

The need for clinical investigation and the significance of risk analysis for medical devices

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The need for clinical investigation

- Millions of medical devices are implanted each year
- However, problems occur
- Role of clinical investigation & risk analysis in ensuring safety & performance/efficacy



EU: No clinical investigation



3M Capital
Hip



Immediately
after operation



8 months



19 months



28 months



32 months

- Setting up of National Joint Registry in UK
- Resulting in changes to 93/42/EEC & 90/385/EEC



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EU Classification

Annex IX

- Class III
- Class IIb
- Class IIa
- Class Im or Is
- Class I

INCREASING RISK

2007/47/EC

- Up-classification to Class III
- Enforcement: every device must provide clinical data
- Clinical investigation required for Class III devices or justification



US Classification

21 CFR 820.30

- Class III
- Class II
- Class I

INCREASING RISK

Class I: exempt or 510K

Class II: 510K
FDA may require clinical investigation and/or post market surveillance study

Class III: PMA

System under review



Artificial Hip Replacements: Differing Regional Regulatory Requirements

US

- Depends on the articulation
 - If metal on metal : Class II 510K substantial equivalence
 - If ceramic on ceramic : Class III PMA required

EU

- Class III
- Post market clinical follow up studies required to demonstrate clinical performance for a period of 10 years

GHTF

- Class C



GHTF Clinical Investigation: SG5/N3: 2010

Primary purpose is to:

- (1) provide guidance on when a clinical investigation should be undertaken



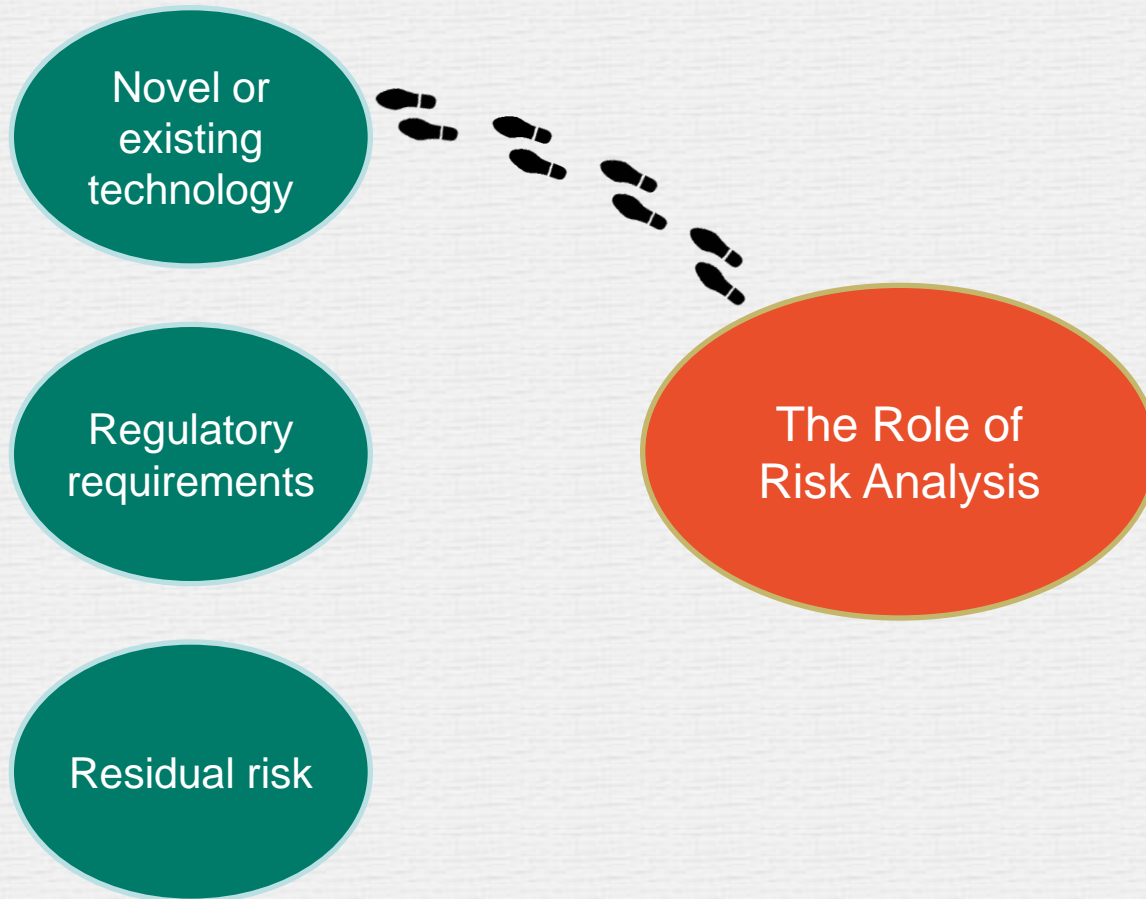
GHTF: the Need for Clinical Investigation

- Clinical investigation necessary when data is not available through other sources
 - literature review
 - preclinical testing

- Clinical investigation necessary to demonstrate safety, clinical performance and acceptability of risk/benefit ratio



When to conduct a clinical investigation: The significance of risk analysis



When to conduct a clinical investigation: The significance of risk analysis

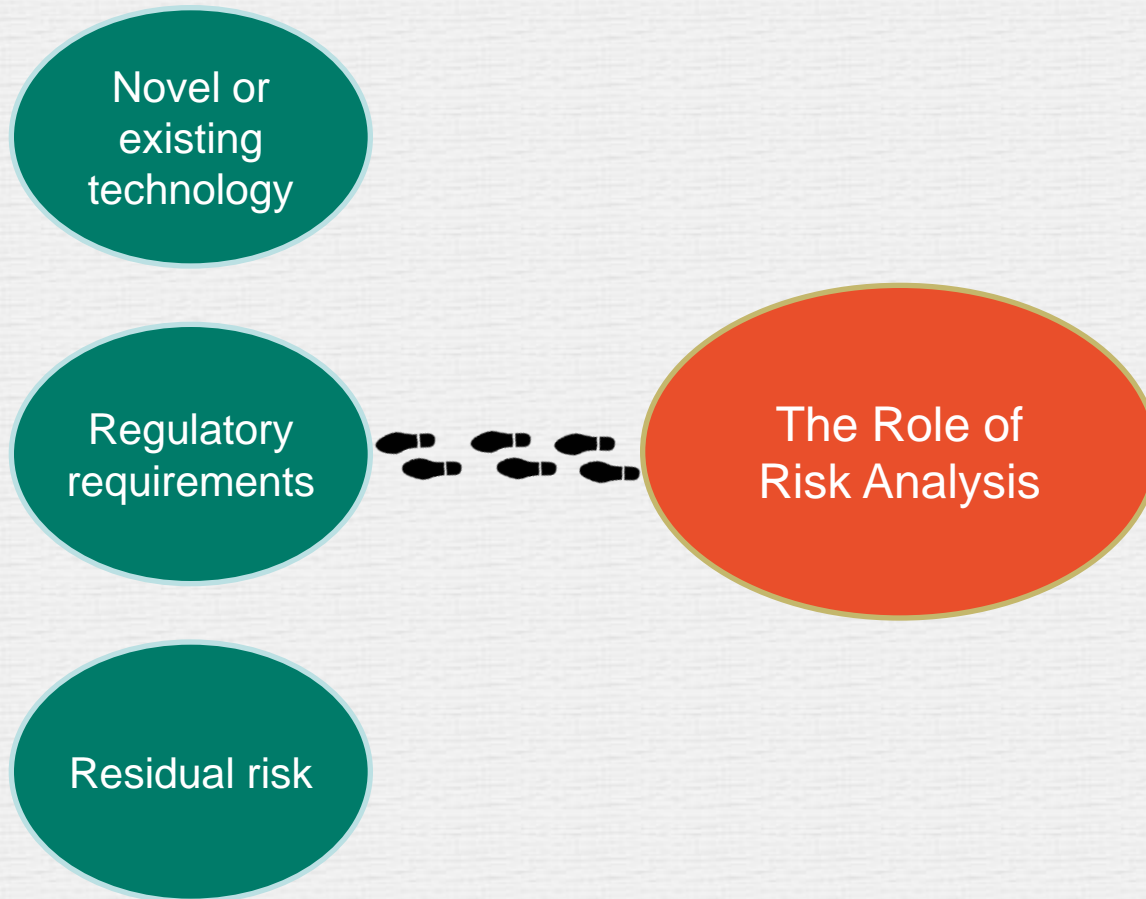
Novel or
existing
technology

Important to consider data from:

- Published literature
- Reports of clinical experience
- Adverse Events



When to conduct a clinical investigation: The significance of risk analysis



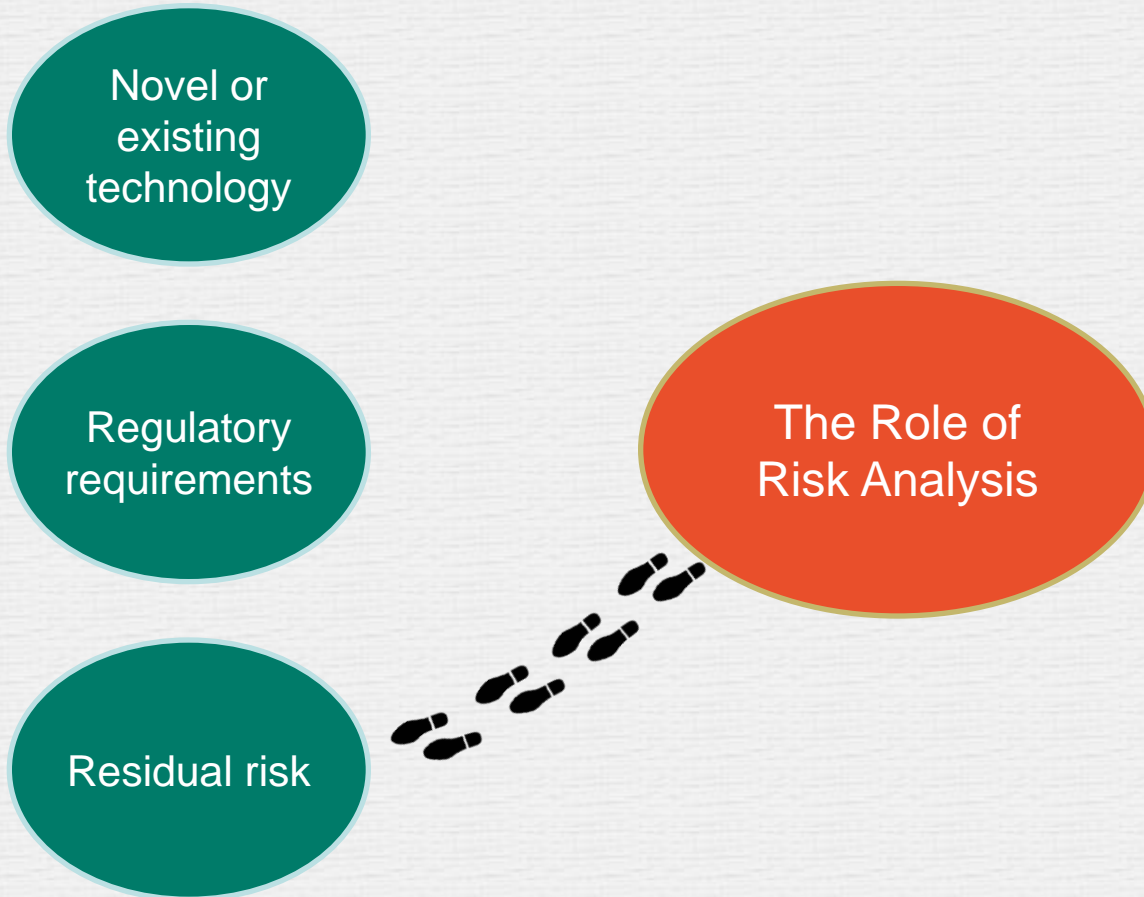
When to conduct a clinical investigation: The significance of risk analysis

Regulatory
requirements

- **US:** Risk analysis is an essential requirement for medical devices
- **EU:** Benefits outweigh the risks for device: Essential Requirement 1
- **GHTF:** Benefits outweigh the risks for device: Essential Requirement 5.1

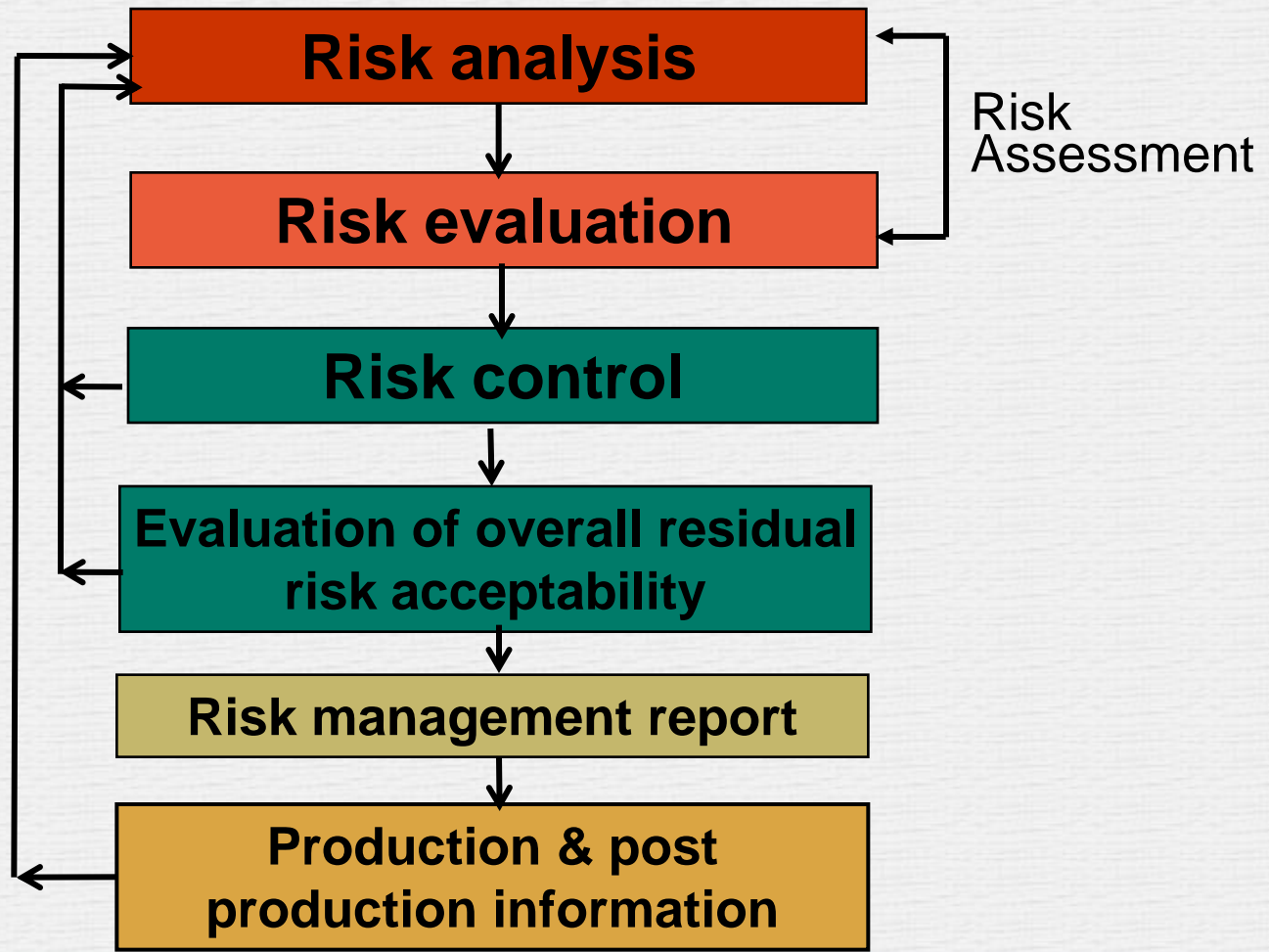


When to conduct a clinical investigation: The significance of risk analysis



When to conduct a clinical investigation: The significance of risk analysis

ISO 14971



GHTF Clinical Investigation: SG5/N3: 2010

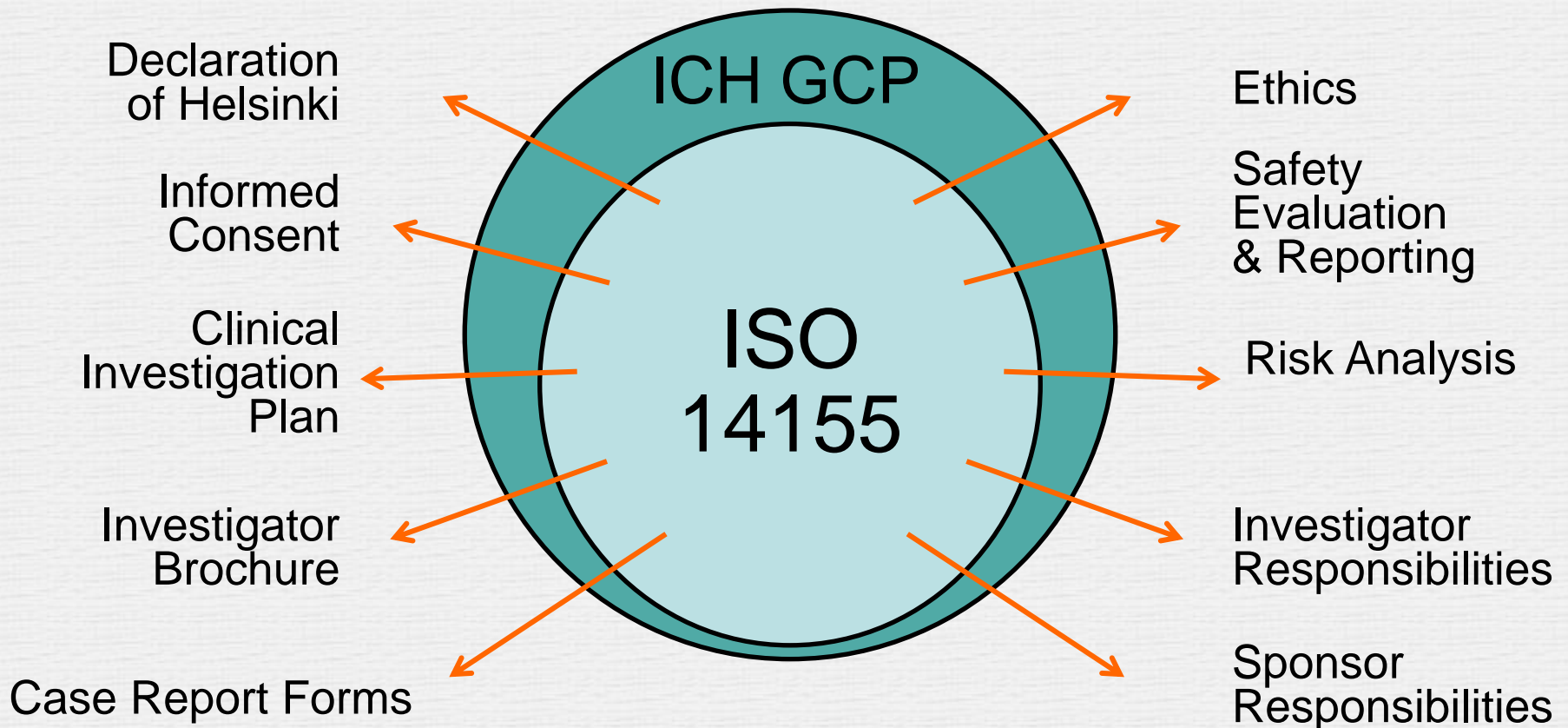
Primary purpose is to:

- (2) Establish the general principles of clinical investigation involving medical devices

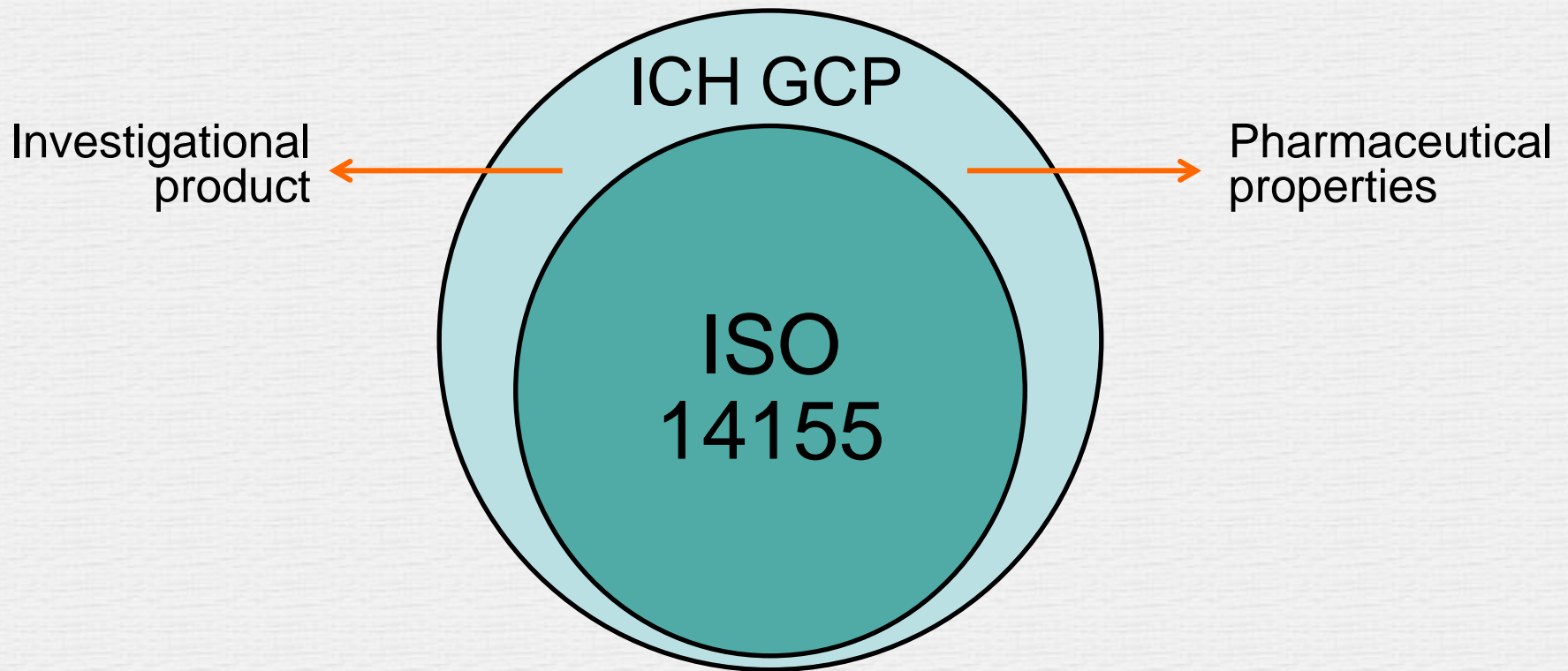
GHTF & ISO 14155



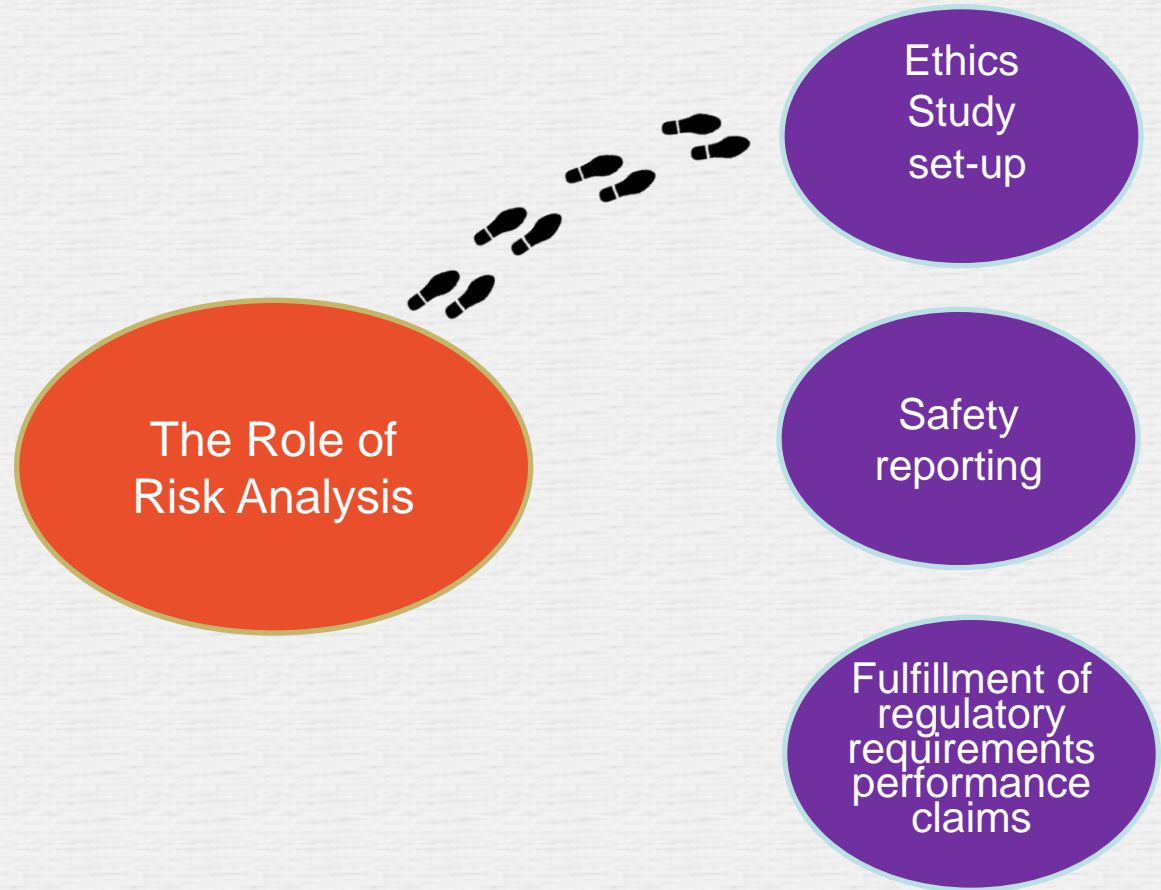
ISO 14155 vs GCP



ISO 14155 vs GCP



The outcome of a clinical investigation: The significance of risk analysis



The outcome of a clinical investigation: The significance of risk analysis

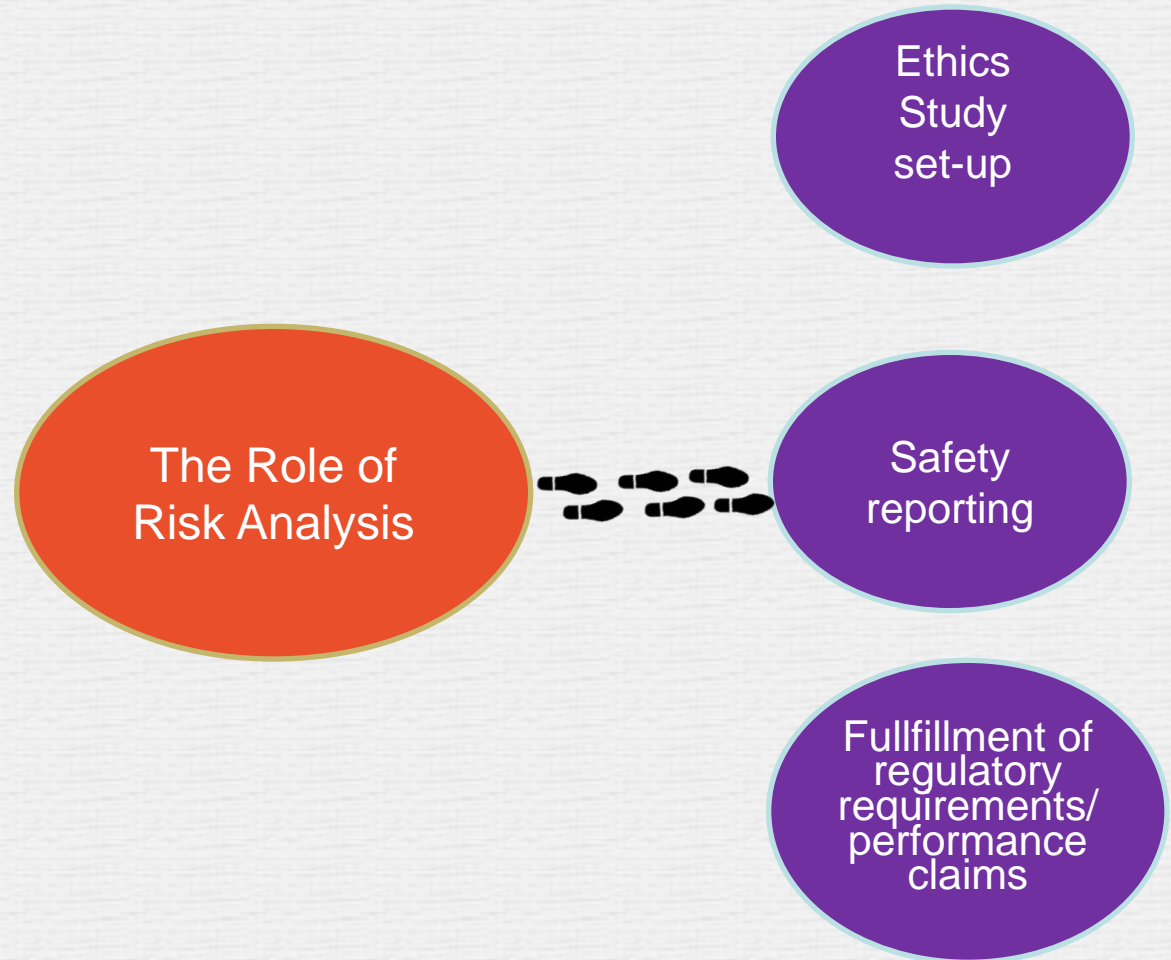
- Declaration of Helsinki
- ISO 14155: 2011
- Clinical Investigation Plan



Ethics
Study
set-up



The outcome of a clinical investigation: The significance of risk analysis



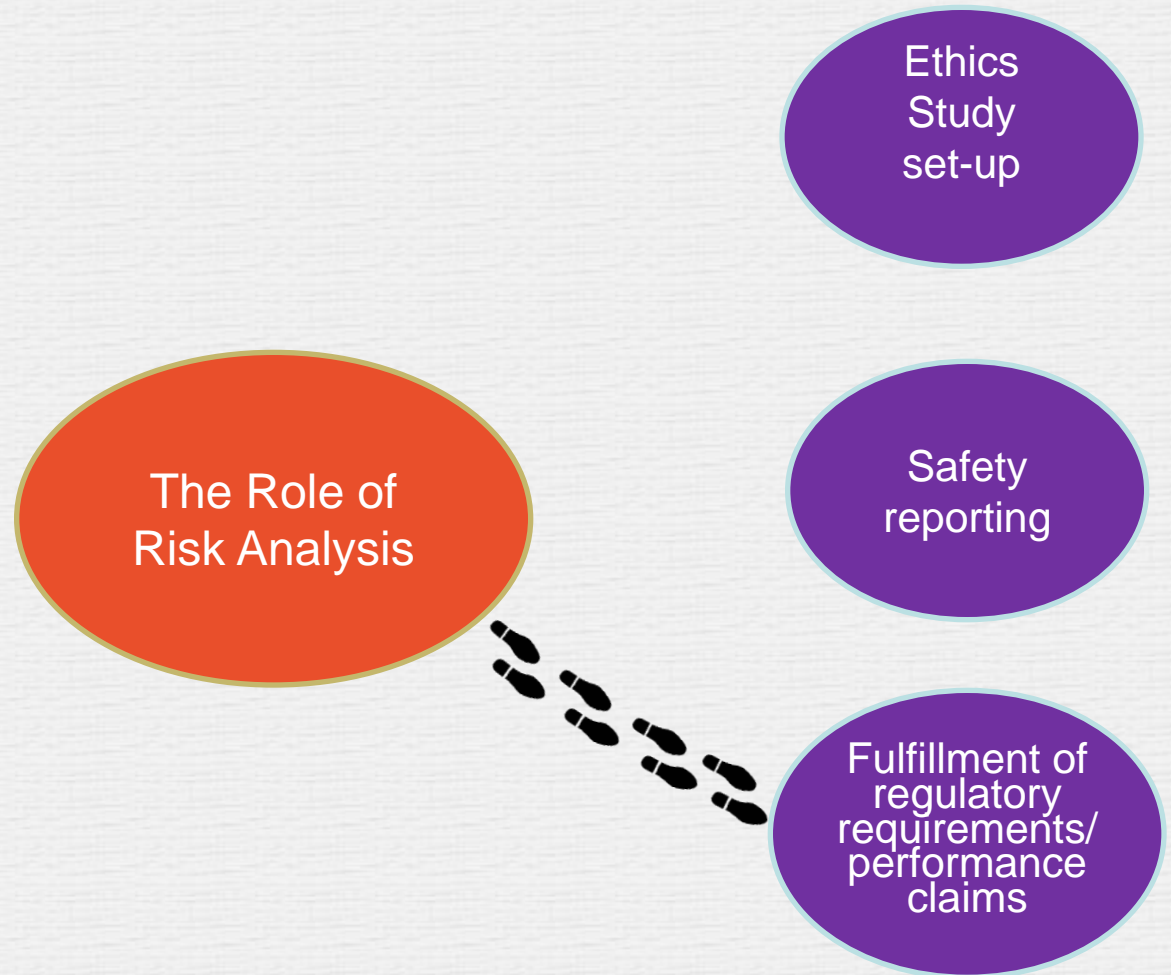
The outcome of a clinical investigation: The significance of risk analysis

- **US** requirements
- **EU**: Serious Adverse Event reporting
- **GHTF** requirements

Safety
reporting



The outcome of a clinical investigation: The significance of risk analysis



The outcome of a clinical investigation: The significance of risk analysis

- **US:** Safety & efficacy
- **EU:** Safety & performance
- **GHTF:** Safety & performance

Fulfillment of
regulatory
requirements/
performance
claims

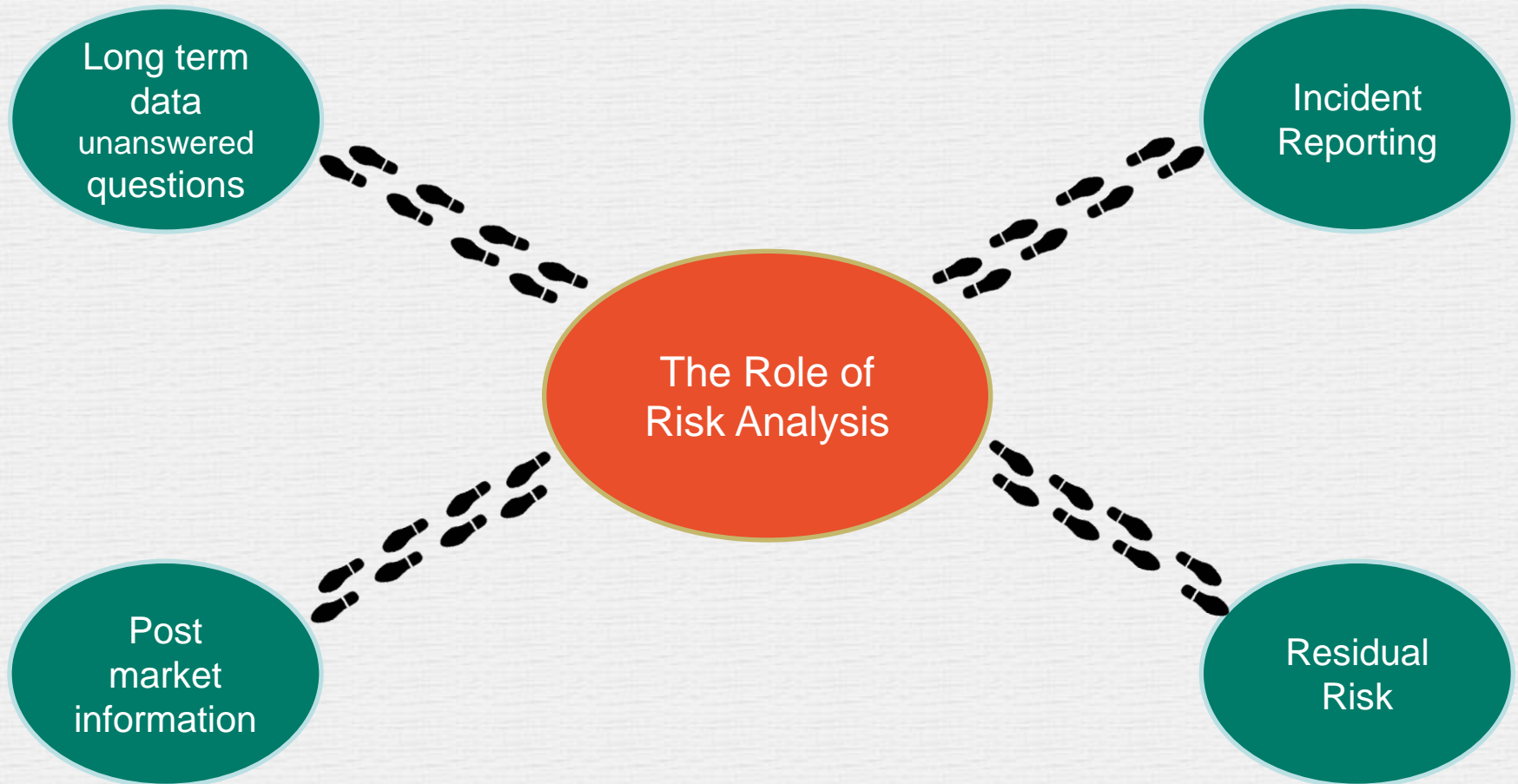


Product Recall

- Approved products continue to be recalled
 - Batch recall: i.e. instructions for use, the quality of the product
 - Recalls: voluntary - the manufacturer can stop producing the product
 - The most serious is a global recall imposed by a regulatory body e.g. FDA



Post Market Surveillance

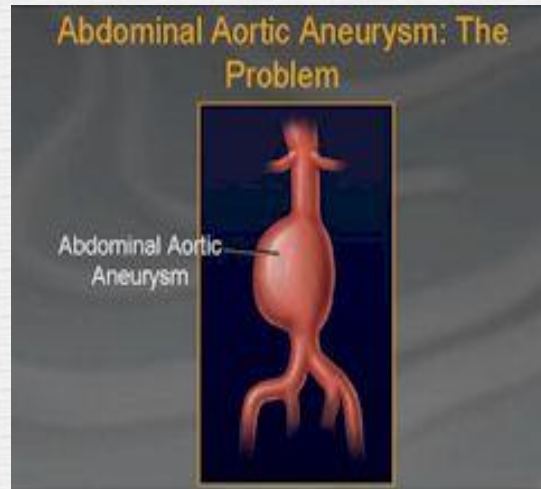


Post Market Clinical Follow-up

- Clinical investigation needed in pre-market and post market phases
- Post market clinical follow up studies
 - GHTF SG5/N4: 2010
 - EU MedDev 2.12–2
 - US FDA imposed



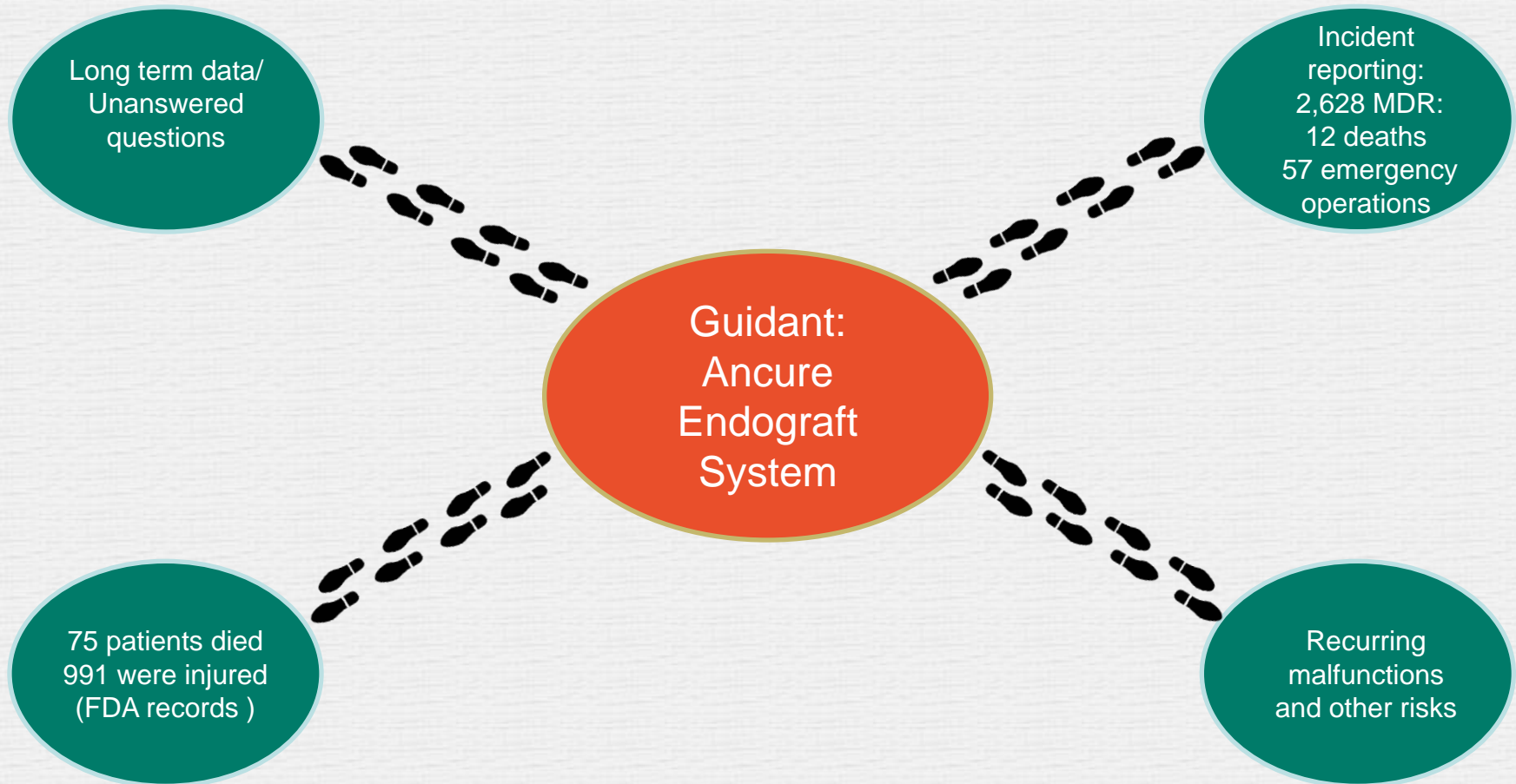
Guidant: Ancure Endograft System



to treat abdominal aortic aneurysm without invasive traditional surgical techniques



Post Market Surveillance



Class Action: Guidant

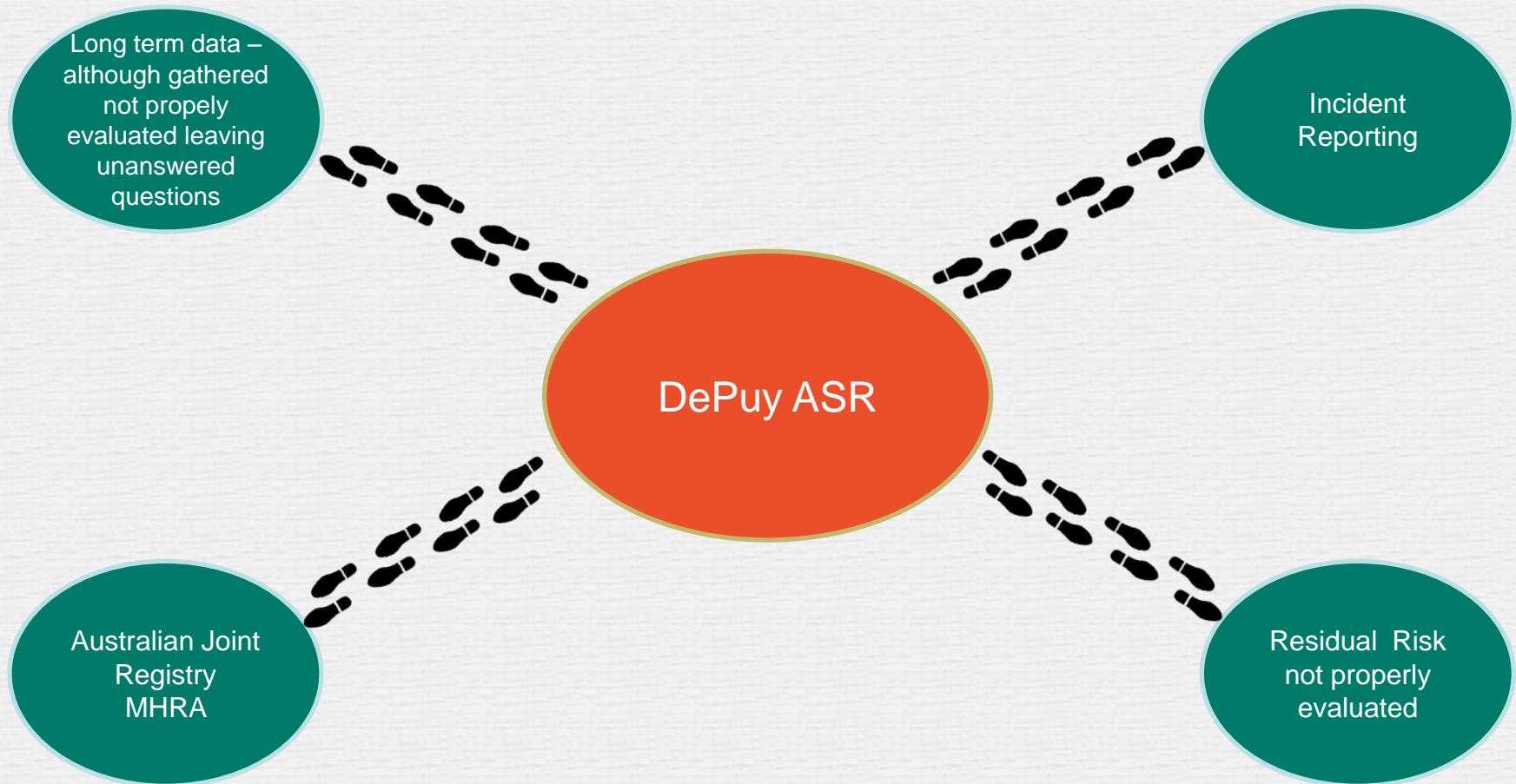
- Approval granted by FDA based on clinical studies of safety and effectiveness conducted by Guidant.
- Unfortunately in the post market phase, the device did not work as promised and the company began to hear of problems not seen in the clinical trials.
- Within 19 months of being released to the public over 2500 Ancure devices had malfunctioned out of a total 7500 sold.



Global Product Recall: Depuy



Post Market Surveillance



Global Product Recall: Depuy

- DePuy voluntarily recalled two of its hip replacement products, after post-market surveillance data showed a high risk of revision rates for patients implanted with the devices.
- The company said it had notified the FDA and other regulatory agencies globally of the recall.
- DePuy has advised all implanted patients to visit surgeons for an evaluation of the product's performance.

FDA: 522 issued on all metal hips



Product Recall

Guidant

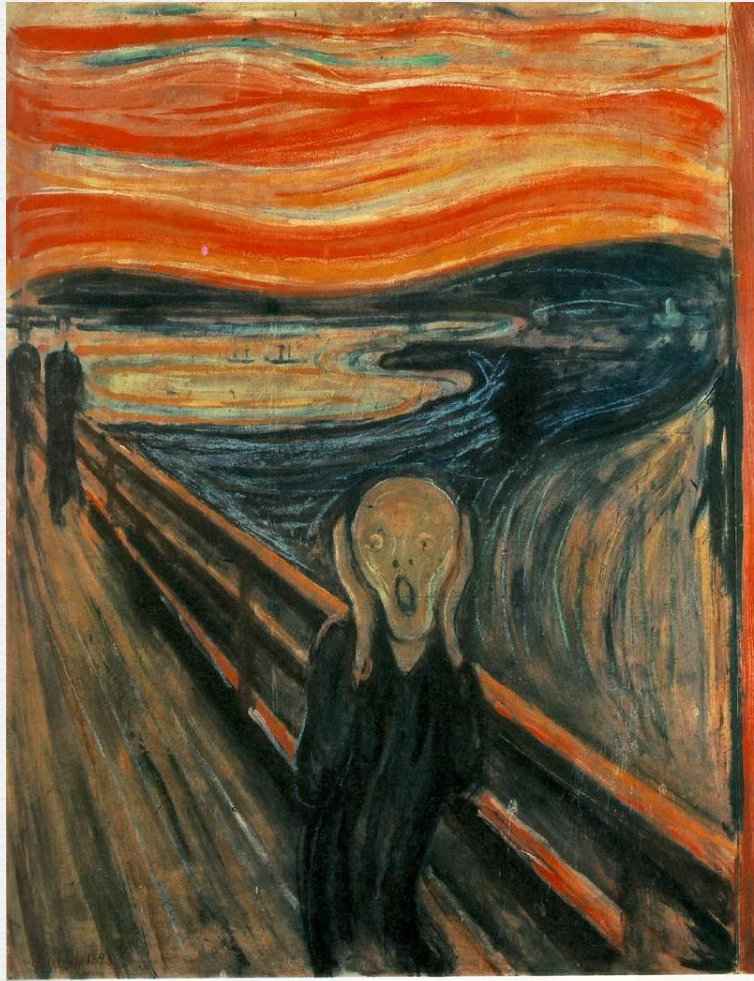
DePuy

Medtronic

Abbott

Boston
Scientific

Roche



Conclusion

GHTF requirements:

- Global standardization of classification and requirements for approval
- Premarket and post market clinical investigations are necessary
- Risk Analysis important in the entire lifecycle of a medical device

