Medical and Drug Delivery Device Design for Biocompatibility

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Presented For:

Society of Plastics Engineers
Medical Plastics Division Presents
MEDICAL PLASTICS MINITEC 2024

Background

PSN Labs was Founded in 1991 as Plastics Services Network to provide support to the legal and business communities regarding failure analyses and product development in the plastics industry.

Over the last three decades, we have expanded our space, equipment, number of employees, and areas of expertise to develop a suite of labs – Engineering Services, an ISO 13485:2016 accredited Material Processing Lab, and an ISO/IEC 17025 accredited Testing Laboratory. While each provide standalone services, they all collaborate to bring products to market with uncompromised quality.

Our unique combination of these services offer our customers quick turnaround at a lower cost because of the flow of communication and cooperation among the different teams.

End-to-End Product Development

Engineering

Processing

Testing

35+ Scientists and Engineers

ISO 9001:2015
ISO 13485:2016
ISO 17025:2017

Erie, PA
Cincinnati, OH
Denver, CO

100+ Clients/Year
Focused on Life Sciences

Optimal Product Development

Engineering Lab

Product Development, Metrology, Test Method Development, M&S

Processing Lab

Functional Prototyping, Material/Process Development, Capability and Cliff Studies

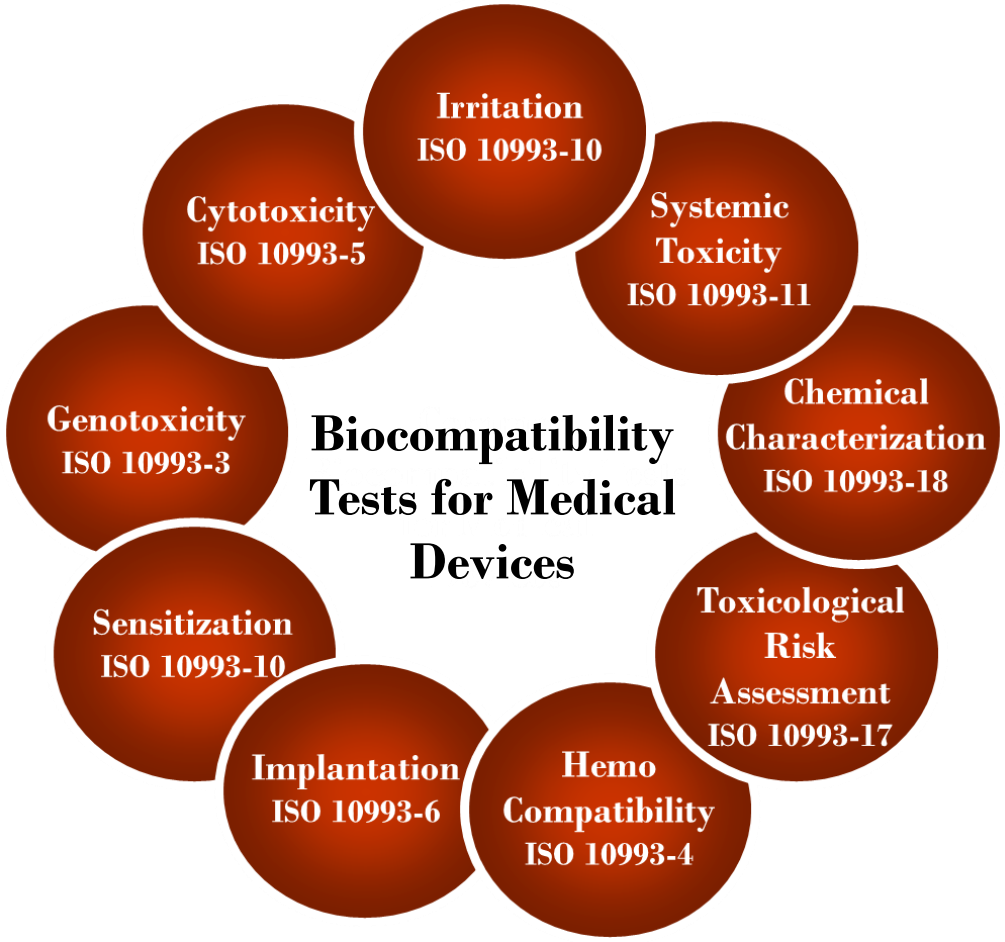
Testing Lab

Biocompatibility, Testing, Material Characterization and Verification

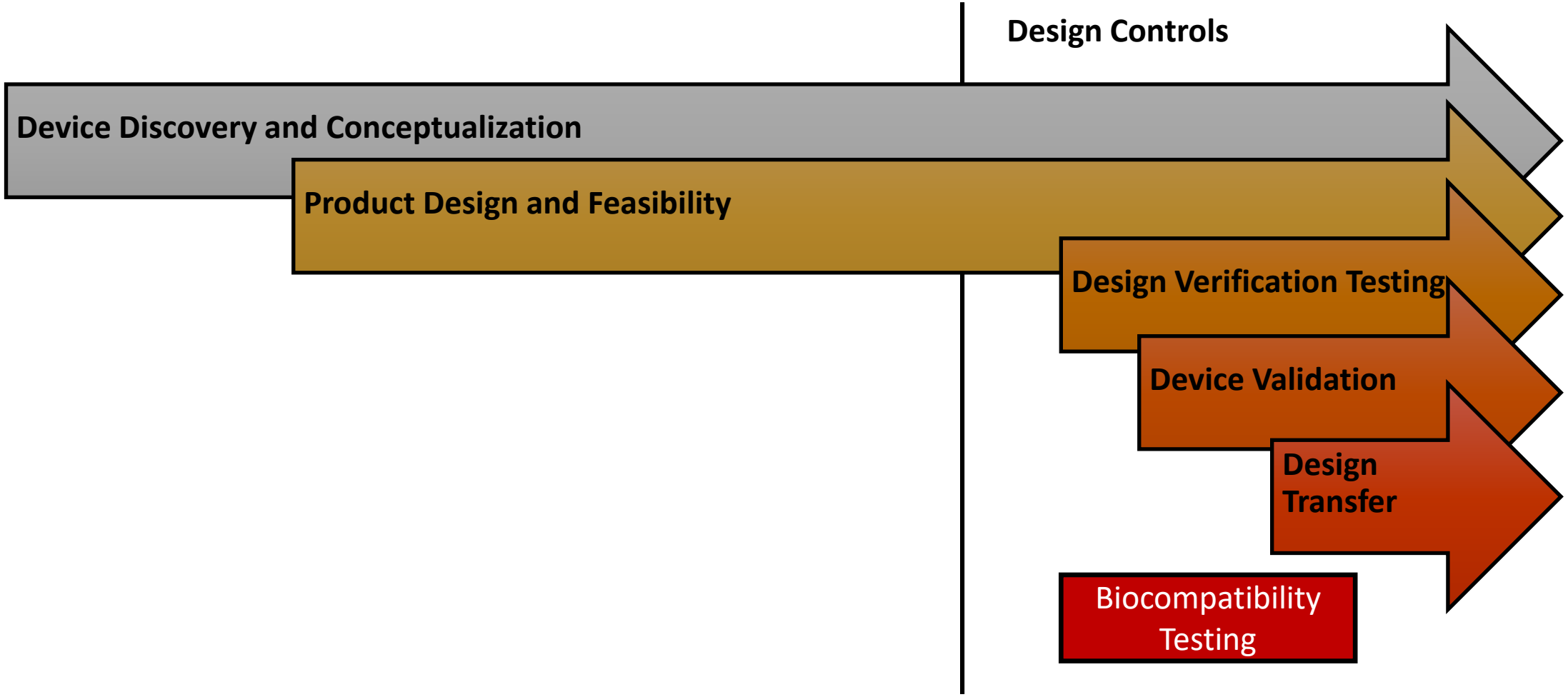
Incorporating these integrated business units into the **product development cycle** allows you to answer engineering questions and develop foundational scientific principles for product and technology development **quickly, efficiently,** and **with data you can trust**.

Importance of Biocompatibility

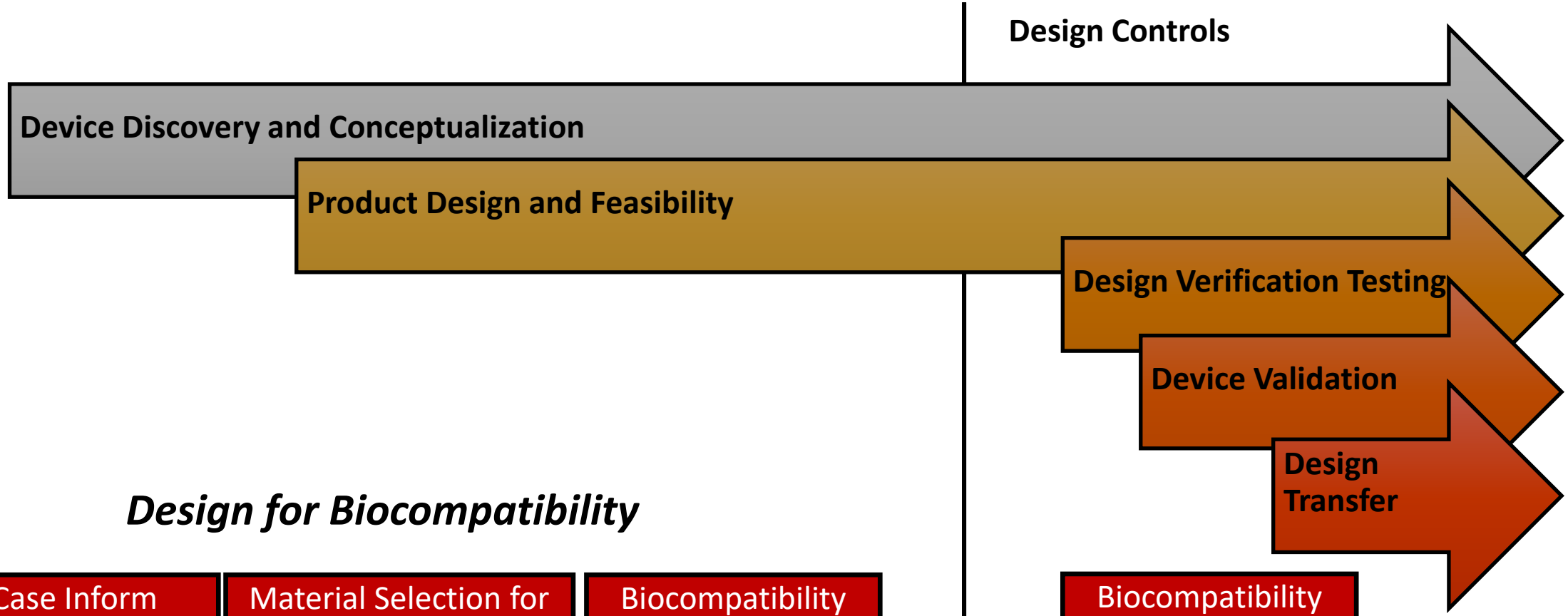
- There is no such thing as a device without risk.
- Our goal is to ensure we evaluate the "actual risk to patient safety" throughout each step of the process and that it is acceptable.
- Our broad multi-disciplinary team allows for sound principles to be applied to each step of the biocompatibility evaluation program.
  - Our team includes a medical doctor and biomedical engineers (how the device intends to deliver therapy and the consequence), engineers (how the device is intended to function), material scientists (how the materials are supposed to behave), and toxicologists (what the actual risk is).



(Most) Biocompatibility Testing Today

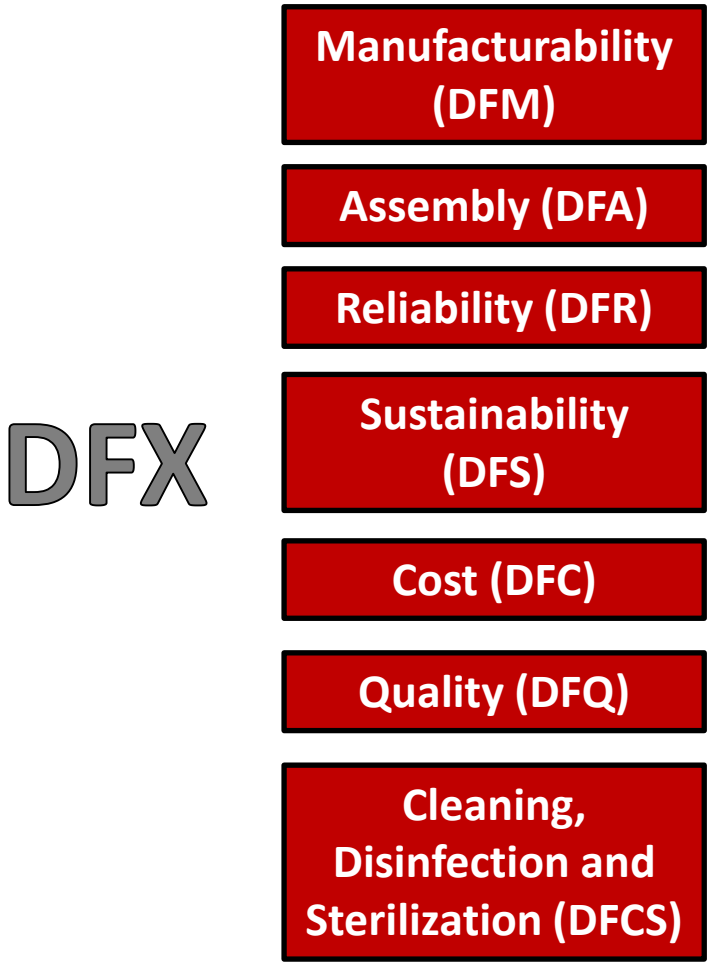


PSN Labs' Approach to Biocompatibility



What is Design For Biocompatibility (DFB)?

- Apply the principals of biological safety up front in the design process to ensure that biocompatibility testing on Final-Finished-Form device is successful.
- Creates the *potential* to treat biocompatibility testing as **confirmational** and **not discovery**!
- Ensures **Device Design Engineers** understand the consequence of decision making and have tools to incorporate DFB principals at an early stage in the product development process (versus two years in!).



Why isn't DFB Always Considered?

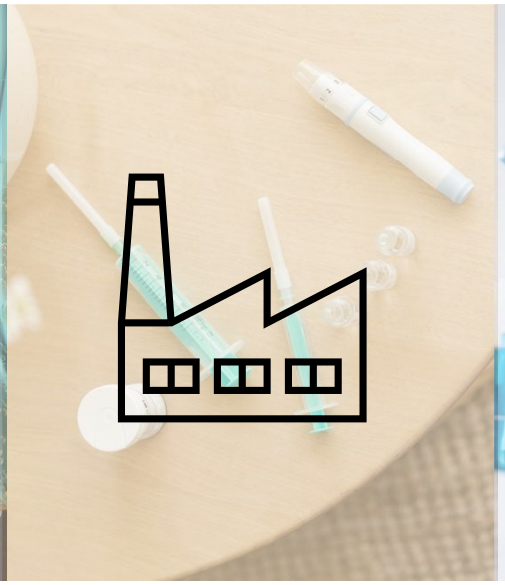
- Lack of correlation:
  - Design Engineers primarily Mechanical, Biomedical, Electrical, and Materials engineers
  - No physical correlation
  - Unknown-Unknown
- Trust in material suppliers and manufacturers.
- Barrier to entry is high (schedule and cost).
- **Evolving Environment – Increased Burden of Proof:**
  - Regulatory
  - Science
  - Instrumentation

How to Ensure DFB is Followed?

Usability

Device Design

Material Selection



Manufacturing

Screening Testing

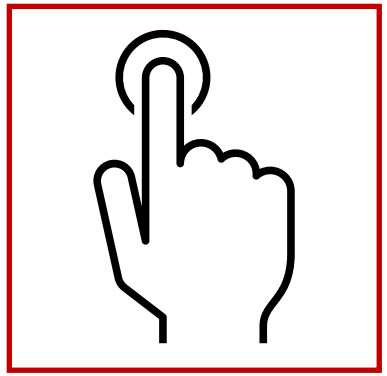
DFB – Usability Considerations

- Final **Form**, **Fit** and **Function** are critical to address biocompatibility concerns.
- Instructions For Use (IFU) should be done with biocompatibility in mind.
- Understanding the risk associated with the use of the device:
  - Severity
  - Occurrence
  - Documented through UFMEA
  - Biocompatibility User Risks should be addressed in these risk management documents

DFB – Usability Guidance

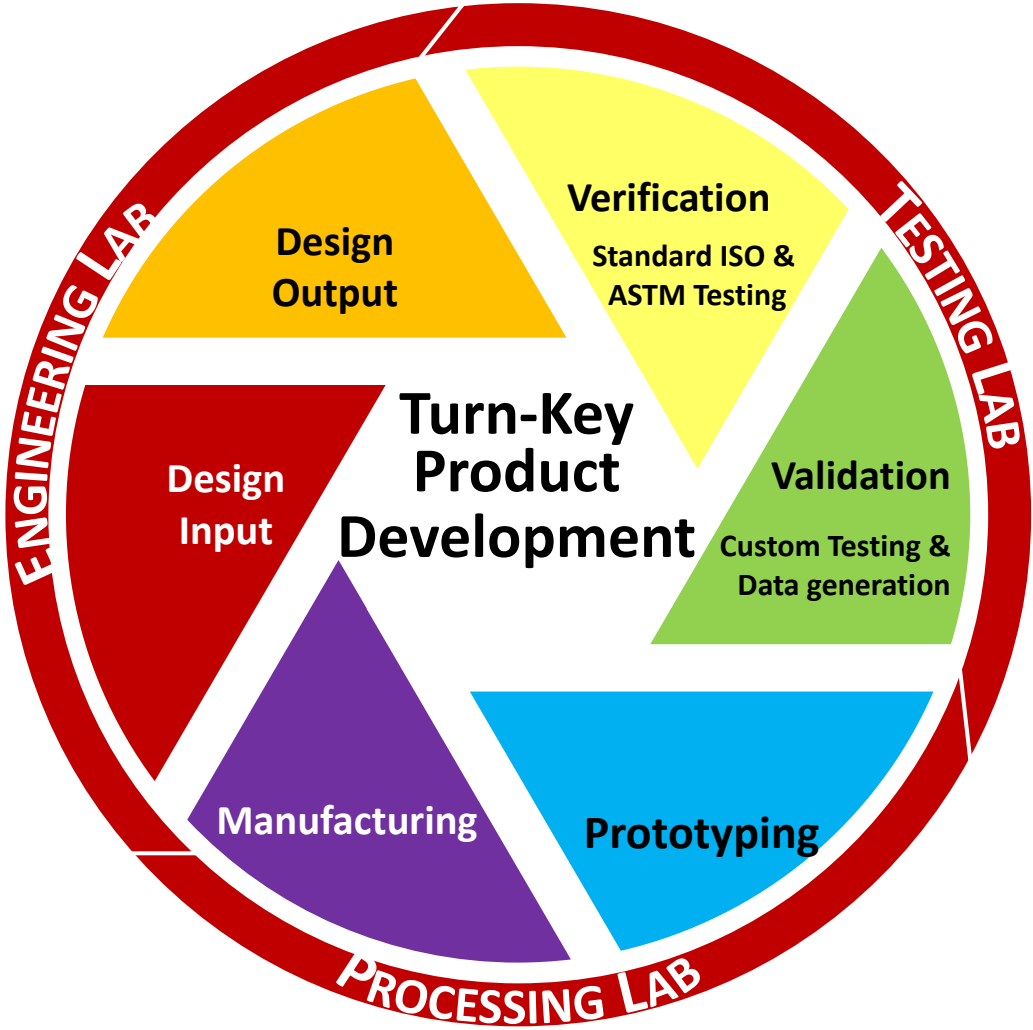
R&D teams should understand the use of the device and its pertinence to biocompatibility:

1. **Single Use, Multi-Use, Re-Processable/Sterilizable**
2. **Patient and/or Practitioners contact duration**
   - Limited (< 24 hrs.)
   - Prolonged (> 24 hrs. to 30 days)
   - Permanent (> 30 days)
3. **Contact Region**
   - Circulating Blood
   - Skin contact
   - Tissue
   - Etc.
4. **Severity of the outcome for failing biocompatibility**
   - Should be understood by the engineer but decision made by clinical and/or regulatory



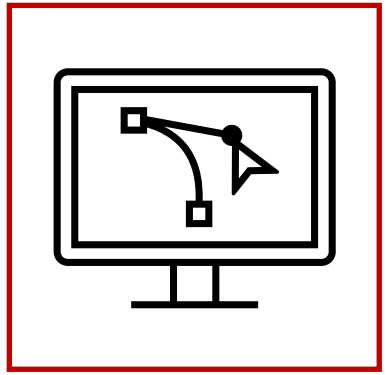
DFB – Design Considerations

- Risk based approach to product development followed for biocompatibility like other design criteria.
- Design inputs capture biocompatibility end goals. Understand the tests required to pass at the conclusion of the development process.
- Engineering Builds incorporate biocompatibility guidance.
  - Attempt to use assumed final finished form early in development phases.
  - Use representative materials and manufacturing processes.
  - Communicate designs early to biocompatibility, regulatory and clinical teams.



DFB – Design Guidance

- R&D teams should understand the design of the device and its pertinence to biocompatibility:
  1. **Understand Shelf Life**
     - Device must demonstrate biological safety across shelf life
  2. **Understand Use Environment**
     - Device must be safe in all environmental conditions (temp, humidity, etc.). End of Life biocompatibility testing!
  3. **Balance functional device performance with biocompatibility safety goals**
     - Manufacturability, Reliability, Cost, Sustainability all equally important
  4. **Understand impact of Manufacturing techniques**
     - 3D Printing is not representative
     - Assembly/joining

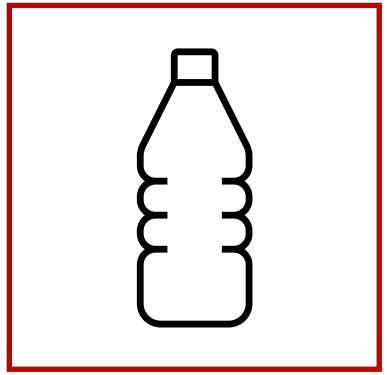


DFB – Material Selection

- Understand the materials of construction and choose based on their ability to meet all requirements.
- The exact grade of tradename and grade, including the constituents should be understood.
  - Plasticizers, additives, colorant, etc.
- Identification of the proper material at the start of the development cycle can minimize risk of biocompatibility testing on the back end.
- Medical/Healthcare grades of materials may not mean it is safe in YOUR *specific device*.

DFB – Material Guidance

- R&D teams should understand materials of construction of the device and its pertinence to biocompatibility:
  1. **Pay attention to material and additives!**
     - PVC is commonly utilized in medical devices but should be avoided in the future if possible.
  2. **Color is important!**
     - Be mindful of the implication of color. Provide context to Industrial Design teams during selection.
  3. **Utilize standards such as USP Class VI materials as guidance but not rely on them!**
     - Even Class VI materials when utilized incorrectly can have negative biocompatibility impacts.
     - FDA exempt lists can also be utilized.
  4. **Medical/Healthcare grade resins are a great start!**
     - This should not be taken as assurance of passing biological endpoints.
  5. **Material selection and how the material is processed should be considered!**
     - Mold release, sterilization techniques, additive changes, etc. can all effect biological safety.

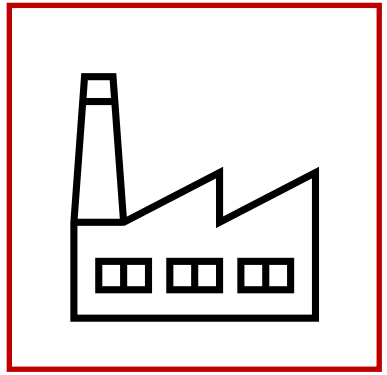


DFB – Manufacturing and Assembly

- Ensuring material processing with appropriate controls is critical.
- Contract manufacturing should be compatible with:
  - Appropriate clean room controls
  - ISO 13485 quality system
  - Change control processes
  - Appropriate material handling and raw material sourcing
- How the material is processed effects the biological end points as well and should be considered.
- Early design risk can be assessed with raw prototype manufacturing methods, but final manufacturing representative prototypes should be utilized earlier in the development cycle.

DFB – Manufacturing and Assembly

- R&D teams should understand manufacturing and assembly of the device and its pertinence to biocompatibility:
  1. **Assembly techniques can significantly influence biocompatibility.**
     - Certain adhesives can have negative impact if in contact with patient or practitioner.
  2. **3D printed components are not biocompatibility surrogates.**
     - Utilize "functional prototypes" aka final manufacturing like processes as soon in the development cycle as possible.
  3. **Processing techniques may degrade the polymer significantly to effect functional and/or biocompatibility requirements.**
     - Processing can break down the polymer in non-desirable ways. Degradation in residence times, residual stress and part dimensions can all negatively affect the product.



Biocompatibility Trends/Headwinds

- ADVAMED working group has published common guidance for specific topics (i.e., Irritation, 10993-18, etc.).
- Reviewers are not reflecting acceptance of some of the new 10993 standards. Harmonization has yet to occur.
- AINN feedback reflects the changes in real-time.
  - FDA recently published 10993-18 guidance in ADVAMED; AINN feedback mirrors the information provided but is still evolving.
  - The information is not trickling down to the test standard itself which provides ambiguity to the manufacturer and the testing laboratories.
  - What has been accepted historically is not necessarily being accepted today.
- Common goal of the FDA:
  - Identify all hazards (i.e., Nitrosamines, inorganics, etc.).
  - Ensure patient safety is maintained even in unlikely/improbable scenarios.

What Else Can be Done?

- Educate and speak to R&D teams early on the development process.
- Ensure that the device requirements incorporate appropriate biocompatibility testing as early as possible.
- FDA Q-sub.
- Understand that AINN will occur, and feedback is to be expected in real-time.

Conclusions

- R&D teams are **not ignoring** biocompatibility purposefully.
- **Education** and understanding internally to the Medical Device organization about the importance of biocompatibility is key.
- Conveying to **Design Engineers** the pain caused by poor biocompatible **decisions** early in the product development cycle.
- There is still **not** a fool proof approach to biocompatibility.
- Attempt to treat biocompatibility testing as **confirmatory** (similar to DVT) and not **informational**.

Questions?

Thank you!

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