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Preparing for and Managing Contract Organizations in the Development of Medical Devices

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Objectives and Disclaimers

- This presentation aims to address use of contract organizations in the development of medical devices.
  - Contract Research Organizations (CRO)
  - Contract Manufacturing Organizations (CMO)
  - Contract Development and Manufacturing Organizations (CDMO)
- Not a ‘one size fits all’ approach to outsourcing elements of medical device product development.
- Cost estimates are based on limited data which may vary greatly from organization to organization and is highly dependent on the complexity of the activity and medical device classification.

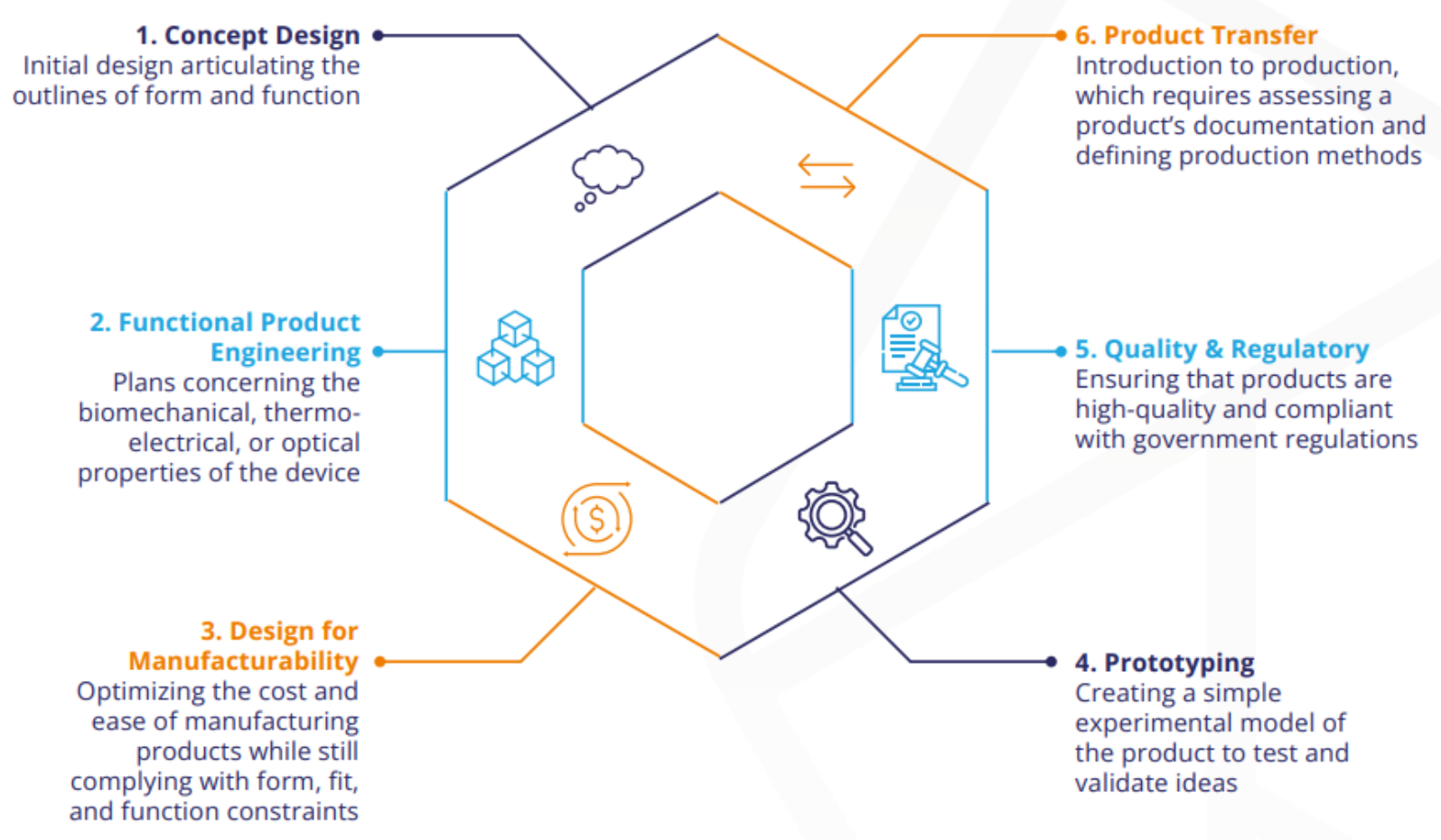
Background

- Limited work has been done to estimate the investment needed to bring a new medical device to the US market.
- One study looking at longitudinal data for Class III Pre-Market Approval (PMA) Medical Device development concluded
  - the average out-of-pocket cost of developing a therapeutic device is around $54 million before conducting post-approval studies, and approximately $60 million with post-approval studies.
    - 37% non-clinical stage related
    - 60% clinical stage (i.e., feasibility and pivotal study) related
    - 3% associated with the FDA review phase

Background, continued

- According to a July 2020 report by *StarFish Medical*
  - the average development cost of a Class II medical device of medium complexity is between $2 and $5 million for the research and development tasks
  - the total cost to get the product FDA-approved is around $30 million.
- Strategy with the largest impact on overall development costs
  - Simplified Clinical Trial Protocols and Reduced Amendments (33.4 %)
  - Improvements in FDA Review Efficiency and Interactions (22.4 %)
  - Use of Adaptive Design in clinical study designs (18.0 %).
- Strategies with the lowest expected development cost savings
  - use of Electronic Health Records (2.9 %)
  - Reduced Source Data Verification (6.0 %)
  - Use of Standardized Contracts (8.3 %)

Device Design and Development Life Cycle



Picture credit: 2023 U.S.MedTech Contract Manufacturing Report

What are Contract Organizations?

- **Typical CRO Services**
  - Regulatory affairs, clinical trial planning, site selection and initiation, recruitment support, clinical monitoring, data management, trial logistics, biostatistics, medical writing, and project management.
  - Take the lead in managing a company's trials and intricate medical testing responsibilities.

- **Typical CMO Services**
  - Manufactures a finished device to another establishment's specifications.
  - Contract Sterilizer - Provides a sterilization service for another establishment's devices.
  - Conducts manufacturing and/or testing of device key components or overall final product.
  - Packaging and Labeling of final product.

- **Typical CDMO Services**
  - A CDMO handles the outsourced manufacturing of medical devices as well as all of the innovation and development work that occurs prior to manufacturing.
  - Tends to be more flexible than a routine manufacturing operation and allows a designer to fabricate one component of their product or take a concept and turn it into a reality.
  - Justified as more economical and efficient to outsource than invest in competence, equipment, and resources.

How to Choose a Contract Organization

- **Expertise & Experience**
  - Specific area you are looking for support in, whether it's conducting clinical trials or running laboratory tests.
  - Assess organization's track record or the types of clients they have worked with in the past to assess their level of expertise.
- **Quality & Compliance**
  - Demonstrate a strong commitment to quality and compliance by providing evidence of their compliance with relevant regulations and standards.
  - Review a CRO's quality management system and any certifications they have to determine their levels of quality and compliance.
- **Cost & Value for Money**
  - Should be competitive and provide real value for money
  - Ask for cost estimates for the services you are interested in and compare them to other CROs.

How to Choose a Contract Organization, cont.

- **Communication & Collaboration**
  - Must communicate effectively and collaborate with your team throughout the project.
  - Ask for references from other clients and to speak with the CRO's team directly to assess their communication and collaboration skills.
- **Timeliness & Flexibility**
  - Deliver the services you need in a timely manner and should be flexible enough to adapt to any changing needs or requirements.
  - Ask about the CRO's availability and their approach to managing project timelines to get a better idea of whether they can meet deadlines and remain flexible in the face of changes.
- **Facility Locations**
  - Location where the work will be done is an important consideration when selecting a partner.
    - If the device you are developing together is expected to be approved in a variety of nations or locations, it will be beneficial—perhaps even necessary—to hire a CRO that has experience with the approval process in each location.
    - Facilities and staff positioned in the target location will ensure knowledge about local regulations for clinical studies and approval.
  - Comparing global CROs and local CROs and assessing how much supervision will be needed can help you understand whether location will be important in your selection.

Top 10 Contract Manufacturing Mistakes

1. Giving Away Too Much Product Control During Contract Negotiation
2. Forgetting The Benefits Of A Good Contract Manufacturing-Client Relationship
3. Being Lenient On Setting The Raw Material Quality Standards
4. Risking Intellectual Property Loss
5. Not Anticipating Overseas Cultural Differences And Challenges

Top 10 Contract Manufacturing Mistakes, cont.

6. Poor Handling Of Unanticipated Project Delays And Manufacturing Capacity Constraints

7. Using Only One Contract Manufacturer For Long-Term Product Production

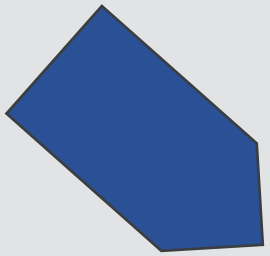
8. Losing Flexibility And Responsiveness

9. Not Negotiating Payment Terms

10. Losing Money To Generic Products

Benefits of Contract Manufacturing Organizations

- Cost savings
- Time savings
- Access to advanced technical skills
- GMP qualified facilities
- Internal product knowledge



Ensure that the signed master services agreement covers all of your intellectual property, quality, timeframe, formulation development, and packaging needs.

Benefits of Contract Research Organizations

- **Understanding clinical research needs specific to medical devices**
  - pre-market feasibility studies
  - pilot first-in-human studies
  - confirmatory studies and large pivotal studies
  - post-market clinical follow-up studies may be required to gather further clinical evidence throughout the lifespan of your device
- **Regulatory Environment Expertise**
  - regulatory framework for device trials differs from pharmaceutical trials
  - EU Medical Device Regulation (MDR 2017/745) which became applicable on May 26, 2021
  - Most Countries require device studies be conducted according to international standards, including ISO 14155:2020
  - **Safety reporting in medical device trials is very specific, includes**
    - unexpected adverse device effects
    - device deficiencies
    - very strict timelines

Benefits of Contract Research Organizations, cont.

- **Specific requirements of essential documents**
  - Unique documents and requirements for medical devices
  - Support you by reviewing these documents to ensure they meet local regulations and standards
  - medical writing services to help you write the documents and essential reports.
- **Therapeutic area expertise**
  - Improve the design and set-up of your trial and reduce the training costs
- **Cost-efficiency**
  - Looks for a track record of approvals for similar medical device trials in the countries you are targeting.
  - Is there a portfolio of the studies the CRO has conducted with devices in this field?
  - Set realistic timelines and Budget goals from the beginning.
    - Less time and money needed for training on the device and therapeutic indication and for learning about local regulatory requirements to get your device approved/cleared.
    - Lessons learned from CRO experience helps to ensure your trial is conducted in the most cost-effective manner.

Types of Contract Manufacturing Agreements

- **Private Label Agreements**
  - Long-term contracts for producing part or all of a product.
    - CMO creates products that the businesses sell as their own with their brand name
    - Private label manufacturing
    - End-to-end manufacturing
    - Select component creation.
- **Agreements for Services and Materials**
  - Involves deals for labor and access to equipment.
  - CMO's team and facilities used but you manage the manufacturing operations.
  - Not all CMOs use the same equipment and materials.
  - Agreements may be needed for more than one CMO to acquire best quality for different activities conducted by each party.
- **International Agreements**
  - Like the above options but third-party supplier is overseas.
  - Unique issues for packaging and shipping into the United States.
  - May prove less expensive, depending on your specific requirements.

General Costs for Medical Device Development

- Ideation – Estimated budget: $0 to $10,000
- Hardware design – Estimated budget: $5,000 to $15,000
- Mechanical engineering – Estimated cost: $4,000 to $40,000
- Electronics engineering – Estimated cost: $4,000 to $40,000
- Prototyping – Estimated cost: $200 – $10,000
- Certifications – Estimated cost: $5,000 to $50,000
- Regulatory Submission – Estimated cost: $50,000 or more
- Packaging – Estimated cost: $2,500 to $5,000
- Manufacturing setup – Estimated cost: $10,000 to $100,000
- First batch manufacturing – Estimated cost: $25,000 or more

Examples of Medical Device Contract Manufacturing Organizations (CMOs)

Note : This is NOT AN ENDORSEMENT

SeaSky Medical

Specialist medical molding company that offers high-grade molding solutions.

Scapa Healthcare

Strategic partner of medical device component manufacturers in cutting-edge wound care and consumer wellness.

Spectrum Solutions

Medical molding full range of services, from product development and prototyping to manufacturing and packaging. They are ISO 13485 certified and registered with the FDA as a medical device establishment.

HAD Technology

Specialize in designing and manufacturing medical devices and components for the healthcare industry, from engineering and prototyping to assembly and packaging.

Alcon Laboratories

Specializing in designing and producing surgical devices and equipment.

Examples of Medical Device CMOs, cont.

Note : This is NOT AN ENDORSEMENT

Advantech Plastics, LLC

Specializing in custom medical device components and assemblies including everything from design and engineering to manufacturing and assembly.

Medtronic

Medical device contract manufacturing company with over 30 years of experience.

Abbott Laboratories

A leading healthcare company that develops and manufactures a broad range of branded and generic pharmaceuticals and medical plastic injection molding producer and diagnostics.

GE Healthcare

World leader in medical device contract manufacturing. They help customers design and develop new medical devices and manufacture and assemble devices to the highest quality standards.

Beckton Dickenson

Complete range of services, from product development and design to manufacturing and assembly. They are ISO 13485 certified and compliant with FDA regulations.

Examples of Medical Device Contract Research Organizations (CROs)

Note : This is NOT AN ENDORSEMENT

ProPharma

Specialists highly qualified to assist you in all aspects of medical device and diagnostic regulation throughout the product lifecycle from concept development through Food and Drug Administration (FDA), international regulatory submissions, and European Union (EU).

MEDIcept

Offers customized study design and project management regardless of product development stage. Extensive experience with first-in-human (FIH), feasibility, pivotal, long-term follow-up, post-approval, post-market, and phase I-IV studies and registries.

Parexel

Offers an array of services including clinical trials management, observational studies and patient/disease registries, data management, biostatistical analysis, epidemiology, health economics/outcomes research, pharmacovigilance, medical communications, clinical pharmacology, patient recruitment, clinical supply and drug logistics, post-marketing surveillance, regulatory and product development, and commercialization to pharmaceutical, biotechnology and medical device industries worldwide.

Examples of Medical Device CROs, cont.

Note : This is NOT AN ENDORSEMENT

Charles River Laboratories

An American pharmaceutical company specializing in a variety of preclinical and clinical laboratory, gene therapy and cell therapy services for the Pharmaceutical, Medical device and Biotechnology industries.

ICON, PLC

A global provider of consulting, and outsourced development and commercialization services to pharmaceutical, biotechnology, medical device, and government and public health organizations.

Syneos Health

A leading fully integrated biopharmaceutical solutions organization built to accelerate customer success. We translate unique clinical, medical affairs and commercial insights into outcomes to address modern market realities.

Examples of Medical Device CROs, cont.

Note : This is NOT AN ENDORSEMENT

Laboratory Corporation of America Holdings

Formerly known as Covance Inc, offers drug development and manufacturing services. Services include research, lead optimization, analysis services, safety assessment and drug safety testing, consulting and partnering, informatics, clinical testing, clinical development, commercialization and manufacturing support, among others.

WuXi AppTec

A global pharmaceutical, biopharmaceutical, and medical device company.
The company covers the development cycle through five core operations, including small molecule R&D and manufacturing, biologics R&D and manufacturing, cell therapy and gene therapy R&D and manufacturing, medical device testing, and molecular testing and genomics.

Medpace

Offers clinical pharmacology and laboratory services including central laboratory, bioanalytical, ECG core lab, and imaging core labs.

Eurofins Scientific SE

Decentralized network of life sciences companies that provide various analytical tests and laboratory services.

QUESTIONS
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Upcoming Events & Reminders

Apply to the Catalyze program:

- Upcoming **product definition** receipt date **February 21, 2024**. Apply through NIH ASSIST or Grants.gov

CRO/CMO Webinar Series

- **February 29, 2024** – Partnering with Contract Organizations for CMC Activities

Have a question or want to learn more?

- Visit us online at **nhlbicatalyze.org**
- catalyze_info@rti.org
- NHLBI_Catalyze@nih.gov

References

Corcoran, Brooke. 2022. What is a contract research organization (CRO)? MED Institute. https://medinstitute.com/blog/what-is-a-contract-research-organization-cro.

Donahoe, G., 2018. *Estimates of Medical Device Spending in the United States,* Washington, DC: AdvaMed.

De Taeye, L. Discover 5 reasons to engage with an experienced Contract Research Organization (CRO) specialized in medical device studies to support you in your clinical research. QBD Group. 2022. https://qbdgroup.com/en/blog/team-up-with-a-contract-research-organization-cro-to-boost-your-clinical-research-strategy.

Mario. 2023. Medical Device Design: A Guide to Service Pricing, Costs, and Rates for Companies. CadCrowd. https://www.cadcrowd.com/blog/medical-device-design-a-guide-to-service-pricing-costs-and-rates-for-companies.

Michael J. Akers. Sterile Drug Products Formulation, Packaging, Manufacture, and Quality. Drugs and the Pharmaceutical Sciences. Informa Healthcare. 2010.

No Author. 2022. Therapeutic Complex Medical Device Development Fina Report. Eastern Research Group Inc.

No Author. 2021. Top Ten Medical Device Component Manufacturers. SeaSky Medical. https://www.seaskymedical.com/top-medical-device-contract-manufacturers/.

No Author. 2024. Top 10 Contract Manufacturing Mistakes Medical Device Startups Should Avoid. MycoScience. https://mycoscience.com/top-10-contract-manufacturing-mistakes-medical-device-startups-should-avoid/.

No Author. 2024. Guide to Choosing & Collaborating with a CRO. Excedr.2023. https://www.excedr.com/blog/contract-research-organizations.

No Author. 2024. Top 10 Contract Manufacturing Mistakes Medical Device Startups Should Avoid. , MycoScience. https://mycoscience.com/top-10-contract-manufacturing-mistakes-medical-device-startups-should-avoid/

Stimamiglio, C, Puzzi, S. Ogdon, E. 2023. The 2023 MedTech Contract Manufacturing Report is released in the U.S. ALIRA Health. https://alirahealth.com/education-hub/the-2023-medtech-contract-manufacturing-report-is-released-in-the-us.