Whitepaper

Three Essential Phases of Medical Device Manufacturing Success

And How to Choose a Medical Device Contract Design and Manufacturing (CDMO) Partner

ARROTEK™

Contents

Introduction to Medical Device Manufacturing Success

Medical device products can have a long lifecycle that includes various stages and milestones. One of the longest stages is the manufacturing stage where, ideally, the product is manufactured in high volumes to meet customer demand.

As a result, the decisions you make on how and where your medical device is manufactured are critical to the product's success. This applies whether you need to manufacture a component, a complete medical device product, or anything in between. It also applies whether your product is still in the development phase or has obtained regulatory approval and is ready for commercialisation.

In this whitepaper, we will explore the three essential phases of medical device manufacturing success - see below.

We'll also look at the steps you should take and the factors you should consider when choosing a CDMO (contract design and manufacturing organisation) for your medical device product.

Three Phases of Medical Device Manufacturing Success

DFM

Design for manufacturing, or design for manufacturability, a phase that takes place during the design and development stages of your product's lifecycle.

Design Transfer

Design Transfer covers the stages in your product's lifecycle where it is moving out of development in preparation for scale-up manufacturing.

Continuous Improvement

Continuous Improvement is an on ongoing process that has relevance throughout the product's lifecycle.

Design for Manufacture

Design for Manufacture (DFM) involves designing products, including medical device products, so they can be efficiently manufactured. This includes ensuring the product can be manufactured within a target manufacturing cost while maintaining consistent quality, safety, and performance.

DFM also takes into account other factors that are crucial when designing minimally invasive medical device products, including regulatory compliance, usability, and the patient experience, but the realities of manufacturing the product remain a key focus.

The DFM process typically involves simplifying and refining the product at all stages in the design process with the aim of making it easier, faster, and less complicated to manufacture with as few steps in the manufacturing process as possible.

The number of parts used to manufacture a medical device product is also important. By going through a DFM process, design engineers will eliminate or combine parts to ensure there are as few as possible. This saves time in production and assembly, while the reduced number of steps to assemble the product (because there are fewer parts to assemble) reduces the risk of errors.

In addition to part reduction, parts standardisation is one of the main goals of DFM.

Benefits of DFM

- Reduces the time it takes to bring a product to market
- Minimises manufacturing transfer timescales and costs
- Reduces the overall cost of designing and developing the product
- Ensures the product can be made profitably
- Ensures a higher quality product
- Reduces the risk of production errors and product quality issues

What Does DFM Entail?

A DFM approach to designing a new medical device product involves questioning all aspects of the product and the design.

Doing this requires experience with similar products and designs. Knowledge of what others have done in the industry is also helpful, while a creative and innovative approach to MedTech product design is essential.

Examples of the questions that engineers will work through as part of the DFM process include:

- Can the product and all its components be manufactured as it has been designed?
- Will the component or product meet the defined functionality requirements?
- Is the manufacturing process cost-efficient?
- What level of variability does the manufacturing process introduce and is that variability within an acceptable range of tolerance?
- Are there changes that can be made to the design to reduce variability?
- Are there changes that can be made to the design to make the product or component easier to manufacture without compromising on performance, variability, etc?
- Can the number of parts or components be reduced or standardised?
- Can the parts be standardised and/or designed more symmetrically to reduce orienting, positioning, and fastening during assembly?

DFM Best Practices

Bring DFM Principles and Processes into the Project as Early as Possible

It is never too early to consider DFM in a medical device design project. In fact, by leaving DFM later in the process, the risk of the project overrunning and becoming more costly increases substantially.

This could be for a range of reasons, including simple reasons such as having to wait for a specific process to be completed. Examples include toxicity studies and similar processes that take time to complete.

The project could also overrun because of more complex reasons if you start DFM late in the process. This includes if a significant change has to be made to the design because of issues identified during the DFM process. After all, the later that changes are made to a product's design, the more time-consuming and costly those changes are to make.

Don't Only Focus on Cost Per Manufactured Unit

The cost to manufacture each individual product or component is important, but there are other crucial factors that should be considered alongside this calculation. Those factors include yield (good parts vs defective parts), manufacturing process reliability, and overall product quality.

Ensure the DFM Process is Fully Documented

All steps in the design process should be

fully documented, including any DFM decisions and considerations. For example, if a change is made to the design based on manufacturing simulation data, it should be possible to see the link in the documentation between the decision and the data.

Think About the Supply Chain

It is important to consider the supply chain as part of DFM processes and decision-making. This includes the availability of materials not just when everything is running smoothly, but also when challenges arise.

Identifying supply chain risks and potential bottlenecks is also important, and it is beneficial to factor in supply chain oversight considerations. For example, how effective is communication and information sharing between supply chain stakeholders?

As part of considering the supply chain, it can often be helpful to consult with key supply chain partners as part of the DFM process. Suppliers can have knowledge that can be helpful to your project as well as ideas that will improve the quality and manufacturability of your product.

Consider All Elements of the Manufacturing Process

Make sure all elements of the manufacturing process are considered. This includes assembly where engineers will often use design for assembly (DFA) principles to ensure the product can be efficiently and effectively assembled.

As well as assembly and the process of actually manufacturing the product, it is also important to consider materials, tooling, metrology, packaging, labelling, and compliance.

Choose a Full-Service Design Partner

Avoiding a siloed approach to product development is important in medical device design projects, where those involved in the project work on their bit with little consideration of anything else.

An integrated approach is much more efficient and effective.

Therefore, it is beneficial to choose a design partner with manufacturing and assembly capabilities, experience, and expertise.

Optimise Post-DFM Processes

Post-DFM processes are also important to ensure DFM decisions are fully optimised. This includes the design transfer process as well as first article inspections (FAI) where production processes are validated to ensure they produce the product or components as specified.

Staff training is also essential for operators who will be involved in production and assembly processes, as is ongoing performance monitoring and continuous improvement.

Factors Considered During a DFM Process

Simplification of Parts

- Minimising the number of parts.
- Minimising the complexity of parts and any other features that will make the medical device more difficult to manufacture and/or assemble.
- Avoiding complex geometries or shapes in the product's components.
- Avoiding manufacturing or assembly processes that are labour-intensive or require specialist machinery.
- Using standardised components.

Error Mitigation and Elimination

Engineers will consider the manufacturing process from start to finish to identify and assess the potential for errors. The focus will be on parts of the manufacturing and assembly process that have a human element. When a risk of human error is identified, engineers will consider how to reduce or eliminate the risk.

Regulations

The design of the product should also

comply with all relevant regulations.

Cost Effectiveness

The aim is to ensure manufacturing costs are aligned with the commercial strategy for the product without compromising on safety, quality, or compliance.

Future Innovation

Minimally invasive medical devices often go through multiple commercial release iterations as products are further developed and improved. DFM processes should take into account the potential for further development of the product.

Manufacturing Process

This involves considering the method used to manufacture the product, i.e. machining, injection moulding, 3D printing, etc. Consideration should be given to tolerances to ensure they are within an acceptable range.

Assembly Process

Sometimes this is referred to as DFA (design for assembly) or DFMA (design for manufacturing and assembly).

Similar principles apply when considering the assembly of a minimally invasive medical device product, i.e., minimising steps and components, reducing the potential for error, and making the process as straightforward as possible.

Automation

Engineers will look at parts of the manufacturing and assembly process that can be automated. Design adjustments can then be made to facilitate automation.

Process Compatibility

Taking into account current manufacturing capabilities. The aim is to minimise the need for new equipment or skills.

Design

The design of the new medical device product must adhere to Good Manufacturing Principles (GMP). For example, the design needs to consider the practicalities of manufacturing the components and then handling them for assembly.

Materials

In a minimally invasive medical device product, materials must be safe and biocompatible. Choosing the right materials also has an impact on product performance as different materials and combinations of materials deliver different performance characteristics.

It is also important to consider the availability of materials in the supply chain, as well as purchasing costs and any impact the material will have on the manufacturing process.

Performance

The product should perform in real-world situations as expected and according to its defined functionality requirements.

Design Transfer

Design Transfer Overview

Design transfer is a phrase that describes the activities and processes that introduce a medical device design to production. Effective design transfer is required by regulators but it also keeps manufacturing costs under control and ensures production milestones and deadlines are met. Furthermore, effective design transfer can reduce time to market and improve product quality.

What is involved in the design transfer process and what are the requirements? At Arrotek, we have a Three-Phase Design Transfer process to prepare a design for commercial manufacturing. The final phase involves a comprehensive checklist that is important for the process itself as well as becoming a crucial component of the Device Master Record.

The Design Transfer Requirements of Regulators

The FDA covers design transfer in FDA Quality System Regulation (21 CFR 820.30(h)):

> *"Each manufacturer shall establish and maintain procedures to ensure that the device design is correctly translated into production specifications."*

That's it. It's short and succinct but it is also clear as to what the FDA wants. It doesn't describe what manufacturers should do in detail, but the expectations are clear.

In ISO 13485:2016, design transfer is covered in section 7.3.8. While providing a bit more detail than the FDA regulations, the basic principles are the same:

"The organization shall document procedures for transfer of design and development outputs to manufacturing. These procedures shall ensure that design and development outputs are verified as suitable for manufacturing before becoming final production specifications and that production capability can meet product requirements. Results and conclusions of the transfer shall be recorded."

As for the EU, design transfer is not specifically mentioned in the EU's MDR as it is covered by the definition in ISO 13485.

Essential Components of an Effective Design Transfer Process

- Good practice is to use a design transfer checklist to ensure all activities related to the transfer have been successfully completed and documented.
- The design transfer process should start as early as possible in the design phase, as the product's manufacturability should be continuously considered. This is known as design for manufacturing, or DFM.
- Furthermore, process validation is closely linked to design transfer, so both should be progressed and documented at the same time.
- All activities related to the design transfer process should be fully documented.

Arrotek's Three-Phase Design Transfer Process

Phase One

Phase One of our design transfer process involves the manufacturing of products for non-clinical use under semi-QA (quality assurance) controlled conditions. This phase is typically for Stage 1 prototypes that are used to assess and refine the product's design.

Phase Two

Phase two involves the production of products for clinical use or validation purposes. Therefore, products manufactured in Phase Two of our design transfer process are fully QA controlled. Stage 2 prototypes are manufactured during Phase Two of the design transfer process.

Phase Three

Phase Three represents the final stage in the design transfer process at the end of which the product will be fully transferred to the production team for commercial manufacturing as a Type One product.

This part of the design process includes a formal meeting between the engineering, production, and quality teams to conduct a full review. A central component of this review is our design transfer checklist.

At Arrotek, we have two versions of the design transfer checklist – one for products designed elsewhere, and one for products designed by us at Arrotek. Examples of the items on our design transfer checklists include:

- Process validation complete?
- Risk management activities complete?
- Statutory and regulatory requirements fulfilled?

Continuous Improvement

Continuous Improvement Overview

Manufacturing medical devices is a complex undertaking. Multiple parts can be required for a single medical device and many of those parts can be extremely small, intricate, and delicate. There are often sterilisation considerations, and every element of the production process is controlled by strict regulations. Where does that leave the concept of continuous improvement in medical device manufacturing?

There are many definitions for continuous improvement in manufacturing, but the basic concept is about adopting a policy of never standing still. You need to constantly make the manufacturing process better, usually through continuous incremental improvements.

Medical Device Manufacturing Complexities

While continuous improvement is important, continuous improvement in medical device manufacturing is challenging – more challenging than continuous improvement in other manufacturing industries. This is because of patient safety and compliance considerations.

In other words, you can't simply change a manufacturing process because it improves a metric or two. Any changes must not compromise patient safety and you must ensure ongoing regulatory compliance. This means any improvements in manufacturing processes and procedures must follow the organisation's quality management system. Any adjustments or changes must also be verified and, when necessary, validated through documentation.

Advantages of Continuous Improvement

- ✓ Improved product quality
- ✓ Enhanced quality consistency
- ✓ Reduced defect rate
- ✓ More efficient compliance
- ✓ Improved productivity
- ✓ Enhanced line speed & efficiency
- ✓ Improved competitivness
- ✓ Reduced operational & business risks
- ✓ Improved responsiveness & agility
- ✓ Enhanced customer relationships
- ✓ Improved profitability

Focus Areas for Improvement

- Product quality
- Raw materials
- Production process steps
- Production line tools and moulds
- Manufacturing equipment
- Operator skills
- Maintenance processes
- Supply chain resilience
- Packaging and labelling
- Quality control processes
- Production planning to meet customer demand
- Waste
- Batch changeover processes

Obectives of Continuous Improvement

- ✓ Ensure products are safe
- ✓ Reduce errors
- ✓ Reduce product defects
- ✓ Adapt to changes in regulations
- ✓ Enhance automation
- ✓ Overcome skills availability challenges
- ✓ Improve employee training
- ✓ Reduce the steps required to produce, assemble, and package the product
- ✓ Reduce the complexity of manufacturing, assembly, and packaging
- ✓ Standardise processes
- ✓ Reduce of the cost of manufacturing
- ✓ Optimise OEE (overall equipment effectiveness) and minimise unplanned downtime
- ✓ Increase throughput
- ✓ Improve product quality and consistency
- ✓ Optimise the supply chain for quality, cost, availability, and reliability
- ✓ Reduce and eliminate risks, including supply chain risks
- ✓ Facilitate the scaling of operations
- ✓ Reduce energy use

Choosing a Medical Device CDMO

Medical Device Contract Design and Manufacturing Organisation

A medical device CDMO (contract design and manufacturing organisation) offers end-to-end services throughout the entire medical device product lifecycle, from the development of the initial concept through all stages of the design process through to the creation of a working prototype ready for testing and clinical trials. CDMOs often also offer regulatory support and, as the name suggests, they can manufacture your medical device when it is ready to be launched into the market.

There are two additional points to highlight. The first is the difference between a CDMO and a CMO. A CMO is a contract manufacturing organisation and is the more traditional type of setup. However, a traditional CMO lacks the design and development expertise that is crucial to many projects and medical device companies.

The second point to highlight is the importance of choosing a medical device CDMO. CDMOs are not unique to the medical device industry, but the medical device industry is unique. Therefore, it is essential to choose a CDMO with a proven medical device track record.

Benefits of Choosing a Medical Device CDMO

CDMOs are the ideal choice for a range of companies in the medical device industry, including start-ups, academic spin-offs, OEMs (original equipment manufacturers), and large international corporations. Here are the main benefits of choosing a medical device CDMO for your product, project, and/or company.

Focus

By partnering with a CDMO, you will have more time to focus on your core areas of competence, whether that's ideation, product research, market development, raising finance, etc.

Time to Market

You will benefit from an accelerated time to market by working with a CDMO that has a ready-to-go team, established processes, and relevant experience.

Easier and Less Costly Scale-Up

When you are ready to scale up production to meet the growing demand for your product, you can do so without having to make a massive investment in technology, equipment, infrastructure, or personnel. Your CDMO partner will already have all of that in place, allowing for a more controlled, efficient, and cost-effective increase in production.

Specialist Knowledge

By partnering with a medical device CDMO, you will get access to specialist knowledge. This includes product-related knowledge such as materials, minimally invasive medical devices, catheter technologies, sensors, etc. It also includes process knowledge and experience, including validation, testing, sterile packaging, manufacturing methods, etc.

Advanced Capabilities

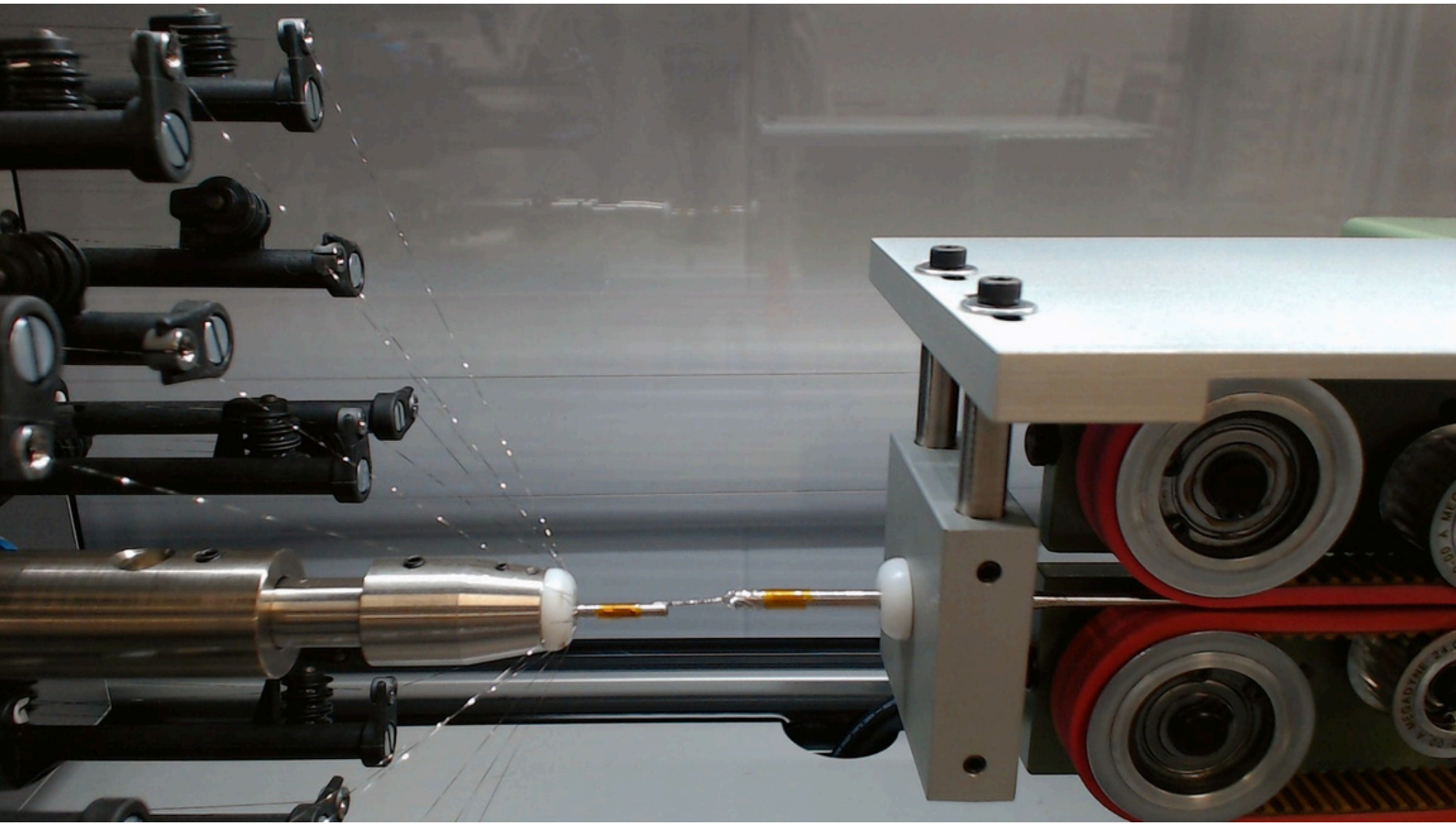
Your CDMO will also give you access to advanced capabilities, from design innovation expertise to prototype production to manufacturing.

Regulatory Expertise

On-tap regulatory knowledge is another important benefit of working with a CDMO. At Arrotek, for example, we start work on compliance at the earliest stages of the product development process, and we continue that work on compliance throughout the entire product lifecycle. This approach reduces the risk of approval setbacks, warning letters, product recalls, and other regulatory challenges.

Certifications and Audits

A medical device CDMO will have a ready-to-go Quality Management System (QMS). Your CDMO should also have a



valid ISO 13485 certification and FDA audit certification.

DFM

DFM stands for design for manufacturing (or design for manufacturability). It involves designing a product in a way that not only delivers the required performance characteristics but can also be commercially manufactured, i.e., efficiently manufactured profitably with minimal quality risks.

Design Transfer

Design transfer refers to the process of handing over the project from the design team to the operational team responsible for manufacturing the product. When you work with a CDMO, those teams will be within the same company, making the design transfer process more streamlined and reducing the risk of errors.

Optimised Processes

A CDMO will have experience ensuring manufacturing processes are fully optimised.

Resource Availability

Many medical device companies struggle with resource availability issues, especially start-ups, although larger organisations can face similar problems. This is where internal resources are overstretched leading to delays and other project challenges. Working with a CDMO will resolve your resource availability issues.

Cost-Effective

Partnering with a CDMO is a cost-effective approach to designing and manufacturing your medical device product. It is also easier to budget and plan.

Flexibility

The best medical device CDMOs offer flexibility in working arrangements to ensure their services align with the varied needs of different customers. At Arrotek, for example, we offer as much flexibility as possible, including operating on a time and materials basis when required. This approach lowers the initial financial outlay and reduces project risks for our customers.

Knowledge Exchange

As medical device products become more advanced, there is an increasing need to access specific and often highly niche expertise to resolve problems and progress projects. Going out to find that expertise from a standing start is difficult and time-consuming. A CDMO will already have relationships with other specialist companies, facilitating faster knowledge sharing and keeping the timeline of your project on track.

Entire Product Lifecycle

Working with a CDMO means you will benefit from dedicated support through the entire product lifecycle. The CDMO will continuously learn, adapt, and improve, benefiting your product and its success in the market.

Factors to Consider in a Medical Device CDMO

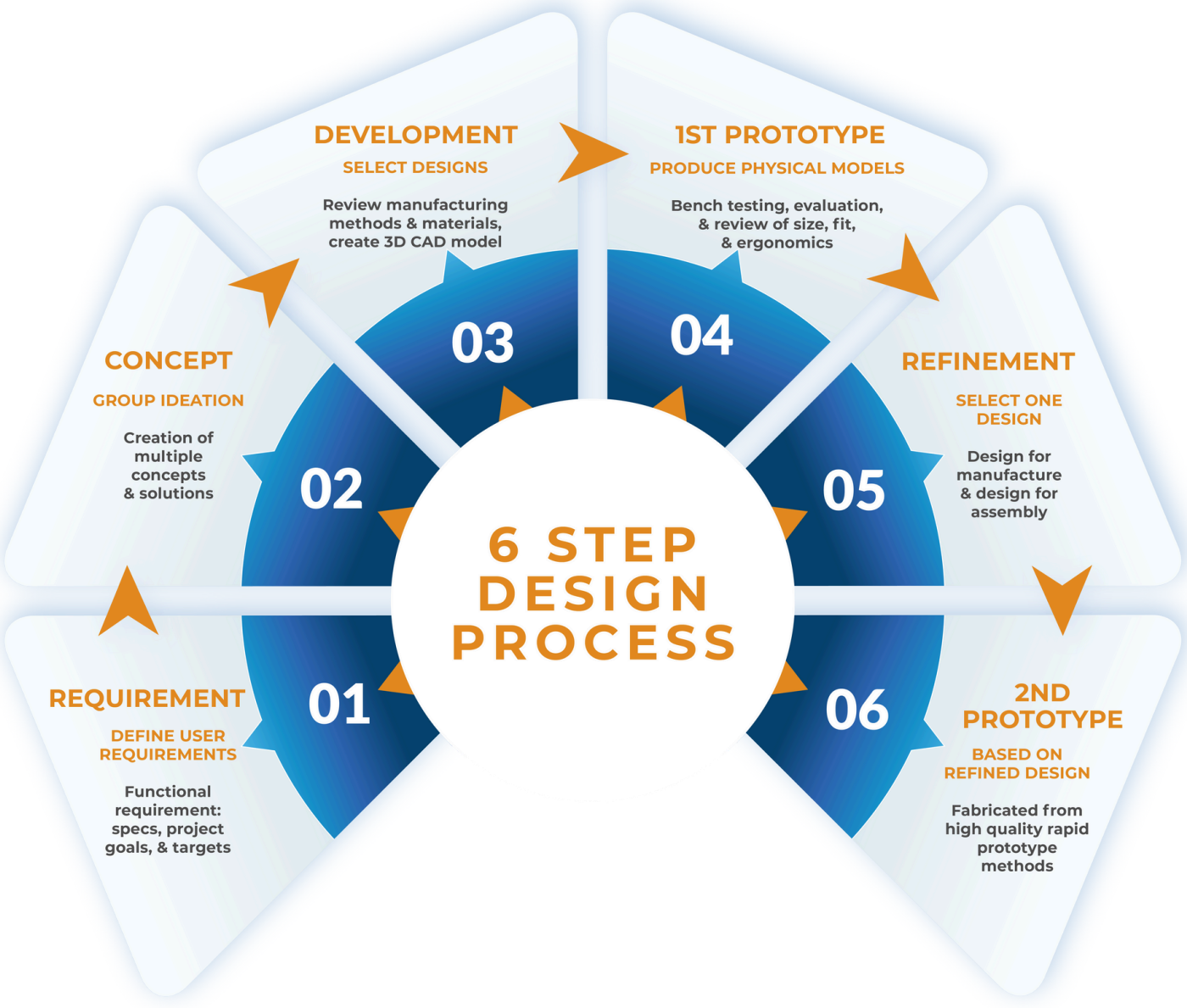
Design and Development Experience

The key difference between a CDMO and a more traditional CMO (contract manufacturing organisation) is the fact a CDMO will have design expertise and product development experience.

It is also beneficial to choose a CDMO with a broad range of product design and development experience. This includes experience managing complete projects, handling all aspects of the design, as well as experience augmenting existing design teams to develop specialist components that are part of a larger product.

Industry Expertise

There are CDMOs and then there are medical device CDMOs. As the medical device industry is unique with the need for an unwavering focus on patient safety, quality, and compliance, direct MedTech industry expertise is essential in a CDMO.



Product Expertise

While medical device experience is essential, it is also beneficial to partner with a CDMO that has expertise in your product area. For example, if your product is a minimally invasive medical device, your CDMO should ideally have minimally invasive medical device expertise.

Alignment With Your Requirements

Your medical device company will have limitations, requirements, and ideal ways of working. For example, you could have financial restraints, milestone requirements, or communication preferences. It is important your CDMO aligns with your requirements.

Capacity

Capacity is an often-overlooked component of a medical device project, but it is essential. Not only should the CDMO you select have available capacity today but also in the future. For example, you need to have confidence the CDMO has the required capacity to design your product and then manufacture it when you are ready to scale up production. The last thing you want is delays caused by capacity issues right when you are about to commercialise your product.

Facilities and Equipment

The best CDMOs have turnkey manufacturing capabilities with state-of-the-art facilities and a wide range of equipment and resources. This includes cleanroom facilities, advanced manufacturing equipment, the latest technology platforms, and skilled staff, as well as assembly, packaging, and sterilisation capabilities.

Investment Strategy

The investment strategy of a CDMO should also factor into your decision-making. Does the CDMO regularly invest in its capabilities – people, technologies, equipment, and facilities? CDMOs that don't invest quickly get left behind.

Problem-Solving Abilities

Medical device products are becoming increasingly complex through innovative design, miniaturisation, complex components, and/or the inclusion of advanced technologies such as sensors. Your medical device CDMO should have extensive problem-solving capabilities and a proven track record to ensure they can deliver on your requirements.

Materials Expertise

The materials used to produce new medical device products are crucial to patient safety, usability, manufacturability, quality consistency, raw material reliability, and, increasingly, sustainability. Therefore, materials expertise is essential.

DFM (design for manufacturing)

DFM is a process that takes place throughout the design stages to ensure the product can be realistically manufactured. DFM objectives include things like reducing the number of components and minimising the complexity of assembly processes. DFM

knowledge and capabilities should be an essential requirement for your medical device CDMO.

Certifications

As a minimum, your medical device CDMO should have an established quality management system (QMS) and ISO 13485 certification. It should also be FDA audited with a valid certification.

Regulatory Knowledge and Support

Compliance with regulations starts at the very beginning of a product development process and is a requirement through the lifecycle of the device. Therefore, regulatory knowledge and support are important considerations when choosing a CDMO.

Your CDMO should have quality and regulatory resources available to give you the support that you need, as well as well-established and robust document control processes.

Supply Chain

Supply chain management is more important than ever given the disruption that many supply chains have faced over the last number of years. The CDMO you choose should have advanced and highly effective supply chain management processes that include strong oversight.

Continuous Improvement

Establishing manufacturing processes to produce your medical device at scale should only be the start of the journey.

The best CDMOs adopt a continuous improvement approach to manufacturing, where there is a constant effort to make improvements in key areas.

The same applies to the design of your product – your CDMO should support your efforts for continuous improvement to make the product more effective, for example, or more profitable to produce.

Communication & Transparency

Communication is important in any business relationship, especially one as close and commercially sensitive as the relationship between a medical device company and a CDMO. The communication should be honest and open, and there should be complete transparency.

IP Protection

It is also important your IP is protected at all times, plus you should always retain 100 percent ownership of your IP. Confidentiality is a non-negotiable component.

The Team

Finally, it's important to get to know the team who will be involved in your project, including the leadership team, design team, quality team, and production team. Do you like and get on with them? Can you work with them? These might sound like low-level considerations, but they are crucially important.

Achieving Medical Device Manufacturing Success

The three production phases highlighted in this whitepaper are essential for medical device manufacturing success, whether you are a start-up or an international, multi-site corporation. As a quick recap, those three phases are:

- DFM - DFM takes place during the design stage of your project and involves making design decisions that optimise manufacturing processes.
- Design transfer - design transfer is the process of moving the project from the design team to the production team to ensure a seamless transition from product development to product manufacturing.
- Continuous improvement - continuous improvement involves making regular enhancements in manufacturing and related processes without compromising patient safety or regulatory compliance.

We also covered the benefits of working with a medical device-focused CDMO, as well as how to choose a CDMO.

At Arrotek, we have designed our services offering to ensure we make a positive contribution to your product's success through its entire lifecycle. This includes offering comprehensive design services and regulatory support. We can also provide you with reliable manufacturing services adapted to your requirements that can scale as your commercialisation strategy develops.

We have facilities in Ireland with specialist catheter manufacturing expertise, the US with specialist needle manufacturing expertise, as well as extensive manufacturing capabilities in Costa Rica.

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