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Ingenuity for life

Siemens Digital Industries Software

Empowering emerging medical device manufacturers

Leveraging the digital infrastructure to align with best practices and accelerate growth

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Detecting and avoiding quality issues

Medical device and diagnostics (MDD) manufacturing is a challenging industry for all players. Not only are technology and products becoming more complex, but regulatory and supply chain factors increasingly compound the requirements bearing down on businesses. The U.S Food and Drug Administration (FDA) is rewarding manufacturers that implement critical-to-quality practices in design and production, shifting its focus to quality first versus compliance. Today, competing in this industry necessitates the proper digital manufacturing foundation to address these growing requirements.

Larger, more entrenched MDD manufacturers have the capital and experienced human resources to implement a digital foundation that improves both quality and cost, creating the most efficient environment for bringing innovation to market. Siemens Digital Industries Software has been a leader in developing that proper digital infrastructure, having worked alongside the FDA throughout its Case for Quality program. The program identifies best practices for moving from detecting to avoiding quality issues. The FDA's work has identified the six pillars of quality manufacturing shown in figure 1.

Siemens has championed the systems that support these quality best practices and is a longstanding leader in manufacturing operations management (MOM) systems tailored for the MDD industry. The MOM systems used by MDD leaders enforce all of the manufacturing behaviors identified above.

Now, small- to medium-sized businesses (SMB) in MDD are looking to create the same infrastructure to get their own innovation to market – rapidly, cost-efficiently and at high quality that achieves regulatory compliance. They are realizing the MOM foundation is not a nice-to-have, it is a must-have to compete in this complex industry. Siemens has recognized this market need and has developed a solution that gives access to the SMB with a scope that meets their critical competitive requirements while reducing the cost and time for implementation and maintenance. The result is a solution that expedites the realization of digital manufacturing, while achieving significant near-term benefits.

SMB MDD manufacturers are proving the value of digital manufacturing. Some of the results from these manufacturers leveraging the Siemens solution – Opcenter™ EX MDD software – include:

- **Reducing** lead time across all products by 15 to 20 percent
- **Reducing** device history record (DHR) review time by 80 percent
- **Reducing** nonconformance reports (NCRs) by 80 percent
- **Completely eliminating** paper costs
- **Taking only two months** from project rollout to measured benefits

This eBook reviews the industry trends in MDD and the unique challenges facing SMB. The requirements for a digital infrastructure that addresses those challenges are detailed, and the Siemens solution developed according to those requirements is explained. Further, we highlight the results achieved by SMB manufacturers that adopted the Siemens solution. Opcenter EX MDD is a part of the Xcelerator™ portfolio, the comprehensive and integrated portfolio of software and services from Siemens Digital Industries Software.

Source: *USFDA as Presented at Siemens PLM – Medtronic hosted Intelligent Design Control and Integrated Risk-Management Event, June 28, 2017*

Traceability
Manufacturers can demonstrate traceability through their production process, suppliers, and distributed products

Control
Manufacturers can demonstrate a focus on establishing, and improving control over their production, supply chain and product quality

Visibility
Manufacturers can demonstrate visibility in their data and metrics. The relevant metrics are visible through all levels of mgt. and staff

Analytics
Manufacturers can demonstrate an effective use of metrics and advanced analytics capabilities

Safety
Manufacturers can demonstrate a high-patient safety focus and responsiveness to issues and speed in identification

Prevention
Manufacturers can demonstrate a strong focus on proactive prevention and continuous improvement

Figure 1. FDA expectations for high-manufacturing quality and manufacturing behaviors.

Trends in the MDD industry

Whether an MDD manufacturer is a global leader or an emerging player, they operate within the same complex environment. They compete to get innovation to market as quickly as possible, with the race against time often an existential challenge for the emerging competitors. MDD manufacturers produce two things – the product and the device history record. Ideally, both must be perfect – perfect product quality, perfect compliance. Yet the trends that face all manufacturers in this segment work against achieving that perfect state.

Increased complexity in products

As innovation and consumer demand pushes us toward mass customization, product complexity is increasing. For MDD products, technologies like the internet of things (IoT), wearables and connected devices are all increasing the complexity in the manufacturing process. As personalized medicine increases, so, too, does the potential impact on the production cycle, leading to concepts of lot size/batch size of one.

The are several implications for this growing product complexity. First, the connection between manufacturing production and product and process design must be strong. Not only do the capabilities of the shop floor need to adjust with the product requirements, but the design teams must understand the constraints of the production environment. As lot sizes decrease, changes to production lines must be done more rapidly. And all of this must be done while maintaining the highest product quality and the details of regulatory compliance.

Global supply chain uncertainty

With the COVID-19 pandemic disrupting global supply chains on a monumental scale, manufacturers have had to reconsider how they plan for and source raw materials and components. For MDD, sourcing requirements have always been significant, with regulatory and quality requirements weighing heavily on supplier selection and ongoing quality monitoring. With 3D printing options becoming more available, component material alternatives have become more significant.

The impact on the manufacturing process includes more complexity in tracking and tracing, as well as supply quality processes. In addition, the options for replacing traditionally sourced components with 3D printed components must be vetted with manufacturing constraints and product quality issues. The opportunity for 3D printing to impact personalized medical devices is also in play.

Growing regulatory requirements

The regulatory environment for the MDD continues to be a significant constraint on innovation and speed to market. In the U.S., the FDA initiatives are shifting its focus to product quality rather than traditional compliance. The European Union (EU) Commission's proposal for Medical Devices Regulations establishes a modernized and more robust legislative framework to ensure better production of public health and patent safety – presenting new challenges for operations in that geography.

Despite regulatory intentions, product recalls are still rising. With social media and consumer engagement, the repercussions of recalls will be increasingly damaging to medical device company brands. Quality inspections will become more difficult to manage, while manufacturers will need to collect data through the entire product lifecycle. Further, the emergence of value-based care will continue to put pressure on costs and production efficiency.

The Unique challenges of SMB

All MDD manufacturers face the challenge described above. But for the SMB, the emerging leaders in this market, there are additional factors that create urgency around speed, efficiency and the path to regulatory approval.

Resource constraints

Emerging MDD companies have a relatively smaller group of process, engineering and information technology (IT) resources to implement, deploy and maintain their hardware and software infrastructure. Every resource consumed has a larger impact on other areas of the business.

In addition, initial investment hurdles are difficult as budgets are constrained. These manufacturers have limited funding, especially if they are getting their initial products launched. They also have limited time – they must get their products manufactured, clear the regulatory process and commercialize faster than their competitors. Although the agility of smaller manufacturers is often an advantage, the constraints associated with deploying the critical infrastructure for success in MDD is daunting.

In this resource-constrained environment, gaining access to critical infrastructure and the mature processes required for compliance has driven the need for a cost- and time-efficient approach to implementing a digital manufacturing foundation. That foundation must come complete with proven processes and an ongoing maintenance approach that fits with the financial position of the manufacturer. Upfront costs as well as recurring costs must be achievable.

Less experienced users and fewer support staff

Typically, the SMB manufacturer workforce has fewer experienced operators and dedicated IT support resources. As these manufacturers move away from paper-based and manual systems to software-guided instructions and data collection, the transition of the workforce may become a gating factor. The value of the systems is directly proportional their adoption, so it is critical for operators to quickly adjust to the new paradigm with minimal training.

This characteristic drives a greater need in the SMB for intuitive, easy-to-use interfaces and workflows that can guide less technology savvy operators. It must support the mobility requirements of the operator. In addition, the maintenance of the systems must be relatively low and proportional to the available IT support.

Speed in the compliance process

Although regulatory approval can make or break an SMB manufacturer, their compliance processes are typically less mature than their larger competitors. These companies have not been around as long, and their employees are often juggling multiple roles. The validation process for high-risk devices is both time-consuming and resource-intensive.

The urgency of an accelerated path to compliance is driving the need for the digital infrastructure itself. It is the infrastructure that systematically supports compliance at scale. The systems needed in the SMB must come equipped with mature processes that reduce the need for expert resources from the manufacturer and accelerate the overall approval process.

Acceleration of growth

Emerging MDD manufacturers must have innovation efficiency if they are to compete with the large industry incumbents. Speed to market is essential, not only to establish a market position, but to bring potentially life-saving products to patients who need them.

If successful, the systems that support that innovation efficiency must scale as the business scales. The digital infrastructure must both accelerate and anticipate growth. As the manufacturer grows in size, product complexity, geographic footprint and supply chain breadth, its systems must be built to grow beyond the initially scoped implementation.

The role of manufacturing operations management

Before we discuss the unique requirements of MOM for the SMB, let's first review the critical role it plays in ensuring product quality, regulatory compliance and speed of innovation. So, what exactly does MOM do?

At its core, MOM is used to create a digital foundation for enabling paperless manufacturing. For MDD, this digital infrastructure creates a self-auditing electronic device history record (eDHR)/electronic batch record (eBR) to support regulatory compliance. Using a digital representation of the manufacturing processes, or the digital twin, MOM enforces the 5Ms of manufacturing – man (operator), machine, material, measure and method. It puts in place safeguards that direct all of these factors of the production process, ensuring products are built as intended. That enforcement builds quality into the product from end-to-end.

MOM creates a single as-built track-and-trace record. It identifies, analyzes and prevents errors. Integrating advanced planning and scheduling as well as manufacturing intelligence capabilities, MOM is used to create the most efficient product environment possible.

MOM can be connected to the larger manufacturing value chain, providing feedback to design as well as enterprise planning. This is called closed-loop manufacturing. The systematic feedback to design and enforcement of changes is key to supporting accelerated innovation. We typically think of five key capabilities that MOM provides in the manufacturing environment.

Five key capabilities of MOM for SNB:

1. **Orchestration:** MOM provides the orchestration and planning of manufacturing and quality operations.
2. **Vertical integration:** MOM bridges the gap between enterprise systems and shop floor automation.
3. **eDHR/eBR:** MOM automatically generates the eDHR/eBR, supporting more rapid compliance processes.
4. **Digital twin:** MOM implements the comprehensive digital twin of the physical production realm, creating a digital representation of the manufacturing process.
5. **Analytics:** MOM transforms big data into IoT actionable information (smart data) and provides the intelligence for continuous improvement and innovation.

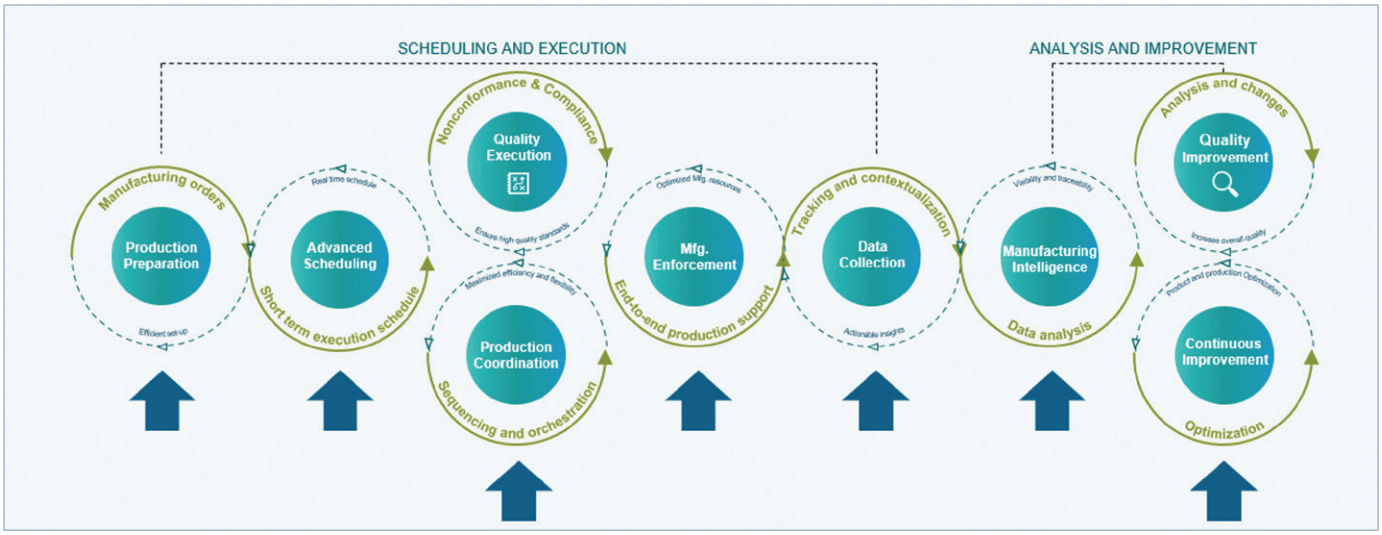

Figure 2. The capabilities of MOM.

Required digital infrastructure for growth of SMB

Given the complexity of both products and the regulatory environment, MOM capabilities are essential for any MDD manufacturer. Opcenter EX MDD is built on a long-time leading manufacturing execution system (MES) platform for MDD, the Camstar™ Medical Device Suite. To make the platform more accessible to emerging MDD leaders, Siemens created the SMB package to address the challenges unique to these companies. The Opcenter EX MDD Rapid Implementation package is a leading digital infrastructure for this segment, tailored for quick and efficient implementation and maintenance while serving as an extensible platform as the manufacturer grows.

The three key pillars of the Opcenter EX MDD Rapid Implementation package includes:

- Standard, preconfigured modules: The prepackaged software configuration that provides the core MOM functionality critical for the SMB
- Rapid Implementation model: An accelerated implementation approach created specifically for the MDD SMB configuration
- Cloud support and maintenance: The option to use Siemens' infrastructure and/or managed services.

Standard, preconfigured modules

The SMB configuration delivers industry-specific, out-of-the-box (OOTB) standard modules, preconfigured for MDD SMB use. These modules include the core functions of MOM that provide the digital manufacturing infrastructure.

With these standard modules, the foundational components of digital manufacturing are provided.

- Enterprise resource planning (ERP) integration: ERP integration is critical for the orchestration of demand and supply into production. Real-time data about orders and the availability of supplied materials and components allow ERP and MES to keep production running efficiently, minimizing interruptions and delays

- Self-auditing eDHR/eBR: eDHRs are paperless electronic systems within MES that enforce production processes and capture all information associated with as-built production records. The self-auditing nature of the eDHR/eBR refers to its capability for error-proofing and real-time visibility necessary to produce consistent product quality every time. Should product quality issues arise, the eDHR or eBR can quickly contain suspect product, either in process or in the field, to take action to address the issue

- Material management: This capability provides full visibility into the movement and consumption of materials across the factory. Material management is critical for factory productivity, tracking the use of materials, evaluating production line capacity and replenishing material as needed

- Tracking-and-tracing: Tracking the status of production and the disposition of work creates the foundation for the eDHR. Status information on qualified personnel, component materials, production conditions, alarms, rework or other exceptions related to the product –

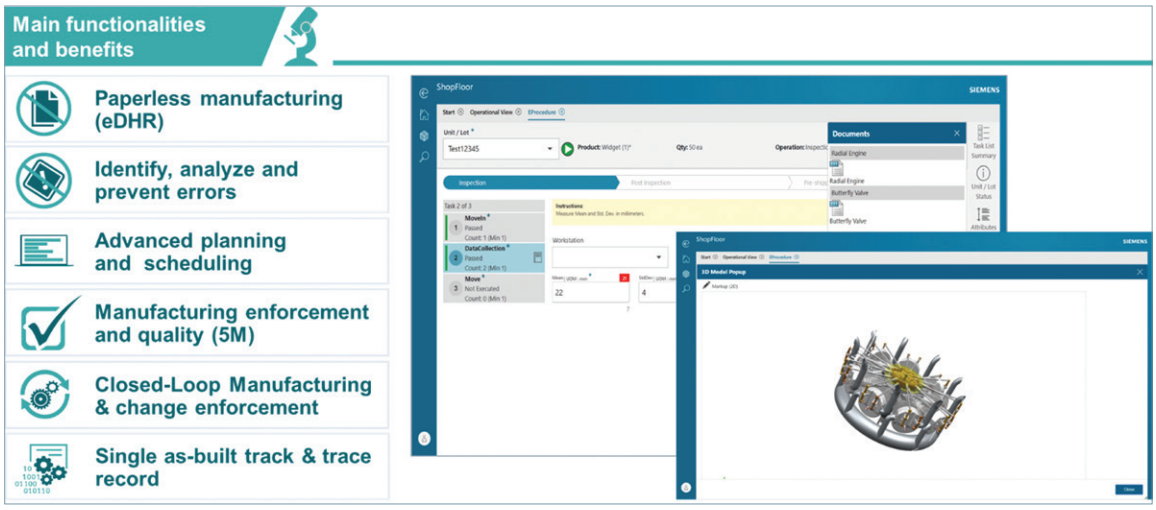

Figure 3. Opcenter EX MDD main functionalities.

essentially the as-built record –is tracked in the system. This detailed production information allows forward and backward traceability of components and their use within each end product

- Sample data collection: Opcenter EX MDD data collection and acquisition capabilities track the real-time status of production equipment and processes as part of the production history. This capability saves time and prevents errors due to manual processes, maximizing productivity while building quality into your products

- Nonconformance management: Opcenter EX MDD improves quality consistency by adhering to global quality policies and orchestrating quality operations. When deviations are detected, nonconformance management capabilities provide exception management, support root cause analysis and enforce protocols to correct the nonconformance. This focus on prevention further reduces the cost of quality, streamlines compliance and reduces regulatory and product risk

- Electronic work instructions (EWI): Comprehensive manufacturing work instructions are provided for the shop floor to create clear process steps. As a result, the most current work instructions are instantaneously where they need to be. Process documentation is automatically updated with revision management, enforcing changes quickly and easily

- eKanban: Electronic Kanban allows manufacturers to efficiently manage their locations and ensure material is properly replenished. eKanban helps control the flow of consumable materials on the manufacturing floor, supports lean manufacturing and provides automatic consumption of materials per the product bill-of-materials (BOM)

Multiple manufacturing process styles are supported, from discrete to batch to process. Given the growing hybrid nature of medical devices and diagnostics, this cross-functional support is critical.

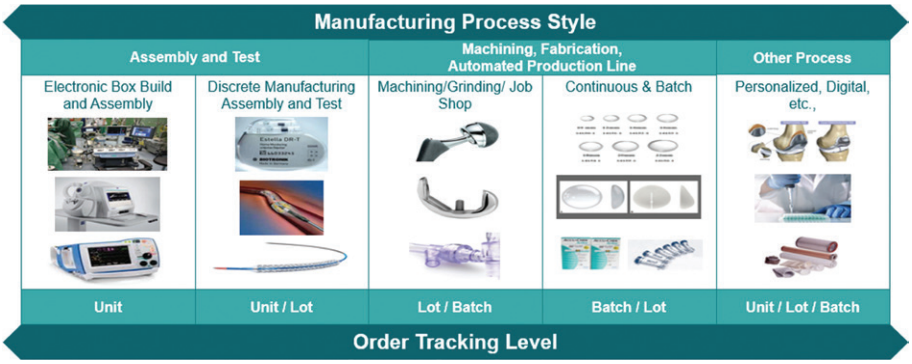

Figure 4. Manufacturing process versus order tracking.

Opcenter EX MDD Rapid Implementation model

Leveraging the OOTB capabilities tailored for MDD described above, the Opcenter EX MDD Rapid Implementation Model (RIM) further streamlines the implementation process to create cost and resource efficiency for SMB manufacturers. The RIM starts with preconfigured functionality and templates to expedite implementation.

The scope of the implementation includes the core functionality that has already been verified as part of the Siemens software development process, saving time and resources. The validation process is further optimized, leveraging Siemens' industry expertise to create a risk-based approach to validation. Risk factors are considered based on severity of impact to a patient, and the probability the impact would occur. Siemens has already identified the functionality that creates patient risk and uses existing scripts to validate those functions.

As you can see, using the preconfigured modules OOTB reduces a significant amount of validation intensity during the project phase.

Risk rating		Testing technique
High	5	Requirement validated using robust scripted testing
	4	Requirement validated using limited scripted testing
Medium	3	Requirement validated using unscripted testing
	2	Requirement validated using ad hoc scripted testing
Low	1	Relies on vendor audit and baseline assurance

Table 1. Risks versus testing requirement.

Patient risk	Out-of-the-box	Configuration	Customization
High	3	4	5
Medium	2	3	4
Low	1	2	3
None	1	1	1

Table 2. Risks versus product feature.

Validation documentation is comprehensive while giving manufacturers the ability to add and remove content. Siemens provides the protocols and the manufacturer updates and executes reports. The output includes:

- Master validation plan: This plan defines the activities, tasks, deliverables and strategy to outline computer systems validation (CSV) strategy and the CSV plan. It shows the scope of validation activities performed, describes the supporting documentation and how the validation project will be conducted
- Functional requirements specification (FRS): The FRS identifies all MOM requirements to be implemented
- Failure modes effects analysis (FMEA): The FMEA documents a risk score for each requirement identified in the FRS. The risk score drives the level of testing required in the course of the validation effort. The risk score is driven by the likelihood of the system failing to meet a requirement, and the seriousness of the system failing to meet a requirement
- Installation qualification (IQ): Verifies the instrument or equipment being qualified, as well as its subsystems and any ancillary systems, which have been delivered, installed and configured in accordance with the manufacturer's specifications or installation checklist
- Operational qualification (OQ): Verifies that the equipment's performance is consistent with the user requirement specification. All the equipment is tested individually
- Performance qualification (PQ): PQ is the final step in qualification processes for equipment. This step involves verifying and documenting the equipment is working reproducibly within a specified range. Rather than testing each instrument individually, they are all tested together as part of a partial or overall process
- Requirements traceability matrix (RTM): This document links requirements throughout the validation process. The purpose of the requirements traceability matrix is to ensure that all requirements defined for a system are assessed in the test protocols
- Validation summary report: The validation summary report provides a summary of testing activities conducted as part of the Opcenter system validation and reports the tasks and deliverables as per the validation plan. It also provides a final disposition of the status of the Opcenter computer system validation and summarizes any exceptions or deviations

Cloud support

Further supporting the resource-constrained environment of the SMB, Siemens offers cloud-based support in various ways. First, virtual implementation support provides access to expert resources at a reduced cost, scaling the use of these more expensive resources. These experts are available to augment the implementation team on the ground as needed.

Second, Siemens provides an infrastructure as a service option, hosting the solution on remote hardware. This option reduces the investment required by the SMB manufacturer, sharing the cost of the infrastructure among multiple clients. In this case, Siemens is the single point of contact for all operating system (OS) updates, security scanning and 24x7 monitoring. The customer is responsible for the VPN/direct connect requirements.

Third, a manufacturer may opt for fully managed services, which includes infrastructure as a service as well as use of the Siemens' cloud services. This team is responsible for the runtime of the system and solution, with guaranteed uptime, scheduled maintenance windows, single point of contact for support and ongoing software patching and security. This service is a significant benefit for companies with limited IT support resources.

Results of digital manufacturing for SMB

Many SMB manufacturers are adopting Siemens Opcenter EX MDD with significant results.

Edwards Lifesciences

Edwards Lifesciences chose Siemens Opcenter EX MDD for paperless manufacturing and built-in compliance with a focus on product quality. Its paper-based DHR included more than 150 pages, 2,100 manual entries, 150 typed entries and 460 signatures. They were suffering from error-prone processes, with 70,000 preventable errors annually. They wanted a renewed focus on quality rather than the historic personnel focus on paperwork. They were looking to eliminate potentially 40 percent of nonconformance reports at the site.

The company realized much greater improvement. Edwards Lifesciences management reports, "The number of NCRs has almost gone away completely. Our team now has excess capacity to do process improvements, to implement cost reductions and improve product quality."

Terumo Cardiovascular

Terumo was experiencing challenges with scaling and errors with the manual process while manufacturing highly complex cardiovascular products.

Terumo chose Opcenter EX MDD based on its reputation as a leading MES in medical device and diagnostics. They wanted a low-risk partner that had successfully completed multiple installations. Terumo leadership comments, "Opcenter EX MDD is a key enabler to help us get beyond quality and compliance and achieve quality excellence. It offers key process improvements like visibility into the manufacturing floor, real-time feedback and hard stops when needed to prevent defects from moving down the line."

MicroPort CRM

MicroPort CRM chose Opcenter EX MDD to increase efficiency, achieve operational excellence, standardize their processes and support a cultural change within the company. Paper-based DHRs and lack of key performance indicators (KPIs) visibility prevented scalability and making decisions based on data.

Opcenter EX MDD eliminated paper with eDHR, gave them detailed manufacturing traceability, enabled parallel processing to reduce queue and lead times, and systematically controlled specifications to enforce product quality and ensure "correct first time." They were able to standardize their manufacturing processes.

Conclusion

Siemens is championing product quality in the medical device industry. With a strong alliance with the FDA and other regulatory bodies across the world, Siemens brings longstanding expertise to their customers, giving them confidence in their journey toward digital manufacturing.

For emerging medical device companies, Siemens is providing access to the same world-class product that leading MDD manufacturers are using to increase efficiency, reduce cost, improve product quality and deliver compliance – all while improving their overall customer experience.

What this means for the SMB companies in the medical device industry is they have a trusted approach that addresses their resource-constrained environment while accelerating their time-to-market. The Opcenter EX MDD Rapid Implementation package tailored for the SMB reduces total cost of implementation, the need for client resources and time to go live.

When MDD companies partner with Siemens, they know they will be fully aligned with FDA and other regulatory requirements. Further, they will have access to the latest best practices and manufacturing innovation and be able to accelerate the approval process, reduce risk and improve the quality of their products. The path to digital manufacturing has never been easier. At Siemens, we are dedicated to the success of every customer and the value realized by patients worldwide.

About Siemens Digital Industries Software
Siemens Digital Industries Software is driving transformation to enable a digital enterprise where engineering, manufacturing and electronics design meet tomorrow. The Xcelerator™ portfolio, the comprehensive and integrated portfolio of software and services from Siemens Digital Industries Software, helps companies of all sizes create and leverage a comprehensive digital twin that provides organizations with new insights, opportunities and levels of automation to drive innovation. For more information on Siemens Digital Industries Software products and services, visit siemens.com/software or follow us on LinkedIn, Twitter, Facebook and Instagram. Siemens Digital Industries Software – Where today meets tomorrow.

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