS Report

The PMCF Plan details how the PMCF is to be carried out. The PMCF plan must specify the methods and procedures for proactively collecting and evaluating clinical data. The PMCF plan must include the following:

1. general methods and procedures, such as collecting clinical experience, user feedback, and review of the scientific literature, review of device registries, PMCF studies, and other sources of clinical data;
2. rationale for the appropriateness of the methods and procedures utilized;
3. reference to the relevant parts of the clinical evaluation report and to your risk management system;
4. objectives of the PMCF;
5. evaluation of clinical data from equivalent or similar devices;
6. reference to relevant Consensus Standards, harmonized standards used, and relevant guidance on PMCF; and
7. detailed and justified time schedule for PMCF activities, e.g., analysis of PMCF data

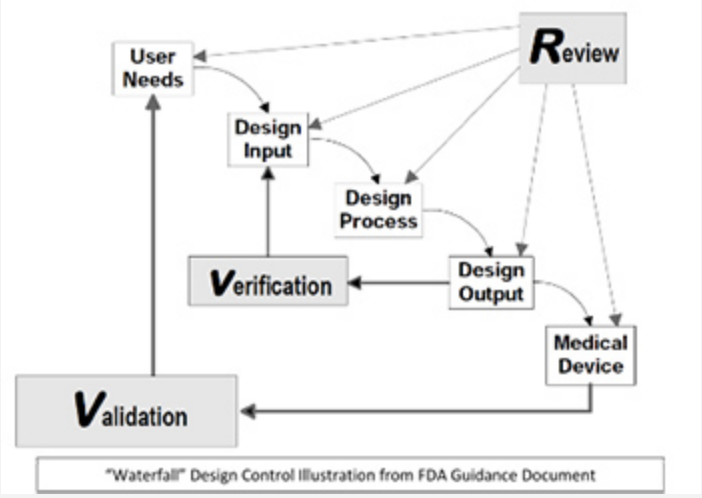
The conclusions of the PMCF evaluation report are to be part of the clinical evaluation and the risk management system. If the PMCF indicates that preventive and/or corrective measures are necessary, identified, they are to be implemented.

In summary, the MDR provides the detail on Post-market Surveillance that the MDD lacked. The Post-market Surveillance requirements are significantly more onerous under the MDR than they were under the MDD. This is consistent with the MDR's life-cycle approach to medical devices and emphasis on safety. Post-market Surveillance must be well planned, and its execution must reflect a proactive approach.

Dr. Mike Andrews is VP of Regulatory and Quality at Boulder iQ

Technology of Interest

Think Fast! Challenging the Phase-Gate Paradigm to Improve the Time to Market



By Jim Kasic and Peggy Fasano, Boulder iQ

THE REGIMENTED PARADIGM

Medical device development is a regulated activity, and rightfully so. The provisions of the FDA Quality System Regulation, international standard ISO 13485 and similar oversight regulations have significantly improved the quality of medical device designs.

They require a Quality Management System (QMS) be established by the developer and in most cases the use of Design Controls along with specific documentation and review requirements throughout the process, including a Design History File (DHF), evidence of Verification and Validation (V&V) testing and a Device Master Record (DMR) on the release of the design to manufacturing. A Design Control process diagram is shown below, excerpted from the FDA Guidance Document "Design Control Guidance for Medical Device Manufacturers."

As part of their QMS, most companies include a "phased" product development process, with specific requirements for each phase. The compliance of meeting the requirements of each phase is strictly enforced by QMS quality policies requiring documented design reviews and phase reviews before completing the DHF for each phase of the process. In many cases, these reviews become the gatekeepers, allowing significant work on the following phase to begin only when the DHF requirements of the previous phase have been satisfied, thus creating a phase-gate approach to controlling the progress of medical device development.

Many tools are available to track activities through the development phases such as Microsoft Project, Playbook, Smartsheet, Agile, etc. But these tools only help implement a specific way of thinking, of proceeding along the development path. We know that significant advantages can be achieved by challenging traditional thinking, without loss of quality control and in full regulatory compliance.

There's nothing inherently wrong with establishing product development phases. It's an appropriate way to set up a project. We've found ways, however, to make dramatic improvements to overall program efficiency while still maintaining project phase controls.

THINK FAST!

Time to market is a critical factor in business success. Once a new product has been conceived, every month, every week it is delayed from entering the marketplace represents lost revenue and presents competitive advantages to others. So how can we improve time to market within a controlled process?

Do everything that is doable up front!

Just because development of V&V test protocols isn't listed until Phase 3 of the development process, doesn't mean they can't be drafted in Phase 1 as soon as the product requirements have been drafted. The same is true for other procedures and documents. Will they change? Of course! They'll need to be refined as additional information is obtained and details determined. But there are significant advantages to doing as much as possible as soon as possible as described below.

Write the IFU first!

In most systems, writing the Instructions For Use (IFU) document for a device is done toward the end of the development process when all the pertinent details are known. We've found great advantage of drafting the IFU as part of the Formative Usability Study (per ISO 62366). The formative usability study typically requires document sketches and presentation of concepts to potential users to confirm that the approach is sound. We go beyond that. In addition to the illustrations, we present an in-service training session to the users following the draft IFU. This is an eye-opener! It really allows the potential user to walk through how the device will be used, but also allows the

developers to think in detail about what they're trying to achieve for their product users. Up front!

This up-front IFU approach has a dramatic impact on the accuracy of the product requirements and specifications. Accordingly, it reduces the number and depth of iterations during the design and testing processes.
Information from the IFU, as modified during the formative usability study, the resulting product requirements document and specifications can then be used to outline test protocols for engineering performance confirmation, verification, and validation to be performed in subsequent phases. Knowing how the design will be tested very early in the process helps streamline the design activities.
Following this Think Fast approach, develop the table of contents for the DHF and for the 510(k) up front. Make an electronic (and physical if desired) file folder for each item in these tables of contents and begin populating them with draft documents as early as possible. Then, as the later phases are completed, there's less time effort needed to complete the DHF and the technical file portions of the 510(k) submittal. They're already mostly done! Think Fast!

Meeting the Documentation and Design Control Requirements

The Think Fast approach doesn't skip anything required. It simply eliminates the "gate" from traditional phase-gate thinking. To complete any given phase, review meetings are held to confirm that all documents required for that phase have been reviewed and approved appropriately. Fine. That doesn't mean that you can't already have a large number of documents drafted for future phases, already for final details to be added then. And by doing those documents early, you force yourself to think about what each will require, thus avoiding oversights that have to be filled in later.

There's a common objection to writing a document, test procedure, or process instruction before the data is ready because "I'll just have to re-do it later." No very much, we've found. Once the IFU, requirements and specifications are in place, the majority of down-stream documents can be drafted with blanks for the details to be filled in later, with all the attendant benefits previously mentioned.

What about templates? Taking the Think Fast approach a step further, can I develop templates to be used in virtually any medical device development project? The answer is yes, to a point.

Each project, each product has its own unique characteristics. Product requirements and specifications for an IV pump and its tubing set are drastically different from those of an electrosurgical generator and its disposable surgical pencils. So, templates tend to be limited, but can still have some value in establishing the major items to be completed.
And what about use of Microsoft Project, Agile approaches, etc.? Those and similar tools can be used with the Think Fast approach as well. The tasks and sprints are restructured to include early implementation of the IFU, test

procedures, DHF and 510(k) submittal document structures and so forth. It's thinking about fast, more efficient product development that's the key to achieving best time to market while maintaining all the appropriate quality requirements and simultaneously complying with all pertinent regulations.

CONCLUSION

Efficient design depends on understanding the breadth of the user needs and testing requirements for the product at the very beginning. Knowing these also allows early drafting of the key documents that will be required in later phases of the project. Think Fast refers to thinking in ways specifically targeted to reducing time to market while maintaining quality and compliance. To Think Fast is also to Thing Smart! The result is time and cost savings in the development process and introducing innovative new products in advance of the competition. It's just good business!

Jim Kasic is Chairman and Founder of Boulder iQ
Peggy Fasano is COO of Boulder iQ and Boulder Sterilization

2021

Sterilization Notes

Quick Turnaround Ethylene Oxide Sterilization

By Peggy Fasano, Boulder iQ

Ethylene Oxide (EO) sterilization is a method routinely used for product that needs to be sterile. EO is particularly great for products that are plastic, have electronics, or sensitive to high amounts of humidity, the gas can penetrate through almost all materials other than metal making it very effective.

These are aspects of EO and despite the large shakeup in the industry over the last year, EO sterilization is here to stay.

Development of EO sterilization cycles is lengthy and costly right now; Boulder Sterilization, a Boulder iQ subsidiary provides a different option than the traditional sterilization channels reducing time, effort and costs. Smaller batch commercially available EO sterilizers here at Boulder iQ enable service organizations to offer quick turnaround (days versus weeks) sterilization services for production lots of product, for prototypes, for animal trial samples, for biocompatibility testing, for sterile packaging testing and for clinical trial purposes. The emergence of such quick turnaround EO services benefits medical device companies needing to test their prototypes, for early production runs and for ongoing production of modest volume, and high value devices.

To learn more about the different types of EO sterilization, please download the white paper.

Peggy Fasano is COO of Boulder iQ and Boulder Sterilization

2021

The Acclerator

Avoiding Failure to Launch

By Jim Kasic, Boulder iQ

A venture capitalist once said that in his experience no really good idea failed due to lack of resources. In my over 25 years of experience, nothing could be further from the truth!

I've seen countless good and great ideas flounder due to lack of resources and lack of good management of resources. It's sad to think how many products never saw the light of day due to inadequate support. But it happens constantly. In come cases it's a lack of understanding of the development process on the part of the inventor. In some cases, it's a lack of connections

to obtain the support needed and in other cases it's simply a lack of physical space, tools, instruments and other capabilities. In all cases, it's a shame to let really good product ideas die, especially in the healthcare field where they could be helping doctors and nurses care for patients.

This is why I founded the Boulder Medical Device Accelerator. I've started several companies myself. I know how hard it can be. I know the myriad of obstacles that stand in the way, and with the Accelerator I intend to provide a way for select startup and emerging companies to leapfrog those obstacles to success!

I'd love to be able to offer the Accelerator to support many, many young inventors and entrepreneurs. The reality in these early days of its inception is that we must be very selective and start with only a few companies to nurture. You can see our philosophy and approach on our website: www.bouldermda.com.

If you're a startup or emerging medical device company in search of a nurturing, supportive launching pad, and have good support from the clinical user community, please contact us. We're interested in finding the few right candidates to support and from there to build and grow our community of successful medical device companies.

Thank you for being an entrepreneur! It's a tough, demanding challenge, but well worth the effort. Keep it up, stay the course and have fun! If we can help, through the Accelerator, Boulder iQ or Boulder Sterilization, it would be our honor to be part of your success!

Jim Kasic is Chairman and Founder of the Boulder Medical Device Accelerator.

2021

Contact Us

Boulder iQ

Regualtory, Quality Engineering, Manufacturing, Packaging

Boulder Sterilization

Ethylene Oxide Contract Sterilization

Boulder Medical Device Accelerator

Medical Device Startup Accelerator

We have great vision

If we see an opportunity to help a client get to the market faster and more effienctly, we'll get it

done.

Peggy Fasano, COO of Boulder iQ

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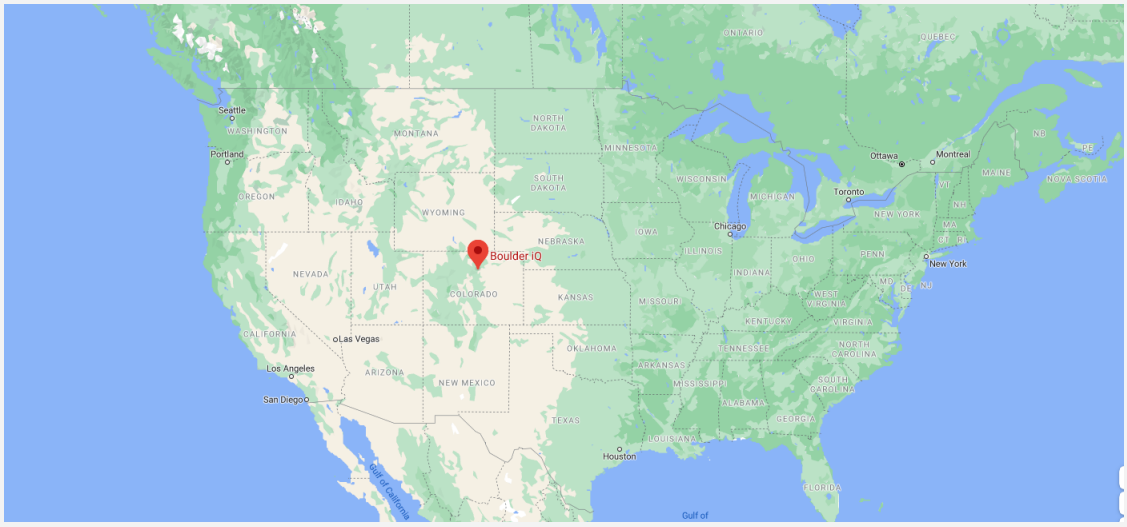
Opening hours

Mon - Fri:
8:00 am to 6:00 pm

Practice Areas

RA/QA
Product Development
Manufacturing/Packaging
EO Sterilization



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