

SIEMENS

Ingenuity for life

Siemens PLM Software

Enabling closed-loop
manufacturing in the
medical device and
diagnostics industry

www.siemens.com/plm

Executive summary

The changing healthcare landscape poses enormous pressure for medical device manufacturers. While they already operate in a complex, highly regulated industry, market dynamics such as global growth in the elderly population and the associated chronic diseases, as well as healthcare reimbursement models that are focusing on patient outcomes, are driving the need for innovation at consistently high quality and controlled cost levels. Globalization of manufacturing operations and the explosion in personalization and smart devices further complicates the process of innovation.

While the medical device industry continues to deliver innovative products to market, the historical focus on quality primarily as a regulatory compliance requirement versus a core business objective has been recognized by industry leaders, as well as regulators around the world. In response to this misplaced focus, the United States' Food and Drug Administration (FDA) has established the Case for Quality program, while the European Union (EU) has completely revamped and modernized its regulatory framework to address quality and safety concerns more comprehensively across the entire device lifecycle.

In this environment, it is clear that the underlying internal development and manufacturing processes and systems also must innovate to enable manufacturers to accelerate product innovation while improving quality – a key metric that will dictate their success with patients and providers.

This white paper explores the process and systems innovation that is inevitable for medical device manufacturers – the digital

manufacturing enterprise. The foundation of manufacturing in this new era must be anchored in intelligent, connected, collaborative systems that accelerate the exchange of information across the entire product lifecycle, driving quality, safety and reliability from idea inception through production and into service, and continuously feeding back relevant intelligence to optimize quality in real time at every step.

At the heart of the digital manufacturing enterprise is a closed-loop manufacturing (CLM) capability, which synchronizes and optimizes production across product design, production planning, manufacturing execution, automation and intelligence. Creating a collaborative, connected information loop, CLM continuously improves the cost, time and quality of the manufacturing process to accelerate the delivery of new innovation.

The benefits of CLM directly address today's medical device industry needs. Namely, the simultaneous achievement of:

- More rapid time-to-market
- Greater flexibility and agility with increasing change
- Improved product quality, safety and reliability
- Increased efficiency to lower costs globally

This step-by-step process to CLM details how a well-engineered infrastructure should operate for the digital manufacturing enterprise. The time has come for manufacturing in the medical device industry to adopt the infrastructure that is essential for improving quality while making innovative, life-saving technology accessible for all patients.

The medical device market faces increasing pressure to innovate – both products and processes

New market challenges are increasing the need for medical device manufacturers to innovate

Demographics and chronic diseases

Globally, the elderly population is getting larger, creating an increased demand for medical care that is characteristic of this demographic. The biggest growth in this population is in countries and regions with emerging economies, with the least ability to pay. Yet they have the same chronic disease patterns seen in wealthier countries. While this growing market is an opportunity for medical device companies, we are faced with the challenge of addressing the needs of the global population, in mature as well as emerging economies. How can we make healthcare affordable for everyone, while leveraging the latest medical technologies and procedures?

Globalization of research and development and manufacturing operations

One way to address the affordability challenge is to globalize research and development (R&D) and manufacturing operations, taking advantage of lower-cost labor, local know-how and regional resources in developing countries such as China and India. But manufacturing devices in several



countries in different global regions presents its own challenges. R&D, quality, regulatory affairs, supply chain, manufacturing, marketing, distribution, sales and service all must now be distributed across the world. Manufacturing enterprises need to train globally and ensure the correct processes are used to perform daily work. And correct revisions and synchronization of information must occur in the midst of constant change.

Patient outcome-driven economics

Another key trend is value-based healthcare, where payment for healthcare services is tied to patient outcome. Rather than the traditional fee-for-services-rendered approach where payment is assured by insurance companies and governments for approved diagnostic and therapeutic procedures, there is a trend toward a fixed payment approach in which the hospital or clinic agrees to a preset payment, and the risks of misdiagnosis or ineffective treatments and therapies are the responsibility of the healthcare providers. When there are complications, healthcare costs may exceed the payments. In this emerging scenario, how can medical device manufacturers make certain that they get reimbursed for the use of their devices when treatments aren't as beneficial as intended? How can medical device manufacturers ensure that providers are correctly utilizing their devices and provide evidence that their devices are not contributing to patient complications?

Relentless innovation

With the increasing proliferation of smart devices comes the dependence of software-based features for critical functionality. Personalization is a major trend, adapting diagnoses and therapies to individual patients. Today's consumer culture is driving patients to be more involved in treatment plans and buying decisions. Patients, along with healthcare workers, are demanding that the usability of healthcare technology be on



par with consumer products such as smart phones. In response, medical device companies are developing new devices with more electronics and software at a faster pace in order to remain competitive and increase profit margins. However, the R&D and manufacturing processes necessary to realize these new devices is significantly more complex than for older, simpler devices. How do manufacturers avoid delays in projects with multidisciplinary engineering teams and new suppliers spread across the globe? How do manufacturers manage the increased risks associated with more complex devices, new manufacturing methods like additive manufacturing and the need for more education to use devices for delivery of healthcare services?

In the midst of these challenges, the medical device industry continues to struggle with quality as their rate of innovation increases.

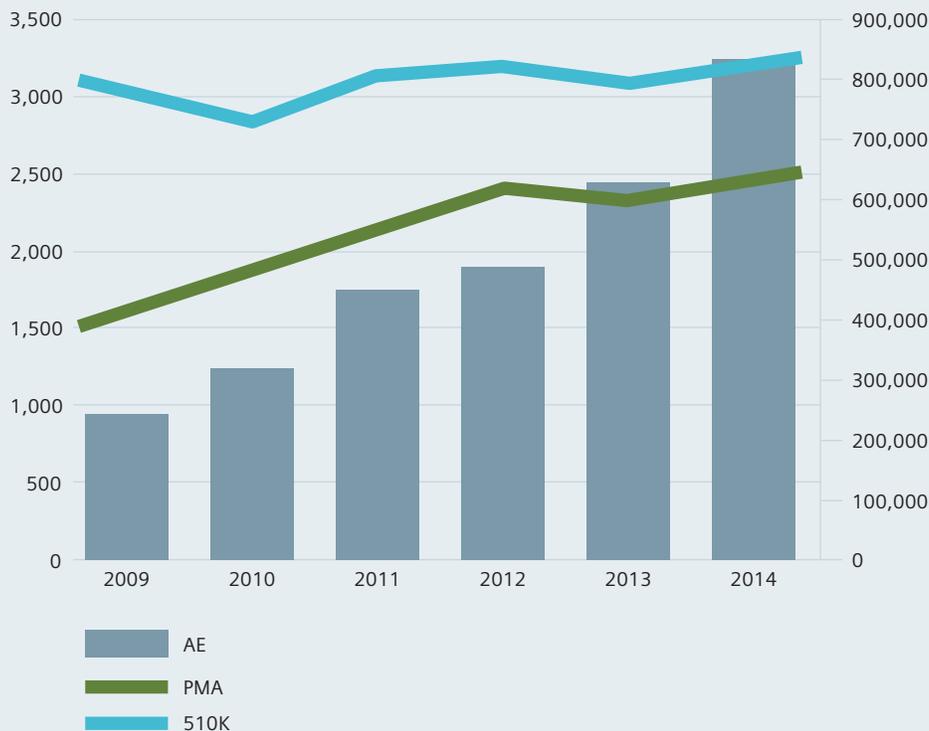


The best efforts with legacy processes are simply not good enough

The graph below depicts the growing flow of innovation from 2009 to 2014, as measured by Premarket Approval (PMA) and 510,000 submissions to the FDA. Overshadowing those gains is the growth in adverse events reported to the FDA, which have tripled during the same time. The challenges facing the medical device market, exacerbated by the pressure to innovate, are contributing to this degradation of performance. The root of the problem is the growing difficulty medical

device companies have in addressing the industry's need for safe and effective devices by using traditional, outdated product development and manufacturing methods. The supporting systems upon which innovative products are being designed and manufactured across the globe are simply insufficient to handle the growing complexity of this market.

Three times increase in adverse events



At Siemens, we propose a holistic approach that transforms a traditional value chain into an integrated product and production life-cycle – from product design to production planning, production engineering, production execution and service. We call this the digital enterprise. It is enabled by an integrated product development and manufacturing platform, model-based product and manufacturing process definition, and digital threads to establish design control surrounding digital twins for both the product and production.

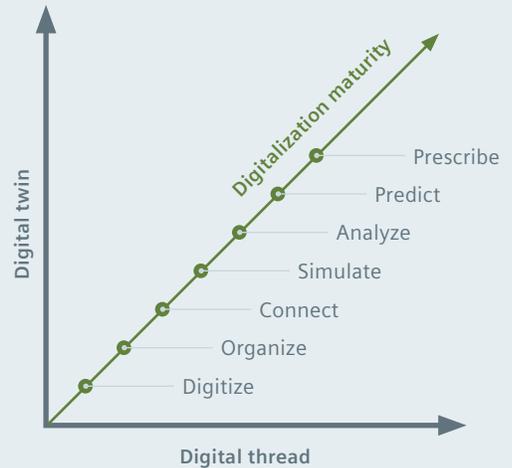
Digital twins are digital replicas of your devices and the manufacturing processes used to produce them. Digital twins enable you to simulate, test and optimize in advance of prototyping and first article production. With digital twins you can explore in a virtual 3D world to find improvements in performance and quality, leading your organization to a better understanding of technical and operational constraints, and learn in advance how close to the edge of failure the device and manufacturing processes will be performing in the real world.

When changes are proposed based on feedback across the digital thread, the impact of those changes across both product and manufacturing engineering domains can be readily traced and carefully evaluated, using updated versions of digital twins.

So how can manufacturers leverage digital twins across the entire lifecycle?

Using production digital twins, we simulate the product and the production process in the virtual world. By running thousands of what-if scenarios, we can identify and resolve product issues, as well as manufacturability issues digitally, in advance of setting up the real plant, assembly lines and fabrication work cells. We also use the digital twins to create electronic work instructions that guide shop floor workers, and automatically generate code to drive automated machines. We use digital twins and digital threads to gain foresight to plan that everything will work perfectly.

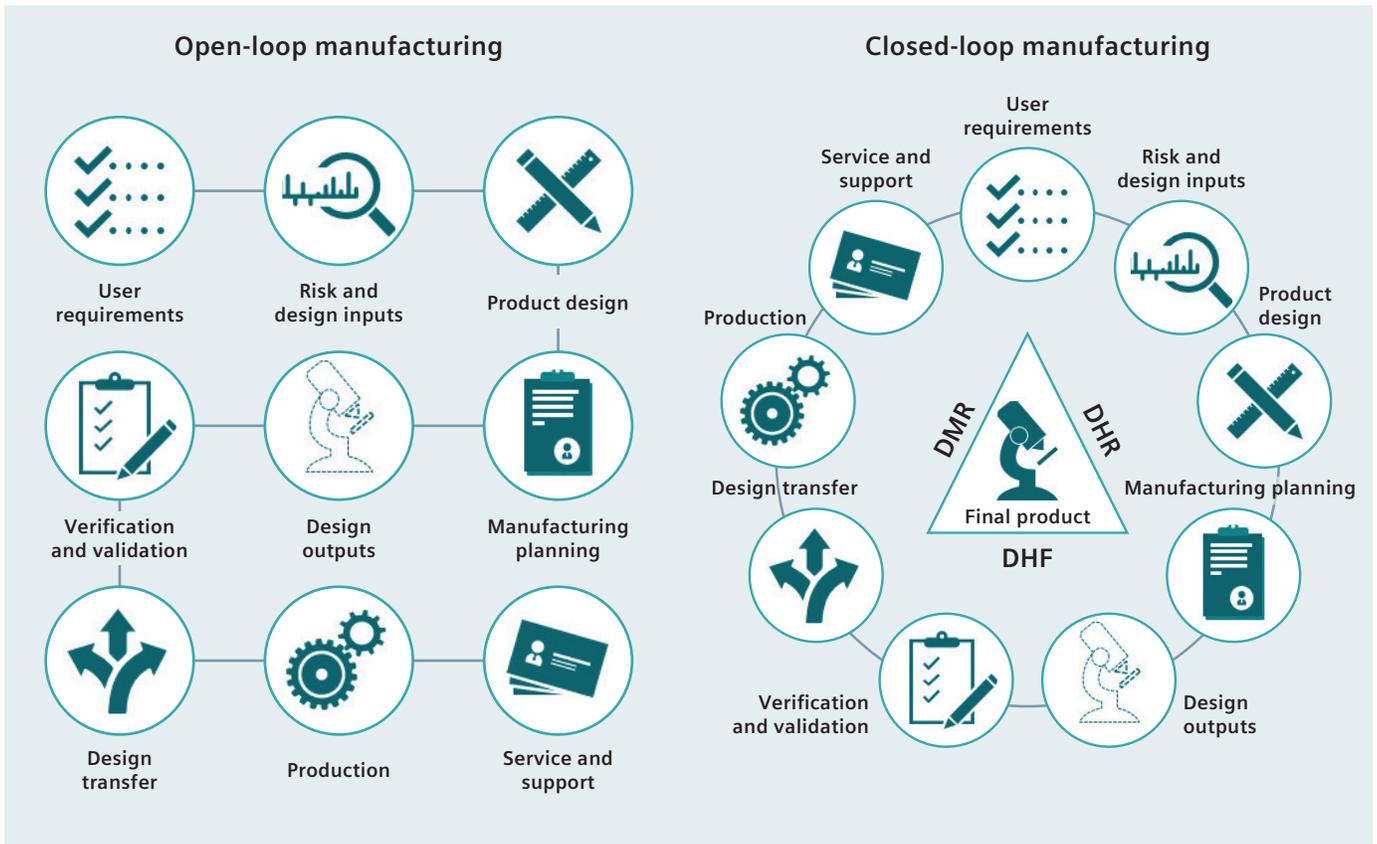
Combining intelligence and connectivity



The value from the production digital twins is further enhanced by re-using the model-based definition of the manufacturing bill of process, already used by the digital twins for simulations, work instruction authoring, and automated code generation: the model-based bill of process is published to the manufacturing execution system (MES), the heart of the manufacturing operations management (MOM).

The bill of process is a manufacturing blueprint that contains the production steps, materials, routings, part programs, quality inspections, work instructions and other items.

It's the job of MES systems to execute that bill of process – to bind the bill of process to an actual manufacturing facility, and coordinate the workflow of the machines, people, materials and logistics in a way that perfectly matches the processes that have been modeled and optimized using the digital twin of production. During execution, the MES captures production data that is analyzed to provide actionable manufacturing feedback, thereby closing the loop to product and manufacturing engineering departments for continuous improvements (that are verified using digital twins) of the released products and processes. This is what we call closed-loop manufacturing (CLM).



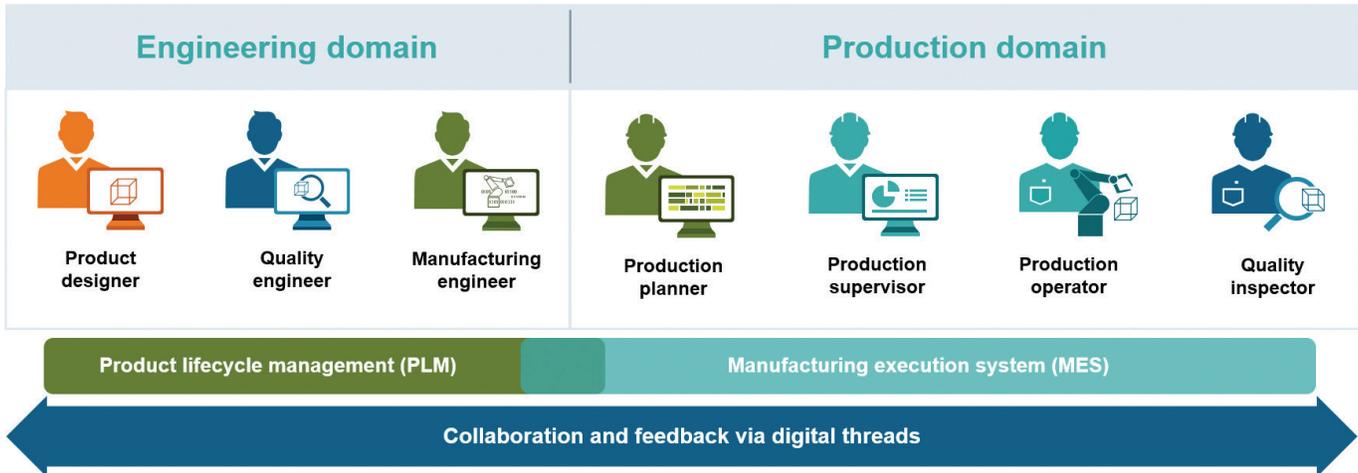
CLM synchronizes and optimizes production across product design, production planning, manufacturing execution, automation and intelligence throughout the entire lifecycle. Creating a collaborative, connected information loop, CLM continuously improves the cost, time and quality of the manufacturing process to accelerate the delivery of new innovation.

These benefits of CLM directly address the needs in the medical device industry today. Namely, the simultaneous achievement of:

- More rapid time-to-market
- Greater flexibility and agility with increasing change
- Improved product quality
- Increased efficiency to lower costs globally

Creating a closed-loop manufacturing enterprise

Connecting the value chain



With the significant benefits of a closed-loop manufacturing approach, why don't we see it universally implemented? A major factor is because it requires the support of an integrated and closed-loop system for receiving product definition, and for creating digital threads to model-based manufacturing process definition with associated production digital twins.

The majority of manufacturers in the medical device industry still operate with manually intensive paper-based processes. And, manufacturers who have invested in automated systems, such as MES, will tend to operate those systems tightly integrated and connected to enterprise resource planning (ERP) for bill-of-materials and process routing data downloads, but not to systems that support early manufacturing engineering tightly coupled with product development and definition.

Unfortunately, the product engineering domain and the manufacturing engineering, planning, and execution domains are commonly segregated. These groups of users are working in silos. Data sharing is manual and error-prone, introducing bottlenecks and non-value added data re-entry causing delays and work product quality issues. The tedious nature of such manual, labor intensive processes is a disincentive to repetitively share work-in-process data, leading to late stage exchange when it is too late to make many changes (without major rework) that affect manufacturability and quality.

In these types of enterprises, which include the majority of medical device manufacturers today, there is a lack of cross-domain visibility and predictive, data-driven evaluation of impact of changes across engineering and

manufacturing. This affects both sustaining engineering and new product introduction and results in business and technical decisions based on incomplete data, without timely analysis of all relevant information across engineering and manufacturing.

CLM brings these domains together on an integrated platform.

Production engineering and process planning

How do these enterprise systems communicate in CLM? Let's look at the process of designing and building a new product, and how communication across functions is enabled in a closed-loop environment.

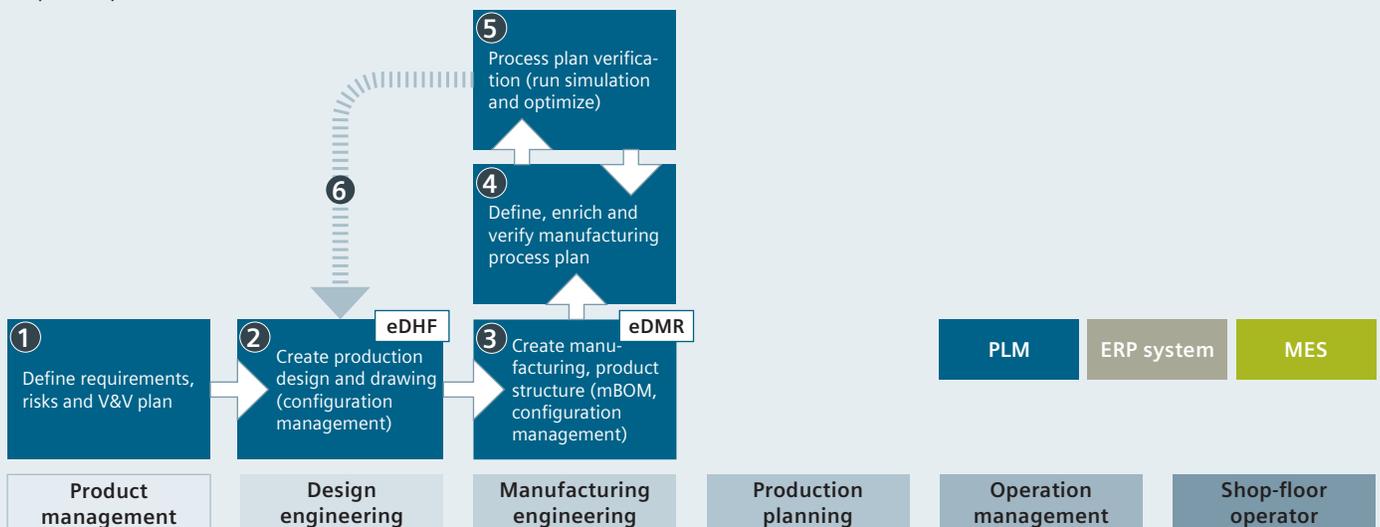
Orienting these functions in "swim lanes" reveals how information flows across functions in a closed-loop environment. The enterprise systems used in this case include:

- Application lifecycle management (ALM). An ALM system is used for design control to manage user needs, decomposition of design input requirements, risk analysis, and traceability to verification and validation test plans and results.
- Product lifecycle management (PLM). A PLM system contains model-based product and process definitions for the design and manufacturing of a product. It stores information like 3D models and drawings of the product, the engineering bill of materials (eBOM), the manufacturing bill of materials (mBOM) and the manufacturing bill of process (BOP), which is the recipe for production, quality assurance, and data collection that can include reference to manufacturing equipment and resources, as well as an association to the physical plant space.

- Manufacturing execution system (MES). MES manages the execution of production, including production orders and data collection.
- Enterprise resource planning (ERP). A generic ERP system in our example will do the material resource planning and coordinate supply chain ordering and receiving.

We will examine the interaction of these four systems across the functional areas that use them – communication in a closed-loop environment across the digital thread. Each step corresponds to the number on the diagram.

1. A product manager uses ALM to define or refine the risks and design input requirements related to a new or modified medical device.
2. Once the new or modified requirements are specified, the design engineer creates/modifies the product design. All the information about the design and the development process for the medical device are captured here. This is where the design history file (DHF) is created and maintained.

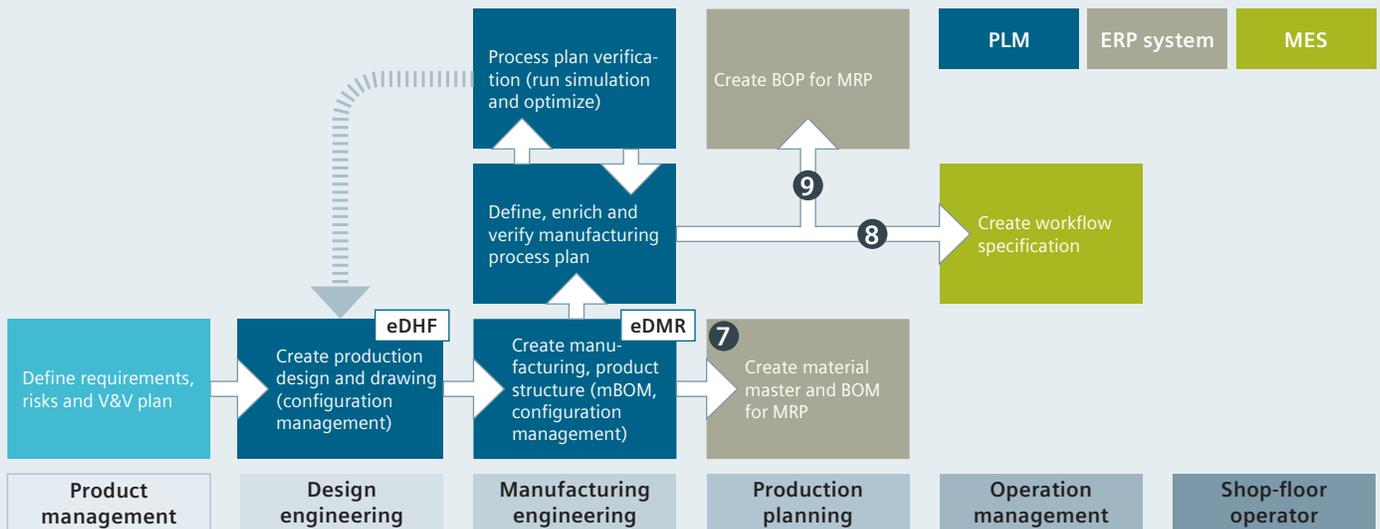


3. Based on the product design, as well as any manufacturing process risks and design input requirements, the manufacturing engineer will define how the new/modified product is manufactured. Throughout this “swim lane,” manufacturing process definition is added to/ updated in the DHF, and in combination with verification and validation plans and results, including clinical trials, all information needed for regulatory submission and design transfer is specified here, establishing the device master record (DMR).
4. The manufacturing engineer creates/ modifies the manufacturing process plan, the recipe for product building, quality testing, and shop floor data collection.
5. The manufacturing process plan is verified using interactive 3D visualization and through simulation using production digital twins, optimizing the efficiency and quality of the process.
6. As a result of process verification, the manufacturing engineer may send feedback to the product designer if the product definition needs improvement. This is the first example of a closed loop that allows design and manufacturing collaboration to improve a product before the product definition is finalized and released.



Product configuration and master data exchange

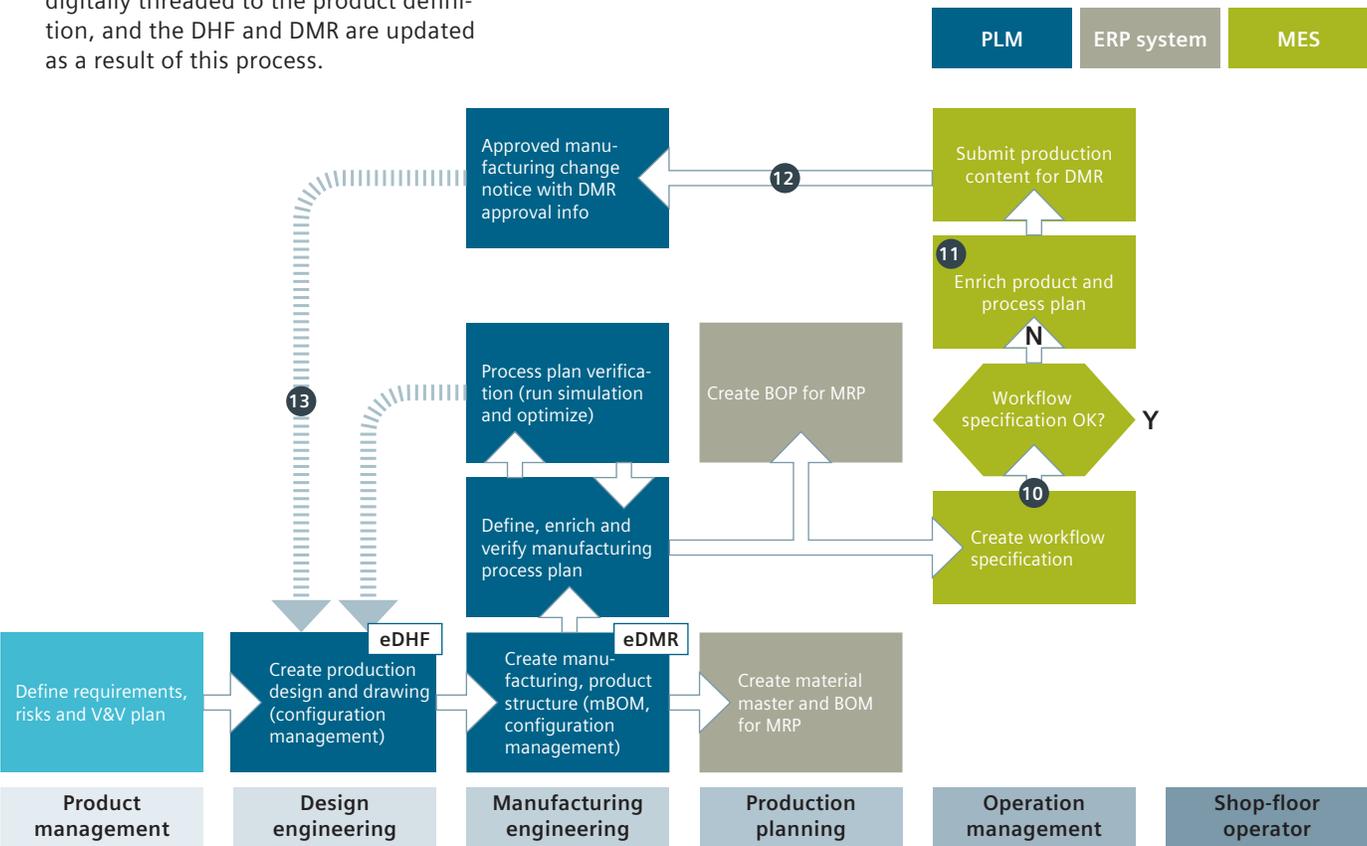
- 7 and 9. Once the model-based definition of the mBOM and the BOP are sufficiently mature, they are passed to the ERP system to keep the MRP up to date.
8. MES, via the digital thread, automatically imports the mBOM and BOP and creates a plant-specific workflow. When the mBOM or BOP is changed, the definitions are automatically updated in MES. Regardless of the number and location of the plants, the new manufacturing process definition will be populated simultaneously and automatically to all plants.



Engineering change and data exchange

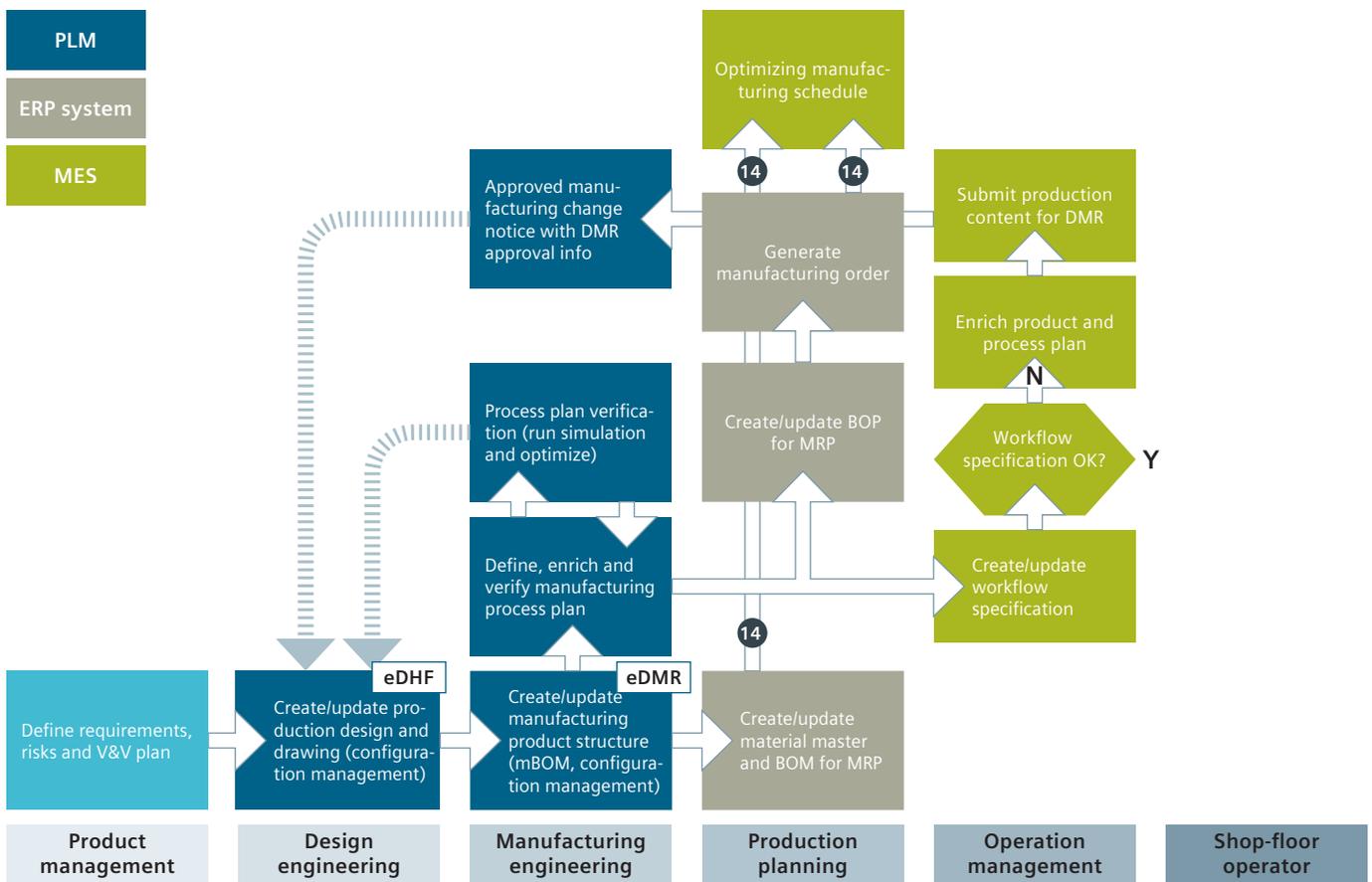
- 10. If a workflow received by MES needs adjustment, or needs additional information for a specific plant, such feedback will be captured and pushed back for modification of the mBOM and BOP.
- 11. MES may also refine and enrich the workflow, using knowledge and information known at the plant-specific operations management level to detail a production-ready workflow.
- 12. The finalized workflow, including plant-specific production content, will be sent to manufacturing engineering for review and approvals.
- 13. In the context of a change notice, the finalized mBOM and BOP revisions and finalized workflow specification, which is the manufacturing process definition, are digitally threaded to the product definition, and the DHF and DMR are updated as a result of this process.

This is CLM, where collaboration across plant-specific operations, manufacturing engineering, and product design improves and optimizes both product and process definitions, using domain expertise to eliminate quality and efficiency issues as early in the lifecycle as possible. All changes progress downstream and/or upstream across the digital threads, enabling comprehensive change impact analysis and fully informed business and technical decisions to result in production of devices with high quality, low cost, and accelerated time-to-market.

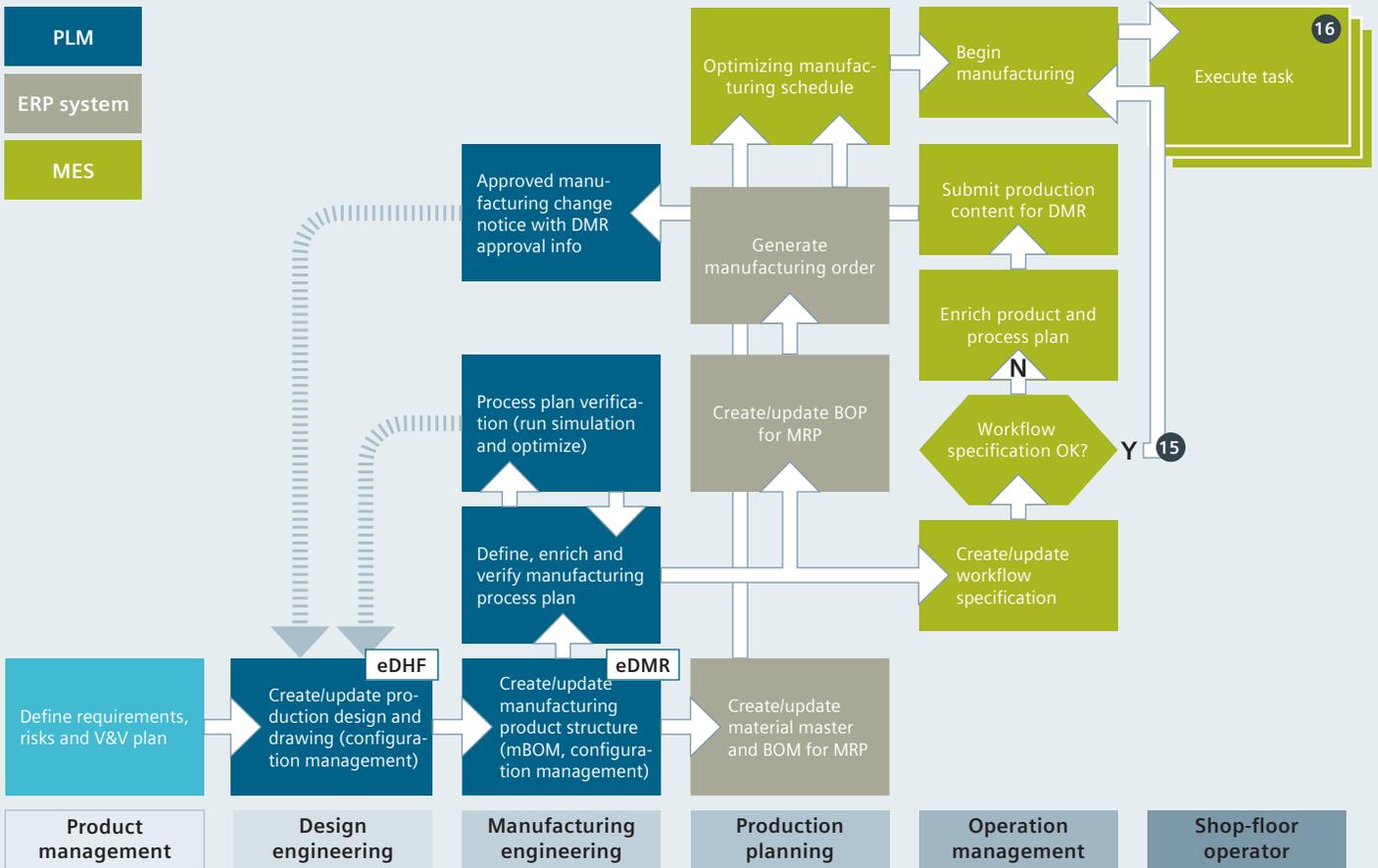


Manufacturing process execution

14. When product and process definitions are finalized and released, ERP is updated and will issue production orders. MES will import all the production orders from ERP and schedule the most efficient execution plan, combining business needs, such as delivery time for a specific production run, with plant-specific information, such as inventory and availability of manufacturing resources.

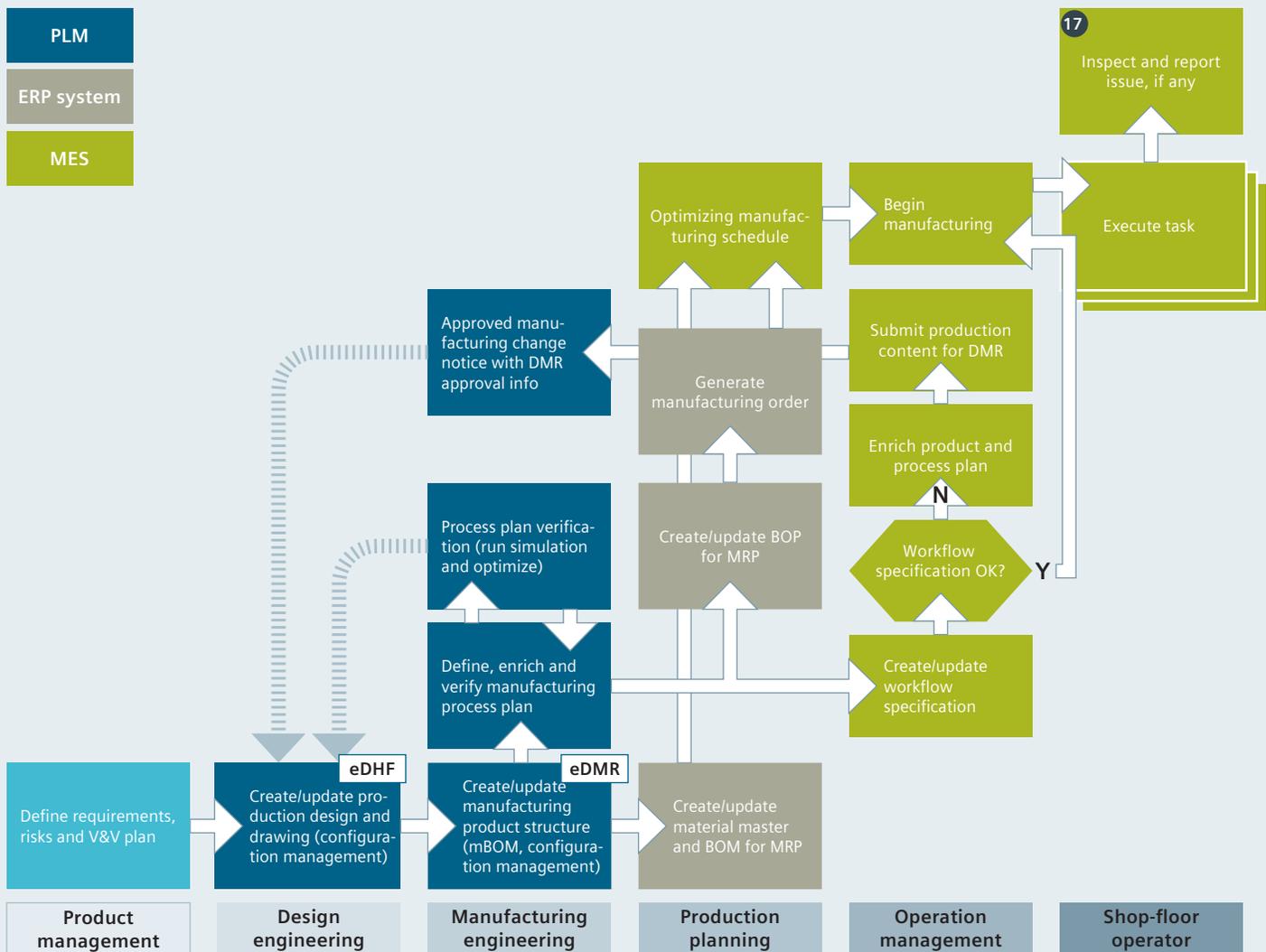


15. With a fully defined and optimized execution schedule, production begins.
16. MES starts the production and executes all the tasks described by the workflow, guiding the operator for manual operations. In the case of automated production, MES runs in the background and automatically coordinates shop-floor equipment.



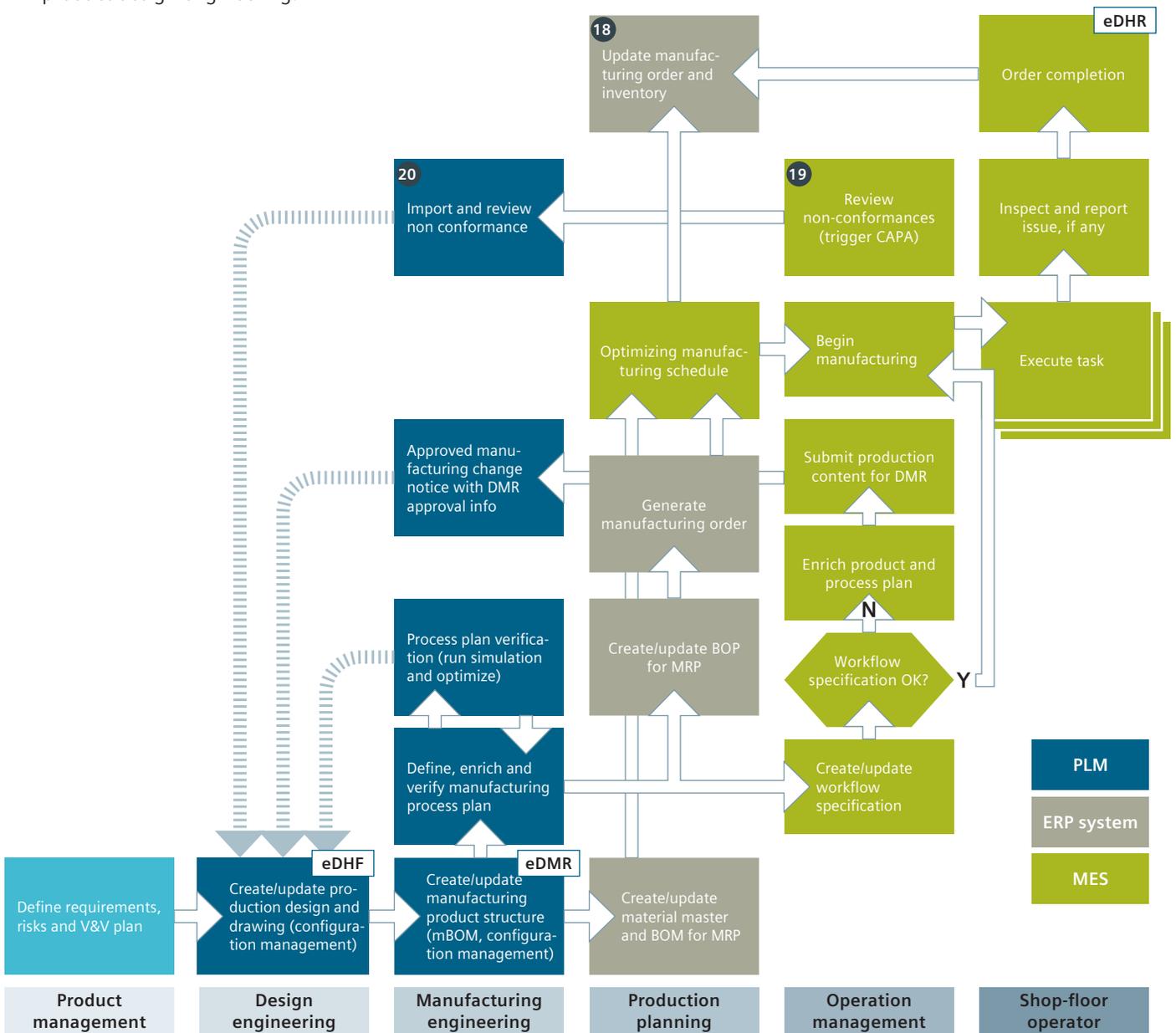
Closed-loop feedbacks for continuous improvements

17. If during manufacturing execution an operator notices an issue (for example, a defect or improvement opportunity), the operator can open a nonconformance to report the issue. Nonconformances may be reported during the manufacturing build tasks, or in dedicated quality assurance tasks. Details may be attached through additional documentation.



18. When the production order is complete, MES finalizes the electronic device history record (eDHR) and updates the ERP with production information such as materials used for the specific order, etc.
19. The supervisor can access MES to review nonconformances and can trigger a corrective and preventive action (CAPA) and/or further escalate the issue if necessary.
20. The manufacturing engineer receives feedback from the shop floor in real time. The manufacturing engineer can evaluate whether this is a problem manufacturing engineering can fix or whether it needs to be further considered by product design engineering.

This feedback loop happens in real time with production of the device and is another example of how CLM can accelerate the discovery and resolution of issues. You can see how feedback across the entire lifecycle is being delivered to manufacturing and product design engineers so that product and manufacturing process definitions can be continuously improved.

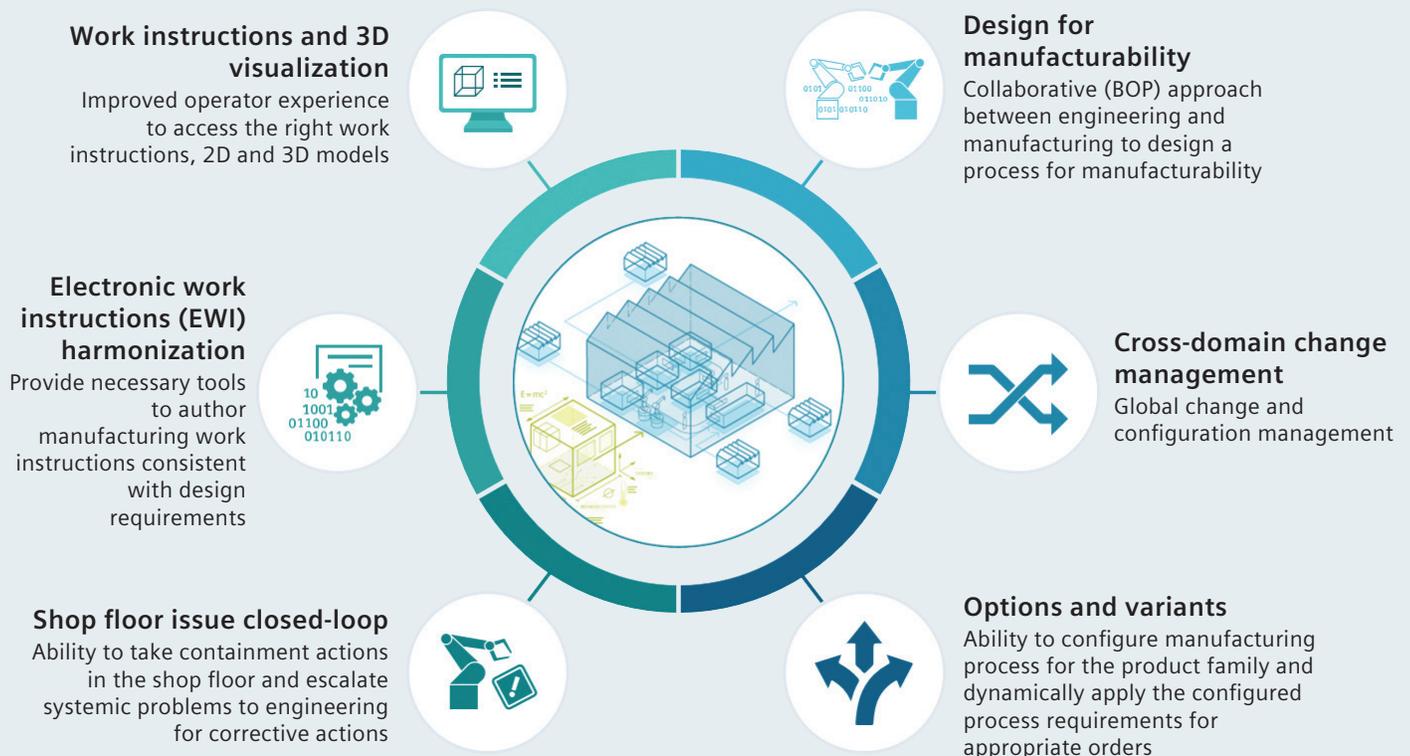


The most frequent use cases for CLM

CLM creates feedback loops that push data upstream as well as downstream. Closing the loop across ERP-PLM-MES systems enables manufacturers to be more responsive and agile. A closed-loop system eliminates replicated information among systems, with software applications focused on domain-specific capabilities. This approach reduces the total cost of ownership while improving system scalability. In a closed-loop environment, users access information they need in the specific system they operate, allowing them to make more informed decisions faster, with digital threads to evaluate and comprehend the full impact of decisions.

There are many use cases for CLM. Some of the most common are:

- Design for manufacturability: With a collaborative eBOM, mBOM, and BOP development approach involving product design, manufacturing engineering, and plant operations management, resulting in designed-in quality and manufacturability early in the lifecycle.
- Cross-domain change controls: Change management becomes aligned across product design, manufacturing engineering, and quality assurance, ensuring valid changes are communicated and enforced across global production sites.



- Options and variants: Manufacturing process definitions can be configured for various product families, dynamically applying the appropriately configured workflows for specific production orders in various locations and facilities.
- Shop floor issue closed loop: Necessary containment actions are immediately enforced on the shop floor, escalating systemic problems to manufacturing and product design engineering for corrective actions.
- Electronic work instruction (EWI) harmonization: Manufacturing work instructions are authored within the context of the product design definition, ensuring the alignment of the as-designed and as-planned product. With work instructions managed and controlled electronically, all operators access the right version every time, regardless of location.

With a collaborative and connected enterprise, problem escalation is easier and faster, resolutions can be determined with immediate access to relevant data, and corrective and preventive actions can be enforced and verified on the shop floor. For example, when correlating product design computer-aided design (CAD) models with shop floor quality data such as critical dimension measurements, engineers will have 100 percent confidence that the CAD model is the correct revision, and that the quality data is resulting from the execution of the correct revision of the manufacturing process and the validated, MES-enforced plant-specific workflow. With this confidence, combined with easy and quick access to product and manufacturing process information across digital threads, problem solving and root cause analysis is accelerated.

The implications for innovation are profound, for both sustaining engineering and for new product introduction (NPI). Design for manufacturability, as well as direct feedback from the shop floor to product design, improves product manufacturability and accelerates NPI. Especially important for NPI, when manufacturability issues are discovered during the design phase, product design change is much less expensive. New products are manufactured right the first time, with high quality and efficiency.



Key takeaways of closed-loop manufacturing

Without such integration, lifecycle processes and necessary data sharing is manual, causing all kinds of errors, bottlenecks and delays, while making it harder to analyze and create actionable insights to improve core business processes. In contrast, an integrated MES-PLM-ERP platform creates a closed loop that enables manufacturers to be more responsive and agile.

Conclusion

CLM, enabled by MES, is fast becoming a competitive differentiator for medical device manufacturers in today's challenging market. The digital enterprise must be anchored in intelligent, connected, collaborative systems that accelerate the exchange of information across the entire product lifecycle. Driving quality early in the process, designing quality into the product and the manufacturing process, and enforcing and monitoring quality all the way through to the production workflows to accelerate time-to-market and lower costs – all while improving the end-product quality.

This is how Siemens is partnering with our leading customers today. It is piquing the interest of regulators as well. The FDA is taking steps to reward manufacturers who adopt these proactive approaches and enabling software systems. Why? Because they are actively encouraging the movement from the old, reactive compliance mindset to one of proactive product quality. The only way to truly get there is through systems that can efficiently and explicitly apply your entire organization's knowledge to improve quality at every step – informing the entire lifecycle with relevant intelligence. This is what it will take to reverse the trends in adverse events and recalls that gauge the entire industry's success on the quality front.



Reducing time-to-market

Reduce manufacturing lead times and production enforcement



Enhancing flexibility

Actionable manufacturing intelligence to avoid recall events



Increasing quality

Reduce cost of regulatory pressure by focusing on product quality



Increasing efficiency

Gain competitive advantage by building higher quality new products, faster and at lower cost

At the end of the day, medical device manufacturers will be able to serve patients more safely and effectively, and receive more financial benefit for their efforts.

- Getting to market faster means lower cost for the manufacturers and quicker access to potentially life-saving products
- Enhancing flexibility allows for rapid change while preserving quality
- Increasing quality creates better outcomes for patients, improving reimbursement for providers
- Increasing efficiency means more access at lower cost to patients everywhere

Now is the time for the medical device industry to adopt the infrastructure that is essential for improving quality while making innovative, life-saving technology accessible for all patients. This type of infrastructure will become the standard over time.

Manufacturers adopting CLM today will be at a clear competitive advantage – and will be achieving their missions with confidence.

About Siemens PLM Software

Siemens PLM Software, a business unit of the Siemens Digital Factory Division, is a leading global provider of software solutions to drive the digital transformation of industry, creating new opportunities for manufacturers to realize innovation. With headquarters in Plano, Texas, and over 140,000 customers worldwide, Siemens PLM Software works with companies of all sizes to transform the way ideas come to life, the way products are realized, and the way products and assets in operation are used and understood. For more information on Siemens PLM Software products and services, visit www.siemens.com/plm.

Headquarters: +1 972 987 3000
Americas: +1 314 264 8499
Europe: +44 (0) 1276 413200
Asia-Pacific: +852 2230 3333

© 2019 Siemens Product Lifecycle Management Software Inc. Siemens, the Siemens logo and SIMATIC IT are registered trademarks of Siemens AG. Camstar, D-Cubed, Femap, Fibersim, Geolus, GO PLM, I-deas, JT, NX, Parasolid, Solid Edge, Syncrofit, Teamcenter and Tecnomatix are trademarks or registered trademarks of Siemens Product Lifecycle Management Software Inc. or its subsidiaries in the United States and in other countries. Simcenter is a trademark or registered trademark of Siemens Industry Software NV or its affiliates. All other trademarks, registered trademarks or service marks belong to their respective holders.

75872-A7 2/19 H