towards high-quality clinical trials and
implementation of genomic medicine

ATLAS Training Program

Course: CRC Training Course

Lecture Title: The Role of CRC in QMS for Cancer Clinical Trials

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Professional Positions

- 2020–Present Head - Quality Management Section, Clinical Research Support Office
- 2020–Present International Professional Education Section/International Medical Care Section
- 2019–Present Deputy Director for Clinical Research Support - Department of Nursing
- 2017–2019 Advisor of Clinical Trial - Research and Development Division, Ministry of Health, Labor and Welfare (MHLW)
- 2014–2017 Head - Clinical Research Coordinator Section, Clinical Research Support Office
- 2003–2013 Senior Head- Clinical Research Coordinator Section, Clinical Research Support Office

Area of Expertise

- Coordinate of Clinical Research
- Clinical Research Nursing/Oncology Nursing
- QMS in Clinical Research

Role of CRC in Quality Management Section (QMS) in Cancer Clinical Trials

Content of today's presentation

- Why QMS is needed in clinical studies
- What is QMS?
- Role of CRC

Role of CRC in QMS in Cancer Clinical Trials

Content of today's presentation

- Why QMS is needed in clinical studies
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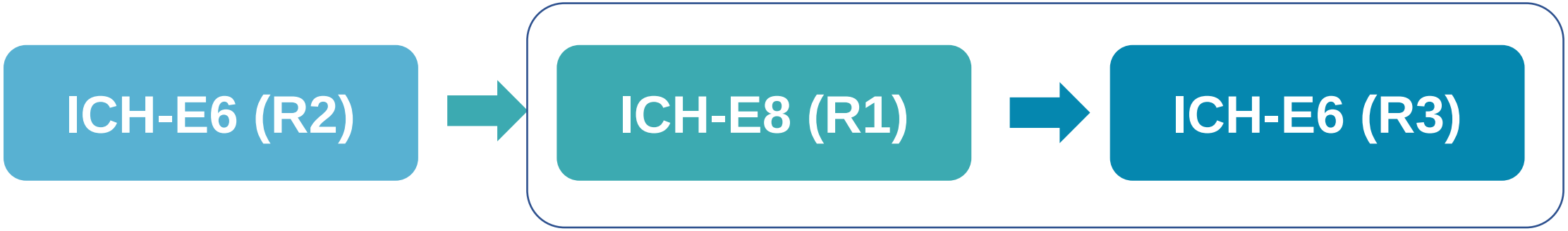
- Role of CRC

To maintain quality

To protect the study participants and ensure the reliability of study results

GCP revision



GCP: Good Clinical Practice

Main revised points of ICH-E6 (R2)

- Quality management
- Risk-based approach
- Risk-based approach to monitoring
- Electronic records
- Trial master file

ICH-E8 (R1)

3.1. Quality by design of clinical studies

3.2. Critical to quality factors

3.3. Approach to identifying critical to quality factors

Role of CRC in QMS in cancer clinical trials

Content of today's presentation

- Why QMS is needed in clinical studies
- What is QMS?
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QMS

Quality Management System

Quality

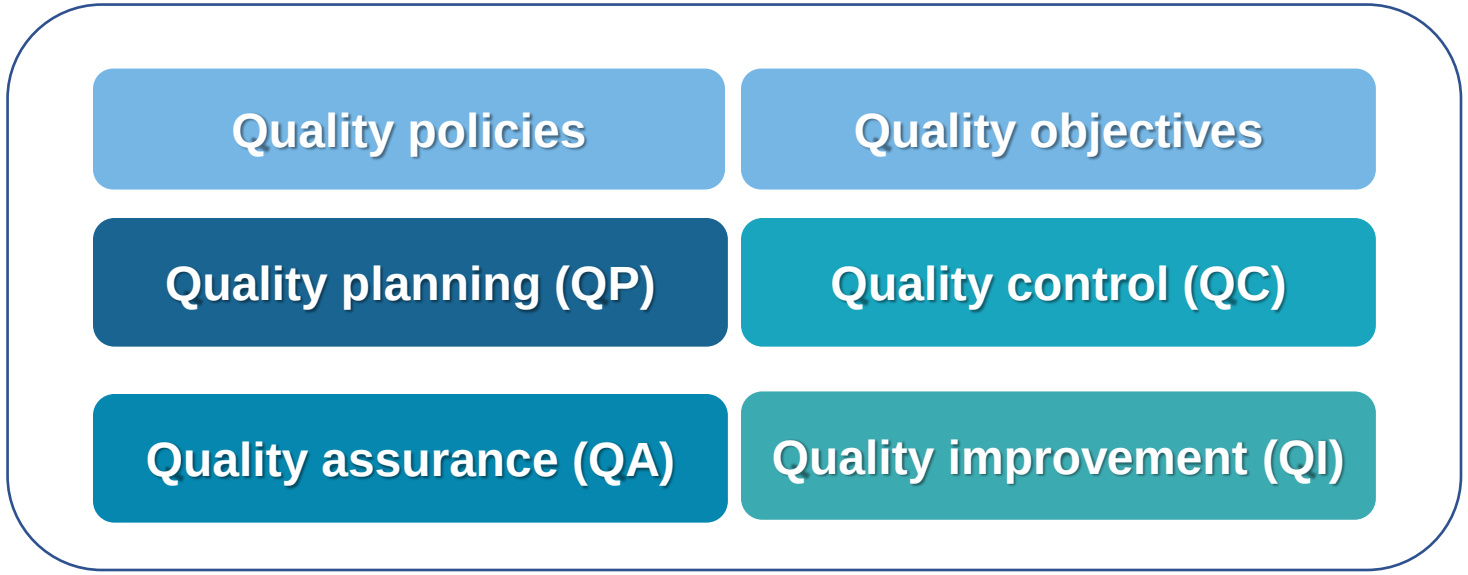
Degree to which a set of inherent characteristics of an object fulfils requirements.

- Object：anything perceivable or conceivable
  e.g., Product , service , process , person, organization , system , resource.
- Inherent：as opposed to “assigned”, means existing in the object
- Characteristics：distinguishing feature
  a. Physical (e.g., mechanical, electrical, chemical or biological characteristics)
  b. Sensory (e.g., related to smell, touch, taste, sight, hearing)
  c. Behavioral (e.g., courtesy, honesty, veracity)
  d. Temporal (e.g., punctuality, reliability, availability, continuity)
  e. Ergonomic (e.g., physiological characteristic, or related to human safety)
  f. Functional (e.g., maximum speed of an aircraft).
- Requirements：need or expectation that is stated, generally implied or obligatory

ISO9000：2015

Quality management

Management related to quality



ISO9000：2015

QMS realization

Process of establishing, documenting, implementing, maintaining, and continually improving a QMS

ISO9000：2015

QMS

Quality Management System

Summary
Operation
Management

Structure

Structure that operates the organization

↓

Systematic blueprints and specifications → **Standardization**

↓

Employees/external → **Visualization**

Advantages of standardization and visualization

- Shared goals
- Have common understanding of standard operations
- Uniform quality of deliverables
- Clarify responsibility and authority
- Prevent individualization of operations
- Improved operating efficiency
- Prompt addressing of process improvements when deviations occur
- Easier to make decisions based on objective facts
- Utilize for education
- Accumulate and inherit technologies with regular updates

ISO

- ISO: International Organization for Standardization
  → bring together experts from all over the world to develop International standards.

ISO website (As of 24/Sep/2022)

Standards for products

ISO9660

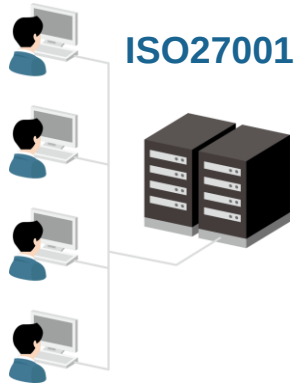
ISO7010

ISO7810

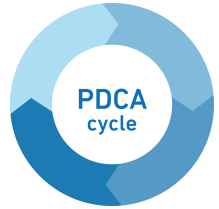
Standards for processes up to supply of products and services

ISO15189

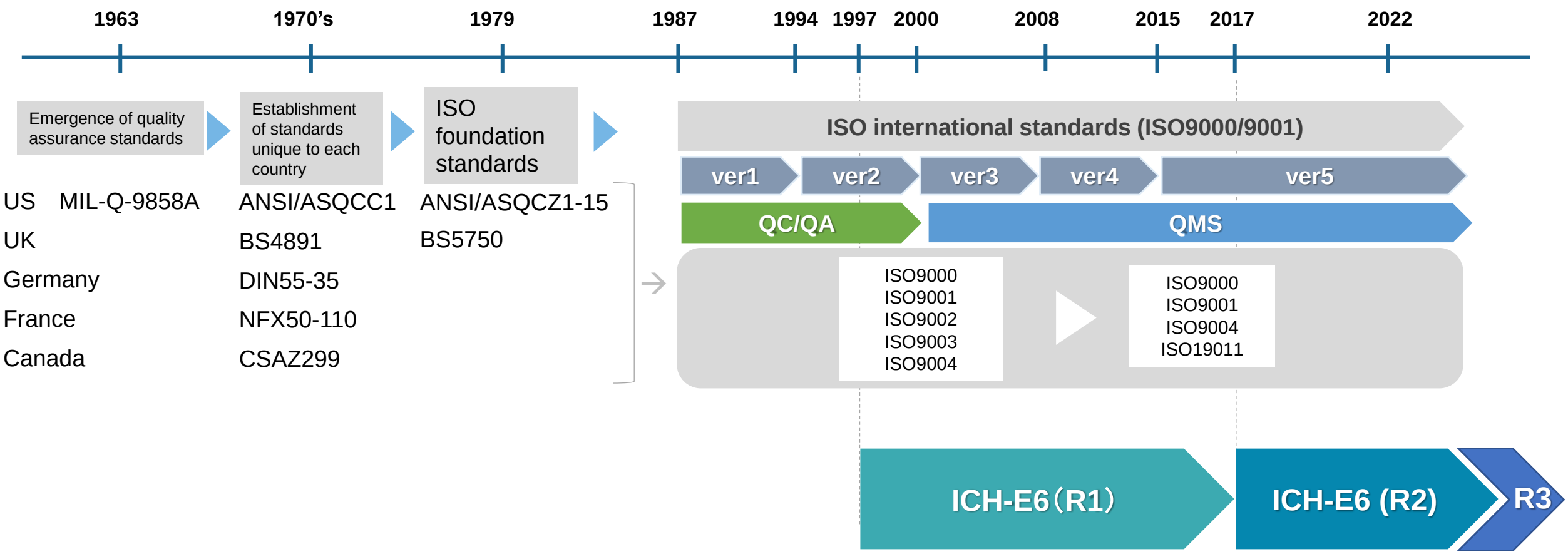
ISO27001



ISO9001



ISO9000/9001 and ICH-E6



Risk-based thinking

- Thinking ahead allows for the formulation of preventative actions rather than resolving a problem once it has occurred
  - ➢Identify and assess risks involved in reaching the goal
  - ➢Consider risk mitigation measures (preventative actions), and include these measures in an advance plan

Reference) JIS ISO9001：2015

QMS serves as a “prevention tool”

Quality management principles

① Customer focus

② Leadership

③ Engagement of people

④ Process approach

⑤ Improvement

⑥ Evidence-based decision making

⑦ Relationship management

ISO9001：2015

Role of CRC in QMS for cancer clinical trials

Content of today's presentation

- Why QMS is needed in clinical studies
- What is QMS?
- Role of CRC

Role of CRCs in QMS

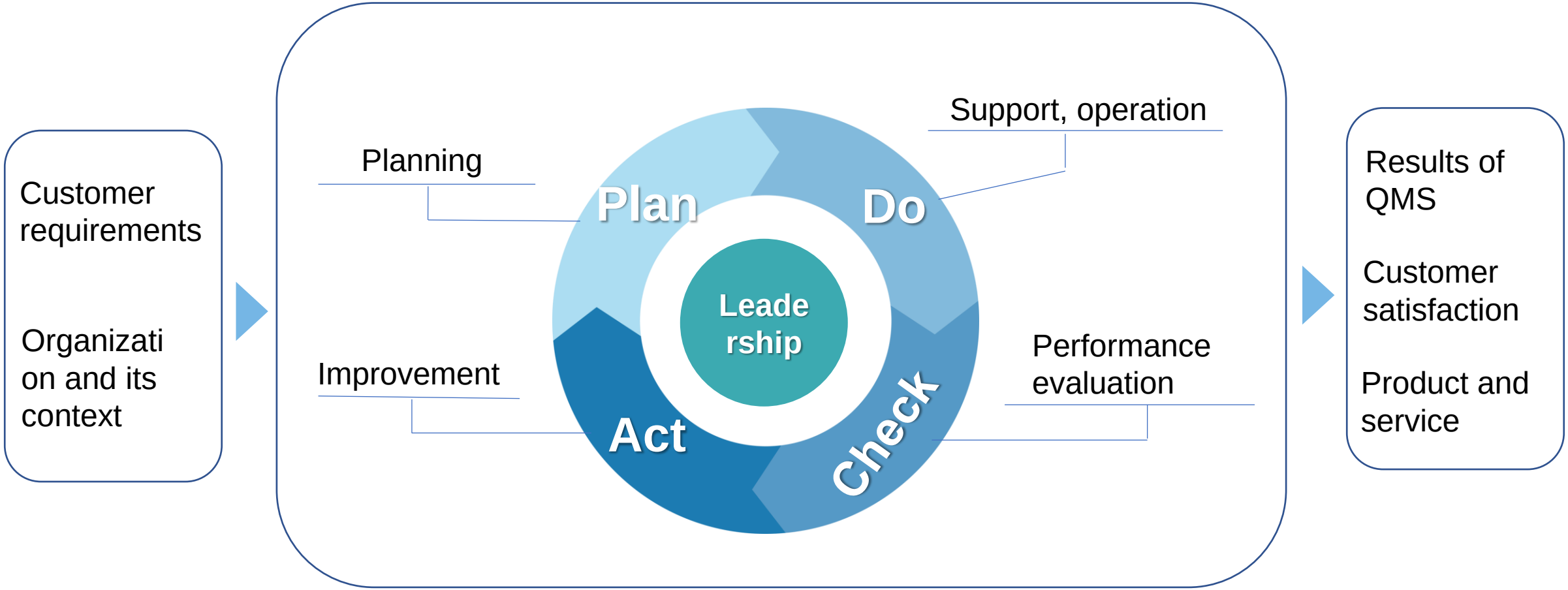
Create and execute a mechanism that ensures quality without variations between CRCs in your own facility

1. Standardize processes using risk-based thinking
   - Consistently assumes risks in clinical trials
   - Relevant to situation at your own facility
   - Specific to each protocol
2. Visualize standardized processes, share with all involved staff, and implement the processes
3. Regular review and continuous improvement

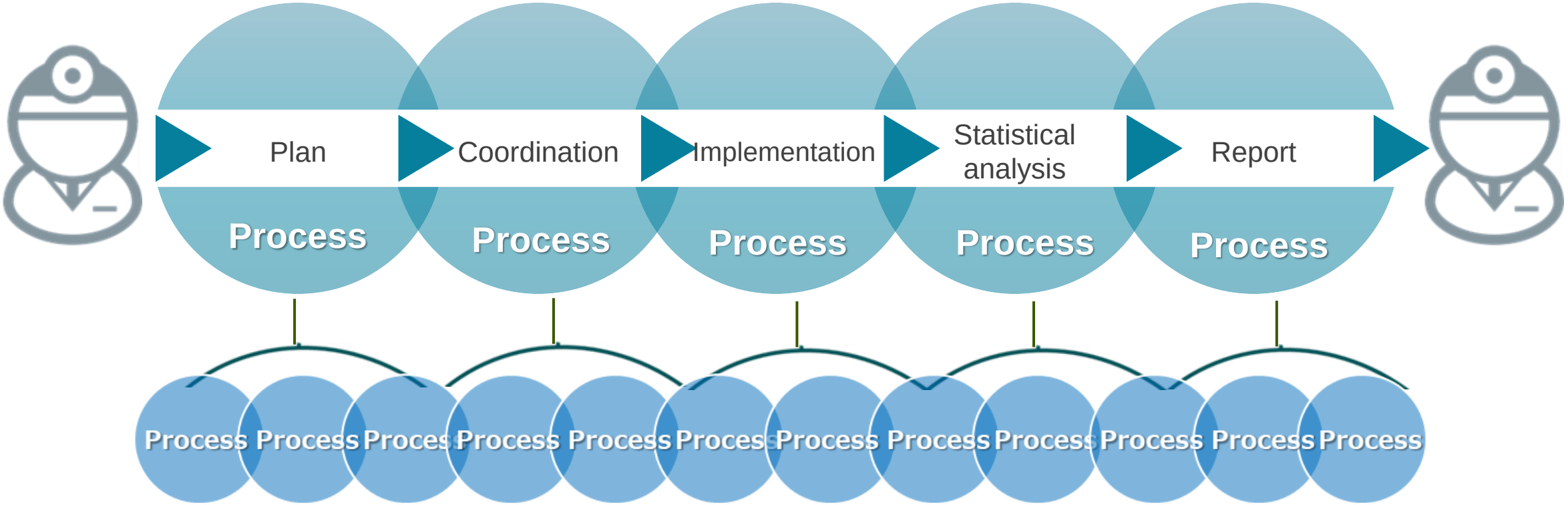
Three points for QMS implementation

- Plan, do, check, and act (PDCA) cycle
- Process approach
- Risk-based approach

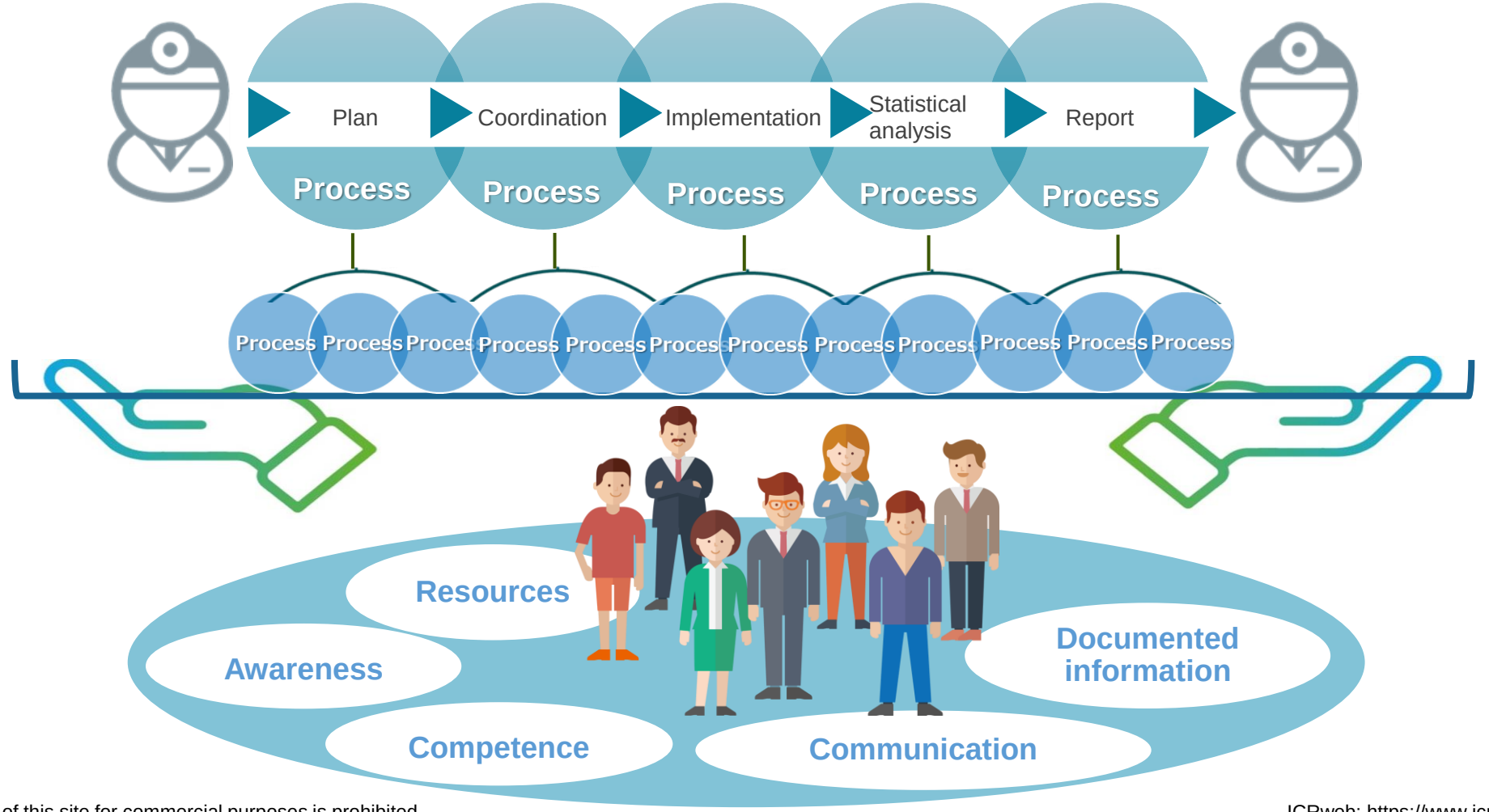
PDCA cycle



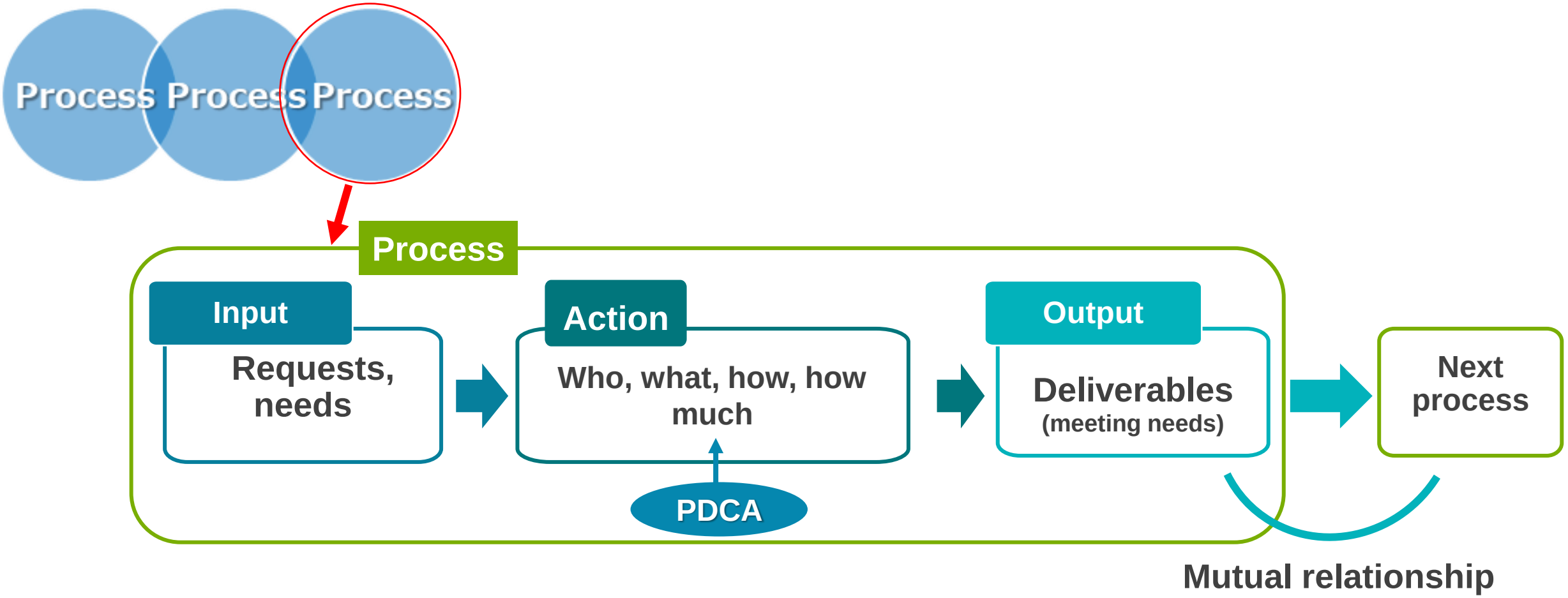
QMS in clinical trials



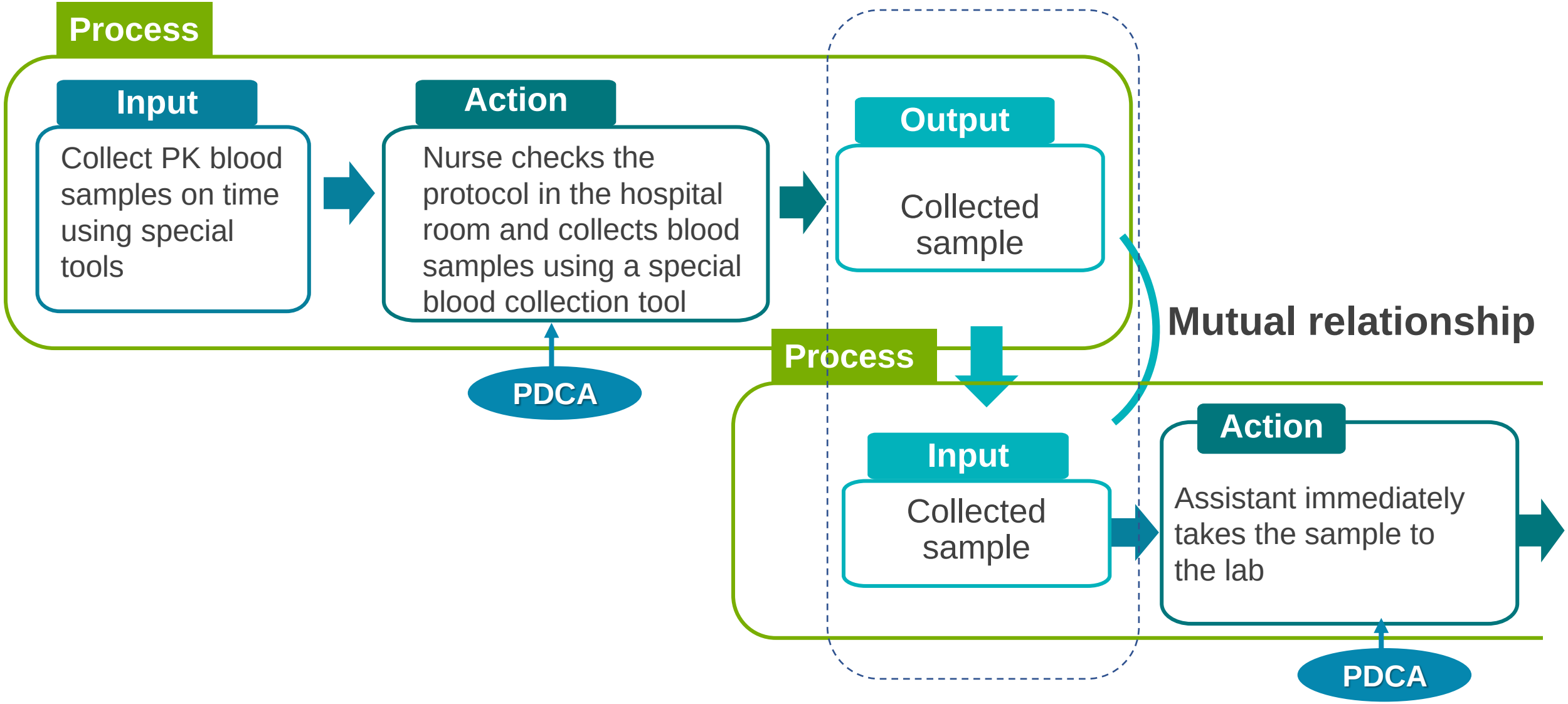
QMS in clinical trials



Process approach



Example of process approach



ICH-E6 (R2): risk-based approach

- 5.0.1 Critical process and data identification
- 5.0.2 Risk identification
- 5.0.3 Risk evaluation
- 5.0.4 Risk control
- 5.0.5 Risk communication
- 5.0.6 Risk review
- 5.0.7 Risk reporting

Risk and issue

Risk

Potential problem

Example) Deviations may occur because there are more blood collection points than normal

Risk management

Preventive action

Issue

Problem that has already occurred

Example) Deviation occurred because blood was not collected at a blood sampling point

Issue management

Corrective action

Preventive action and corrective action

- Preventive action
  - Eliminates the cause of a potential non-conformity or other undesirable potential situation.

- Corrective action
  - Eliminates the cause of a detected non-conformity or other undesirable situation.

ICH Q10

Examples of critical process and data

Common to all studies

Critical process

- Informed consent
- Confirm eligibility
- SAE response
- Critical AE response
- Management of drugs used in the clinical trial
- Test procedures
- Maintaining blinding

Critical data

- SAE
- Critical AE

Study-specific

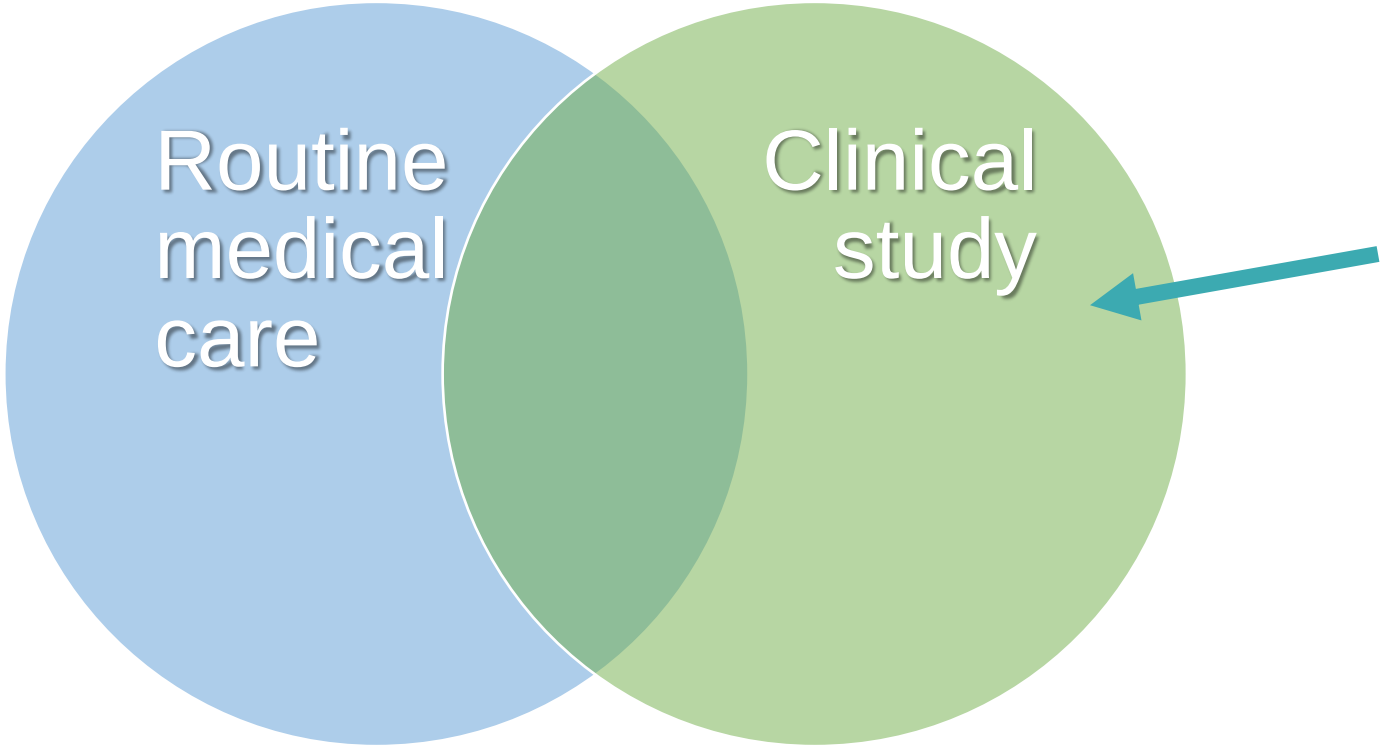
Critical process

- Study-specific separate informed consent
- Confirm eligibility
- Allocation
- Administration method
- Changing dose, drug interruption, drug discontinuation
- Study-specific AE that results in discontinuation
- Study-specific test procedures

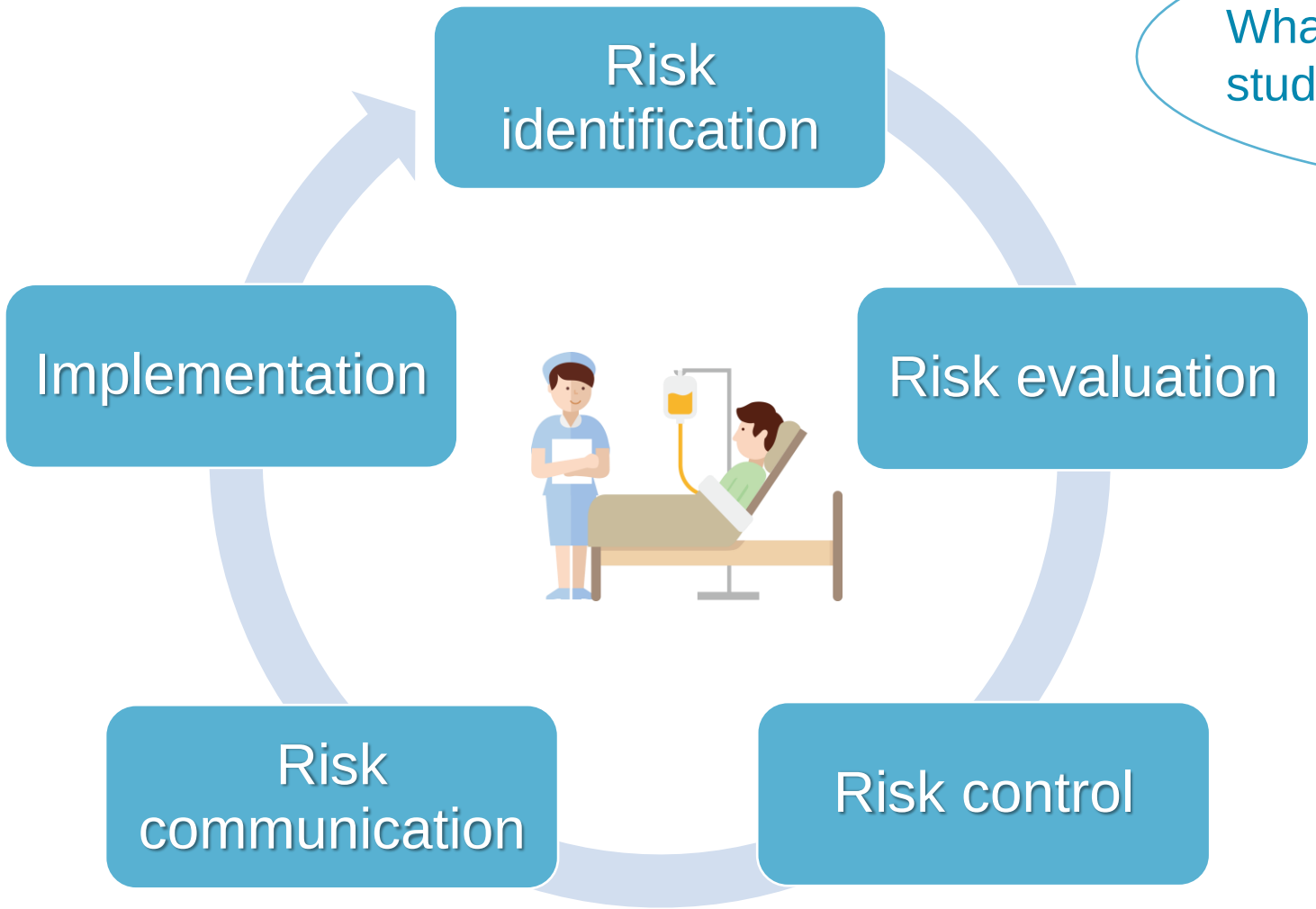
Critical data

- Data that affects the primary endpoint

Risks in medical facility implementing the clinical study

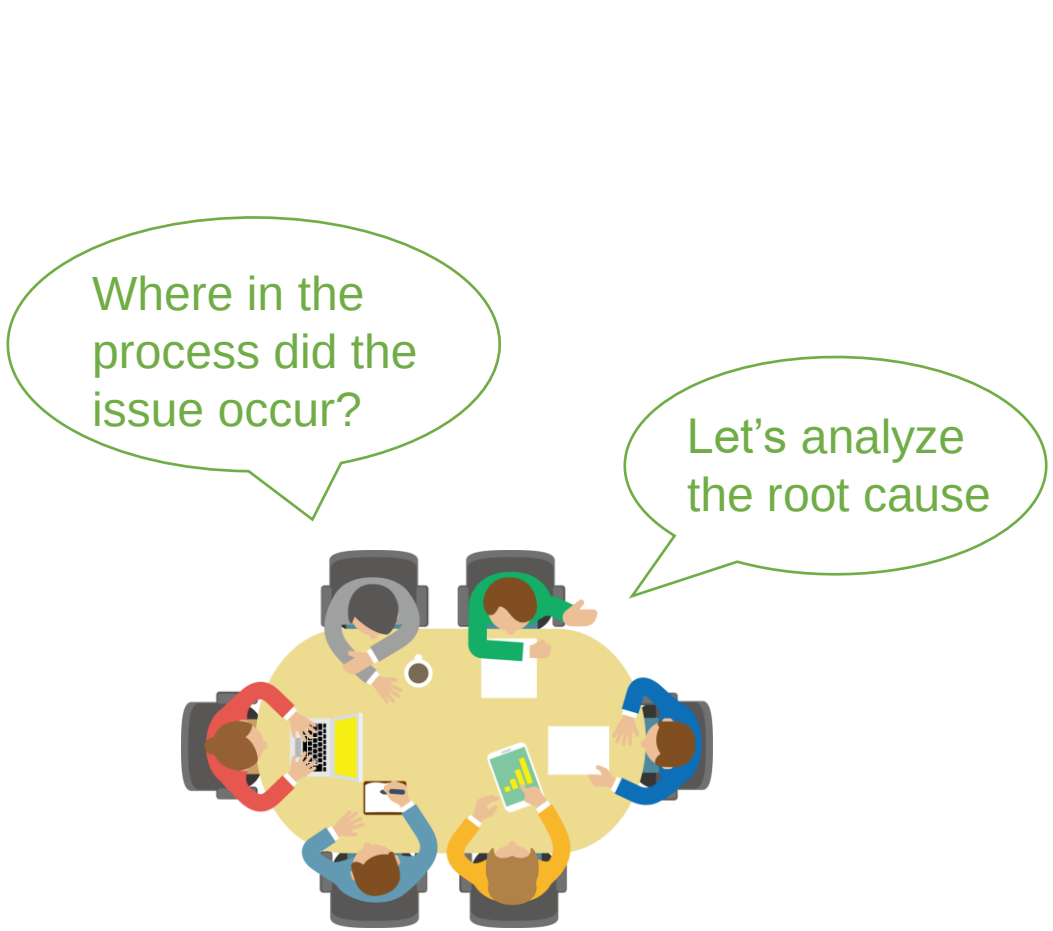


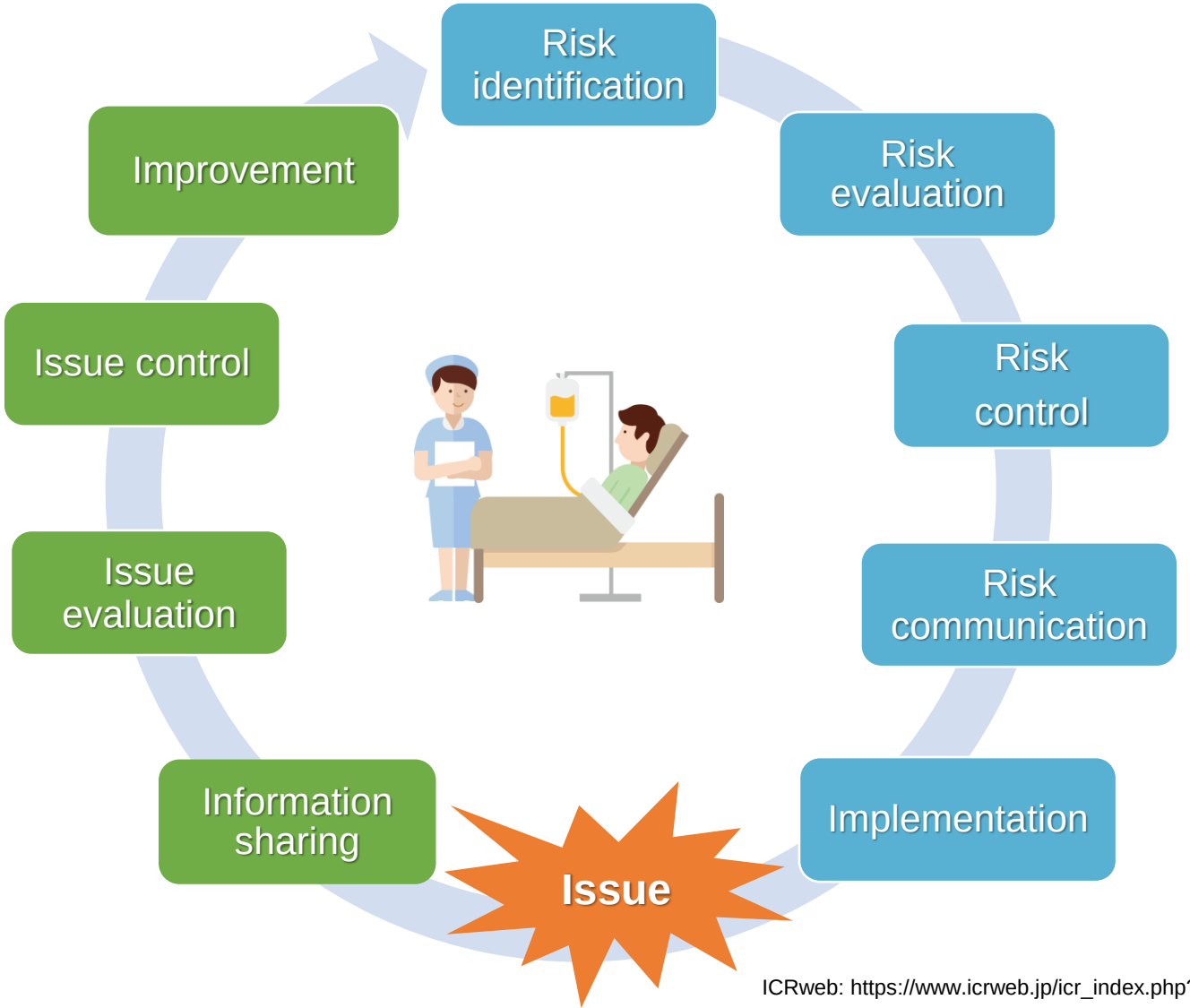
Risk management



What are the critical risks when the study is implemented in this hospital?

Issue management





Drawing out information when building a QMS

Organizational structure
Organization's philosophy, strategies and direction
Organizational conventions
Medical institution rules
Regulations

Easy to document

Unconscious behaviour
Tacit knowledge
Wisdom and tips from experts

Difficult to document
→ Difficult to verbalize

Setting up a QMS is not particularly difficult

- Visualize familiar procedures performed daily by CRCs
- QMS is not the goal, but rather a means to achieve the goal
- Standardization and visualization brings the research team together