INSIGHTS

into **MedTech Innovation**

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IDENTIFYING & MITIGATING PREMARKET SUBMISSION RISKS

Submission Quality Issues: What's Really Going On?

In 2021, FDA reviewers found major deficiencies in an estimated 80% of PMA submissions and in 67% of 510(k) submissions.[1]

These submission failures are a serious problem—the business and healthcare ramifications can be significant. Submission quality issues lead to denials and rejections that oftentimes result in time and cost overruns, time-to-market delays, and reputational harm.

The numbers associated with premarket submission failures are interesting and truly alarming, but on their own tell only part of the story. To offer additional real-world context, we compared this data against our client portfolio, relationships, and our own experiences working with device OEMs. We did this to get to the story behind the numbers and to offer insights on mitigating risks for both "pre-", and potentially, "re-" submissions.

Our findings indicate that **Design History File (DHF)**-related submission deficiencies and their causes can be the main culprit tripping up medical device OEMs. Common root causes based on general compliance issues are the most prevalent and can be addressed in a straightforward manner. However, we also come across less common root causes such as cyber requirements, UX needs, DHF organizational deficiencies, and more advanced concerns. These issues can be more challenging to mitigate correctly. History also provides some context to this challenge, specifically how FDA scrutiny, and the resultant impact to the DHF, has evolved.

The DHF has always been the primary aspect of the submission per 21 CFR 820, but what it includes and how it's evaluated has changed over time. Going back 10-15+ years ago, there were fewer compliance requirements. User experience and cybersecurity, for example, had a more minimal role in approval of medical devices. Process expectations were lower as guidelines such as IEC 62304 were not the de facto standard. DHFs were smaller so the tolerance for DHF organizational irregularities was higher.

Fast forward to today, and the process has evolved as new compliance considerations have taken effect, along with increased overall submission scrutiny. Common issues from yesteryear still occur, but new issues have moved to the forefront as the FDA's expectations have expanded and evolved.

In our experience, the DHFs built by most medical device organizations don't stand up to FDA rigor for the following reasons:

- **Quality & Consistency** - Incomplete, unclear/ confusing, inconsistent content across artifacts
- **Obsolescence** - Artifacts not kept current with existing systems or procedures
- **Compliance Deficiencies** - Missing artifacts, missing signatures, trace deficiencies
- **Risk** - Risk and associated design controls are not clear or adequate
- **Missing or inadequate coverage in key areas** - cybersecurity, UX studies, new risk management approaches/considerations

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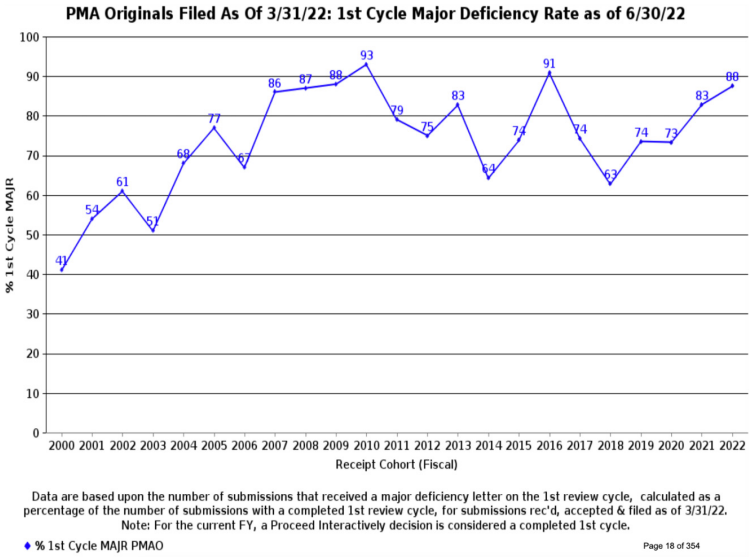
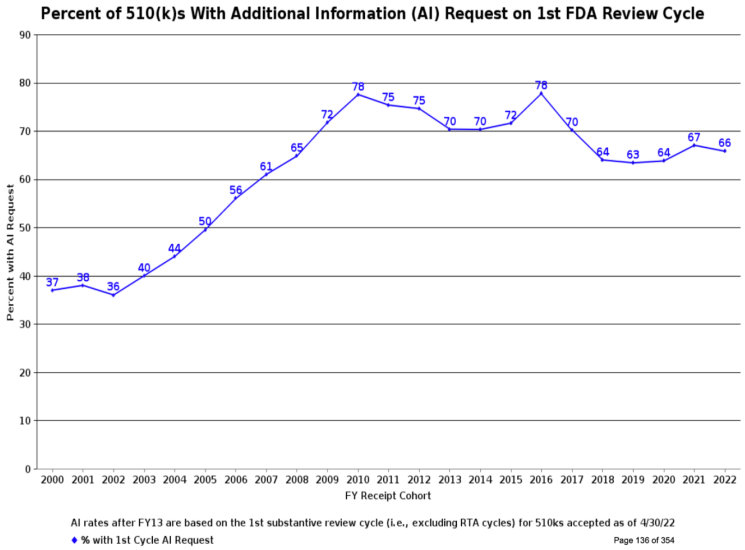
In this article, we'll take a closer look at the ever-changing regulatory landscape and offer insights into how medical device manufacturers can learn to align and evolve to ensure successful premarket submissions.





Evolving Regulatory Landscape

Looking back a decade or more, there was a higher tolerance for submission variations. Organizations were able to navigate straightforward issues such as missing signatures, artifact quality, minor compliance gaps and cohesion throughout the submission package. Today, these failures are still prevalent, but the FDA's higher expectations and increased scrutiny has raised the sophistication, breadth and depth of the issues. This increased rigor and complexity can pose a formidable challenge to an organization's submission efforts.

Adding to the challenge, the submission process has evolved significantly as new compliance considerations have taken effect. New and evolving standards, including **cybersecurity and human factors,** are primary influencers of this evolution. Cybersecurity, as we all know, gets a lot of press, but it remains a primary source of failed submissions. And other issues are on the rise such as non-intuitive user experiences and FDA adjustments leading to an increase in expiring predicates.

Just when organizations feel they have a handle on these items, DHF-specific concerns such as package organization, structure and similar can rear up. As the packages have grown much larger, more complicated and unwieldly, it's no surprise that DHF-specific deficiencies have spiked over the last decade. FDA reviewers have greater expectations and are less tolerant of sloppy DHFs that are not organized in a familiar fashion.

Looking to the future, expect submission issues to increase as submission requirements continue to change and evolve as the technical and operating context of medical devices expands.

Mitigating Premarket Submission Risk

A failed submission can lead to financial impacts due to cost overruns and time-to-market delays. But sometimes just as concerning, **failures can also cause reputational harm both in the market and with the FDA.** And we mustn't forget that failures also leave innovative and potentially lifesaving healthcare solutions sitting on the shelves helping no one. Organizations need a strategy to mitigate submission risks to ensure a successful submission.

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An overarching approach for addressing submission issues must align with these common-sense tenets:

- **Early Risk Reduction** - Follow good risk management practices by identifying and mitigating risks/issues as early as possible
- **Work Smartly** - Employ the appropriate tools and automation with manual processes to minimize compliance and data accuracy gaps
- **Pragmatic Approach** - Understand the true needs and intention of the FDA guidance to ensure the strategy actually addresses the problem

Along with these overarching tenets, we find that across our client portfolio, employing these specific strategies increases the probability of success:

- **DHF Elevation** - Integrate the DHF package components into the DNA of your development process
- **Clear RACI** - Define clear ownership and responsibilities for all aspects of the DHF
- **Quality Focus** - Capture, control, and review package artifacts in real time during the development process
- **Diligence** - Apply a careful and persistent effort, as the upfront impact on development timelines is minor compared to the downstream impact of a failed submission
- **Get Help** - Consult experts when you have questions, gaps, or doubts

Getting to the Root of the Problem

Sometimes the issues are complex and require specialized attention and custom approaches. When a submission failure occurs, it's critical that organizations perform an **objective root cause analysis** with a trained eye–looking at their organization, processes and specific approaches. Sometimes an organization-wide approach is required to identify possible systemic organizational issues that are behind submission deficiencies. This can be tough for most organizations. When a failed submission is the result of months, even years, of development work, it's natural for organizations to start pointing fingers rather than looking inward for answers. *Why did this happen? What are we missing? Where do we start?*

Once there is a clearer picture of potential cause(s), pragmatic mediations can be implemented to help ensure a smoother submission process that will withstand FDA scrutiny. Generally, this can take the form of simple SOP alignment changes and inclusion of best-practice development approaches, to deeper organizational changes that require expert mentoring and guidance. Inflection is not easy and there is no one size fits all, but these issues can be solved.

A partner who understands current FDA requirements and has deep experience applying medical device development best practices can help you successfully navigate these waters. The combination of both can bear the most fruit for medical device manufacturers.

Avoiding the Problem

MedAcuity helps medical device OEMs understand new compliance considerations specific to your device or solution and successfully navigate submission requirements. Our clients leverage our deep regulatory experience to assess and improve the handling of issues, from tactical and broader systemic organizational issues to mitigation of submission risk. We offer a wide range of services designed to help device OEMs avoid problems with their submissions - from up-front assessment and planning to regulatory-experienced full lifecycle software development.

And, if you are on the receiving end of a failed premarket submission, we can conduct a gap analysis and remediate the identified problems. Let us guide you in building an appropriate DHF that will stand up to FDA scrutiny, even as FDA expectations continue to become increasingly exacting.

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1. *3rd Quarter FY 2022 MDUFA IV Performance Report - September 7, 2022 | https://www.fda.gov/media/161485/download*

ABOUT MEDACUITY

MedAcuity, a software engineering firm, partners with companies to address the business and technical challenges inherent in developing complex software-intensive solutions. Offering a combination of strategic consulting services focused on aligning product technology strategy with business goals and full lifecycle software development expertise, we accelerate the pace of innovation for leading companies and innovators in the MedTech, Life Sciences and Robotics industries. With over a decade of experience in software design and development methodologies for highly regulated and compliance-driven environments, our technical capabilities span all levels of software from embedded systems to mobile devices, the cloud and enterprise technologies. Contact us at **medacuitysoftware.com**

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