IMPERIAL

MedTechONE

Knowledge Base

What is the journey through pre-clinical trials & how is it influenced by your medical device class?

1 Planning and Study Design

2 Pre-Clinical Testing and Experimental Work

3 Data Analysis and Results

4 Reporting and Regulatory Submission

The journey through pre-clinical trials for a medical device consists of essential steps that help verify its safety, functionality, and regulatory compliance before testing in humans. The pre-clinical process is influenced by the device's classification (Class I, IIa, IIb, III in the UK), with requirements becoming more stringent as the class and associated risk increase.

1. Planning and Study Design

1.1 Objective: To create a structured plan that aligns with the device's regulatory requirements and class-specific risks, ensuring the design, testing, and objectives are well-defined.

1.2 Step-by-Step Process:

- **Determine Device Classification Early:**
  - Conduct a regulatory assessment to classify the device into Class I, IIa, IIb, or III based on intended use, risk level, and contact with the body.
  - Class I: Simple devices requiring minimal safety evidence (e.g., surgical gloves).
  - Class IIa: Moderate-risk devices with greater oversight (e.g., dental drills).
  - Class IIb: Higher-risk devices needing Notified Body involvement (e.g., infusion pumps).
  - Class III: High-risk or implantable devices that sustain life or are critical to patient care (e.g., pacemakers).

- **Engage with Regulatory Bodies:**
  - Schedule a pre-submission meeting with relevant bodies (e.g., MHRA, Notified Body) to discuss required evidence based on the device's classification.
  - Class III devices, in particular, may benefit from multiple consultations for clarity on high-stakes requirements.

- **Set Specific Study Objectives and Endpoints:**
  - Define what safety, biocompatibility, and performance metrics are necessary to prove compliance.

- **Examples:**
  - Class I: Demonstrate basic functionality and minimal toxicity.
  - Class IIa and IIb: Show consistent performance in varied settings (e.g., different pressures or temperatures).
  - Class III: Prove long-term reliability and compatibility with human physiology.

- **Develop the Risk Assessment and Management Plan:**
  - Use tools like Failure Modes and Effects Analysis (FMEA) and Hazard Analysis and Critical Control Points (HACCP) to assess risks.
  - For Class III devices, perform a comprehensive analysis of potential failure modes and patient safety impacts.

- **Select Testing Models:**
  - Determine appropriate in vitro (cellular or lab-based) and in vivo (animal) models to test the device.
  - Class IIb and III devices often require complex models to assess high-risk aspects under realistic conditions.

2. Pre-Clinical Testing and Experimental Work

2.1 Objective: Execute testing to gather evidence on the device's safety, efficacy, and performance under controlled conditions.

2.2 Step-by-Step Process:

- **Biocompatibility Testing:**
  - Ensure materials in contact with tissues are non-toxic and do not cause irritation, following ISO 10993 standards.
  - Techniques:
    - Class I: Cytotoxicity tests for skin-contact materials.
    - Class IIa and IIb: Sensitization and irritation tests for short-term tissue contact.
    - Class III: Long-term implantation tests, assessing chronic toxicity and genotoxicity.

- **Mechanical and Functional Testing:**
  - Test durability, mechanical strength, and functionality under simulated use.
  - Techniques:
    - Class I: Simple stress tests and functional checks.
    - Class IIa: Fatigue testing for devices subjected to repeated use (e.g., catheters).
    - Class IIb and III: Comprehensive durability tests under varied stresses, thermal cycling, and device lifetime projections.

- **Electrical Safety and Electromagnetic Compatibility (EMC):**
  - Essential for electronic or powered devices to ensure reliable function around other electronics.
  - Techniques:
    - Class IIa and IIb: Basic electrical safety tests.
    - Class III: Full EMC testing, including susceptibility to radiofrequency interference per IEC 60601 standards.

- **Software Verification and Validation:**
  - Verify that the software operates as intended and can handle error conditions.
  - Techniques:
    - Class IIa: Verification testing for basic software functions.
    - Class III: Extensive testing, including unit tests, system integration, and failure recovery scenarios.

- **Animal Studies**:
  - Conducted for implantable devices and devices with high physiological impact to understand interactions within a biological system.
  - Techniques:
    - Class III: Long-term studies assessing tissue integration, inflammation, and biological degradation.

3. Data Analysis and Results

3.1 Objective: Interpret test data to confirm that the device meets safety and performance benchmarks specific to its class.

3.2 Step-by-Step Process:

- **Collect and Clean Data:**
  - Consolidate test data from all sources, cleaning for inconsistencies or anomalies.
  - Class III devices, for instance, require especially rigorous data integrity due to the high regulatory scrutiny.

- **Analyze Data According to Regulatory Standards:**
  - Techniques:
    - Class I: Simple pass/fail criteria based on meeting basic standards.
    - Class IIa and IIb: Statistical analysis on consistency and reliability, particularly for repeated-use devices.
    - Class III: In-depth statistical methods, possibly involving Kaplan-Meier survival analysis for long-term functionality in life-sustaining devices.
  - Interim Analysis for Iterative Testing:
    - Conduct interim reviews to identify any need for design adjustments or further testing.
    - Class III devices benefit from ongoing analysis to catch early issues in complex devices.

4. Reporting and Regulatory Submission

4.1 Objective: Compile all findings and document compliance in a report for regulatory submission, adapted to the class of device.

4.2 Step-by-Step Process:

- **Prepare a Comprehensive Study Report:**
  - Document testing methods, results, risk management activities, and any interim changes.

- Reports for Class III should include high-level analysis of risk-benefit, safety profiles, and evidence of device functionality.

- **Develop Class-Specific Documentation:**
  - Class I: Basic documentation, including test reports and safety certificates.
  - Class IIa: Detailed Technical File covering safety, functionality, and performance.
  - Class IIb: Technical File and expanded Design Dossier, including data on usability, risk analysis, and effectiveness.
  - Class III: Exhaustive Design Dossier with complete risk management documentation, all testing results, and animal study data if applicable.

- **Submit for Conformity Assessment:**
  - Class I: Most devices undergo self-certification unless they are sterile or measuring.
  - Class IIa and IIb: Involve a Notified Body to review the Technical File and grant certification.
  - Class III: Submission to a Notified Body and MHRA, often requiring detailed feedback and response cycles for high-risk devices.

- **Prepare for Next Steps: Transition to Clinical Trials:**
  - Class IIb and III devices, if cleared, proceed to human trials following successful pre-clinical completion.
  - Ensure a Clinical Investigation Plan (CIP) is ready for Class III devices, detailing the objectives, endpoints, and study design for first-in-human trials.

This journey through pre-clinical trials ensures that medical devices are rigorously tested and documented according to their classification and associated risks. By following this structured path, developers can meet regulatory standards and confidently proceed to clinical trials or market entry.