PROCESS CHART

臨床研究の品質向上ツール作成WG

本研究の目的

- 現時点において品質管理システムあるいは品質管理計画に基づく、Goal志向のデザインアプローチとなるQuality by Design（QbD）において、プロトコルに必須の領域あるいは実臨床に関連する領域での品質管理指標として、何を基準にどのように推奨するかについて、まだ汎用的なツールがないのが現状である。
- 本研究では、被験者保護、データの質確保を目標として、QbDによる実施計画書の作成に必要なツールを検討及び作成し臨床研究の品質向上を目指す。

本研究で整備目標としたQbDツール

QbD概念に対する教育コンテンツ

PPT提示

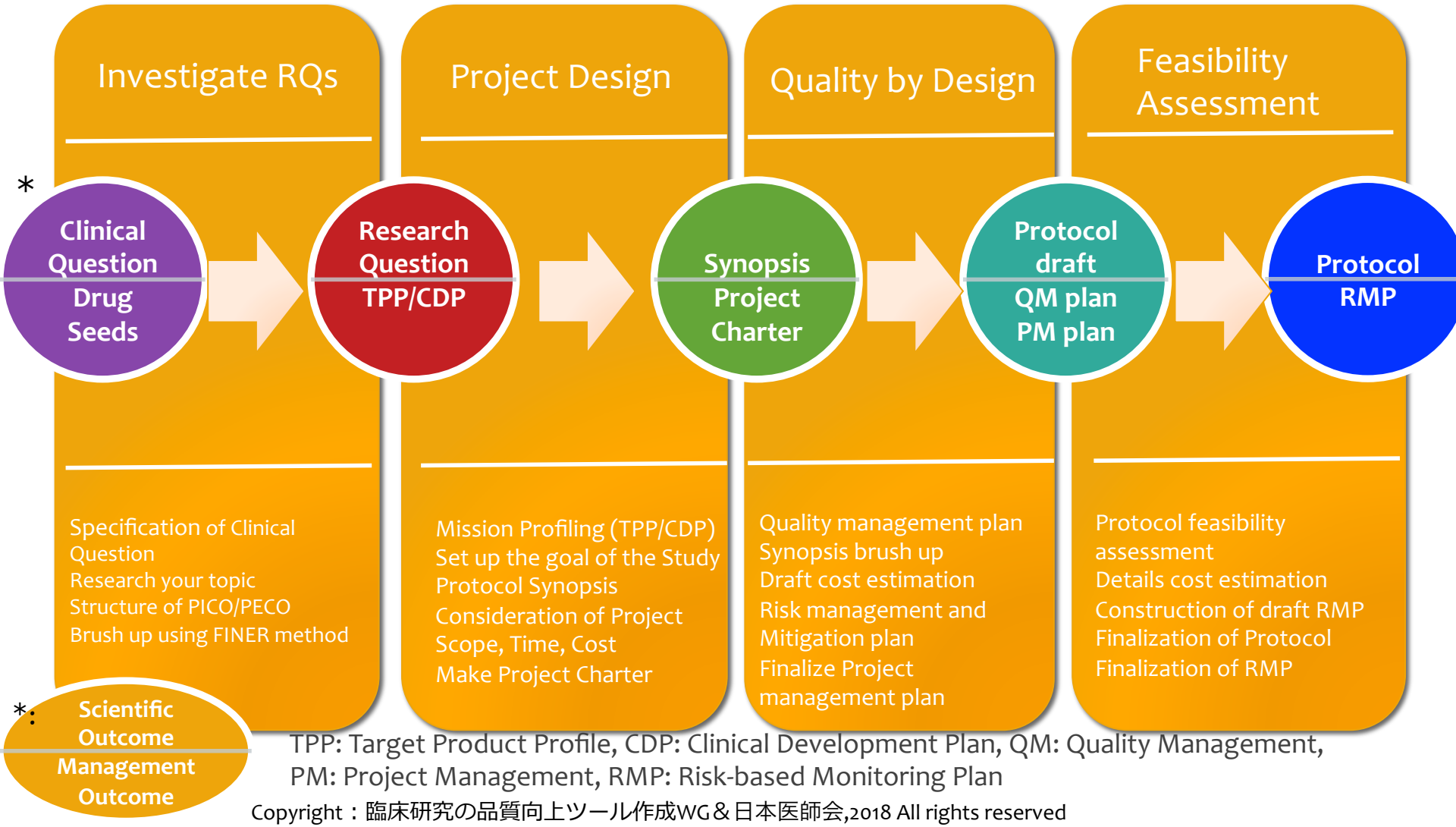
QbDによるプロトコル開発プロセスチャート

フローチャート提示

品質管理項目を組み込んだ実施計画書

次期活動で検討（H30年度）

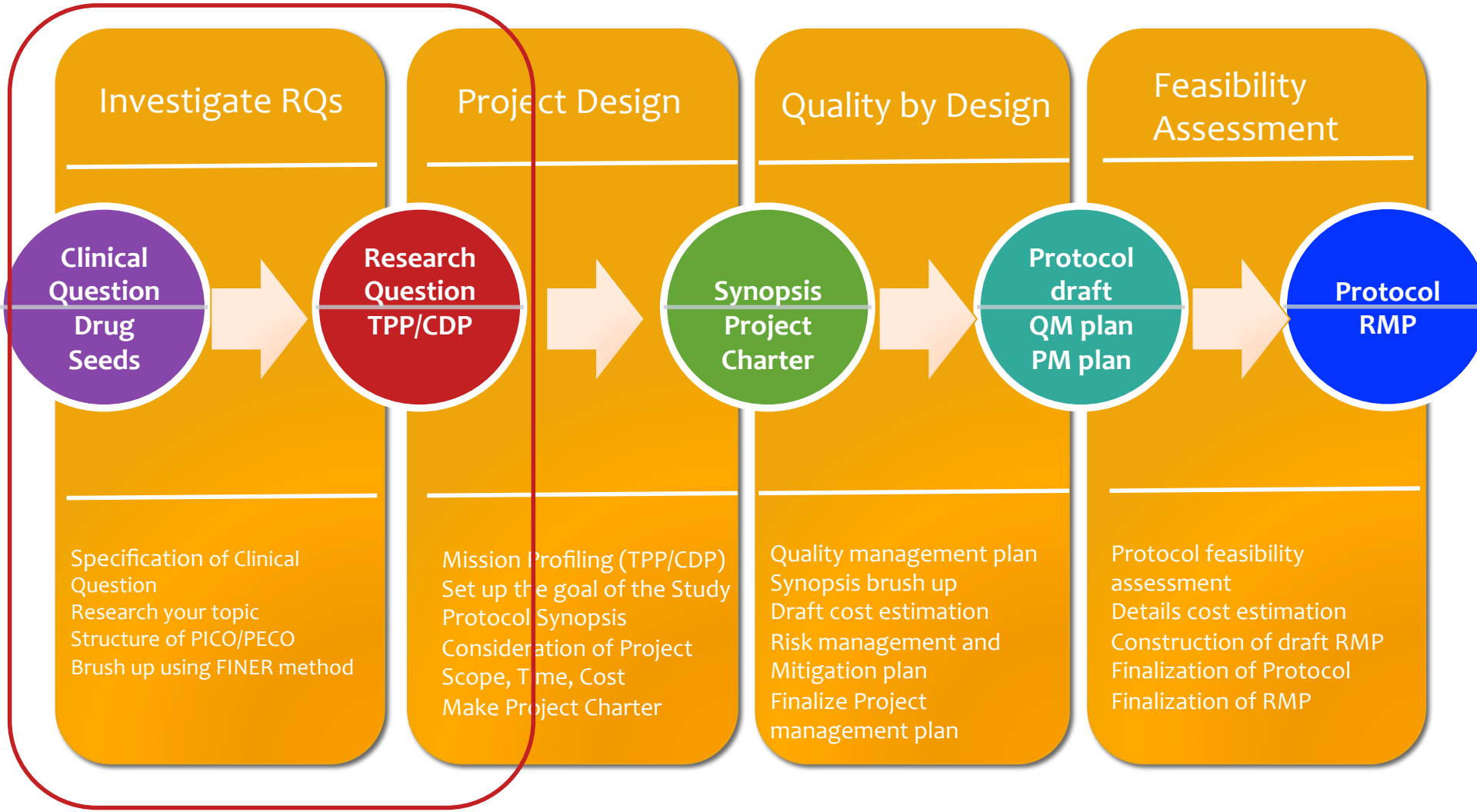
Whole Process of QbD protocol planning



TPP: Target Product Profile, CDP: Clinical Development Plan, QM: Quality Management, PM: Project Management, RMP: Risk-based Monitoring Plan

INVESTIGATE RQs

Whole Process of QbD protocol planning



Investigate Research Questions

input

Clinical Question

Specification of Clinical Question

Research your topic

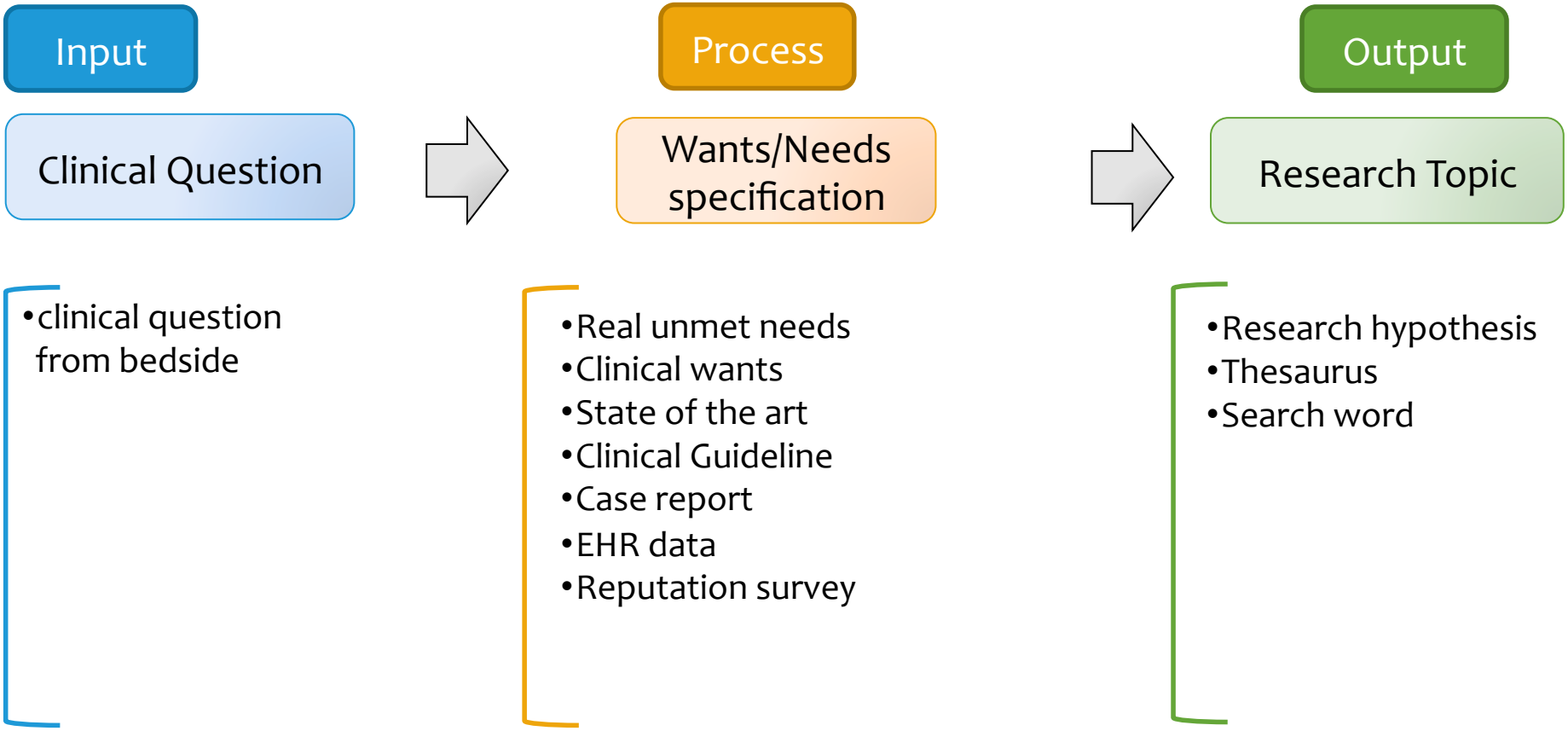
Structure of PICO/PECO

Brush up using FINER method

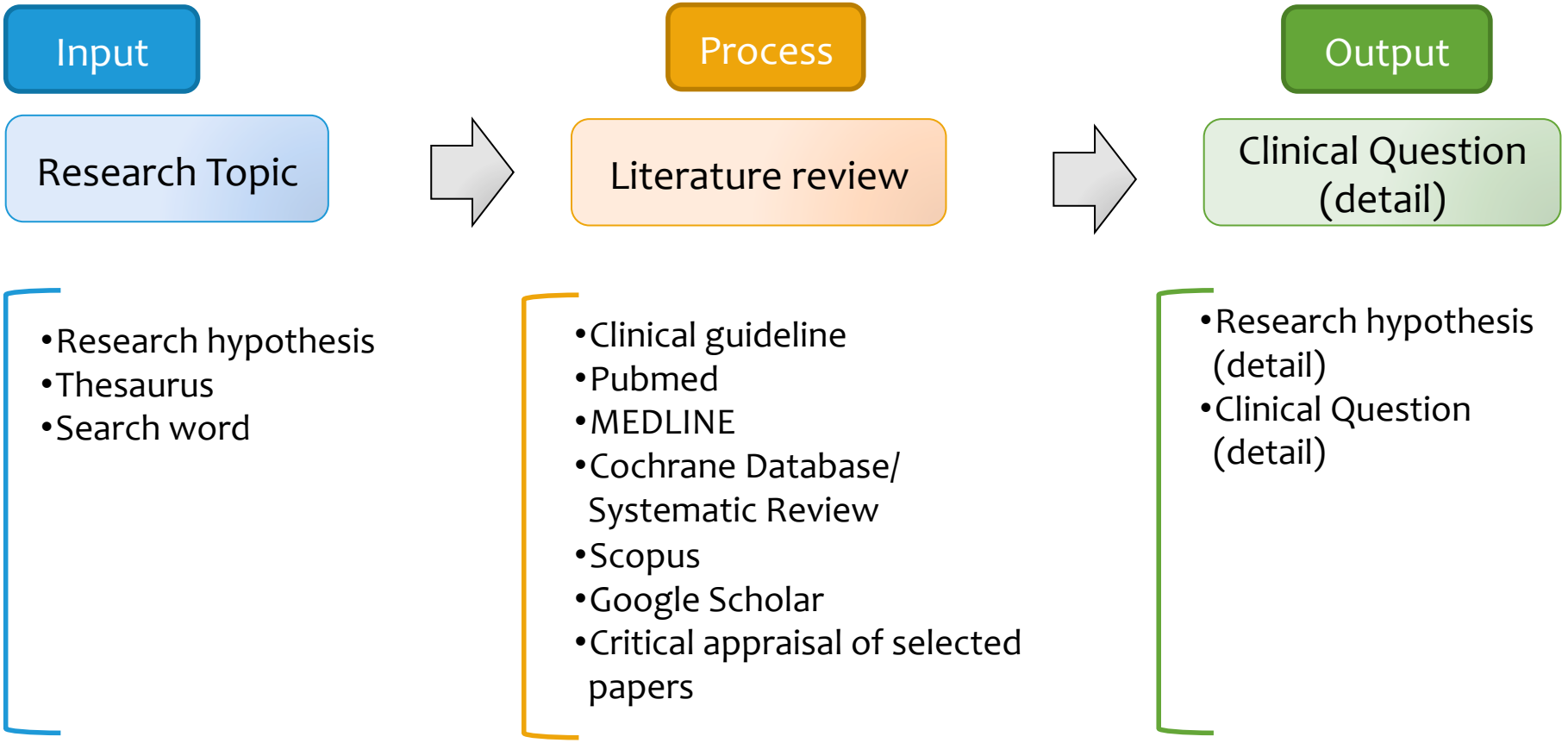
Research Question

Output

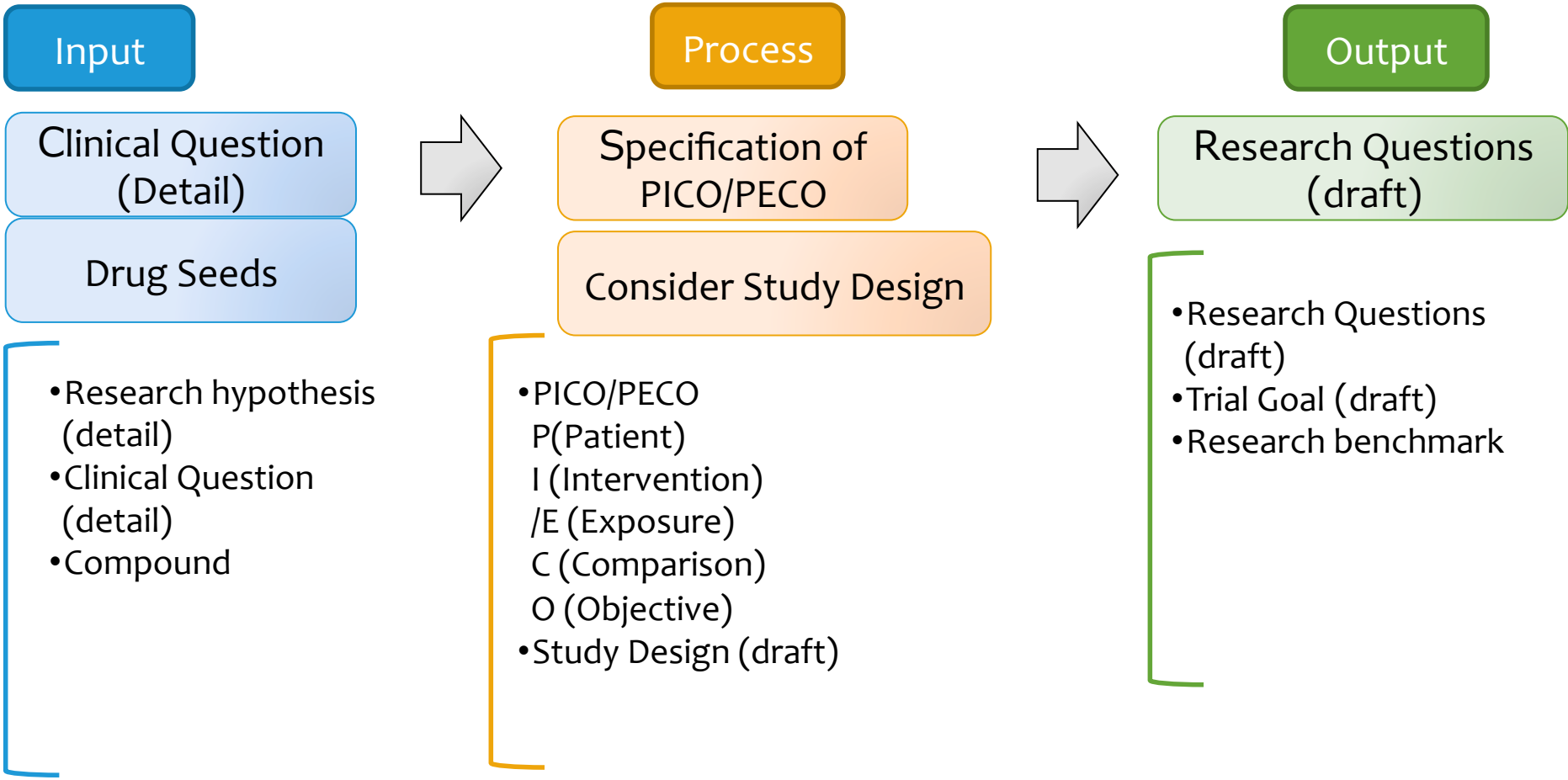
Specification of Clinical Question



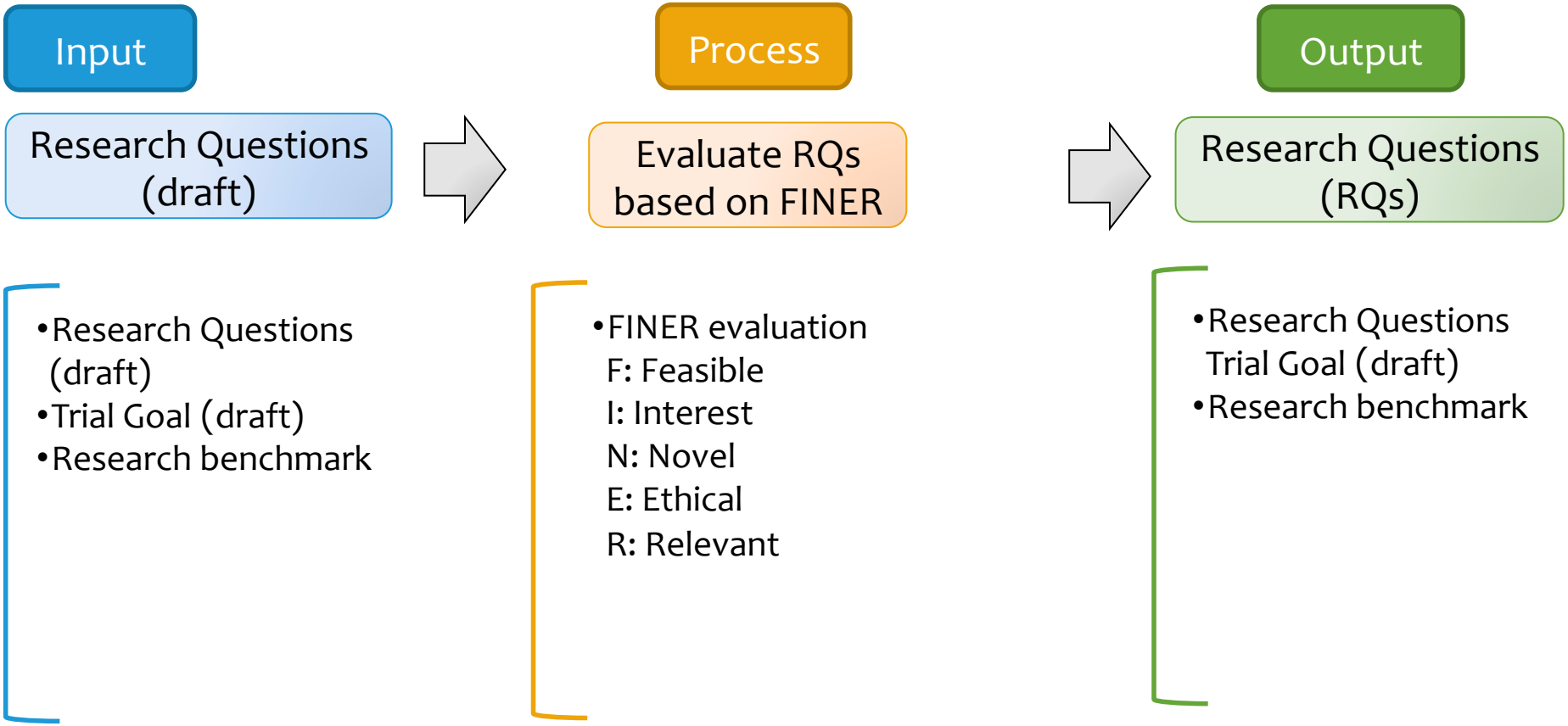
Research your topic



Structure of PICO/PECO

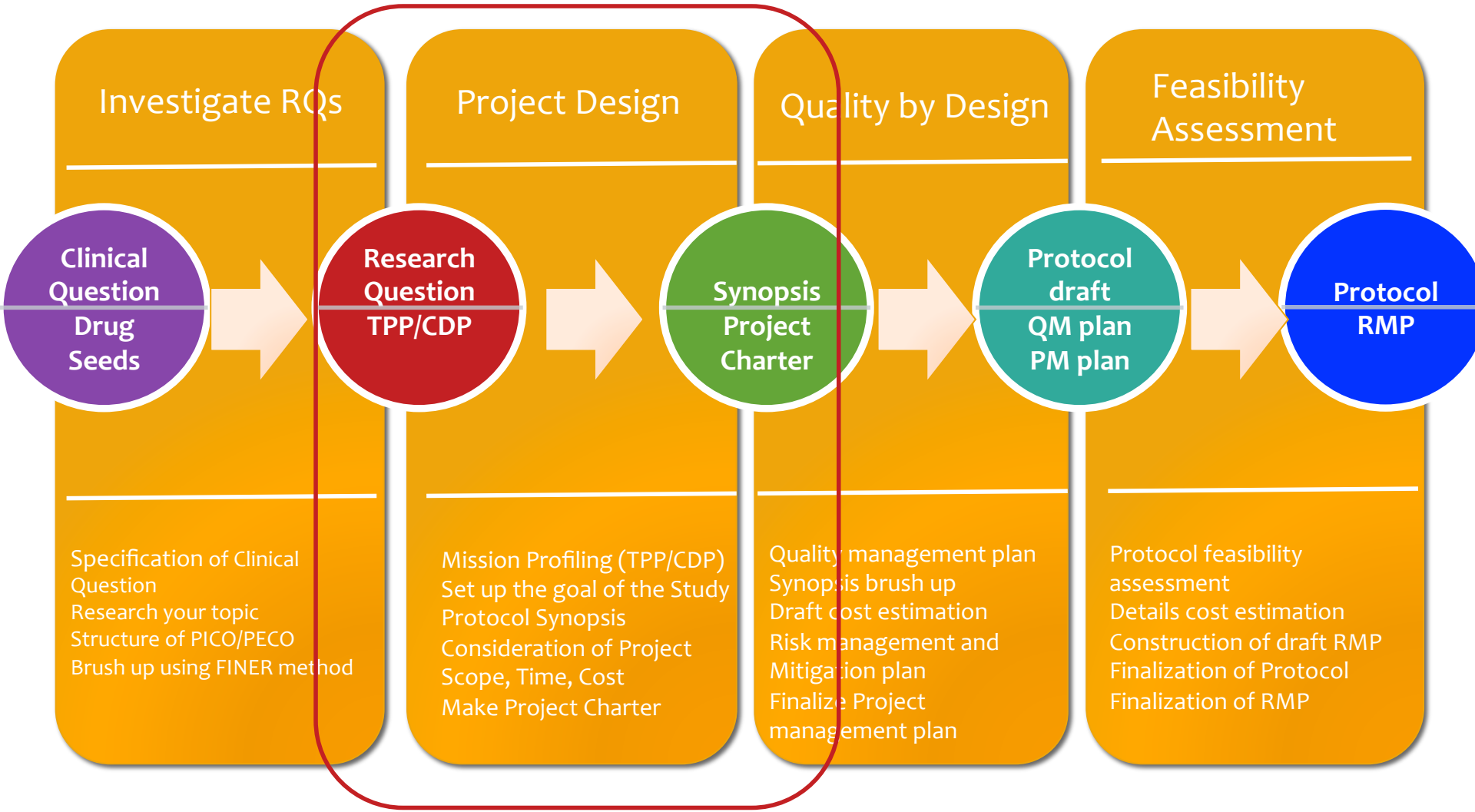


RQs brush up using FINER method



PROJECT DESIGN

Whole Process of QbD protocol planning



Project Design

input

Research Question

Mission Profiling（TPP/CDP）

Set up the goal of the Study

Protocol Synopsis

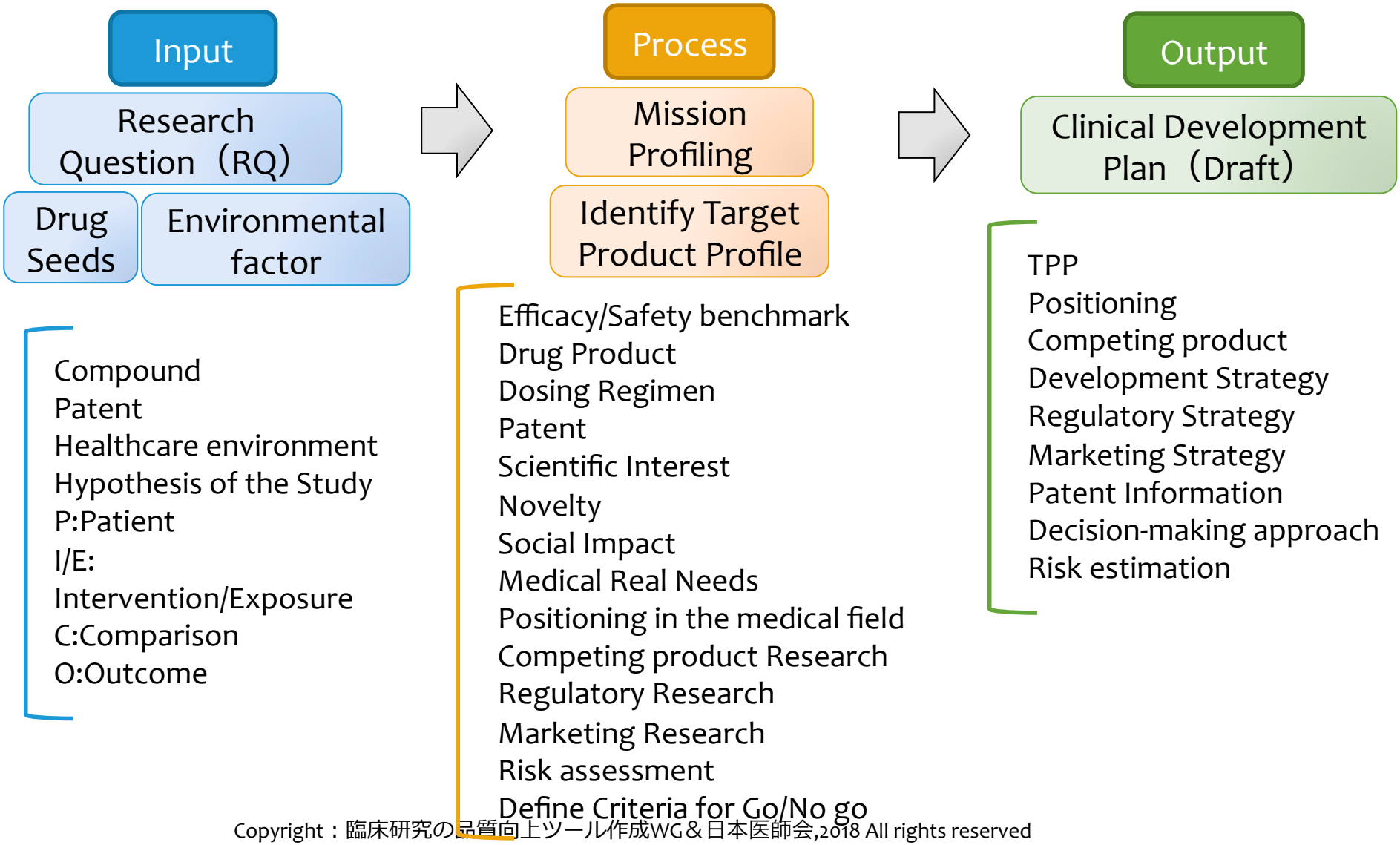
Consideration of Project Scope, Time, Cost

Make Project Charter

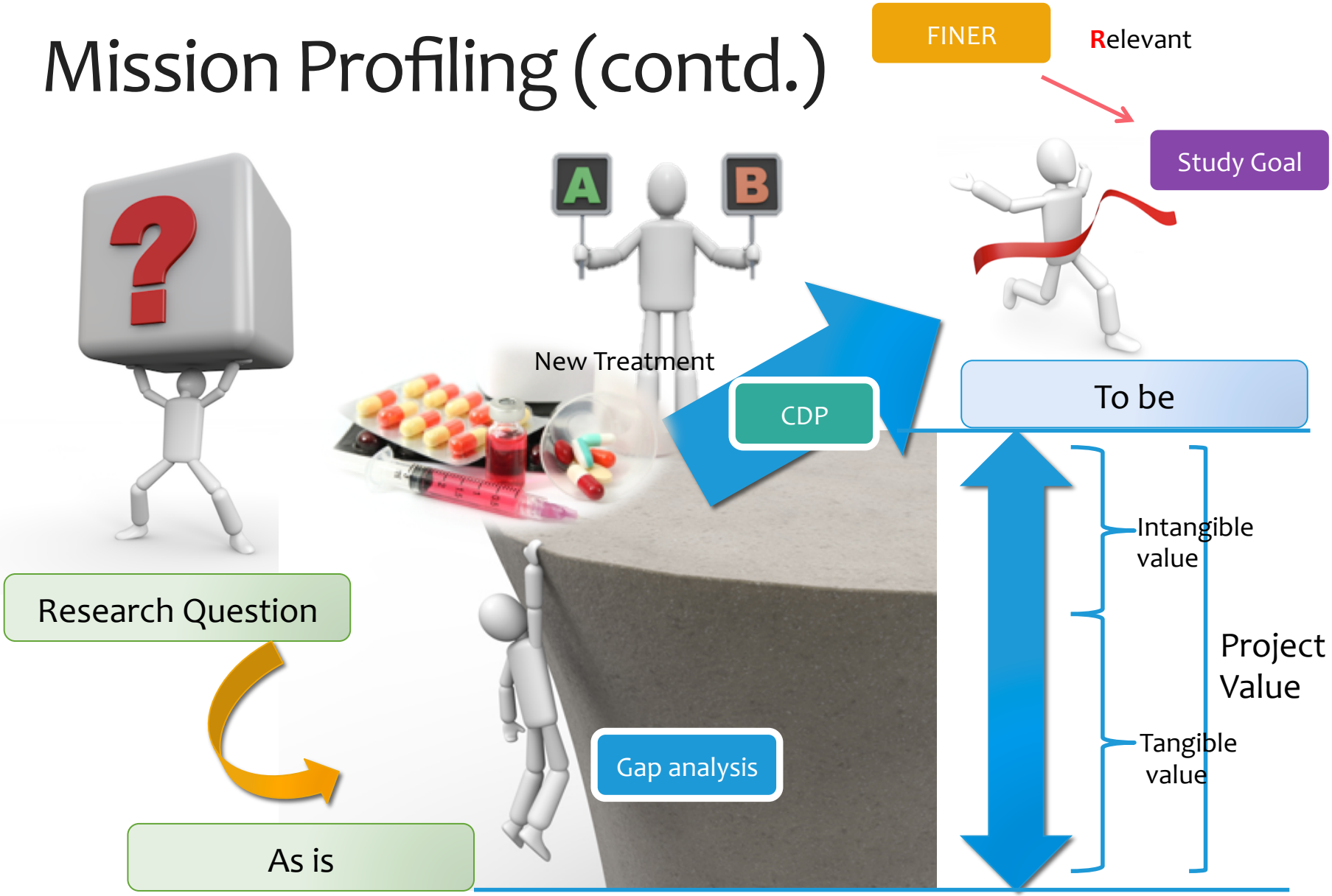
Synopsis Project Chater

Output

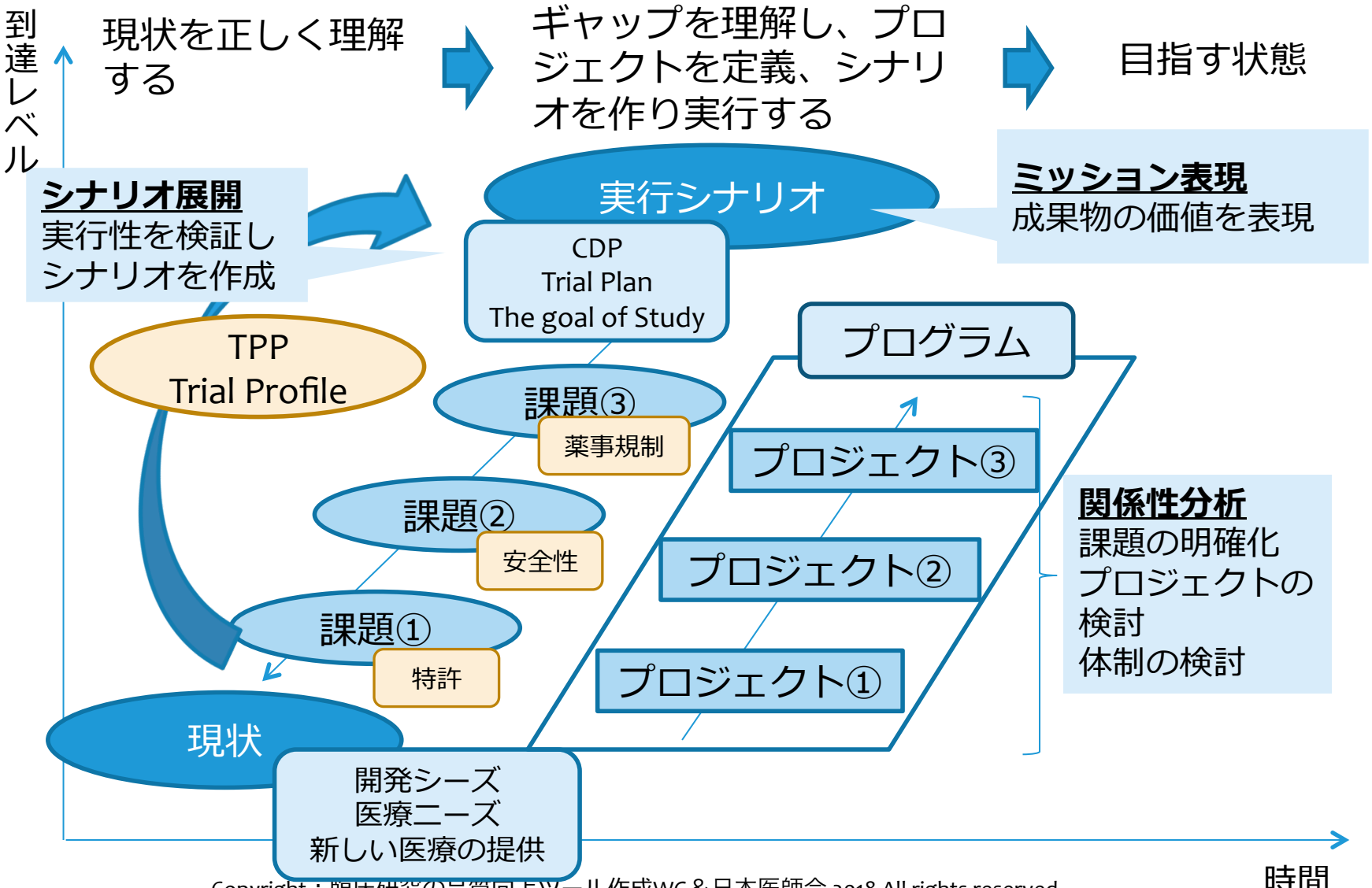
Mission Profiling



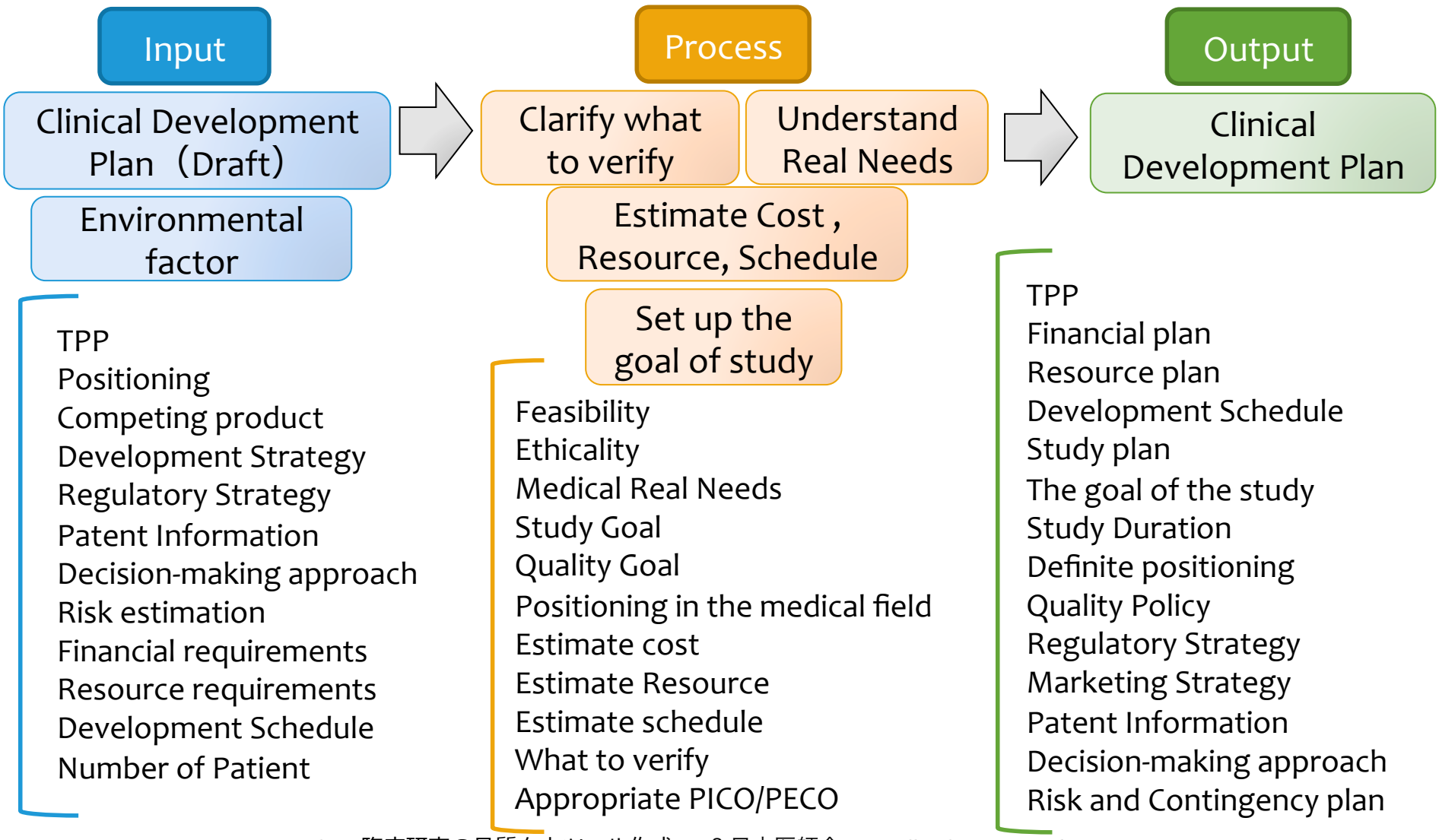
Mission Profiling (contd.)



Mission Profiling 概念図



Set up the goal of the Study



Target Product Profile（TPP）

- TPP:承認申請に必要な開発プログラム全体の意図が記載され、その時点での適切な情報が記載されているもの。開発のゴールが明記されている。(2007年3月FDAガイダンス)

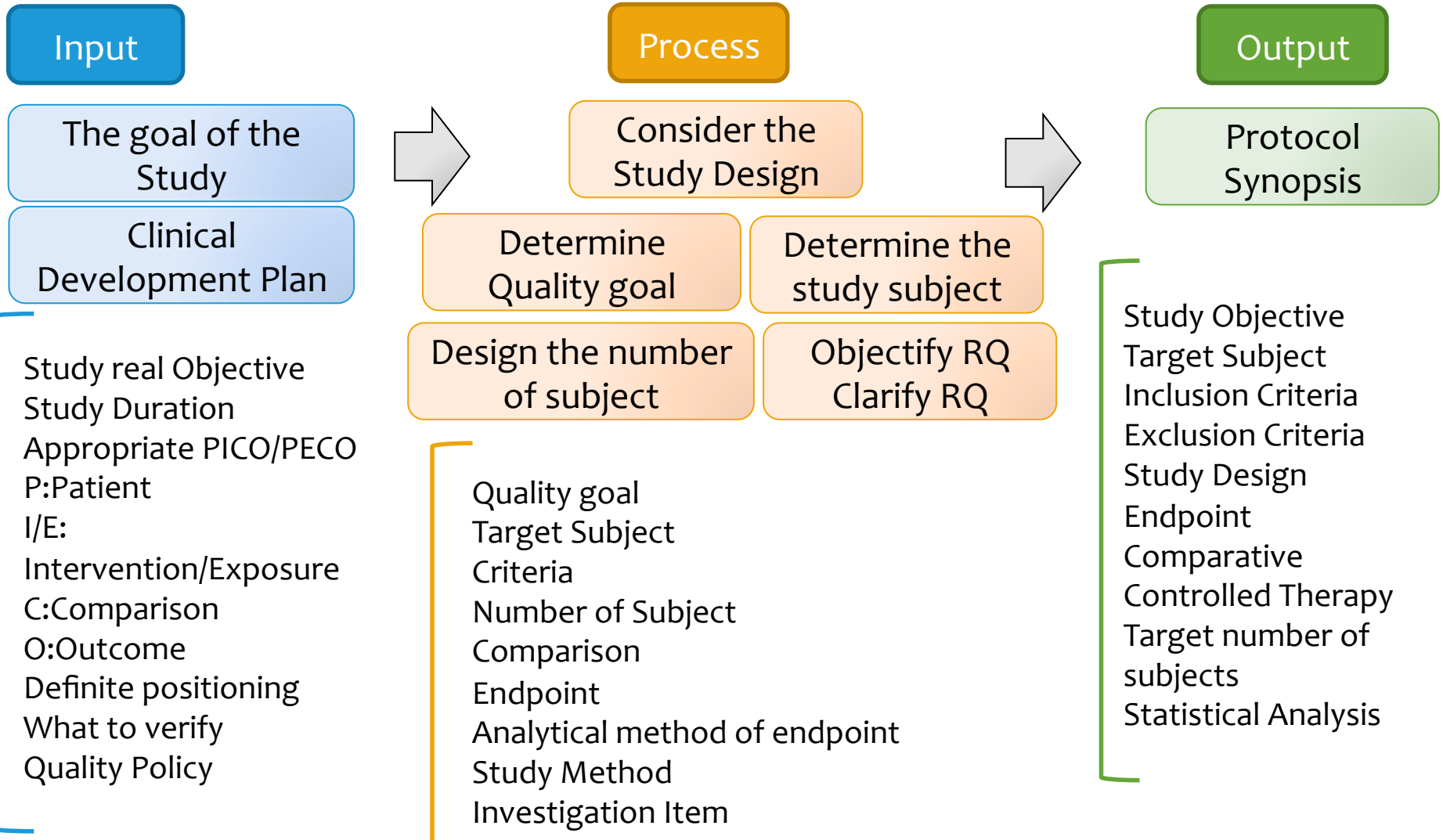
- TPPに記載すべき項目（例）
  - 製品の概要
  - 疾患セグメント
  - Keyとなる項目
    - 有効性：有効性のベンチマーク、Go/No goの判断基準
    - 安全性：安全性のベンチマーク、Go/No goの判断基準
    - 製剤：規格・安定性や扱いやすさ（保管条件）
    - 投与計画：経路・用法用量

Clinical Development Plan（CDP）

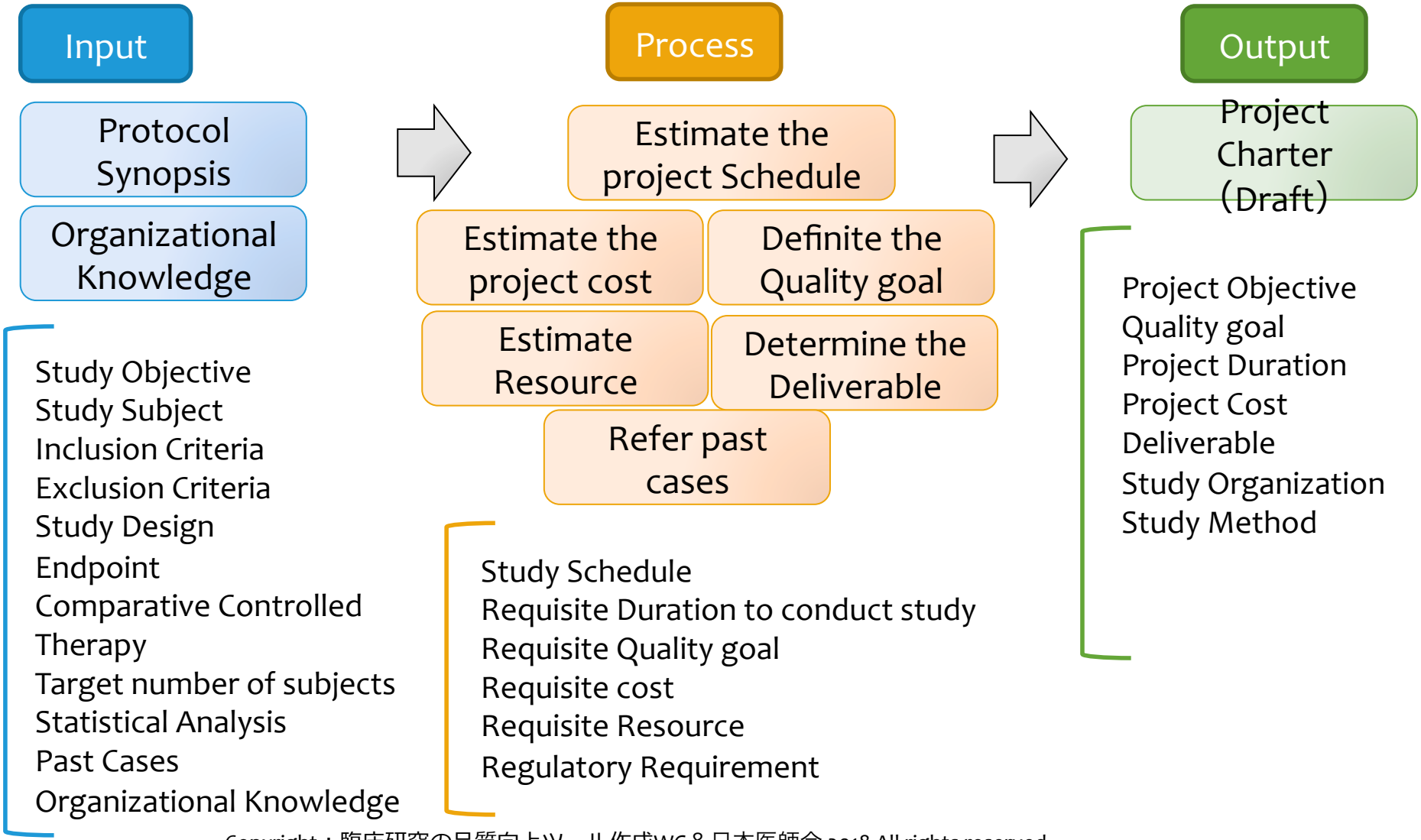
- 臨床開発計画（Clinical Development Plan、CDP）
  - どのようなターゲットに対して、どういう試験を実施するかについてまとめたもの

- CDPの項目の例
  - 開発の経緯
  - 薬効・薬理の概略
  - 臨床的な位置づけ
  - 類薬の開発状況
  - 用量探索・有効性及び安全性評価計画（I相～III相、長期試験等）
  - リスクとその対応策
  - 人員、資金計画
  - タイムスケジュール
  - 意思決定方法

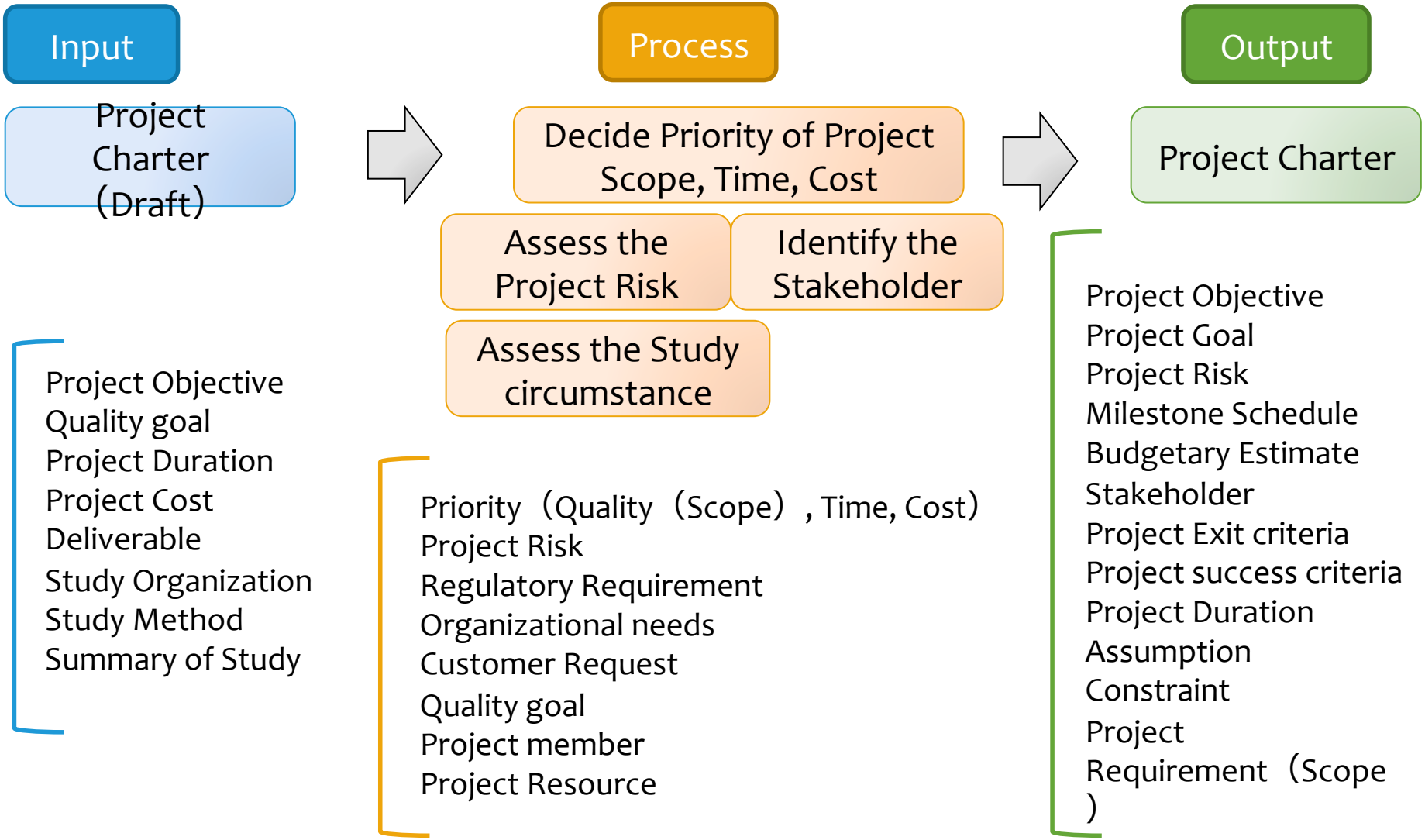
Protocol Synopsis



Consideration of Project Scope, Time, Cost

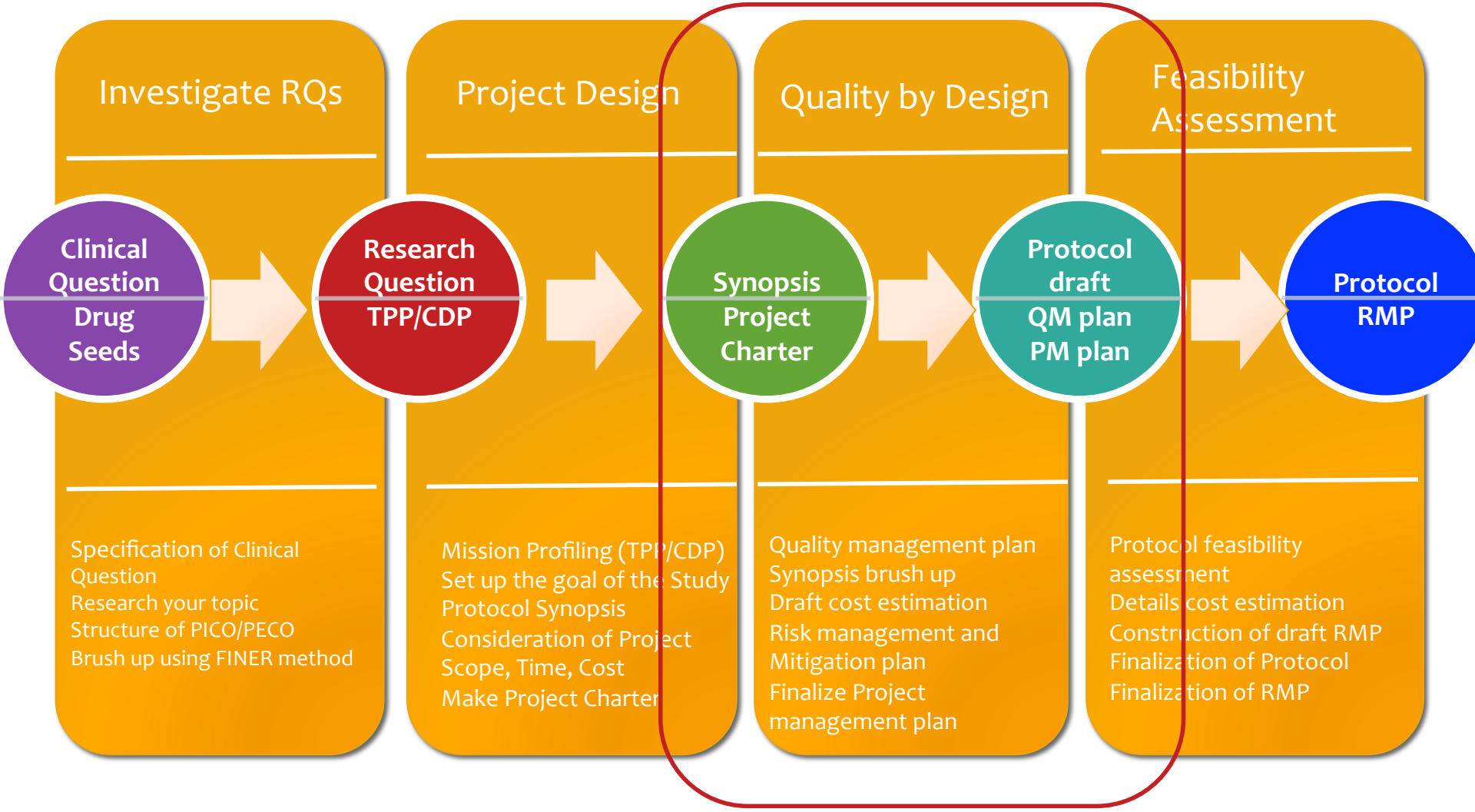


Make Project Charter



QUALITY BY DESIGN

Whole Process of QbD protocol planning



Quality by Design

input

Synopsis
Project
Chater

Quality management plan

Synopsis brush up

Draft cost estimation

Risk management and Mitigation plan

Finalize Project management plan

Protocol draft
QM plan
PM plan

Output

Quality management plan

Input

- Project Charter
- Protocol Synopsis

Project Objective
Project Goal
Project Risk
Milestone Schedule
Budgetary Estimate
Stakeholder
Project Exit criteria
Project success criteria
Project Duration
Assumption
Constraint
Project Requirement

Process

- Identify the Project Risk
- Define the quality policies, measurements

Clarify the goal of the clinical trial
Define the quality policy
Define the quality objectives
Risk assessment

Output

Quality Management Plan

1. Quality policy of the trial
2. Requirements of the trial (customer, laws and regulations, implementation system)
3. Scope and authority
4. Risk identification and risk management plan
5. Quality management plan
6. Quality management (monitoring methods, monitoring methods)
7. Quality assurance (the presence or absence of audit, system of the audit)
8. Change management
9. Education and training

Quality Management Plan

- ☐ Clarify the goal of the clinical trial
- ☐ Define the quality policy
- ☐ Define the quality objectives
- ☐ Risk assessment

↓

Preparation for the quality management plan

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Planning the protocol well-behaved from the quality management plan

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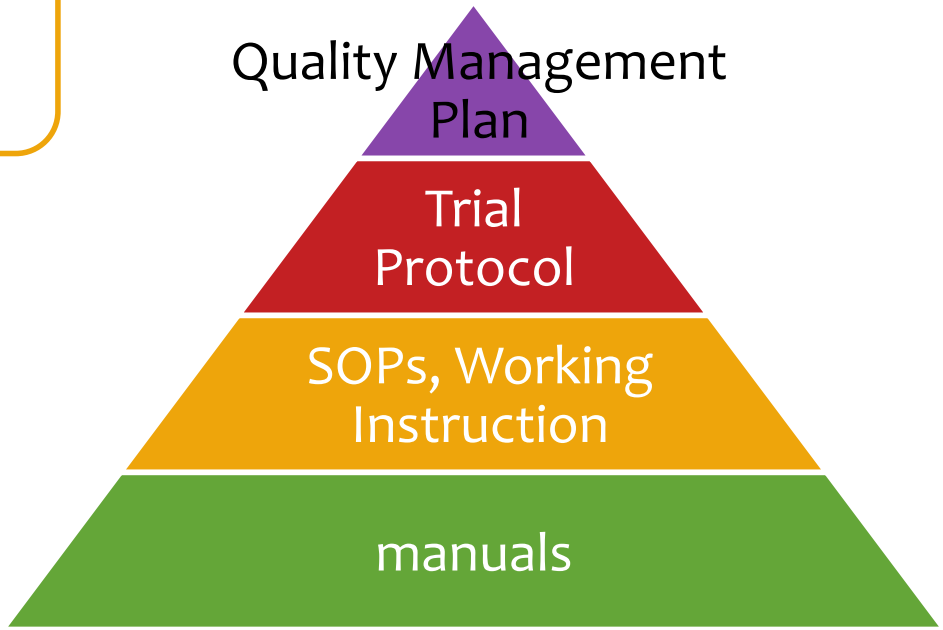
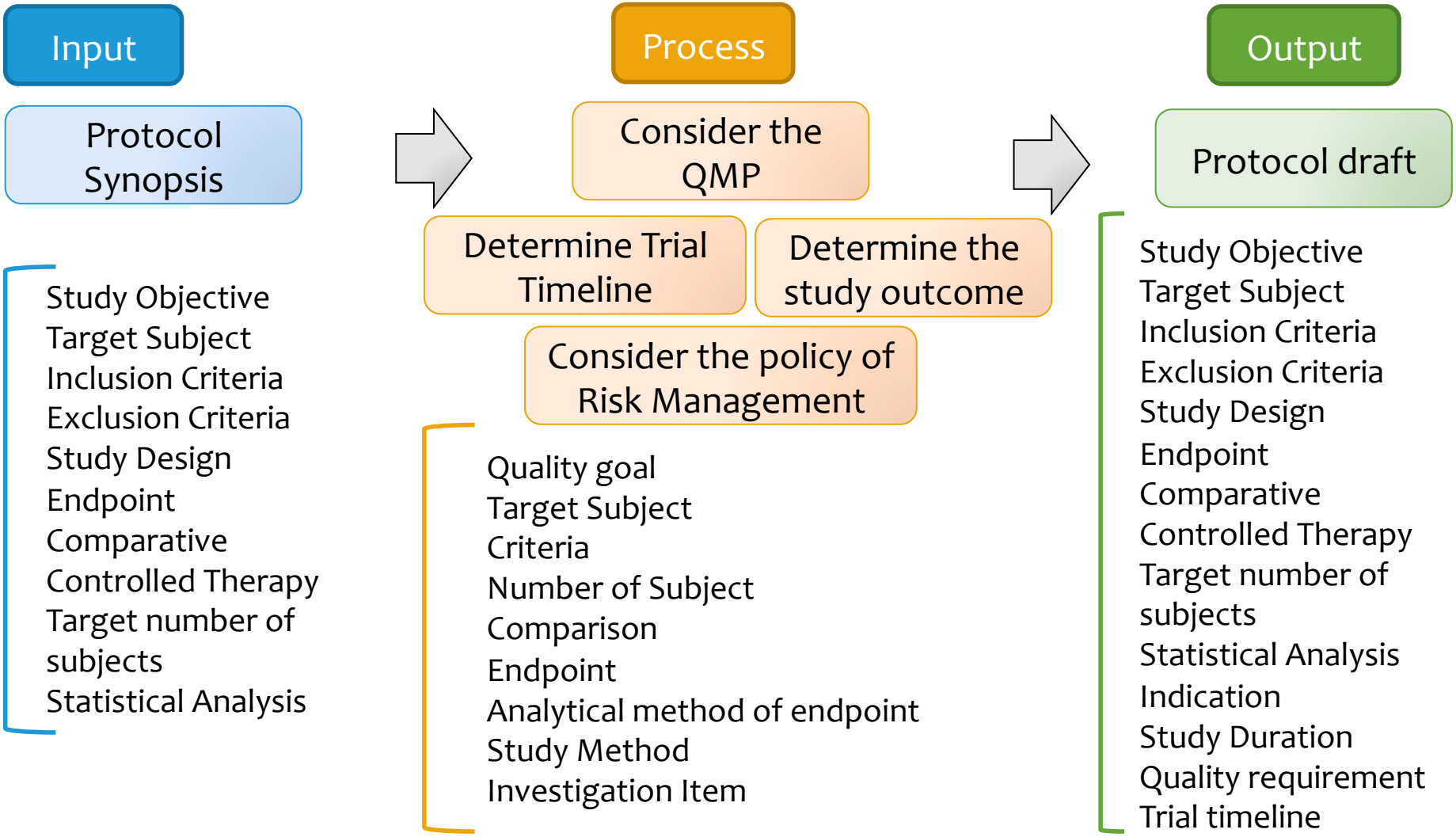
Preparation for the operating procedure or instructions for trial monitoring and auditing

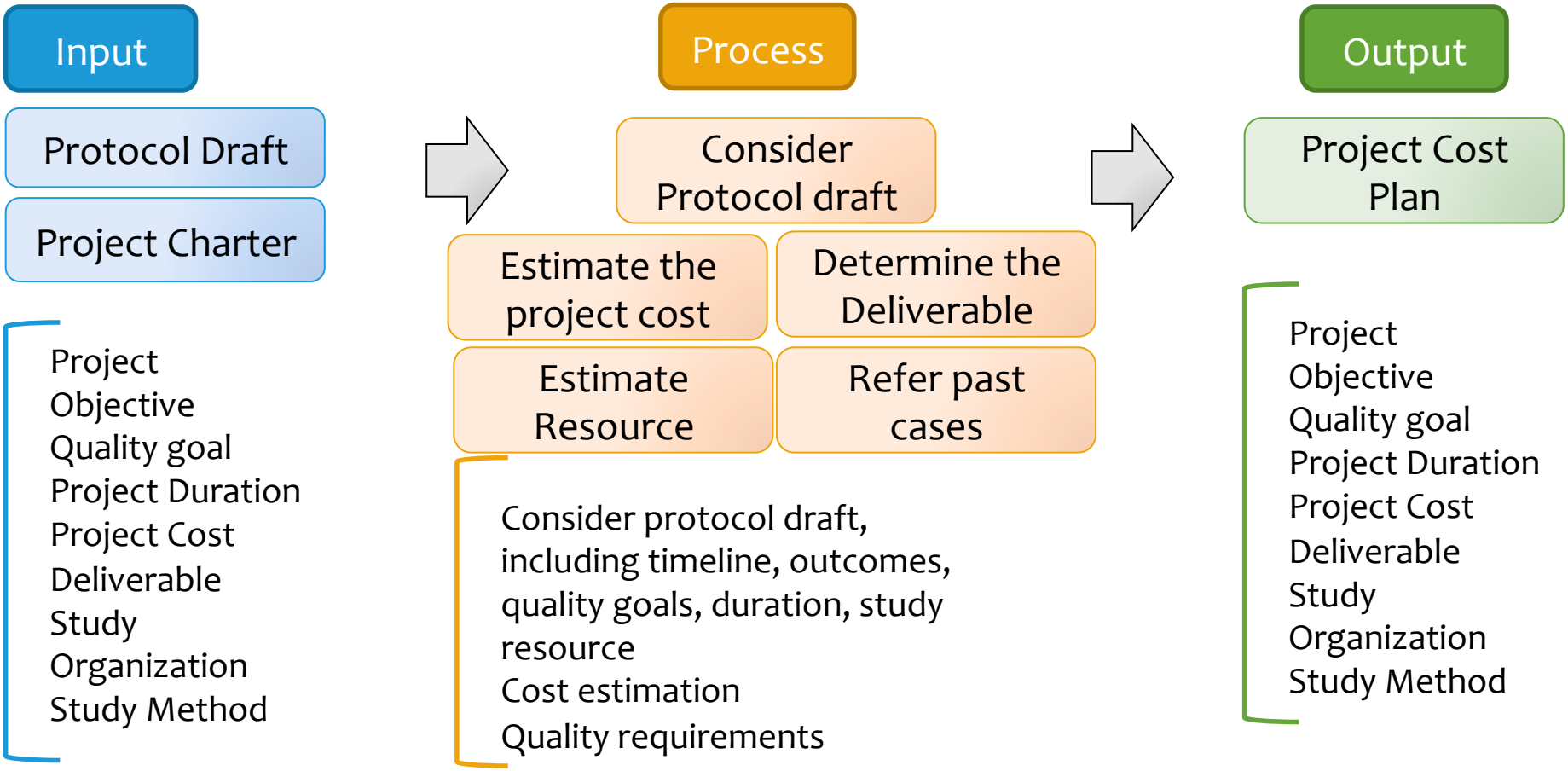


- Quality Management System (SOPs, Computerized systems, human resources, outsourcing, infrastructure)
- Clinical trial protocol（investigational new drugs, trial design, data collecting process, monitoring process, documents or records）

Synopsis brush up



Draft cost estimation



Risk Management and Mitigation plan

Input

Quality Management Plan

1. Quality policy of the trial
2. Requirements of the trial (customer, laws and regulations, implementation system)
3. Scope and authority
4. Risk identification and risk management plan
5. Quality management plan
6. Quality management (monitoring methods, monitoring methods)
7. Quality assurance (the presence or absence of audit, system of the audit)
8. Change management
9. Education and training

Process

Consider Risk and Assessment

Consider CAPA plan

Consider Risk Mitigation Plan

Consider Risk Management plan
Identify Risk
Risk analysis: Quantitative and Qualitative analysis
Consider Risk Mitigation and Risk Control
Consider CAPA plan

Output

Risk Management and Mitigation Plan

1. Risk Management
2. Risk Quantitative Analysis
3. Risk Qualitative Analysis
4. Risk Mitigation plan
5. Risk Control
6. CAPA plan

Finalize Project management plan

Input

- Risk Management and Mitigation Plan
- Project Cost Plan
- Quality Management Plan

Project
Objective
Quality goal
Project Duration
Project Cost
Deliverable
Study
Organization
Study Method

Process

- Define Project Activity
- Consider Risk Management plan
- Consider resource, cost, duration, stakeholders

Corrective and Preventive Action
Consider Quality Management plan
Define project activity and scope
Define project development and change management method
Consider Risk Management plan
Consider Protocol Draft

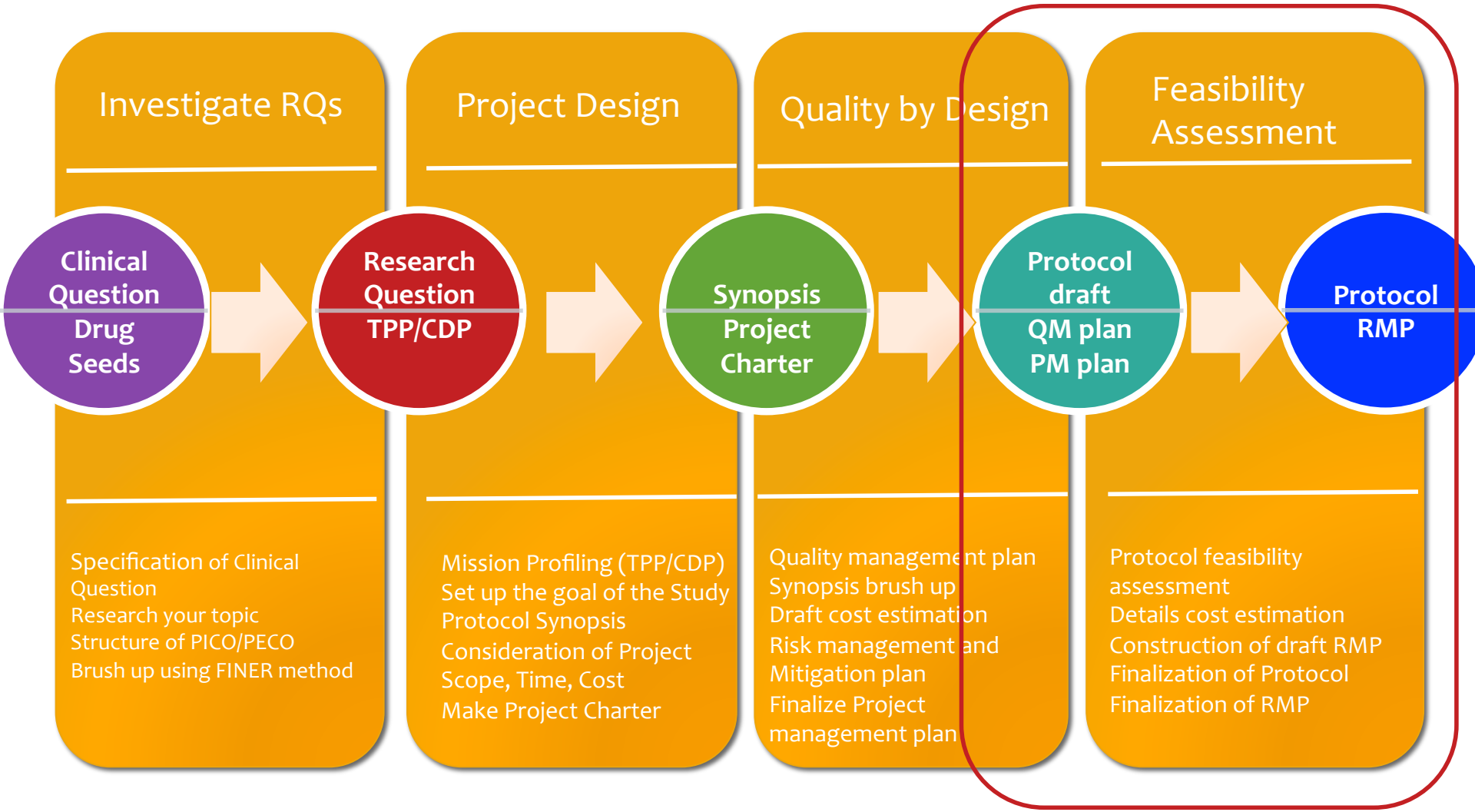
Output

Project Management Plan

1.Scope Management
2.Project Requirements
3.Schedule Management
4.Cost Management
5.Quality Management
6. Resource Management
7. Communication Management
8. Risk Management
9.Procure Management
10. Stakeholder Engagement
11. Change Management
12. Configuration Management
13. Scope baseline
14. Schedule baseline
15. Cost baseline
16. Performance baseline
17. Project Lifecycle
18. Development Method

FEASIBILITY ASSESSMENT

Whole Process of QbD protocol planning



Feasibility Assessment

input

Protocol draft
QM plan
PM plan

Protocol feasibility assessment

Details cost estimation

Construction of draft RMP

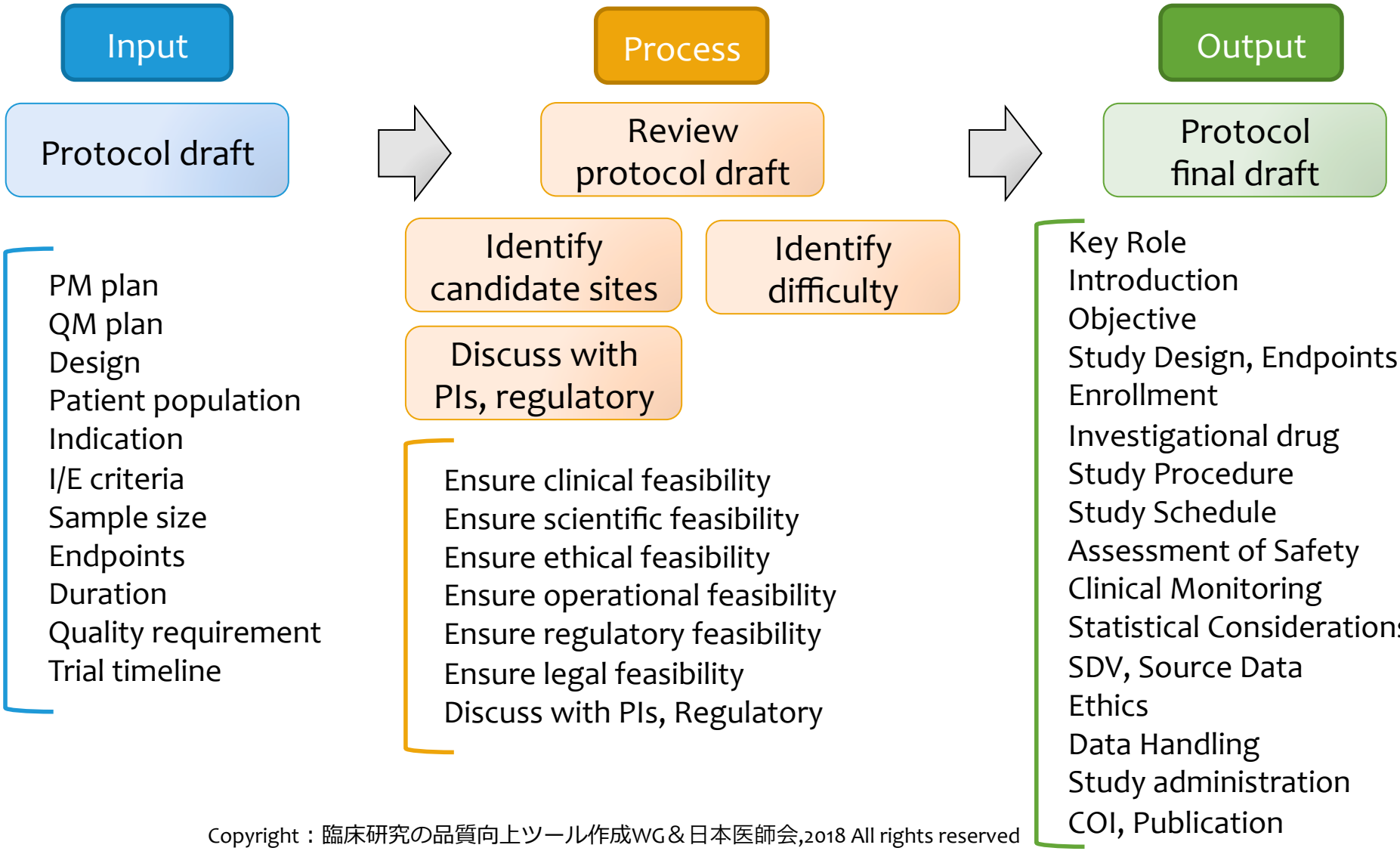
Finalization of Protocol

Finalization of RMP

Output

Protocol
RMP

Protocol feasibility assessment



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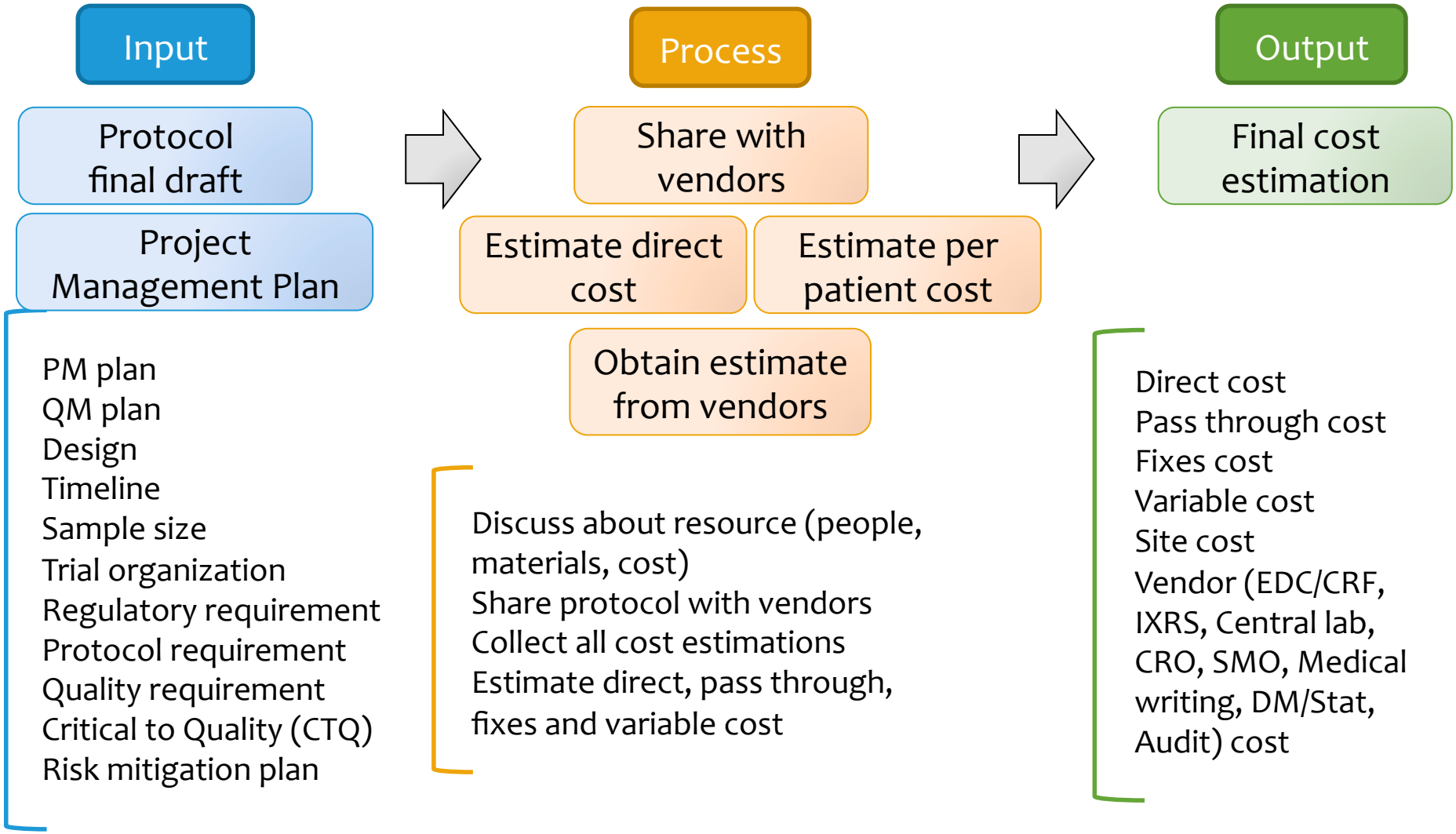
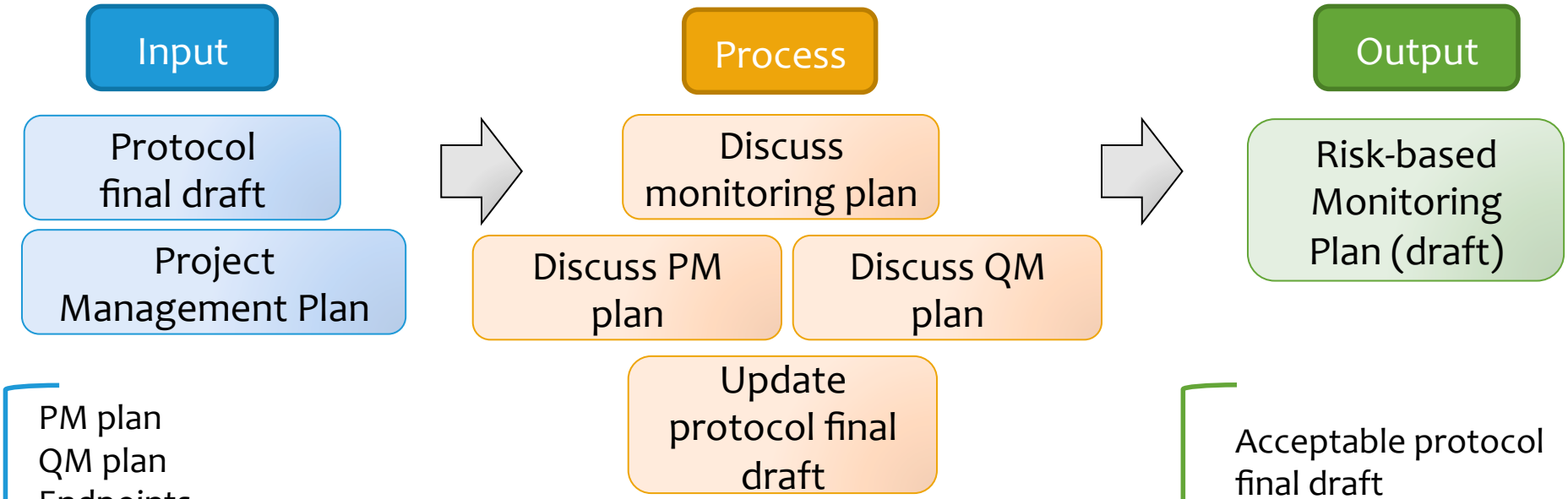


Construction of draft RMP



PM plan
QM plan
Endpoints
Candidate patients
Budget estimate
Trial cost
Trial organization
Trial complexity
Potential risk
Fixed timeline
Quality requirements

Confirm acceptance of procedures
Discuss key risk indicators
Discuss quality requirements
Decide monitoring type (central, on site)
Decide monitoring frequency
Update protocol draft
Prepare monitoring plan

Acceptable protocol final draft
Monitoring type
Monitoring frequency
Monitoring team
Key risk indicators
Risk mitigation plan
Draft audit plan

Finalization of Protocol

Input

- Final cost estimation
- Draft RMP

Design
Patient population
Indication
I/E criteria
Sample size
Endpoints
Analysis methods
Trial timeline
Trial cost
Trial organization
Trial complexity
Trial difficulty
Potential risk
Monitoring plan

Process

Finalize protocol

Input feasibility result into draft protocol
Re-confirm voice of customer
Re-confirm customer requirements
Discuss output data (Table, Figure, List etc)
Update draft protocol
Protocol review by team
Protocol review by expert

Output

Full protocol

Fixed full information for protocol
Fixed trial cost
CRF index

Finalization of RMP

PM plan
QM plan
Endpoints
Analysis methods
Trial timeline
Trial organization
Trial complexity
Monitoring type
Monitoring frequency
Monitoring team
Key risk indicators
Risk mitigation plan
Draft audit plan

Confirm acceptance of procedures
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Acceptable final monitoring plan
Monitoring type
Monitoring frequency
Monitoring team
Key risk indicators
Risk mitigation plan
Audit plan