BrightInsight

WHITE PAPER

How an Unregulated Internet of Things Platform Increases Your Risk and Delays Time to Market

Understand the limitations of a Medical Device Data System (MDDS) and how you can future-proof your platform strategy with BrightInsight

Table of Contents

Executive Summary

There is a common misconception that determining whether you need an unregulated Internet of Things (IoT) platform or a regulated IoT platform is about the product(s) hosted on the platform.

This is not the case, however. The need for a regulated platform is predicated on the intended use of the data collected and where the data are processed or analyzed, not about whether you're hosting data from a regulated Class II or III (FDA) or Class IIa, IIb or Class III (EU) device.

In this white paper, we outline the limitations of an unregulated platform, or a platform for transferring data (known as a Medical Device Data System (MDDS) in the United States), including the types of use cases that an unregulated platform can and can not support.

We also discuss the importance of developing the regulatory strategy for your digital health products now, to be prepared for the future. Most MDDS platforms do not offer a sustainable regulatory infrastructure to support more mature digital health solutions.

From our code to our culture, BrightInsight is built to support regulated digital health solutions. We understand the highly regulated environment that our biopharma and medtech customers operate in, and as such, have built a team that's committed to quality and a platform that is compliant with the standards and regulations needed by our customer's various digital health solutions.

The purpose of this white paper is to clearly explain how the regulated BrightInsight Platform differs from an MDDS platform, and help you decide which type of infrastructure you need today and in the future.

Uncertainty Surrounding Digital Health Regulations

There is substantial confusion around the digital health regulatory landscape.

Through our market research, interviews with regulatory thought leaders and conversations with customers in the field, it is apparent that global medical device software regulations are nuanced and that there are a number of complexities in the specific digital health use cases that biopharma and medtech companies are looking to deploy.

> **Within the evolution of digital health, an increasing number of progressive U.S. and European Medical Device regulations have come into effect. This forward-thinking positioning can cause a lot of uncertainty on how to qualify and validate digital health platforms and medical software. Biopharma and medtech executives usually don't have the time to go through all this legal documentation and need support in navigating through the complex and constantly evolving regulatory maze."**
>
> — Tanja Rohark, CEO & Founder, Digital Chameleon

The numerous updates on digital health from the FDA and other global authorities in recent years suggest that regulations for software products will evolve at an increasing pace, adding complexity to biopharma and medtech companies' already demanding regulatory responsibilities. While authorities should be lauded for keeping up with the fast-moving digital health market by issuing new regulatory updates, keeping tabs on the current thinking has proven to be a regulatory challenge in its own right.

> **When it comes to the regulatory landscape for software used with drugs, you are layering uncertainty on uncertainty. There is uncertainty from the Center for Devices and Radiological Health (CDRH) and from the Center for Drug Evaluation and Research (CDER). The trend overall seems to be toward more regulation."**
>
> — Bradley Merrill Thompson, Epstein Becker & Green, P.C.

Biopharma and medtech execs also encounter a myriad of conflicting marketing materials and sales presentations from vendors attempting to blur the lines between underlying infrastructures that are "medical-grade" or ones that support "GxP", the "good practice" quality guidelines. "GxP" is the general abbreviation where the "x" can stand for various fields, such as "GMP" / Good Manufacturing Practice or "GLP" / Good Laboratory Practice.

Having an infrastructure and the quality systems in place to show good practices for your manufacturing or IT systems is very different – and is regulated differently – than Software as a Medical Device.

> **Traditionally, biopharma companies only deal with regulated software when it comes to their IT systems involved in the drug development and manufacturing process and are typically limited to GxP. When we started our digital health journey we did not know what we did not know, and assumed we had the systems and the skills in place to support regulated digital health software development, but we did not."**
>
> — Senior digital health product executive formerly with a top 25 biopharma company

GxP requires validation of IT systems and not of the medical device software.

> **GxP is a term you increasingly encounter in both the biopharma and medtech industry and refers to guidelines for "good work practice". This is specifically important within software development as adhering to these guidelines promotes quality, such as having batch numbers or quality numbers for your drug or device. However, Digital Therapeutics or Software as a Medical Device (SaMD) are regulated differently than GxP, and the requirements vary greatly, including the way you conduct risk assessment, usability testing, clinical evaluation, validation and more. Our daily challenge is helping our customers understand these differences and to ensure their solutions are compliant and harmonized in both regulatory worlds."**
>
> — Anne Woitzik, Senior Manager Quality & Compliance, Digital Chameleon

Limitations of an Unregulated or MDDS Platform

Many biopharma and medtech executives grapple with whether or not to build solutions on top of a regulated or an unregulated software infrastructure. There are varying opinions on which strategy to take because there is no clear delineation, definition, or existing guidance document to make this decision any easier.

The first thing to understand is that comparing an unregulated platform, or a platform for transferring data (MDDS Platform) to the regulated BrightInsight Platform is like comparing apples to oranges.

Determining the need for an unregulated platform versus a regulated platform is predicated on the intended use of the data and if you're analyzing the data on the platform, not about whether you're hosting data from a regulated Class II or III (FDA) or Class IIa, IIb or Class III (EU) device.

To make this crystal clear, we've included some examples here:

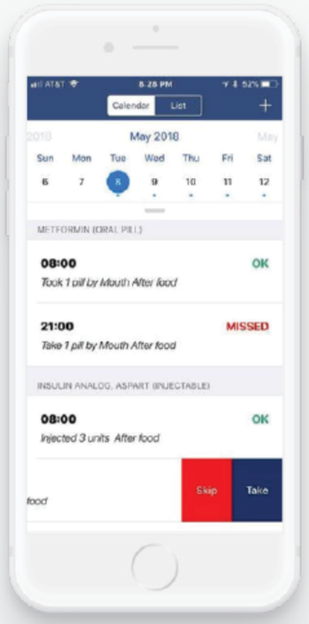
Example Modality/Device	Unregulated intended use of data includes handling device data and results	Regulated intended use of data includes interpretation and analysis
Connected Combination Product	Companion app that sends clinical guidance data across the platform based on generally recognized standard of care, e.g. asthma risk factors for patients using an inhaler	Companion app that provides clinical guidance based on platform analysis of the patient's drug/device utilization data, e.g. recommend inhaler use due to smog warning
Software as a Medical Device (associated with a drug)	Syncing patient treatment plan through a software app that is built on the platform, e.g. doctor uploads Rx dosing plan via the platform for patient access via the mobile app	Sending dose reminders to patient through a software app that is built on the platform, e.g. automated reminder is generated through platform analysis, triggering a patient alert via their mobile app
Class II (FDA) wearable	Data transmitted via the platform from a pulse oximeter (SpO2) that is used as a "general wellness product", e.g. Oximeter data can be analyzed on the platform for breathing events impacting sleep health	Data transmitted via the platform from a pulse oximeter (SpO2) that is used as a medical device, e.g. Oximeter data can be analyzed on the platform for diagnosing sleep apnea

Figure 1: Unregulated versus Regulated use cases

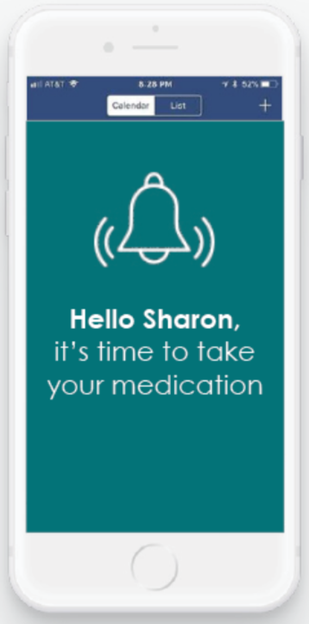
We have two other example use cases from a patient and physician viewpoint to crystalize this concept of regulated intended use of data.

Use Case: From a Patient's View

Here's an example of using data from a connected combination product in an unregulated versus a regulated way.



Unregulated use case:
Displaying medication history



Regulated use case:
Telling a patient to take their medication

Figure 2: Unregulated versus regulated use case from a patient's view

Use Case: From a Clinician's View

Here's an example of using remote monitoring data in an unregulated versus a regulated way in a clinical trial.

Let's say a patient is wearing a Class II (FDA) medical device that transmits data to caregivers. If a doctor were to review raw patient data and make a clinical decision about it, that is an unregulated use case. However, if you were to develop a Software as a Medical Device (SaMD) algorithm that analyzes data on the platform and makes clinical recommendations, that is a regulated use case.

Unregulated use case:
Clinician reviews raw patient data and makes a clinical decision.

Patient wears a Class II medical device during a clinical trial that transmits data to caregivers.

Regulated use case:
SaMD algorithm analyzes data on the platform and makes clinical recommendations.

Figure 3: Unregulated versus regulated use case from a clinician's view

Contemplating your Regulatory Roadmap

Digital-savvy biopharma companies see adding new regulated functionalities as a way to improve patient engagement, deliver actionable insights to providers, and provide more value around their products and therapies.

Moving up the digital health regulatory maturity curve brings biopharma companies from developing simple companion apps, to capturing data from connected medical devices, to generating meaningful insights around the data, to building SaMD solutions. The more advanced regulated solutions include more robust feature sets, such as artificial pancreas systems, connected drug delivery devices, personalized drug dosing systems, and more.

Introducing more advanced capabilities like these can create operational efficiencies through automation and scale, improve patient outcomes through interventions and engagement, and ultimately optimize the value of connected drug, device or combination products. To unlock these benefits and deploy regulated digital health offerings, you need a strategy that includes a regulated IoT infrastructure.

Hopefully the earlier sections of this white paper make it clear that determining whether you need a regulated platform or an unregulated / MDDS platform is all about intended use of the data, not the regulatory status of the product(s) hosted on the platform.

As a biopharma or medtech company, it is important to understand that your intended use of the data will likely evolve over time, and you should plan for that.

> **Whether or not a biopharma or medtech company needs to use regulated software in their clinical trials is a complex question. We regularly encounter this precise challenge with our clients. One of the issues is determining if a software system used in a clinical trial does or doesn't have a medical intent. A "medical intent" is the basis on which the classification of software as a medical device is determined. But—the regulatory authorities in the EU are becoming increasingly demanding and the scope of their interpretation of what is considered a medical device is expanding. Given this evolution, making the determination is not necessarily simple or straightforward."**
>
> – Elisabethann Wright, Partner, Hogan Lovells

You must contemplate your digital health solution roadmap and what type of regulatory strategy you need to support future products. MDDS platforms will not offer a sustainable regulatory infrastructure to support more mature digital health solutions.

Here's an example for a connected inhaler, and how the intended use of the data changes over time:

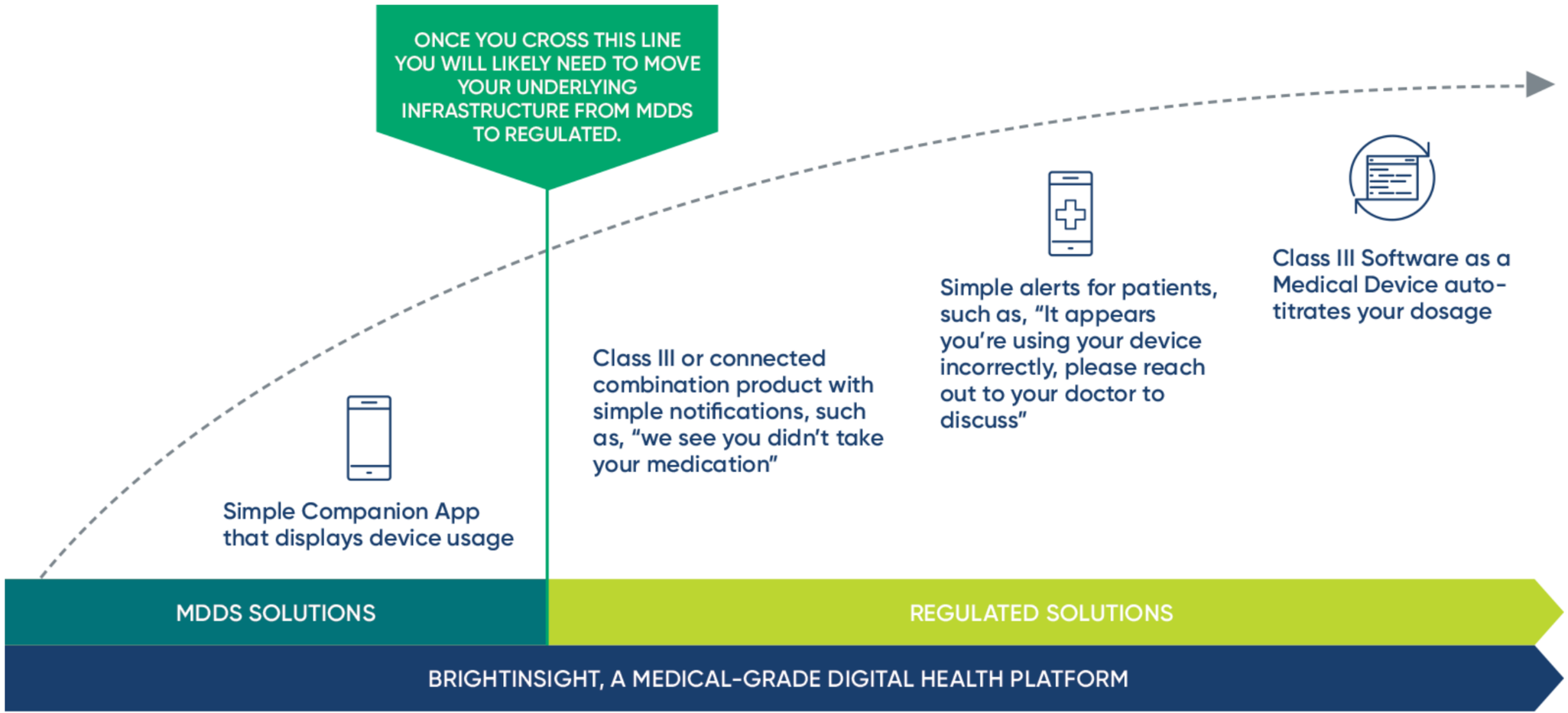


Figure 4: Digital health regulatory maturity curve

You may launch a simple companion app that displays inhaler usage. That's not a regulated use case. But overtime, you want to improve patient adherence and outcomes so you deliver notifications and / or dosing recommendations based on an individual patient's data analyzed on the platform. Once you make the leap from displaying inhaler usage to delivering dosing recommendations, that feature needs to be supported by a regulated infrastructure, with supporting documentation, quality system and more.

> **If your platform solution does anything beyond transferring, storing, converting the format or displaying medical device data – the definition of a Medical Device Data System (MDDS) – the chances are high that some aspect of a biopharma's software will be regulated. If you want to manage risk, you need to adopt a more conservative point of view to future-proof your business."**
>
> – Bradley Merrill Thompson, Epstein Becker & Green, P.C.

Thinking even further down the line, you will likely want to be able to send alerts about using a product or therapy incorrectly, advising patients to reach out to their doctor, or even SaMD that can auto-titrate a patient's inhaler dosage.

Remediation Effort Required to Upgrade an Unregulated Platform to Support a Regulated Use Case

If you have an MDDS platform and you have a regulated intended use of the data on the platform, it might be possible to use your MDDS platform, but there's a significant amount of remediation that needs to occur and that path is uncertain.

Let's take the inhaler example from the previous section. You start with a simple companion app but decide you want to provide alerts to your patients about incorrect inhaler usage from SaMD on the platform. In order to introduce this functionality, you need to invest significant time and resources to secure approval on the regulated intended use of the data.

The below table displays the main ways the required remediation effort will impact your company, including delayed time to market, increased risk and more.

IMPACT AREA	LEVEL OF IMPACT
Time to market	Delayed by months, possibly years to document software modules managing the regulated use case
Internal effort	New documentation and additional testing which takes focus away from core product development
Resources	Need to hire new people with specific regulated medical device and digital health software expertise
Product development	Necessary software architecture redesign for separation of regulated components and data
Process development	Need to develop Quality Management System processes for state-of-the-art software design lifecycle
Regulatory compliance risk	Findings by regulatory authorities may delay product market authorization and require more remediation
DevOps/Maintenance	Advanced change management to control continuous integration/test and delivery environments

Figure 5: Main impact areas of remediation effort required to upgrade an unregulated platform to support a regulated use case

We started our digital health journey and assumed we had the systems and the skills in place to support regulated digital health software development. It was only a year later as we were approaching the first regulatory hurdle that we realized our QMS was misaligned with both US and EU medical device regulations. We then began the long journey to rebuild our QMS amounting to direct and indirect costs of millions of USD. Right before our product launch, another significant gap was discovered in our ability to support post launch activities, something that biopharma companies usually don't have to deal with as it relates to software. In total, our incorrect assumptions on regulatory, QMS and operations requirements for medical device software cost us more than a year of delays which could have been prevented by partnering with a company that had such expertise."

– Senior digital health product executive formerly with a top 25 biopharma company

We all know the devil is in the details, so let's dive deeper into the FDA's requirements to support up to Class III intended uses. Note that your platform will not be compliant with FDA regulations if you are missing these components.

	FDA REQUIREMENTS FOR REGULATED USE CASE	REGULATED BRIGHTINSIGHT PLATFORM
DESIGN CONTROL DELIVERABLES	Level of Concern determination	✓
	Detailed Software Description	✓
	Device Hazard Analysis	✓
	Software Requirements Specification (SRS)	✓
	Detailed Architecture Design	✓
	Software Design Specification (SDS)	✓
	Traceability Matrix	✓
	Software Development Environment Description	✓
	Revision Level History	✓
	Unresolved Anomalies Plan	✓
	Risk Management File	✓
	Usability/Human Factors Assessment	✓
	Cybersecurity Risk Management	✓
SOFTWARE VERIFICATION & VALIDATION	Unit Level Tests	✓
	Integration and System Level test protocols	✓
	Test reports, test summary and test results	✓
	Usability/Human Factors Assessment	✓
		+ Code Reviews, Static Code, Vulnerability Assessment ✓
		+ 3rd Party Design History File Audit ✓
		+ 3rd Party Security testing including HITRUST Certification ✓
GENERAL CONTROLS	Quality Management System – CFR 820	✓
	Medical Device Labeling – CFR 801	✓
	Medical Device Reporting – CFR 803/806	✓
	Registration and Listing – CFR 207	✓
		+ ISO 13485:2016 Certification ✓
		+ EC Certificate for Platform (MDD) ✓
		+ Except Registration and Listing replaced with availability of Device Master File (MAF) ✓
POST MARKET	Complaint Handling	✓
	Change Control on Cloud	✓
		+ Risk assessment of complaints ✓
		+ Software component and unit risk-based decomposition ✓
		+ Risk assessment and continuous review of Software of Unknown Provenance (SOUP) ✓

Figure 6: FDA requirements to support up to Class III intended uses

Impact to your Company, Product Launch and Quality Systems

Building on the "Main Impact Areas" above, here are more details on how upgrading an unregulated or MDDS platform to support regulated use cases will delay your time to market, distract your team and increase compliance risk.

> **Having led the Regulatory and Quality programs for an MDDS platform in a prior role, I can confirm that the level of effort required to support a regulated use case is extensive. The work required from a Quality Management System and documentation standpoint alone requires an entire team, distracts from the core business and isn't a sustainable strategy."**
>
> – Mark Tarby, Vice President, Regulatory and Quality Management System, BrightInsight

RISK AREAS	MDDS PLATFORM	IMPACT TO BIOPHARMA
REGULATORY & COMPLIANCE	• **Platform's Design Control:** An MDDS Platform ("Platform") built following MDDS classification have risk controls that are designed/implemented according to a lower safety class • **Product/Application's Design Control:** The internal product owner of each application on the Platform will be responsible for the product's overall regulatory compliance • **Product Portfolio:** Products on the platform are likely not considered regulated, and are either non-regulated or CDS (Clinical Decision Support) • **Quality System:** IT's quality system is likely not ready to support Medical Device Reporting (MDR), which requires discussions with Notified Bodies • **Change Control:** Platform is dependent on releases from their cloud provider (AWS, Microsoft Azure, etc), without any way of knowing when lower level changes are coming or any control over the runtime environment	• **Risk:** Future regulated projects will need to take on more risk by implementing additional controls, and some might not even be possible, which could lead to compromises to the product and/or overall project • **Development Effort:** Additional effort required to implement risk controls • **Maintenance:** Internal team is responsible for full build and ongoing performance monitoring of the App/ Product, and maintenance/updates of the Design History File (DHFR), rather than leveraging a Master File • **Focus:** Internal team will have to also improve the core platform "regulatory level", which defocuses team's effort from the actual product launch
PLATFORM FUNCTIONALITY	• **Clinical Decision Support (CDS)-focus:** Platform services are focused on functionalities supporting clinical decision support use cases vs clinical trial or patient-facing use cases • **Closed Ecosystem:** Platform and process does not allow anybody outside of Biopharma to develop applications/ products or integrate data into third-party Health IT systems such as EHRs, Payers and more • **Version Control:** There is likely only one instance of the Platform per region, and thus, the Platform version will continue to evolve and will impact all co-located product	• **Development Effort:** Effort required to implement patient-facing use cases, such as ePRO, Device Data Integration, etc. • **Siloed:** The closed nature of the platform and process does not allow other organizations to develop/collaborate, making the Product a "closed" product • **Unnecessary Regulatory Re-filing:** Internal team will be forced to re-file new Platform releases to regulatory authorities even if the release may not be relevant to the specific Product(s)

RISK AREAS	MDDS PLATFORM	IMPACT TO BIOPHARMA
OPERATIONS	• **Multi-tenancy:** The Platform is multi-tenant, which means sharing of the same platform instance across multiple applications • **Shared Responsibility:** Product teams are responsible for deployment and support/ maintenance of their applications	• **Shared Downtime:** A shared instance means Platform maintenance window will impact all products on the platform, with no control from any single product • **DevOps Resources:** Deployment of applications, traditionally done by DevOps, may fall under the responsibility of individual Product teams. IT resources will be constrained. • **Support Resources:** Individual Project/ Product teams will need to allocate resources to support the application software running on the Platform, including Level 1, 2, and 3 support.
DATA PRIVACY	• **Identified Data:** The internal IT team, and maybe the broader biopharma, is not allowed to have visibility into identified data	• **Re-identification:** Inability to have visibility into identified data means it is not possible to re-identify data after the data is anonymized, which limits potential future use of the data • **Risk:** De-identification and anonymization of the data falls under the responsibility of the biopharma company. Any error in this process opens the biopharma to broad organization risk • **GDPR compliance:** Biopharma needs to be able to address questions around how they are able to service patient requests on their data, such as Right to be Forgotten or Right to Modify Data
TEAM COORDINATION & DE-FOCUS	• **Domain Experience:** Internal IT team's experience in the life science industry is likely limited to medical devices with no biopharma background. • **Focus:** Internal IT's mission is to maintain the Platform versus developing products/ applications running on the Platform. Focus becomes on plumbing rather than the differentiated Products, such as Software as a Medical Device	• **Organization Effort:** Project team will need to take on the effort of educating the IT team about all of these risks in parallel to developing the actual product(s) • **Conflict of Interest:** Project team will have to continue to monitor IT resources and how they are allocated across the Products vs the Platform • **Coordination:** Due to the multiple groups involved, additional effort will be needed to ensure coordination

Figure 7: Risk areas that can impact your biopharma company

Transitioning Products from Clinical Trials to Commercialization

In our discussions with biopharma companies, we are regularly asked about whether or not they need a regulated IoT Platform for clinical trials. There is often a desire to use an unregulated platform that is homegrown for a low cost, quick way to capture data in a trial setting.

This is not a solid strategy, however, and will delay your time to market and increase your regulatory risk once you transition the product from clinical trials to commercialization.

If you use an unregulated platform when trialing a new therapy, combination product, companion app, or SaMD where data analysis takes place on the platform, you will run into issues when submitting your product to the FDA for approval. You will need to complete the remediation effort we discuss in the previous section of this white paper, which will delay time to market and introduces regulatory complexity and risk.

> **It's important to use a regulated platform from the very beginning, starting with your clinical trials. Many biopharma execs believe that software regulations don't apply when the software is used in clinical trials. Regardless of whether you choose to commercialize your Software as a Medical Device, you will have needed to document the design of the software from the beginning, before the trial even starts."**
>
> – Paul Upham, Head of Smart Devices, Roche/Genentech

Our customers who have trialed products on BrightInsight are grateful when it comes time to commercialize as all of the necessary documentation, quality systems, testing and more are in place for a seamless transition and product launch. If you use BrightInsight's regulated infrastructure and QMS from the start of a trial, your regulatory approval will be much smoother as you will not have to make infrastructure or data transaction changes. The entire system (the IoT infrastructure and the clinical product) has already been validated within the clinical trial.

BrightInsight, your Regulated Solution

As the leading regulated IoT platform for biopharma and medtech, BrightInsight has achieved the utmost privacy, security, regulatory and quality certifications to minimize customer risk and protect sensitive health information. BrightInsight is built from the ground up to securely manage regulated medical device data and personal health information and is designed to support up to Class III medical device and combination product intended uses.

> **At Roche, most of our commercial products and clinical trials are multi-national, so our regulatory strategy needs to be contemplated across regions and across varying regulations. This will be the case for most leading biopharma companies. If you leverage a solution like BrightInsight that meets the most stringent requirements and maintains compliance as part of their managed service, you don't have to worry about your regulated digital solutions in the U.S. versus Europe versus U.K. and so on. You just know they're compliant."**
>
> – Paul Upham, Head of Smart Devices, Roche/Genentech

Biopharma and medtech companies wouldn't accept a sub-par security, privacy, regulatory or quality system for their traditional drugs or devices, and the same rigor should be applied to their digital health offerings.

> **We are unquestionably moving towards a time where software used in clinical trials will require a regulated infrastructure in the EU. In the interest of caution, a regulated infrastructure is preferable because manufacturers can rely on this infrastructure to demonstrate the appropriate classification and, where necessary, the safety and effectiveness of their software solutions."**
>
> – Elisabethann Wright, Partner, Hogan Lovells

We are committed to the highest quality standards and BrightInsight, Inc. is EN ISO13485:2016 certified and our software development lifecycle process follows EN / IEC 62304. As part of our managed service, we maintain all of the required documentation and processes to ensure regulatory compliance globally.

From a security perspective, the BrightInsight Platform is HITRUST CSF® v9.1 Certified and HITRUST Certified of the NIST Cybersecurity Framework to manage risk, improve security posture and meet compliance requirements. The BrightInsight Platform also has certification for compliance with EN ISO 27001:2013. To support our commitment to the utmost privacy standards, the BrightInsight Platform is HIPAA and GDPR compliant and certified under both the EU-U.S. and Swiss-U.S. Privacy Shield frameworks. The BrightInsight Platform has also achieved the French HDS ("Hébergeur de Données de Santé") certification, validating that BrightInsight ensures data confidentiality, integrity, and availability for our biopharma and medtech customers.

Contact our team today to learn how we can accelerate your digital initiatives while minimizing risk, reducing costs, and getting your products to market faster.