Sharing Best Practices as a Sponsor for Medical Device Clinical Trials

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Johnson & Johnson
MEDICAL DEVICES COMPANIES

Disclaimer

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Introduction

Geraldine Seow,
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- 20 years of experience in international clinical research for pharmaceuticals & medical devices: clinical development strategy, evidence generation strategy, clinical operations, quality & training, clinical IT systems implementation & management in collaboration with cross-functional, cross-business, international/ local teams management
- Registered pharmacist in Singapore with experience in hospital and retail pharmacy practice.

Topics

- The role of a Sponsor in a medical device clinical trial
- Differences between medical device and pharmaceutical clinical trials
- Case Study

Sponsor Definition

- Individual or organization taking responsibility and liability for the initiation or implementation of a clinical investigation

Company Sponsored Study (CSS)

NOTE:
When an investigator initiates, implements and takes full responsibility for the clinical investigation, the investigator also assumes the role of the sponsor and is identified as the sponsor-investigator.

Investigator-Initiated Study (IIS)

Reference:
ISO 14155:2011(E): Clinical investigation of medical devices for human subjects — Good clinical practice

Two types

Company Sponsored Study (CSS)

- The Company assumes all Sponsor responsibilities as per GCP including:
  - Protocol writing
  - Conducting & monitoring
  - Report writing
  - Trial Products
  - Finance
  - Quality Assurance & Control
  - Selection of qualified Investigators & Sites to conduct the study

- Investigator conducts the study at the Site and is responsible for the enrolment, medical treatment & care of subjects as per protocol and clinical trial agreement.

Investigator-Initiated Study (IIS)

- The Investigator assumes all Sponsor- Investigator responsibilities as per GCP including:
  - Protocol writing
  - Conducting & monitoring
  - Report writing
  - Trial Products
  - Finance
  - Quality Assurance & Control

- Company provides support:
  - Funding/ Product/ Technical support

- Investigator conducts the study at the Site and is responsible for the enrolment, medical treatment & care of subjects as per protocol and clinical trial agreement.

Differences Between

Medical Device & Pharmaceutical Clinical Trials

Clinical Trial/ Study/ Investigation

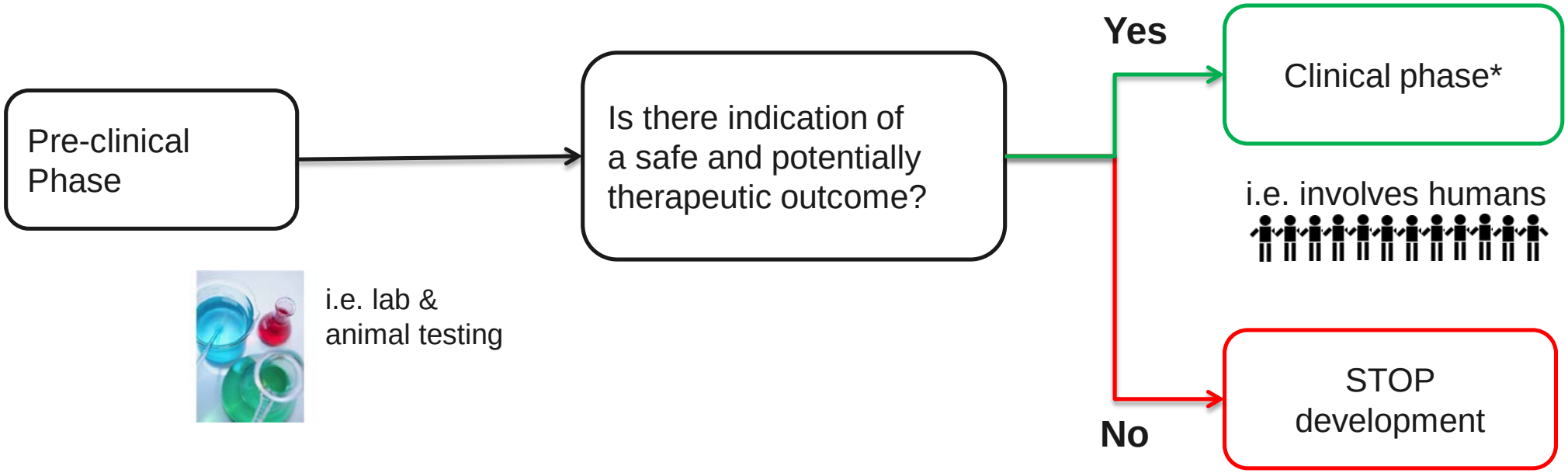
Medical Device

ISO 14155:2011(E):
Clinical Investigation:
Systemic investigation in one or more human subjects, undertaken **to assess the safety or performance of a medical device**.
Note: “Clinical trial” or clinical study are synonymous with “clinical investigation”.

Pharmaceutical

ICH Guidelines E6(R2) for GCP, 1.12:
Clinical Trial/ Study:
Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.

Clinical Research Phases



Medical Device: From design to patient: ~ 5-10 years

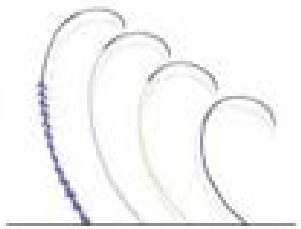
Pharmaceuticals: From molecule to patient: ~ 10-15 years

*Clinical Phase:

- For medical devices, the clinical testing requirements differ based on the type of device and whether it is permanent.
- For experimental pharmaceutical agents, the clinical testing process is extensive and follows a specific sequence.

Medical Device Study Phases

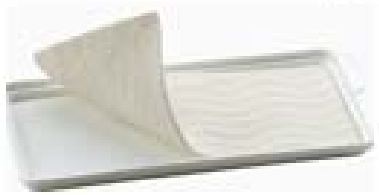
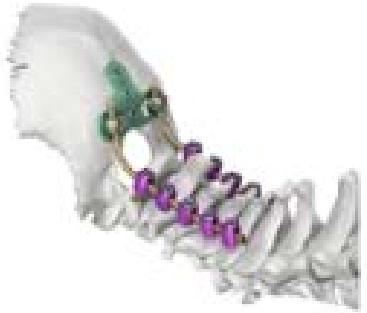
	Phase	Description
Preclinical	**In vitro (bench-top) testing**	In vitro research takes place in the laboratory. (In vitro means 'in glass' – referring to the test-tubes of the lab.). Laboratory researchers attempt to simulate conditions of the human body, conducting multiple tests to establish whether the device is effective, safe, and functioning properly.
Preclinical	**Animal studies**	Initial tests to establish safety of the product or materials in question will be conducted on animals.
Clinical Trials	**Feasibility (pilot) studies**	A feasibility, or pilot, study will be conducted to test safety and performance of the product in question. Usually these will be multi-centre studies, and the number of subjects can range from 30 to about 200. The duration of the study generally ranges from 30 days to 6 months.
Clinical Trials	**Pivotal trials**	Pivotal trials are conducted to gain evidence of safety and effectiveness. These are also usually multi-centre studies, with the number of subjects generally ranging from 100 to over 1,000. The duration of the study can range from 30 days to several years. These are the studies used to obtain regulatory approval from the relevant approval body (e.g., FDA in the US).
Clinical Trials	**Post-marketing studies**	After the launch of a product, post-marketing studies will be conducted to monitor long-term effects and to gain additional safety and effectiveness data. Post-marketing studies will also be conducted for commercial reasons (i.e., to increase market penetration).












New
Radiant Bright
New
Radiant Charm
NATURAL
SHINE™
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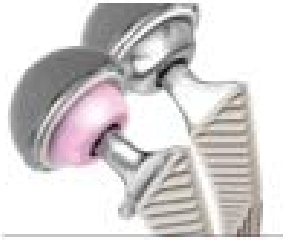
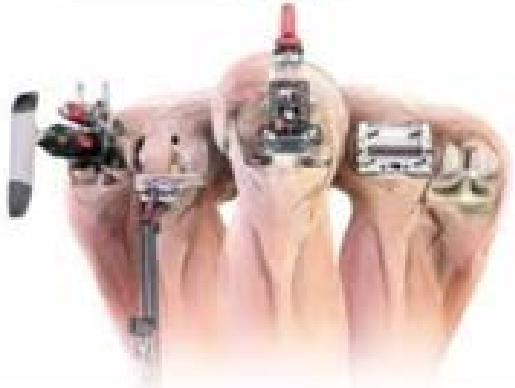








Medical Devices- Classification

CLASS	RISK LEVEL	DEVICE EXAMPLES
A	Low Risk	Surgical retractors / tongue depressors
B	Low-moderate Risk	Hypodermic Needles / suction equipment
C	Moderate-high Risk	Lung ventilator / bone fixation plate
D	High Risk	Heart valves / implantable defibrillator

Classification of a medical device will depend upon a series of factors, including:

- How long the device is intended to be in use
- Whether the device is invasive
- Whether the device is implantable
- Whether the device is active
- Whether the device contains a drug or biologic component

In general, whether there is a need for clinical trial(s) to be conducted or clinical evidence to be available for an unregistered medical device before it receives registration approval depends on the regulatory registration pathway associated with its risk-based classification.

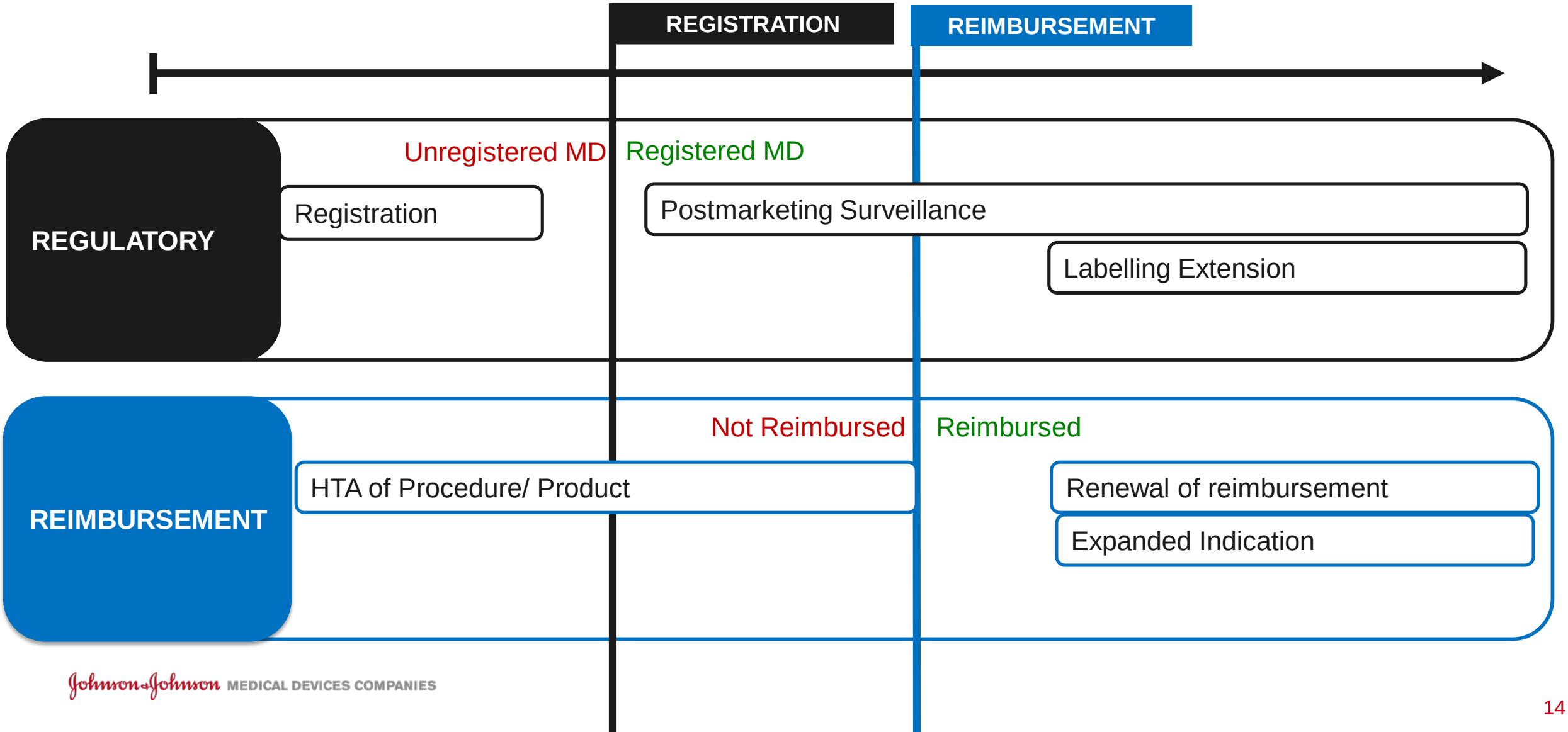
Sponsor’s rationale for conducting a medical device clinical study

- **Collecting credible clinical evidence for market access & adoption**
  - Safety, efficacy/ performance (& cost-effectiveness)
  - Registration requirement
  - Premium price
  - Local data

- Decision based on:
  - ✓ Mandatory requirement
  - ✓ Strategic Alignment
  - ✓ Scientific merit
  - ✓ Budget
  - ✓ Resources

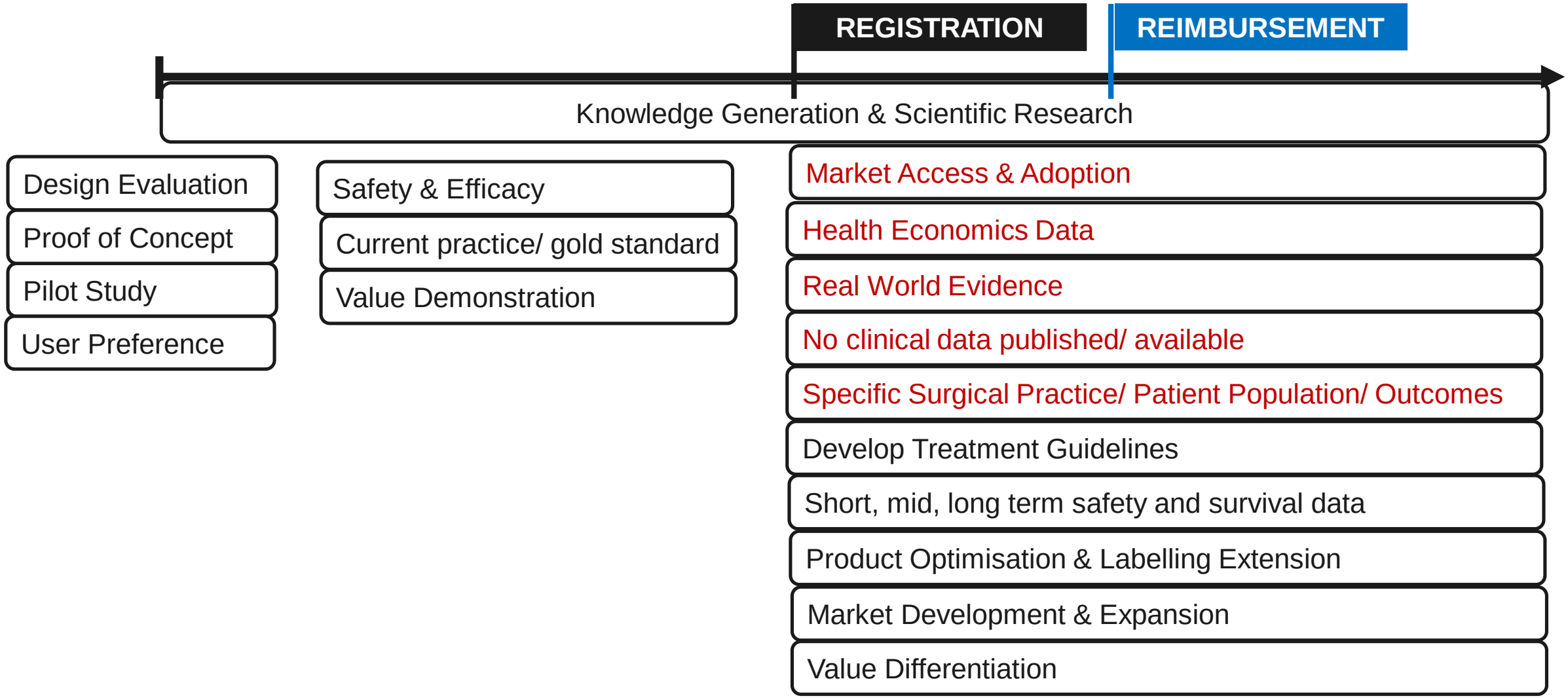
Sponsor's rationale for conducting a medical device clinical study

* For countries where there is local clinical study requirement for registration and/ or reimbursement

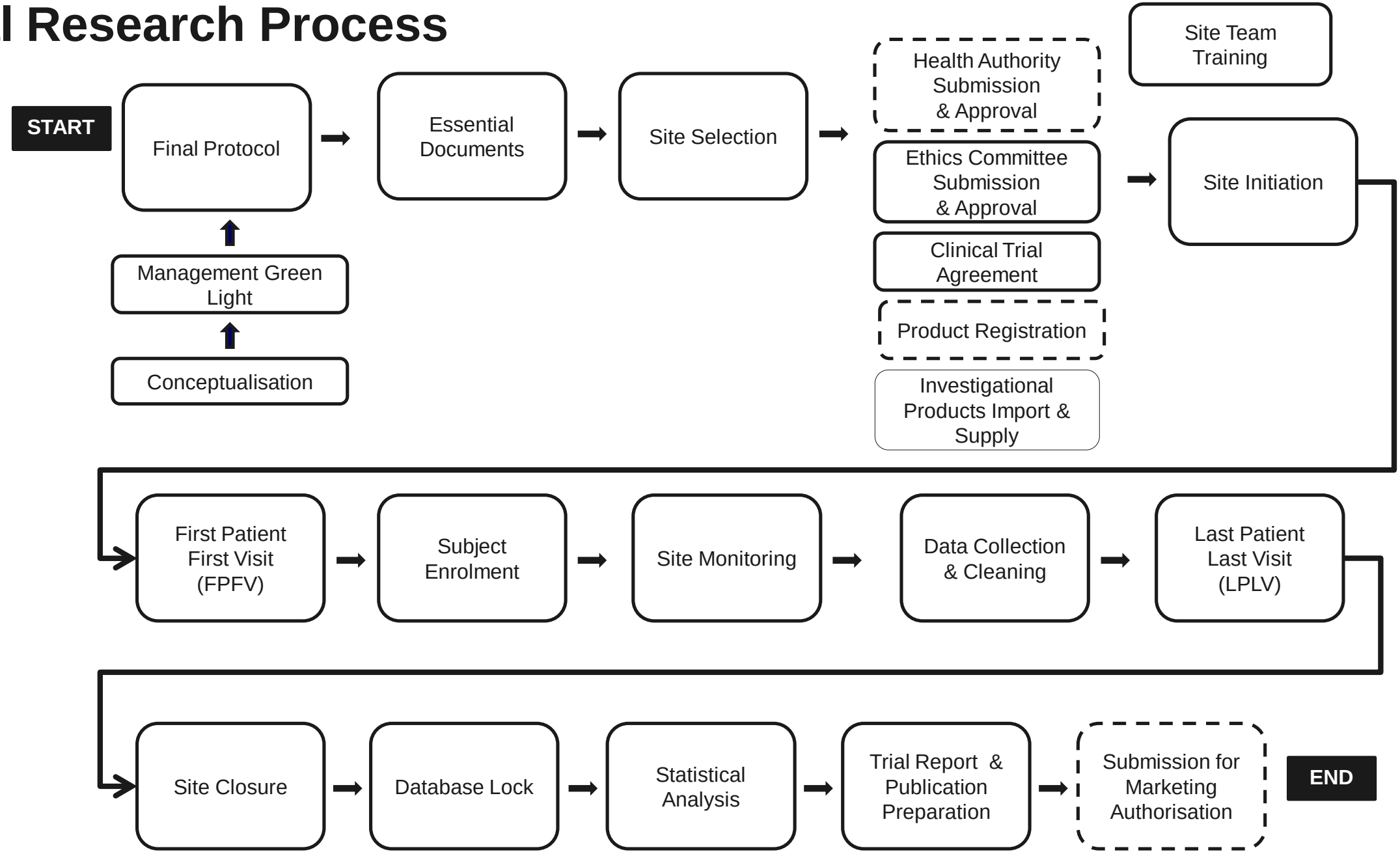


Sponsor’s rationale for conducting a medical device clinical study

* When there are Clinical Evidence Gaps



Clinical Research Process



Country & Site Selection Considerations

Best Fit

Similar requirements but specific considerations:

Investigator:
- Product type preference
- Surgical technique
- Qualification and experience with treating the condition plus procedure (i.e. no. of cases)
- Experience with research (which type)
- Availability for clinical research

Patients:
- Demographics/ Epidemiology
- Preference/ suitability for drug versus device treatment options
- Device (size) match with patient anatomy and surgeon
- Reasons/ expectations for seeing doctor

Country:
- Type of evidence required for registration, reimbursement, market access, etc.
- Gold standard treatment guidelines followed
- Availability of product
- Regulatory pathway & timelines for starting a MD clinical trial

Study Site:
- IRB review and Contract review processes
- Study design
- Relevance of gold standard/ existing devices and surgical technique
- Site infrastructure e.g. facilities, imaging
- Target timelines
- (Min/ Max) Number of cases/ site

Protocol

Information from IB/ IFU	More mechanical test results, preclinical research, data from earlier/ similar device/ procedure, minimal “side effects”. (No SPC/ PIL. No PK/ PD data, dosage, drug interactions, overdose, effect on metabolism.)
Investigator training/ qualification requirements	Surgical training and qualification- wet lab, patient cases, case observation. Requirement to complete training and/ or a number of cases. Learning curve. Run-in period.
Study design	Tends to be single arm (challenging to have comparator arm or RCT e.g. unethical, non-existent, hard to be blinded). Comparison could be with a retrospective cohort
Sample size	Depends on end point, type of study and budget but tends to have much smaller sample sizes than drug trials and could be not statistically powered
Endpoints	Could be an assessment based on the clinical judgement of the Investigator. Which endpoint can best demonstrate the outcome due to the investigational device alone. Which endpoint is measurable and is clinical significant.

Protocol

Screening | Enrolment | Pre-Op | Op & Hosp | Post-op | Follow-up

Visit Schedule	**Screening→ Enrolment → Admission → Procedure → Discharge → Post-op Follow Up** (more data intensive upfront; more SC- dependent during follow up)
Assessments	Higher usage of imaging, expert assessments/ judgement, QOLs & specialised tests than lab tests.
Safety Reporting	**Adverse Device Effect (ADE), SADE, USADE.** Adverse events related to device and procedure. Consider Expectedness and Seriousness. Need to report for study data (e.g. post-op fever, pain, etc.)?
Product Complaints (and Device Deficiencies)	In addition to adverse event reporting. Reporting to the Sponsor/ manufacturer/ importer. Reporting to the health authority.
Independent Reviewer/ Central Lab	Central review of imaging/ ECG/ surgical videos for data analysis

Investigational Product

- **One Device System** consisting of many devices or One device.
- **Instrument sets**: limited, sterilization after use, availability, secure storage
- **Capital equipment** (e.g. Generator): On loan versus purchased from the Sponsor; Installation of equipment in the hospital; space allocation, infrastructure and power supply.
- **Consumables**: One time use device versus reprocessed device; reloads; catheters, guidewires, sterilized packaging (once opened, considered used!).
- **Product sizes**: Various product sizes required/ suitable for subjects
- **Subject-customised devices**: Custom made for a patient.
- **Digital surgery**: Connectivity to cloud based systems, cybersecurity, data privacy laws.
- **Expiry date**: Watch out for expiration date of sterilized product in sealed packaging
- **Storage**: Location (where device will be used), Locked/ Secure Access, Temperature control, Pre/ Post-Sterilisation, Space, Power Supply, Mobility, physical requirements.
- **Biohazard management** of devices removed from subject- blood, body fluids, tissue, explants.

Collaboration with Operating Theatre Team

- **Understand study pathway** for the subject, device, site team and Sponsor team
- **Unused device storage** in locked cabinet/ secure area/ OT fridge
- **Used device handling** (and disposal)
- **Device decontamination and sterilization**:
  - how to ensure device is safe enough to be used on another subject
  - Logistics for turnaround of devices which need to be sterilized from one case to another
- **Training** of OT nurse/ technician on device system, e.g. instrument sets, prior to study start
- **OT access**: Application for permission to be in the OT area or in the OT room where the procedure takes place. Familiarity with OT layout and subject pathway.
  - **Site Team**: Meet subject in the recovery room before/ after the procedure, be in the OT room during procedure to record specific source data points which are not usually documented in the surgery report and should consider appropriate documentation methods/ tools.
  - **Sponsor staff** may be required to be in the OT for case support: application for permission to be in the OT area or in the OT room where the procedure takes place. Training of sponsor staff on OT requirements.

Case Study

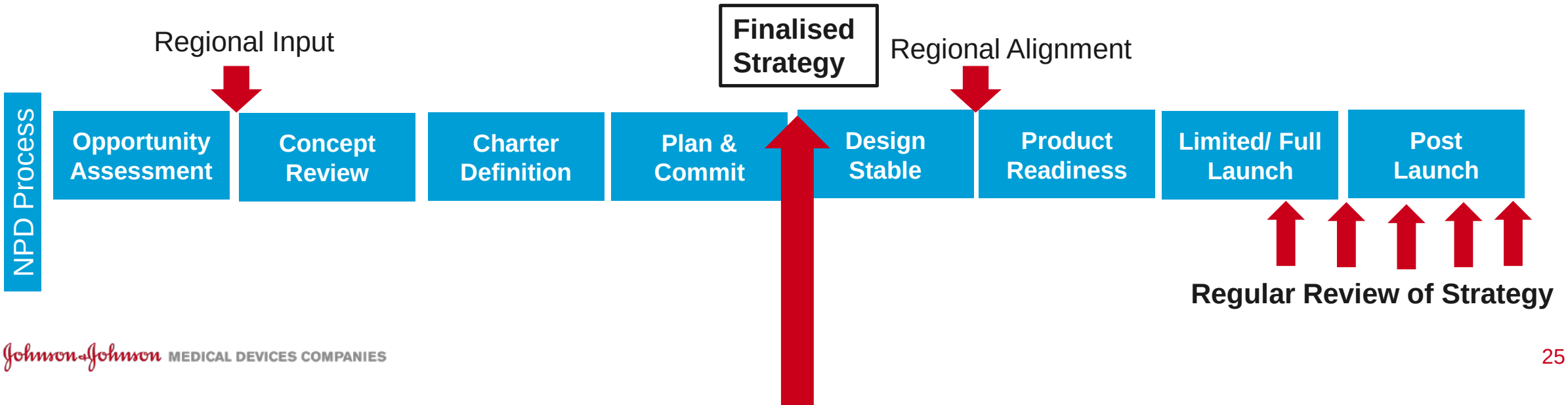
Case Study

- Product X is an innovative medical device system.
- The regulatory strategy is to submit for approval in the US via the **510(k) pathway** and in EMEA via **CE mark**.
- There are multiple items within the system which must be used together in a procedure.
- This product requires surgeon to change their technique slightly.
- At the time of approval, there will only be benchtop data and no clinical data available since there is no IDE requirement.
- The plan is to launch Product X in all Asia Pacific countries with a premium price.

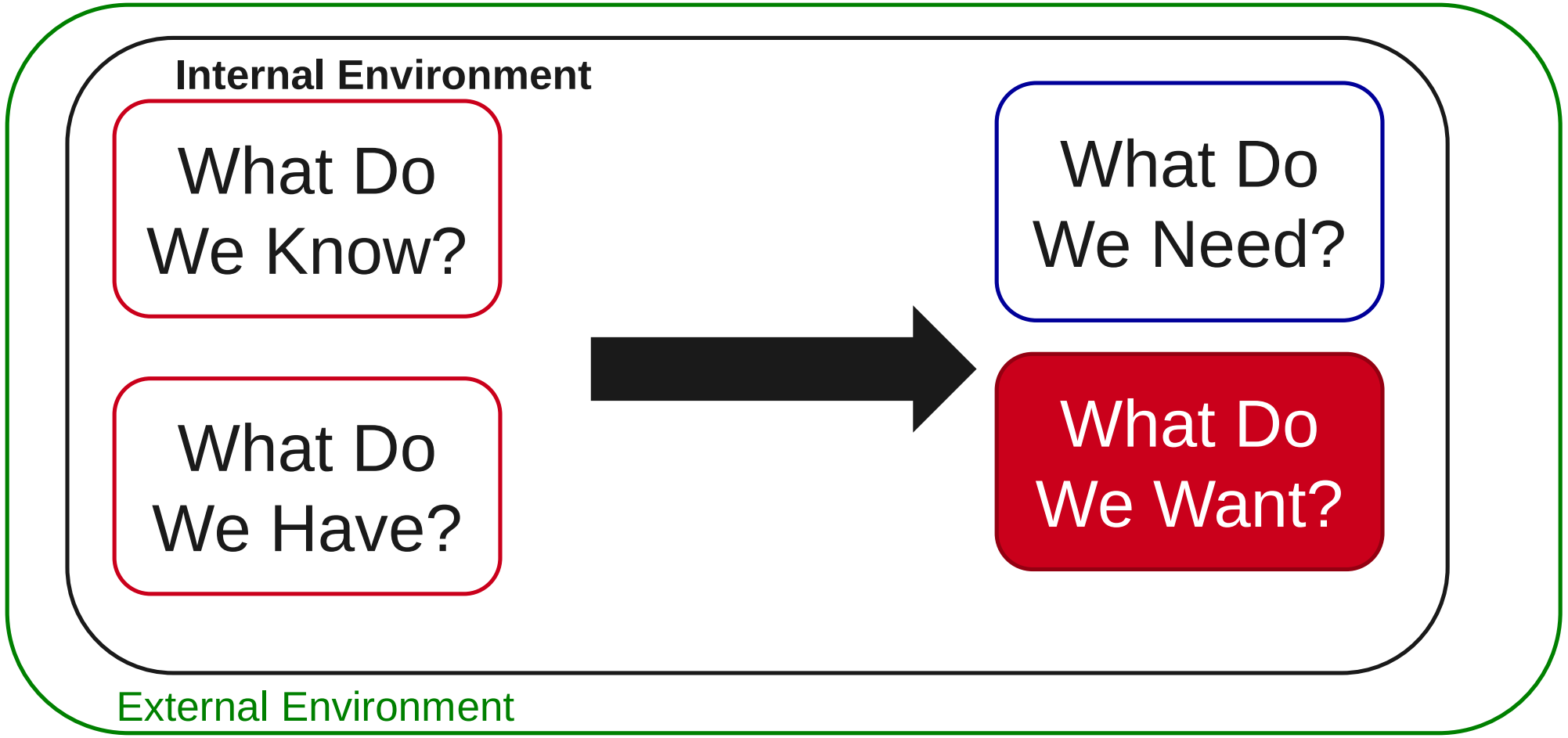
Planning

Evidence Generation

- It is a strategic & collaborative activity.
- It is not a checklist activity.
- It requires conversation and discussion among cross-functional team members at country, regional and global levels



What are the Evidence Gaps?



Engage Stakeholders

A Cross-Functional Team of Stakeholders Develops An Evidence Generation Strategy (EGS)

Responsible for ensuring evidence is created for regulatory approval in regions where product is targeted to be sold.

Ensures product design meets performance targets defined in TPP. Designs and executes bench-top studies.

Responsible for defining target marketing, customer unmet needs, benefit of the product, and desired claims.

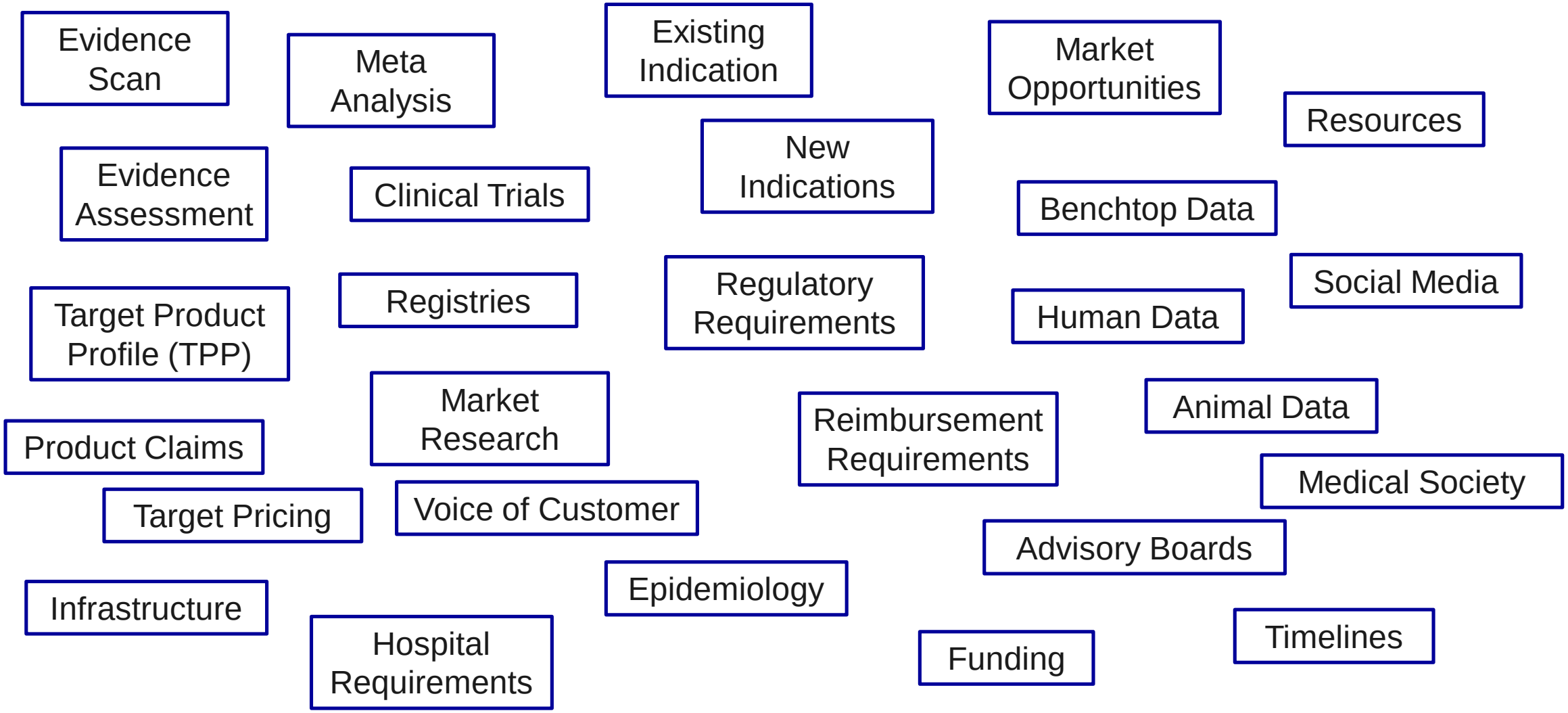
Responsible for designing preclinical studies to support projects.

Responsible for designing and obtaining healthcare economic data to support economic value of the product.

Responsible for designing clinical research studies to support the clinical value of the product.

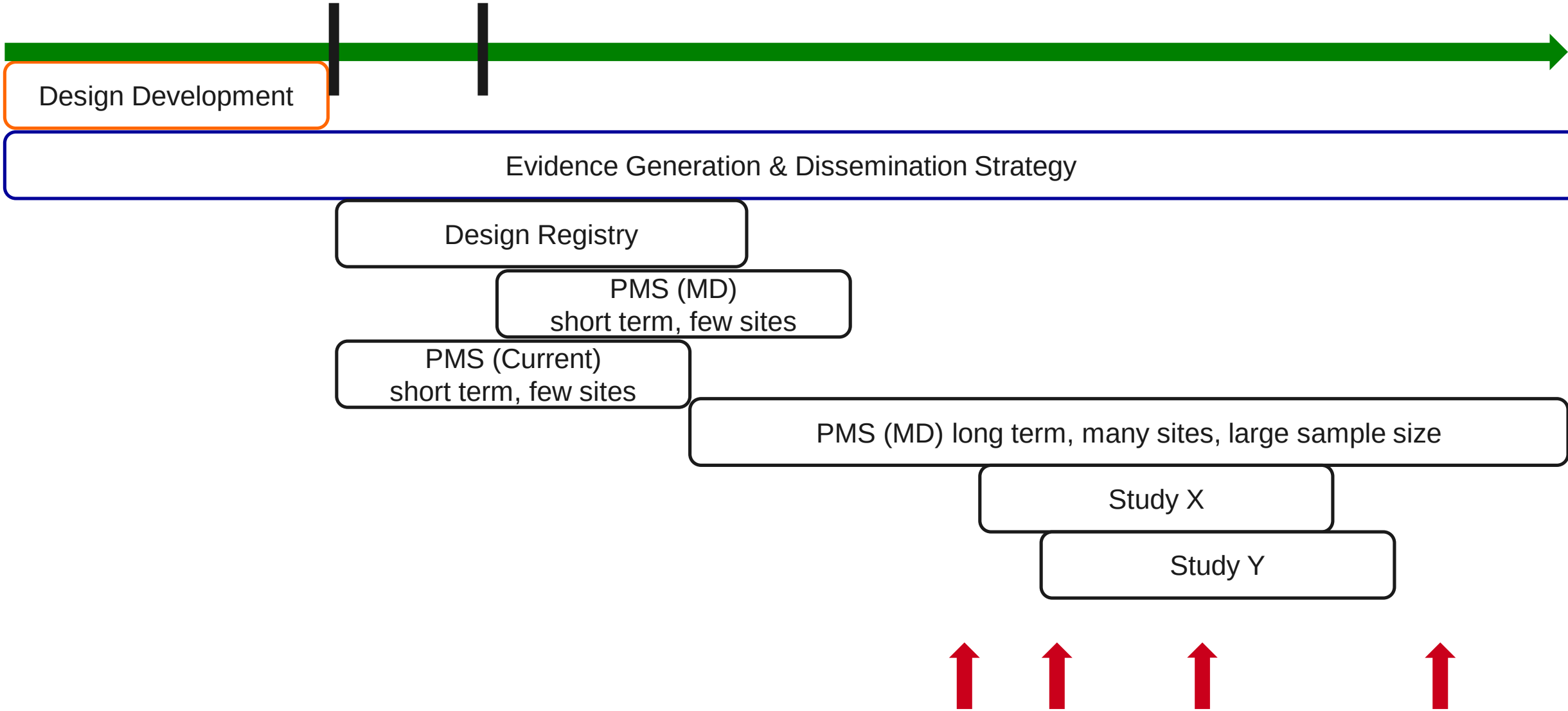
Ensures product benefit and evidence are clinically relevant and meaningful.

Gather Insights



Analyse & Prioritise→ Develop Strategy

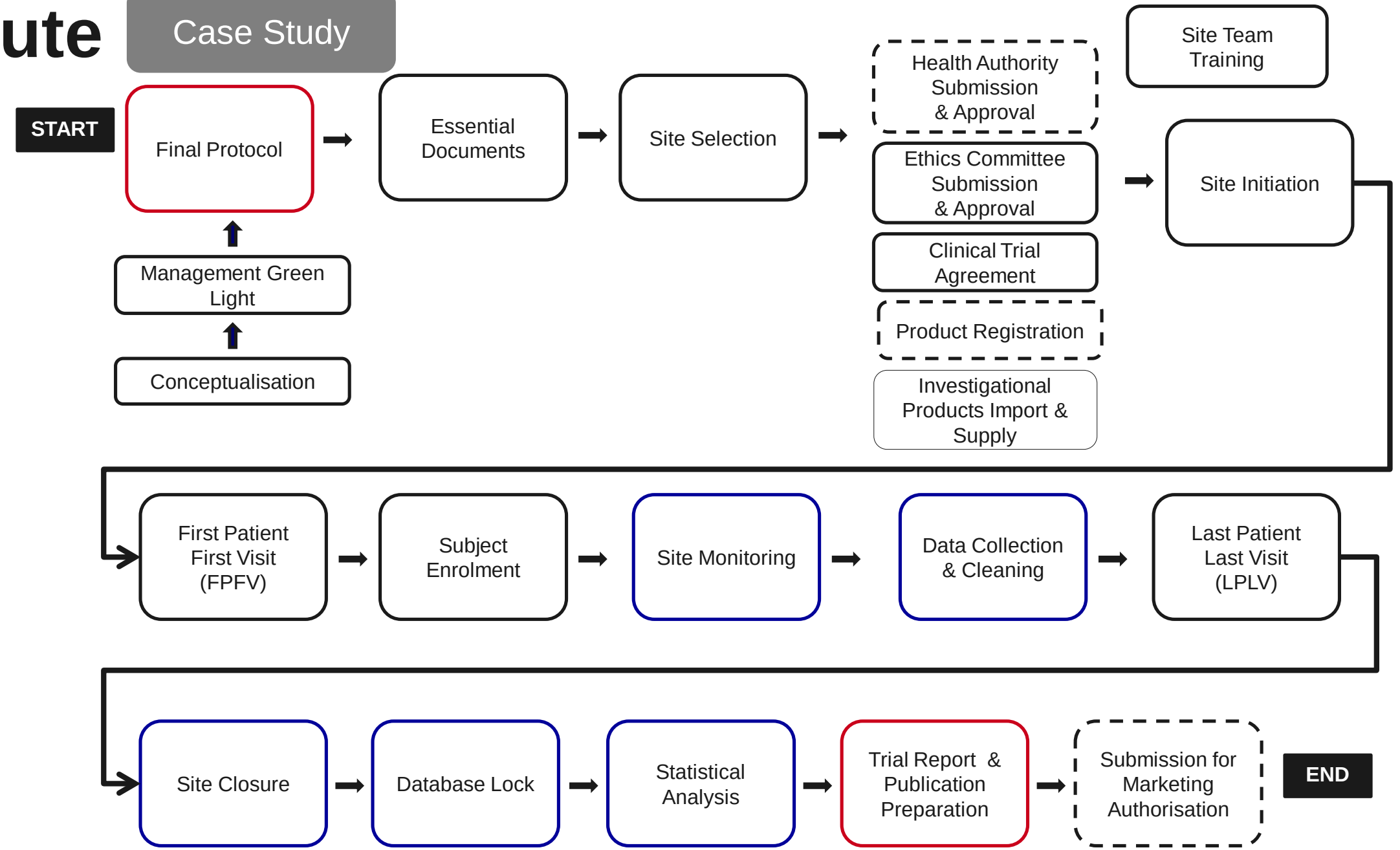
Case Study



Execution

Execute

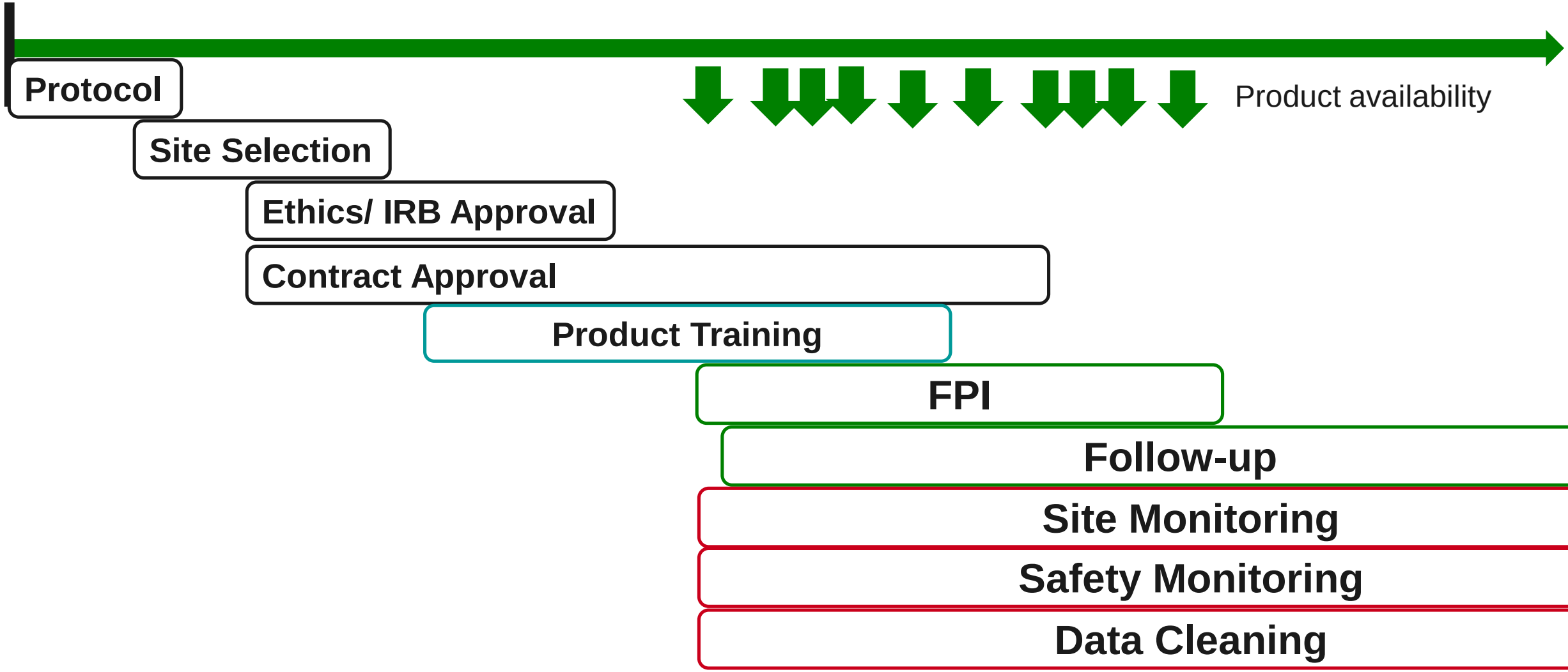
Case Study



Execute

PMS (MD) long term, many sites, large sample size

Case Study



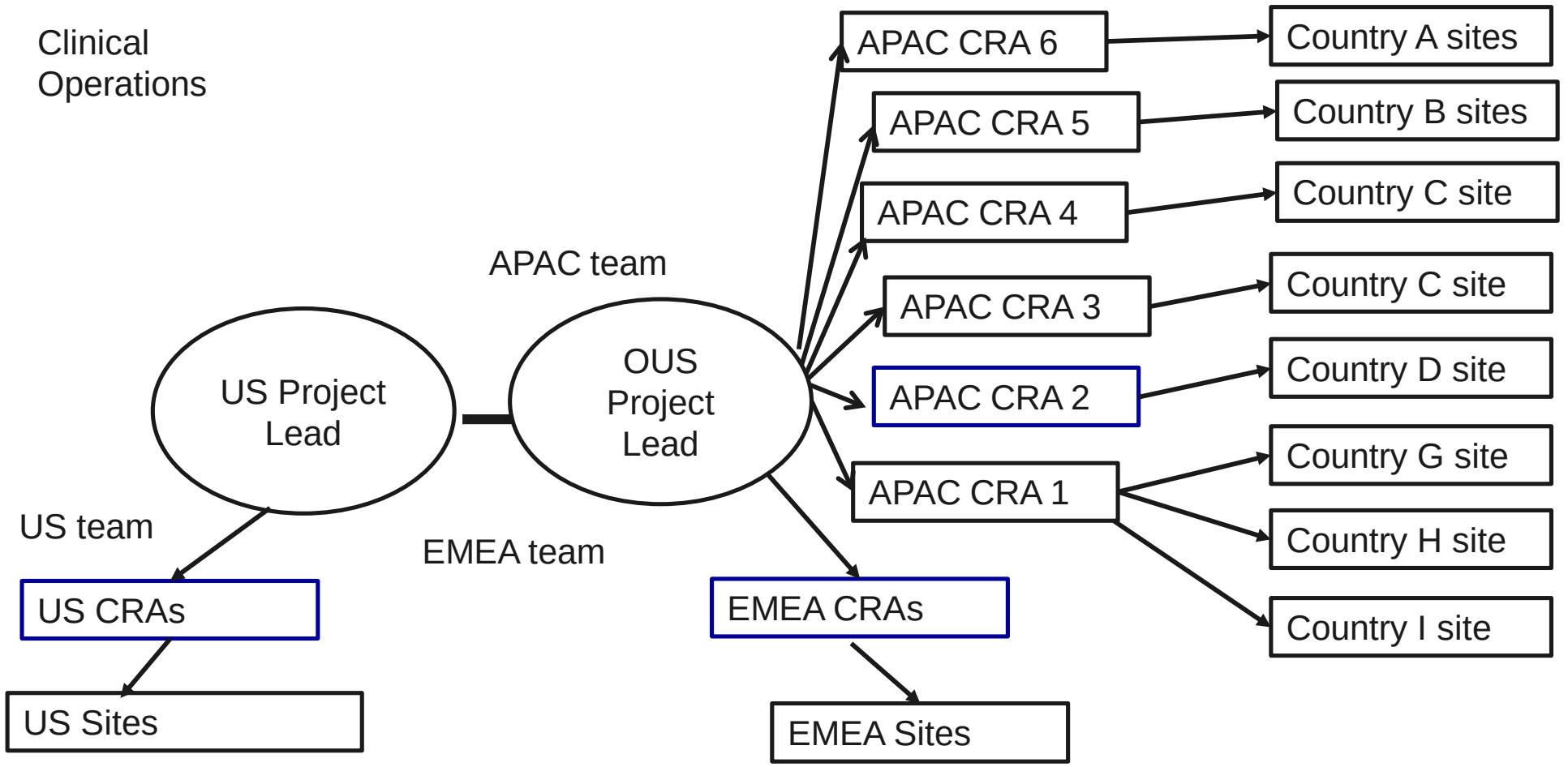
Execute

PMS (MD) long term, many sites, large sample size

Case Study

Project Team

- Clinical Franchise
- Medical Affairs
- Medical Safety
- Data Mgmt
- Biostatistics
- Central Lab



Execute

- One clinical trial cannot solve ALL evidence gaps
- Combination of evidence sources is required
- Sponsor tracks and maintains the EGS for the product or platform
- Needs may change with time
  → Check- in regularly on relevance & timeliness of the clinical trial results
- Agility that is founded on The Credo & GCP

Thank you!