



# Quality Assurance for Device Trials The Process of Updating Design Risk Analysis based on Clinical Data Output and Complaints.

Patricia Aherne 13 July 2011

*Let's think about it*



**WHAT IS HAZARD?**

**WHAT IS RISK?**



# WHAT IS HAZARD?



A **real or potential** condition, situation or agent that **could cause immediate or long term harm** to people or an organization.

**Damage or loss** of a system, an equipment, a property, the environment or other things of value.

# WHAT IS RISK?



Risk is the possibility that human activities or natural events will lead to consequences that affect what people value.

It is a measure of the potential ability to achieve overall program objectives within defined costs, schedule, and performance criteria.



**What could go wrong?**

**What is the probability of failing to achieve a particular outcome?**

**What is the impact of failing to achieve a particular outcome?**

## Risk Outcomes



# DEFINITION



- **Hazard**

Potential source of harm.

- **Risk**

Combination of the probability (*or likelihood*) of occurrence of harm, and the severity of that harm.

- **Risk Management**

Systematic application of Quality Management, policies, procedures and practices to the tasks of assessing, controlling, communicating, and reviewing of risk.

*(ISO/IEC Guide 51:1999)*

# REFERENCES AND STANDARDS



- **HACCP- Hazard Analysis Critical Control Point**

Was implemented in 1993 by Food Processors Institute

- **ICH Q9 -Quality Risk Management**

Was approved by International Conference on Harmonization (ICH) in November 2005 and implemented in Japan & USA during 2006 and in EU in March 2008

- **ISO/IEC Guide 73:2002 -Risk Management - Vocabulary**

- **ISO 14971:2007-Medical devices-Application of Risk Management to Medical Devices**

- **Code of Federal Regulations- 21 CFR 820**

## Why did we need ICH Q9/ ISO 14971?

- To ensure a **common understanding of Quality Risk Management** among industry and competent authorities.
- To facilitate **moving to the “Desired State”**:
  - Facilitate Communication and Transparency
  - **Move from Fire Fighting to Quality Risk Management**

### ICH Q9/ISO14971

Define common language and process worldwide  
Design methodologies for QRM  
Explain How QRM can add value

# PRINCIPLES OF QUALITY RISK MANAGEMENT



1. The **evaluation of the risk** to quality should be based on **Scientific Knowledge** and **link to the protection of the patient**.
2. The **level of effort**, formality and documentation of the quality risk management processes should be **commensurate with the level of risk**.

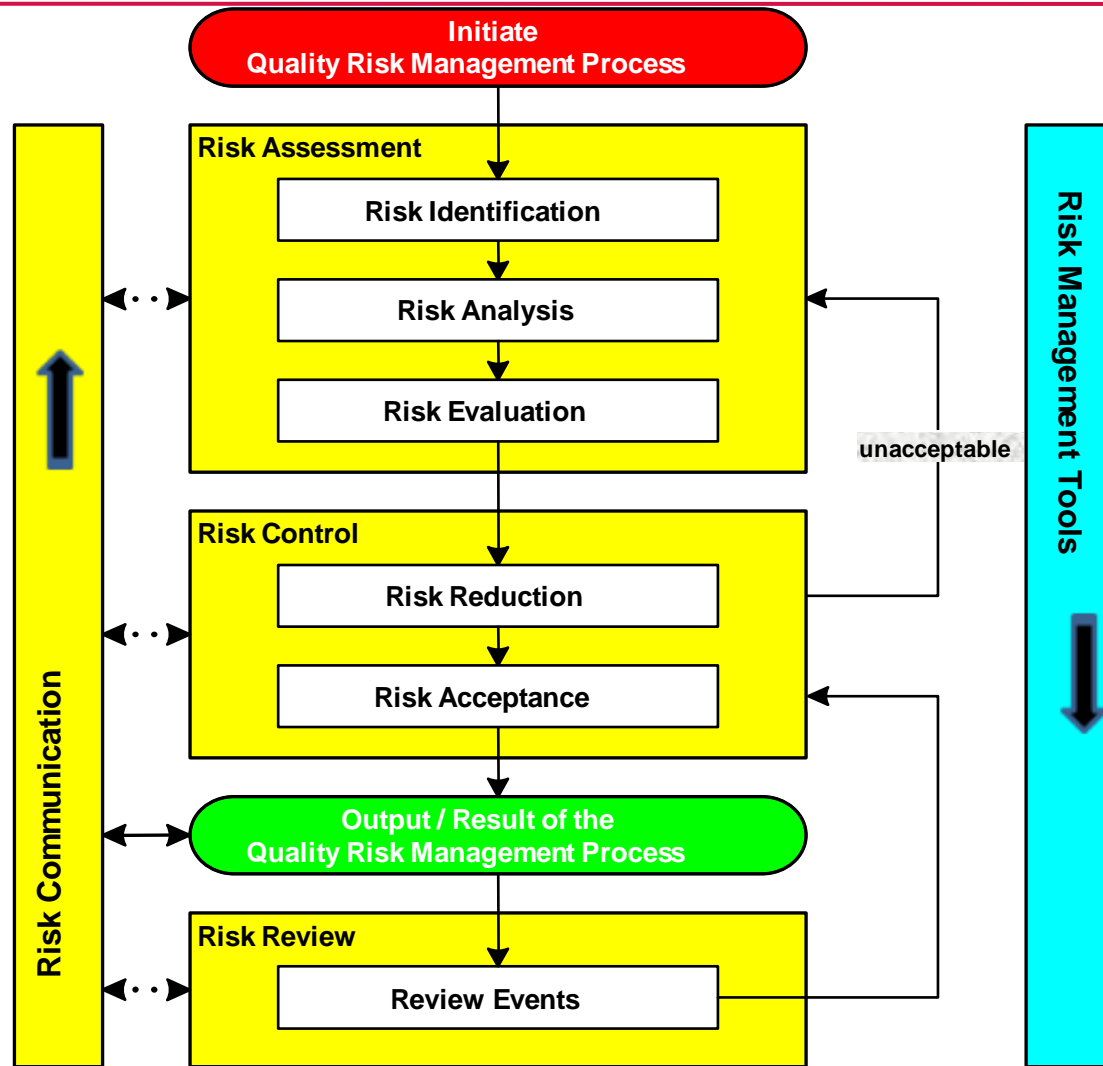
## In order to manage risk, Hazards must first be identified

By **evaluating** the potential consequences of hazards and their likelihood, a measure of risk can be estimated.

This value is **compared to the company's risk-acceptability criteria** and, **if it is too high**, the risk needs to be mitigated.

**Because risk cannot be completely eliminated,  
the risk that remains must be Managed**

# QUALITY RISK MANAGEMENT PROCESS



## The following steps can be used in a QMR Program

- Develop written definitions of **what needs to be done and how to do it.**
- Define **responsibilities** and **accountability.**
- Define what needs **authorization** and **who is responsible** for handling it.
- Define **the skills and knowledge** necessary to implement the system and a provision for training those who do not possess these skills.
- Develop and maintain **written documentation to demonstrate conformance to policies and procedures.**
- Incorporate **measures** to cross-check and **verify that procedures are followed.**
- **Verify that systems are in place and functioning properly.**

# QUALITY RISK MANAGEMENT TOOLS



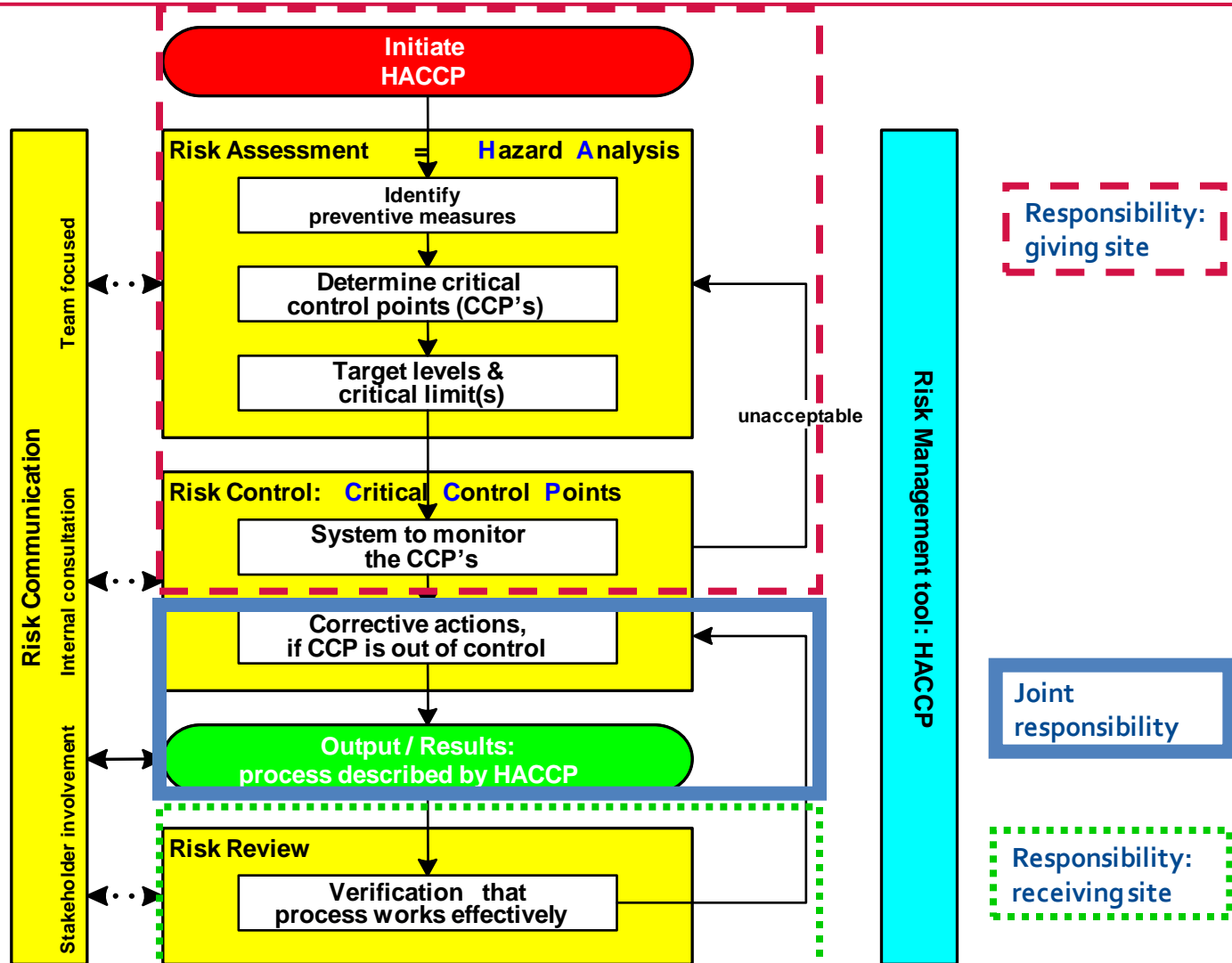
- Failure Mode Effects Analysis (**FMEA**)
- Failure Mode Effects and Criticality Analysis (**FMCEA**)
- Fault Tree Analysis (**FTA**)
- Hazard Analysis of Critical Control Points (**HACCP**)
- Hazard Operability Analysis (**HAZOP**)
- Risk Ranking and Filtering
- Preliminary Hazard Analysis (**PHA**)
- Supporting statistical tools



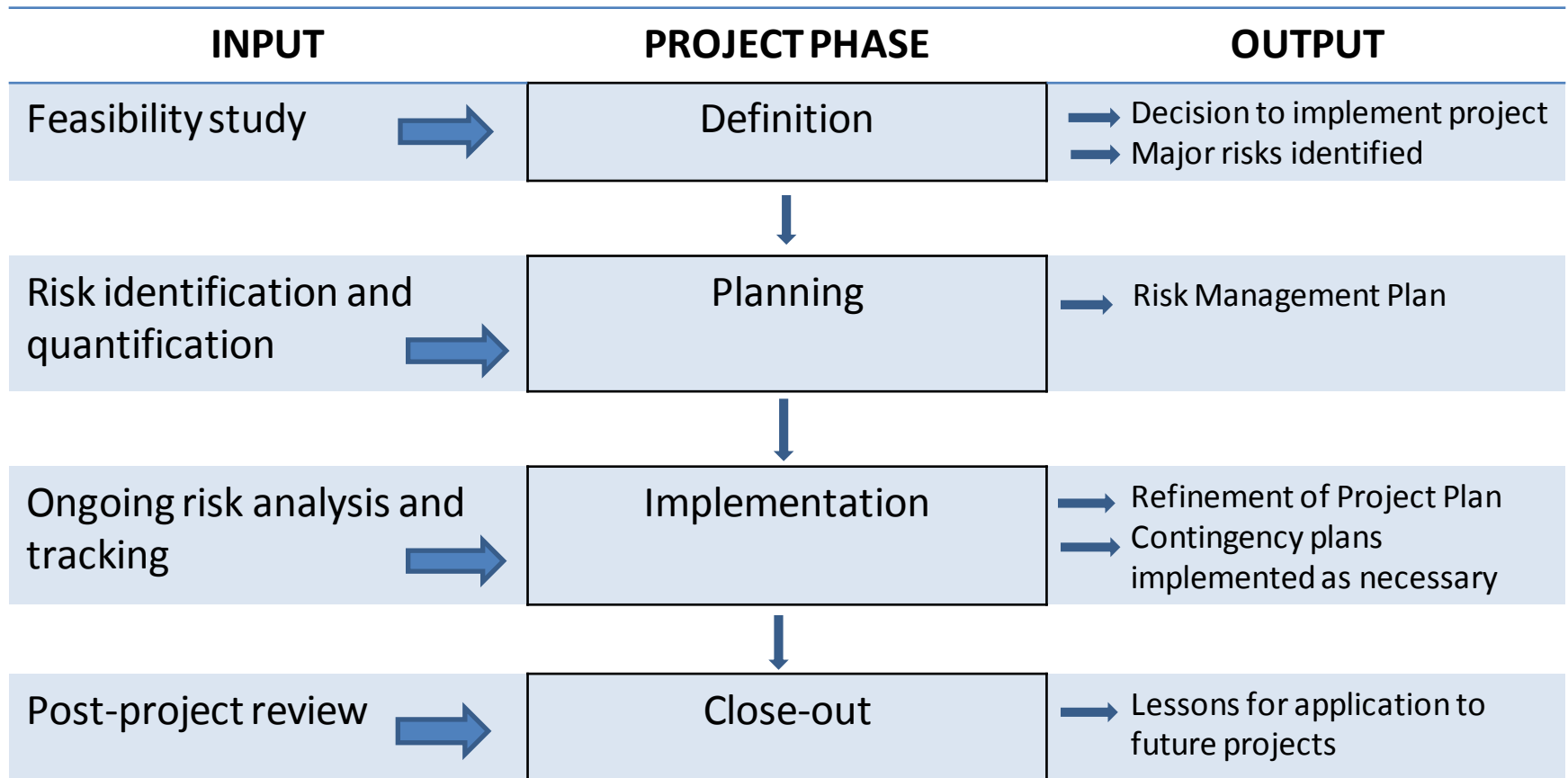
# Hazard Analysis and Critical Control Points



Site change



# Risk Management as a Function of Project Phase



# PRACTICAL





## Risk Management in Medical Device Design

*Early and continuous evaluation of a product's hazard potential increases the likelihood of correcting these faults and producing a device with a low probability of causing harm.*

- FDA's quality system regulation is intended to give manufacturers "**the flexibility to determine the controls that are necessary to be commensurate with risk.**"
- **FDA sees risk analysis as an essential requirement of the regulation** but gives little guidance on specific risk analysis approaches and procedures such as fault tree analysis (**FTA**) or failure mode and effects analysis (**FMEA**).

# Advantage of using QRM as a technique?



- **Improves decision making**

  - Identifies what gives most benefit to the patient

- **Scientific and Data-driven**





  - Reduces subjectivity

- **Ranks risk - Allows prioritization**





  - Better use of resources

- **Means of building in Quality and Improves transparency**





  - Inside organisation and

  - Builds trust with Competent Authorities

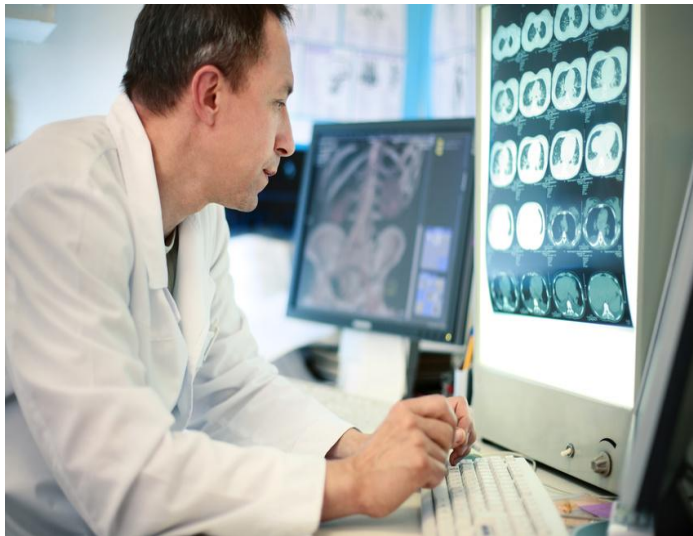
A pink, rounded rectangular callout box with a reflection below it. The text inside reads "Benefits apply throughout product lifecycle".

Benefits apply throughout product lifecycle

# Clinical Evaluation (Annex X) (1)



- Risk/Benefit Ratio must be assessed
- The evaluation must follow a defined and methodologically robust procedure based on either:
  1. Evaluation of scientific literature (clinical or post market)
  2. Evaluation of results of all clinical investigations
  3. Combination of 1 and 2



# Clinical Evaluation (Annex X) (2)



- Clinical investigations shall be performed unless it can be justified to rely on:
- existing clinical data, particularly for implantable devices and class III devices
- Clinical evaluation plan, process, and outcome shall be documented
- Clinical evaluation documentation is part of the technical file/dossier



# Risk Assessment



- Identify the product and describe the intended use
- Identify possible hazards, probability of occurrence, and severity
- Characteristics which could affect safety
- Estimate the risk, and... mitigate!



# Conformity Assessment Routes for Class I



## Class I

The manufacturer is responsible for ensuring that their product complies with all the relevant Essential Requirements of the Directive and must draw up a written statement to this effect (self-declaration). Once the manufacturer is satisfied that their products meet all the relevant Essential Requirements, they must register with the Competent Authority (eg MHRA in the UK by completing and returning form RG2). They may then CE mark their products and place them on the market.

# Annex I : Essential Requirements



## Currently 14 Essential Requirements

### Essential Requirement 1

- The devices must be **designed** and **manufactured** in such a way that,
- when used under the conditions and for the purposes intended, they
- **will not compromise the clinical condition or the safety of patients, or the safety and health of users or**, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.

# Essential Requirement 2



- The solutions adopted by the manufacturer for the design and construction
- of the devices must conform to safety principles, taking account of
- the generally acknowledged state of the art.
- In selecting the most appropriate solutions, the manufacturer must apply
- the following principles in the following order:
  - eliminate or reduce **risks** as far as possible (inherently safe design and construction),
  - where appropriate take adequate protection measures including alarms if necessary, in relation to **risks** that cannot be eliminated,
  - inform users of the **residual risks** due to any shortcomings of the protection measures adopted.

# Clinical Trial Medical Device



**Clinical Data** means the safety and/or performance information that is generated from the use of a device.

**Clinical data** are sourced from:

— clinical investigation(s) of the device concerned.

or

— clinical investigation(s) or other studies reported in the scientific literature, of a similar device for which equivalence to the device in question can be demonstrated.

or

— published and/or unpublished reports on other clinical experience of either the device in question or a similar device for which equivalence to the device in question can be demonstrated.

# To meet essential requirements



- **Chemical, physical and biological properties**
  - Choice of materials used, particularly as regards toxicity, and where appropriate, flammability.
  - The compatibility between the materials used and biological tissues, cells and body fluids, taking account of the intended purpose of the device.
  - The devices must be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues. Particular attention must be paid to the tissues exposed and to the duration and frequency of exposure.

# To meet essential requirements



- **Chemical, physical and biological properties**
  - The devices must be designed and manufactured in such a way as to reduce to a minimum the risks posed by substances leaking from the device.
  - Devices must be designed and manufactured in such a way as to reduce, as much as possible, risks posed by the unintentional ingress of substances into the device taking into account the device and the nature of the environment in which it is intended to be used.

# To meet essential requirements



- **Infection and microbial contamination**
  - The devices and manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the patient, user and third parties.
  - Tissues of animal origin must originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues.
  - Devices delivered in a sterile state must be designed, manufactured and packed in a non-reusable pack and/or according to appropriate procedures to ensure that they are sterile when placed on the market

# To meet essential requirements



## ▪ Infection and microbial contamination

- Devices intended to be sterilized must be manufactured in appropriately controlled (e. g. environmental) conditions.
- Sterilization methods shall be validated.
- Devices must be designed and manufactured in such a way as to remove or minimize as far as is possible:
  - the risks of injury, in connection with their physical features.
  - the risks connected with environmental conditions, such as magnetic fields, external electrical influences, electrostatic discharge, pressure, temperature.
  - the risks of fire or explosion during normal use.



# ISO 14971: 2007 Risk Management

