

Optimal Use of Experience Gained in Post-marketing Surveillance in Medical Device Regulatory Policy

Some *personal* reflections

Global Harmonization Task Force Conference

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Caveats

- Personal comments
- Broad, complex topic
- Not an exact science
- Risks in generalizing
- More questions than answers

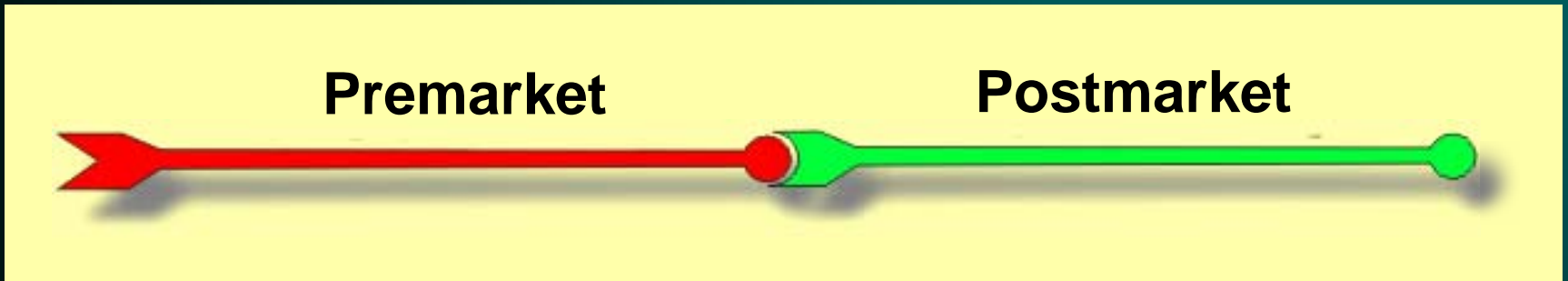


Premises

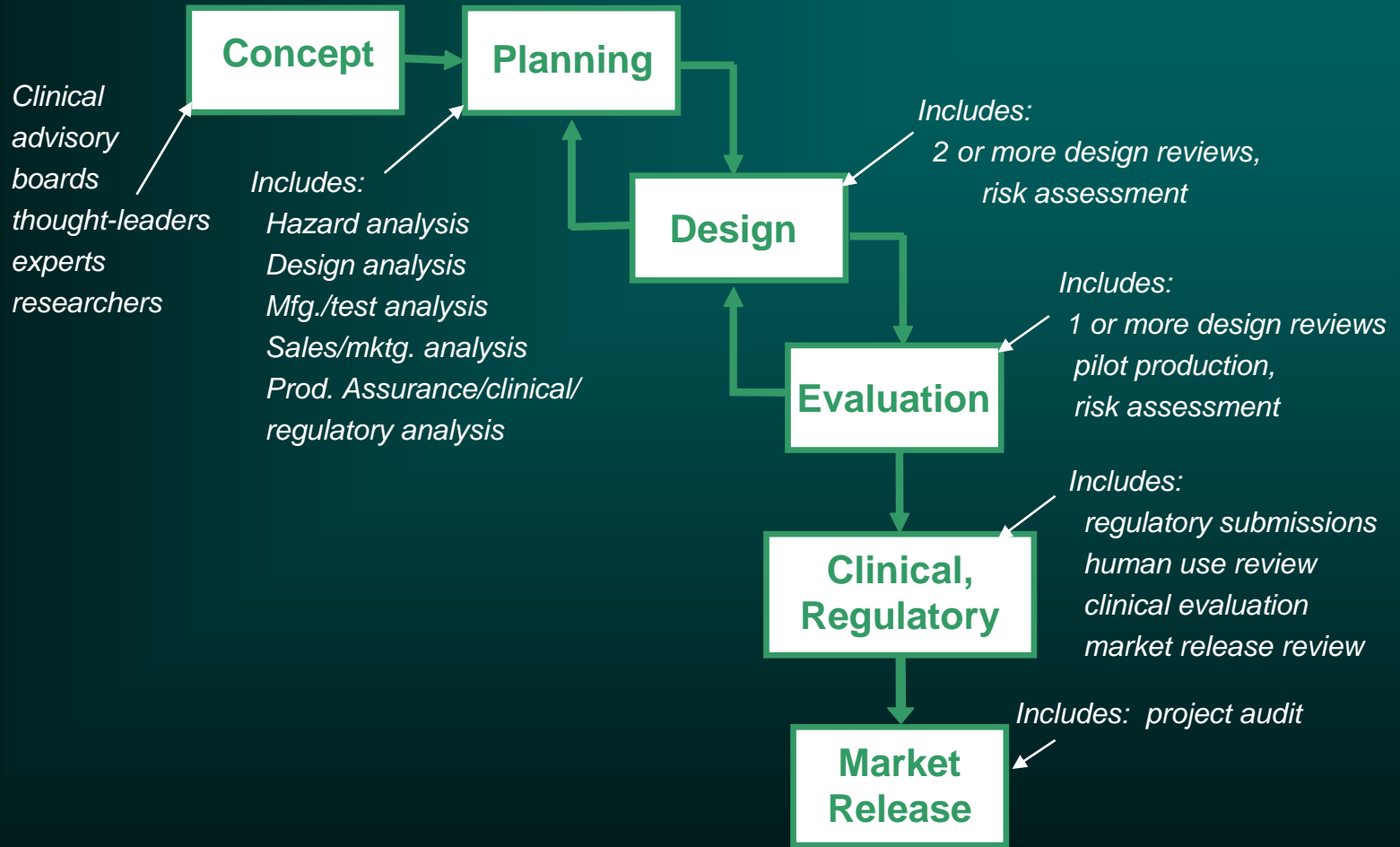
- Medical technology, clinical outcomes, safety, and regulatory practices should (and generally do) improve over time
- Systems approach required
- Observations could apply to health care systems generally
- Regulatory policy defines medical technology industry and, in part, determines rate of innovation



Product life cycle and regulatory controls



Product development life cycle (representative)



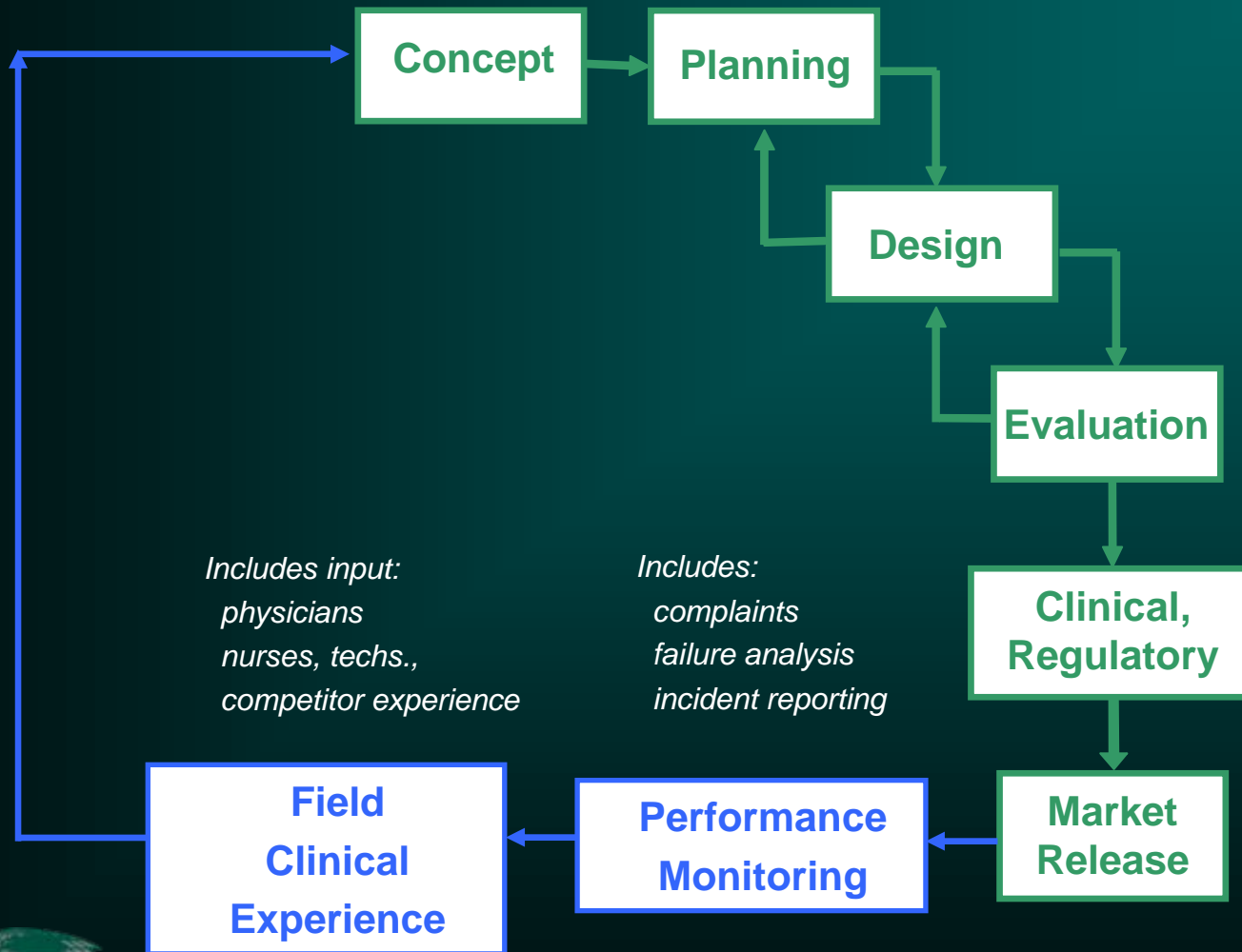
Product development life cycle (representative)



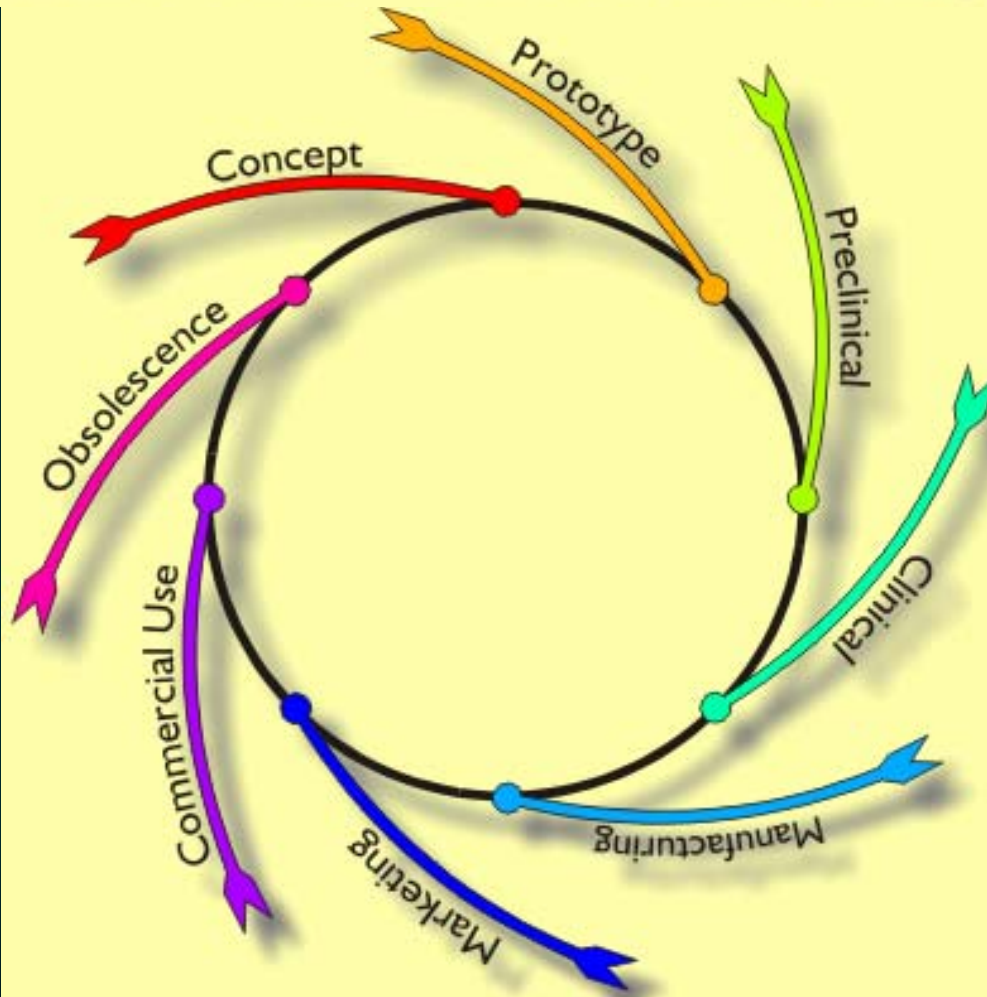
Inherent limitations in what is, and can be, known at pre-market stage



Product development life cycle (representative)



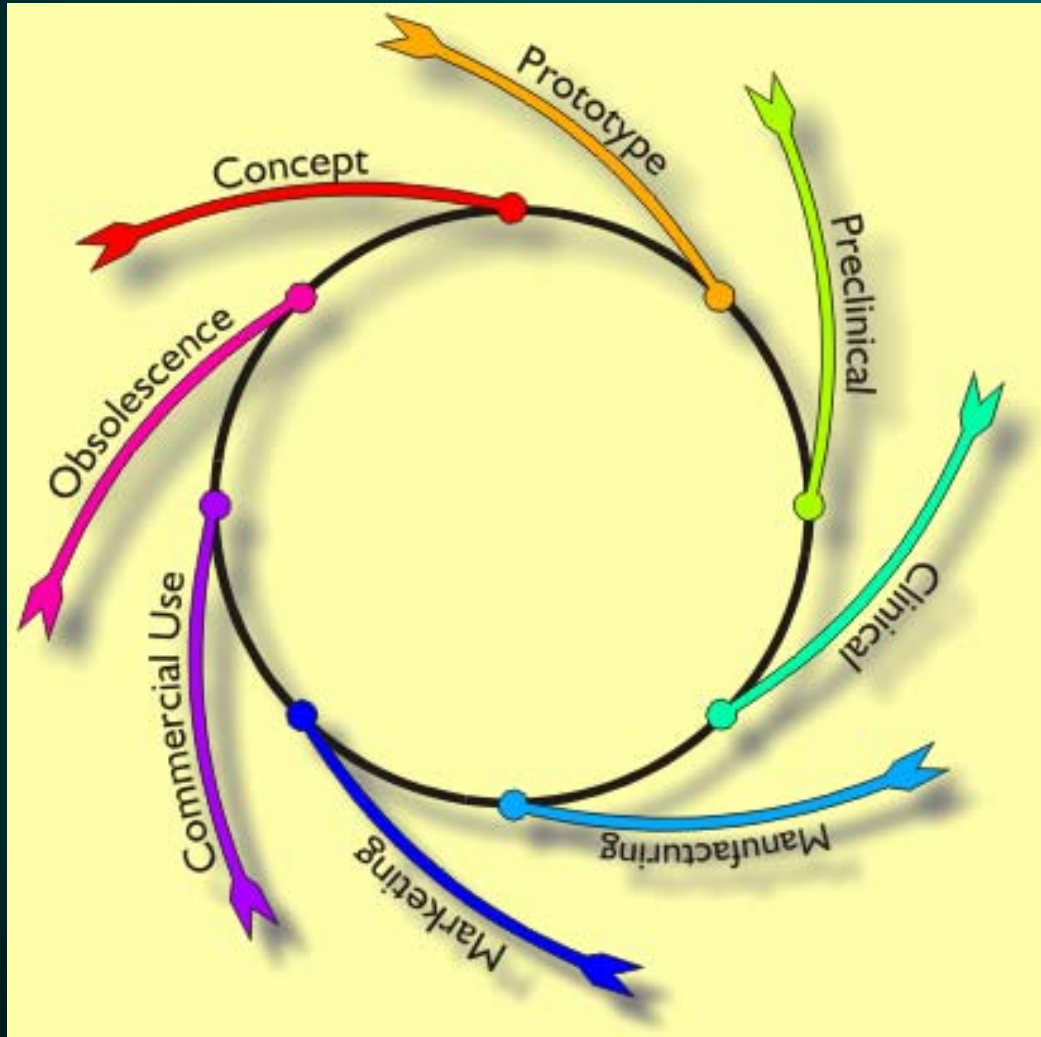
CDRH Vision - Total Product Life Cycle



Source: US Food and Drug Administration, Center for Devices and Radiological Health, Strategic Plan 2001



Post-marketing surveillance or life cycle surveillance?



Sources of post-marketing experience data

**Product
Experience**

Sources of post-marketing experience data

**Product
Experience**

Product performance data comes from many sources
and in many different forms



Sources of post-marketing experience data

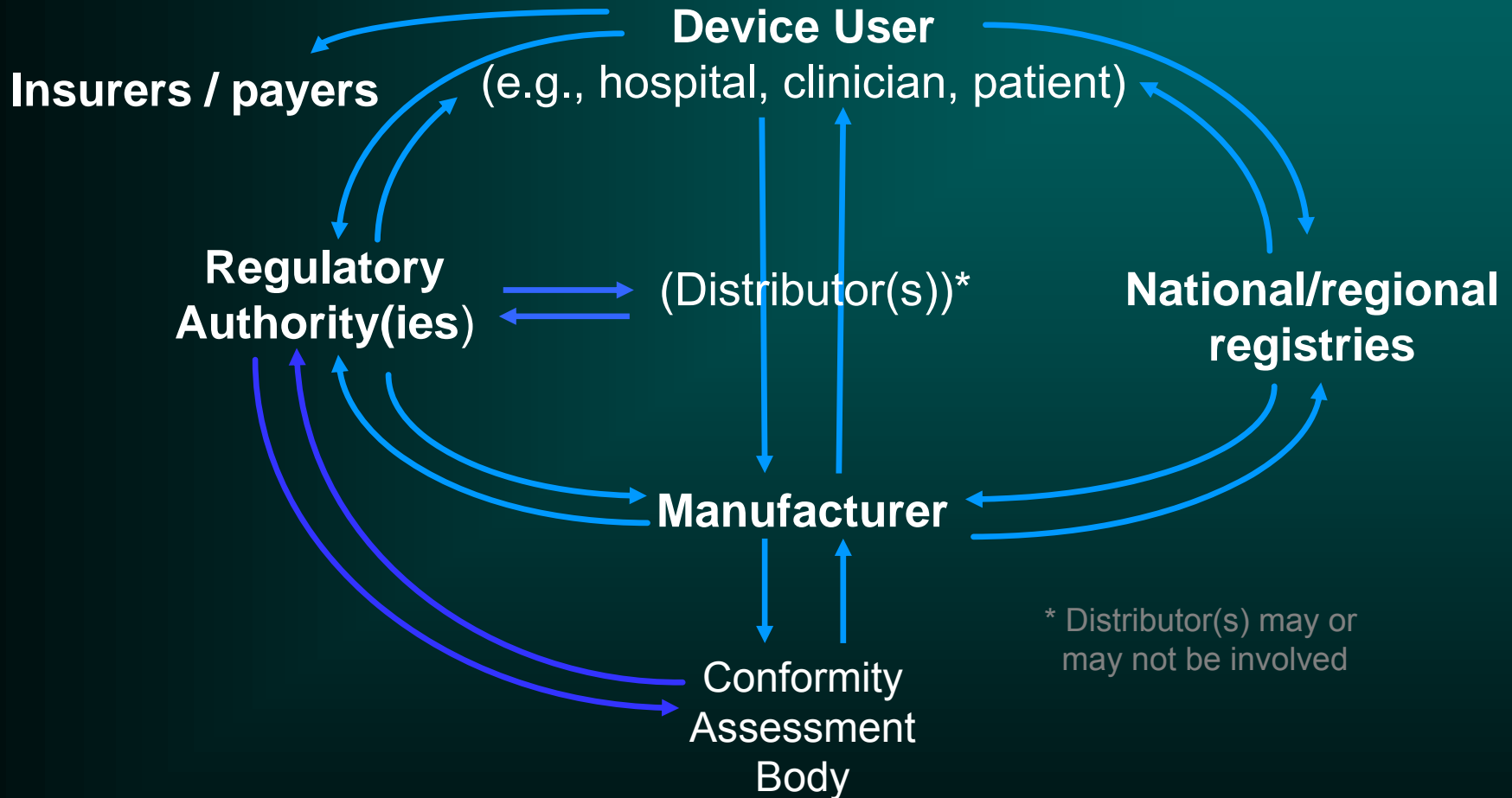


Medical device performance information – user feedback

- Experience reporting by users often differs across geographic regions
 - Clinical practices
 - Clinician expectations
 - Reporting culture
 - Litigation climate
 - Efforts of regulators and industry
 - Local representation of manufacturer
 - Language
- Affects quality, reliability, and timeliness of data
- Limits in comparability and applicability



Flow of post-marketing experience data (generalized)



Flow of post-marketing performance data

- Pathways vary depending on device
- No single party controls all pathways
- Failures can and do occur in any of these pathways
- Complexity of pathways attenuates signals



Obstacles to performance information flow and event analysis

- Discarded product
- Lack of timely access to product
- Complexity of use environments and difficulty in parsing interactions
- Difficulty in reaching users
- Lack of reported detail on events
- Complexity of information chain



Obstacles to performance information flow and event analysis

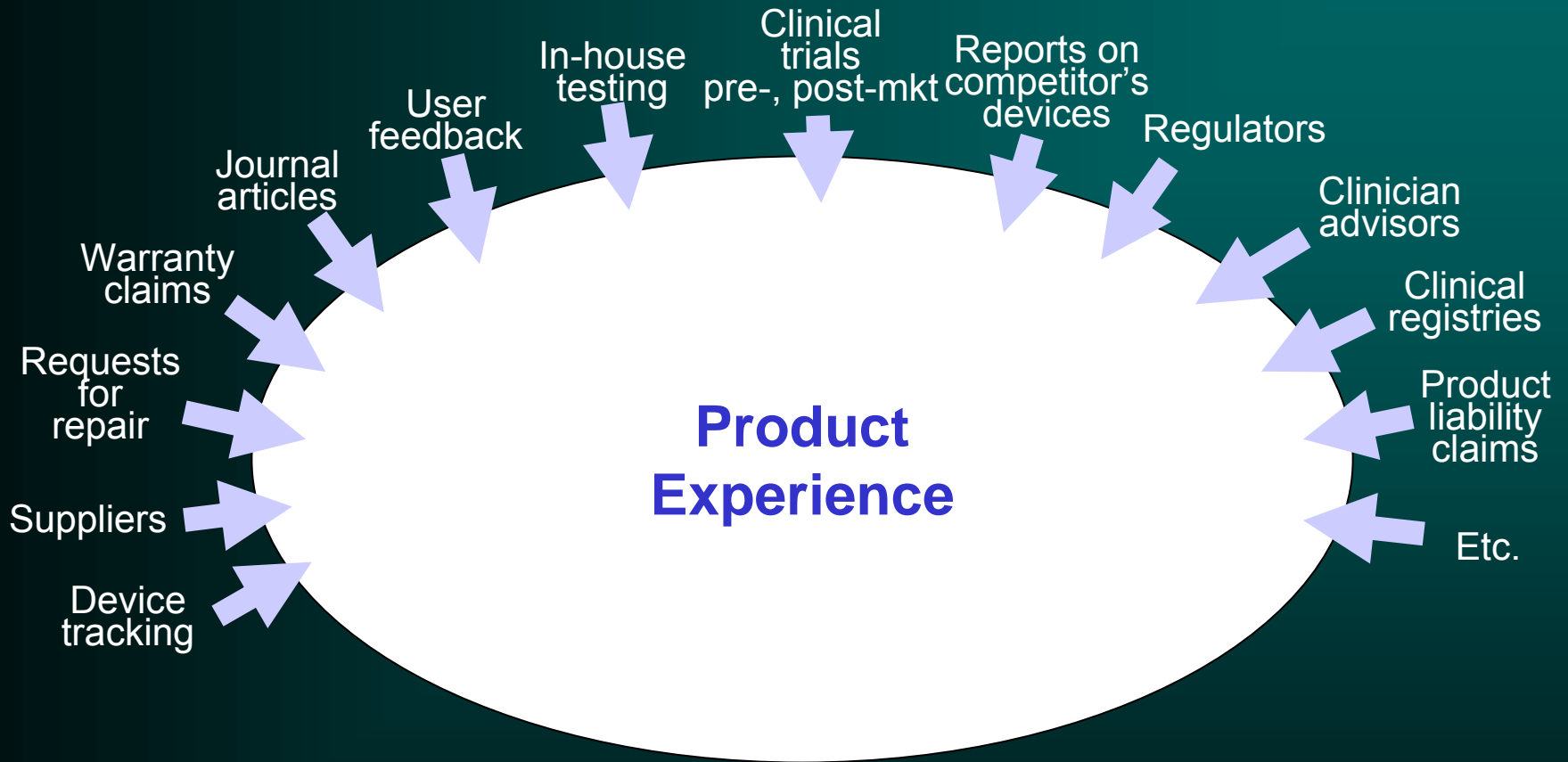
- Possibility of device combinations
- Need to respect patient privacy and patient – physician relationship
- Breakdown between local representative and manufacturing site
- Distrust between parties
- Possible contribution of use error



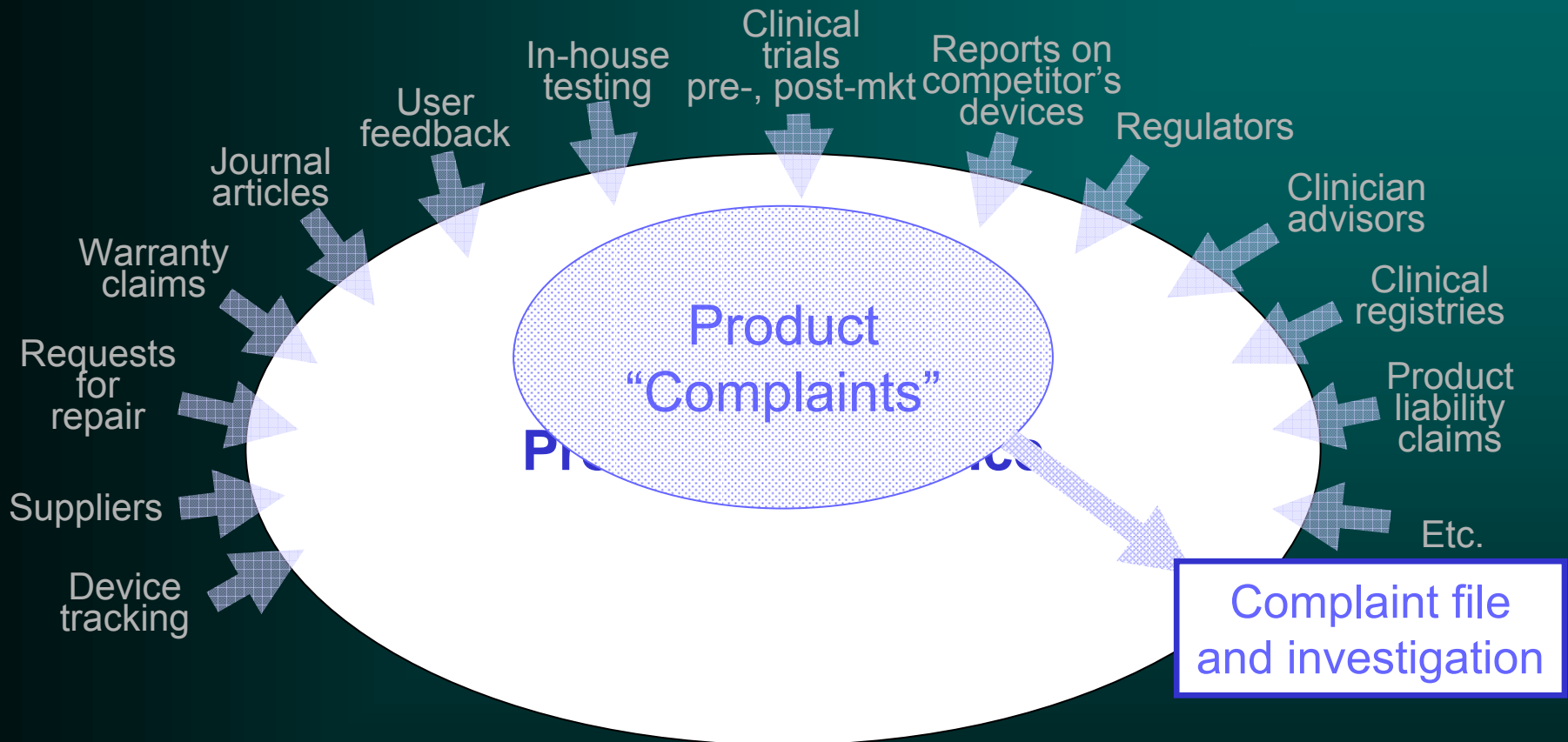
Sources of post-marketing experience data



Sources of post-marketing experience data



Uses of post-marketing experience data – complaints

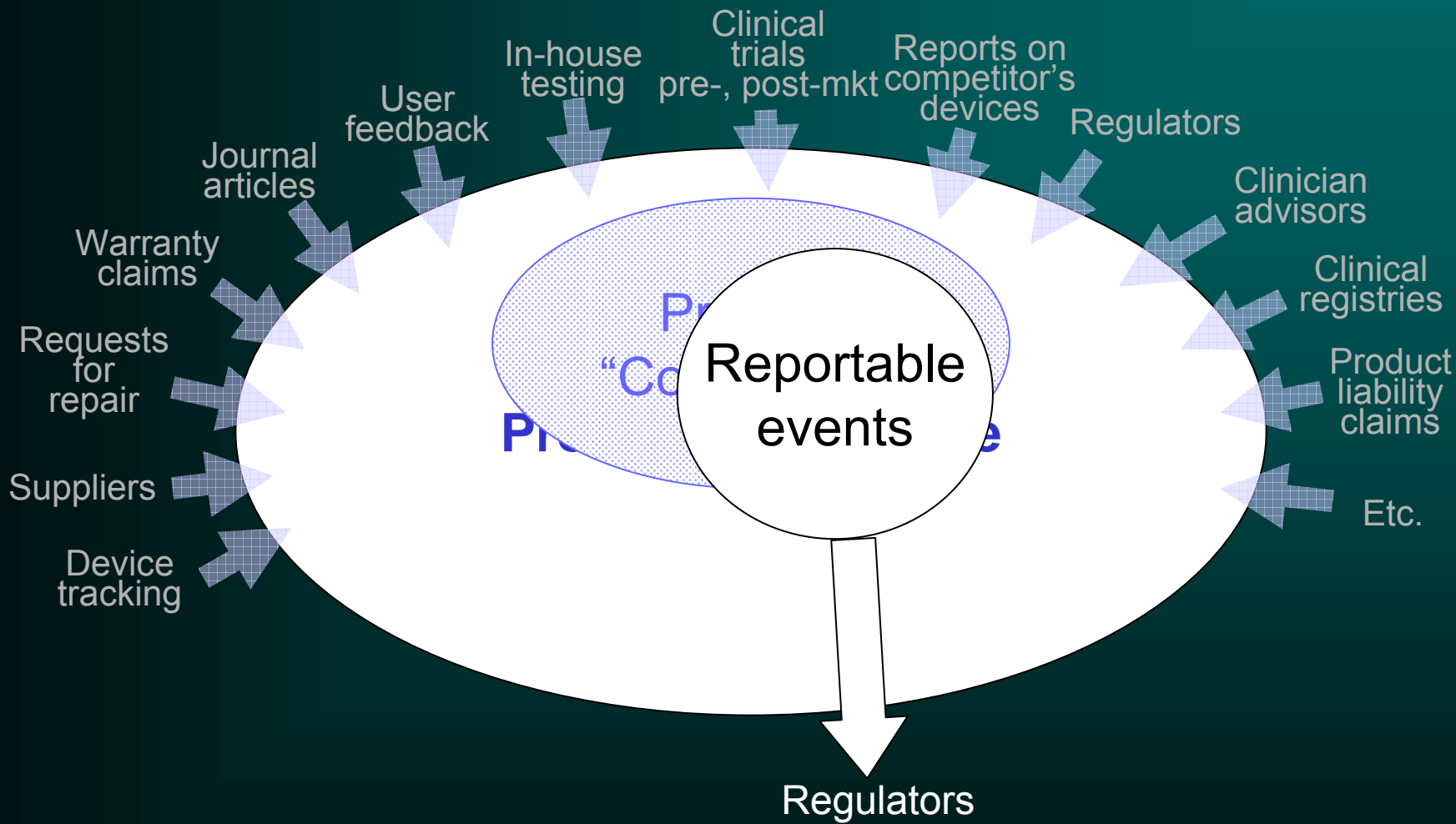


“Customer Complaint: Written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety or performance of a medical device that has been placed on the market.”

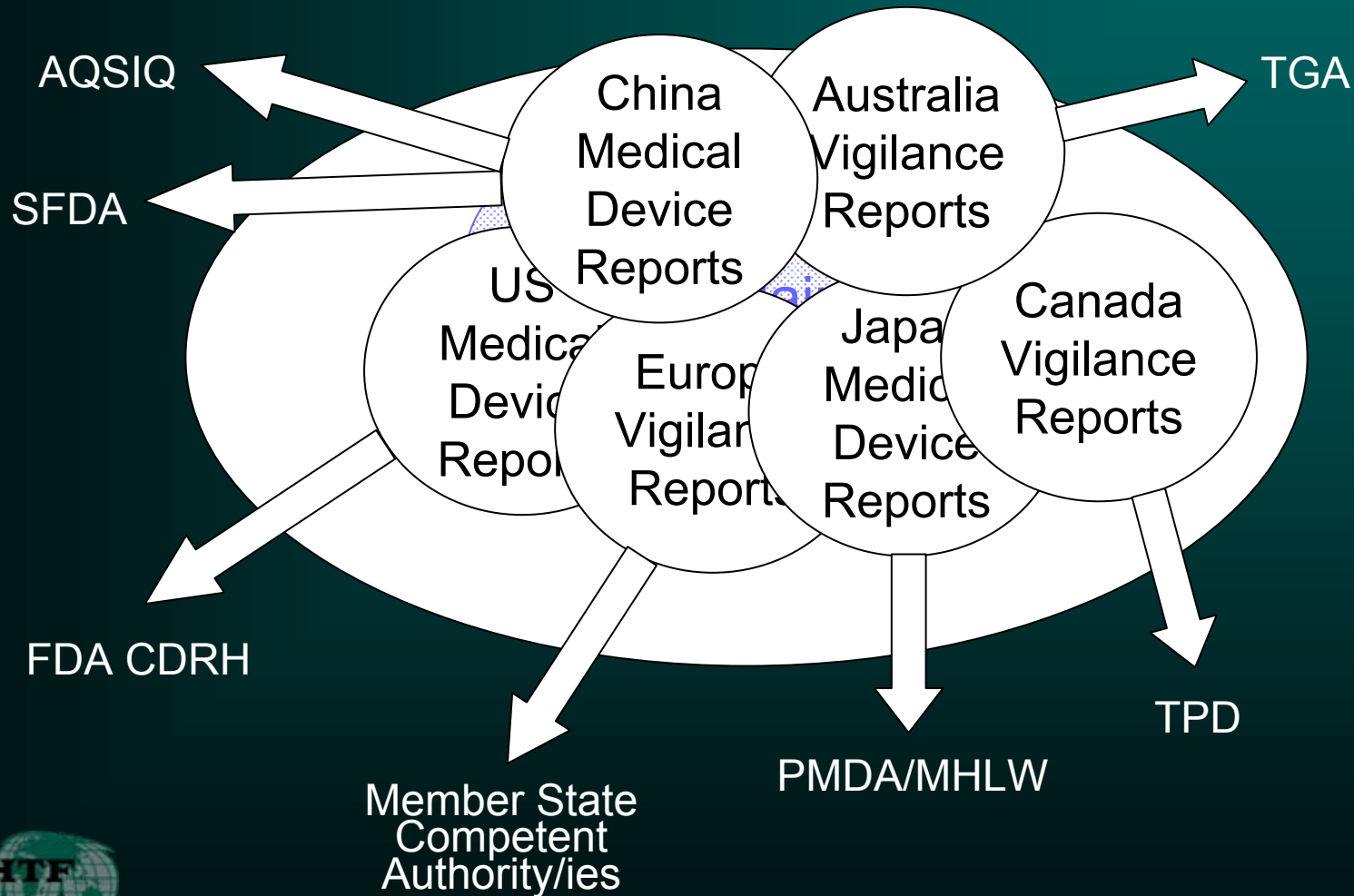
Source: ISO 13485:2003



Uses of post-marketing experience data – vigilance



Uses of post-marketing experience data – vigilance



Medical device manufacturer vigilance reporting

- Un-harmonized reporting criteria
- Un-harmonized reporting timelines
 - Trade-off between rapidity and quality of reports
- Un-harmonized reporting formats
- More reporting in future?
- Opportunity for electronic reporting?



Medical device manufacturer vigilance reporting

GHTF/SG2/N54R8:2006



FINAL DOCUMENT

Global Harmonization Task Force

Title: Medical Devices Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices

Authoring Group: Study Group 2

Date: 30 November 2006

A handwritten signature in black ink, appearing to read 'Georgette Lalis'.

Georgette Lalis, GHTF Chair

The document herein was produced by the Global Harmonization Task Force, which is comprised of representatives from medical device regulatory agencies and the regulated industry. The document is intended to provide *non-binding* guidance for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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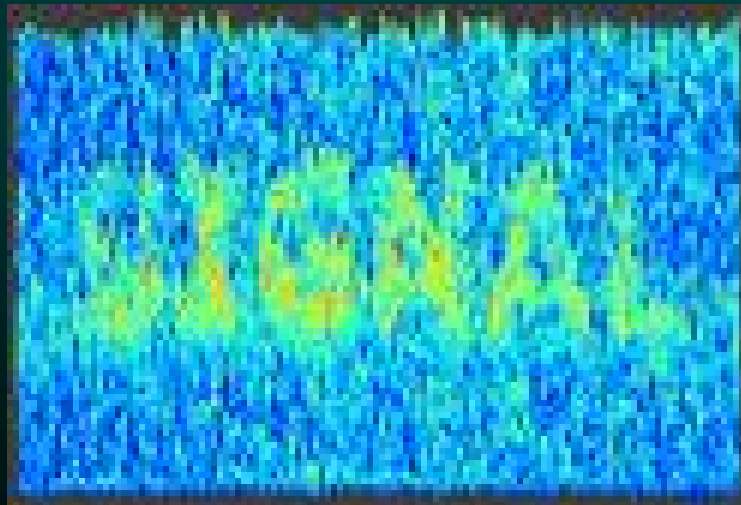
Medical device performance reporting systems (to and from manufacturers)

- Inherently based on single incidents or near incidents – tend to be “lagging indicators”
- Individual reports may or may not be confirmed
- Individual reports may or may not indicate a systemic problem
- Individual reports may not allow determination of root cause
- Appropriate corrective and preventive action for individual events varies



Parties receiving data must have systems to

- Catalogue and collate data and allow searching
- Enhance “signal to noise” ratio
- Search for and prospectively identify potentially significant trends
- Establish priorities for further investigation



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Uses of post-marketing experience data

**Product
Experience**

Trend analysis

Medical device performance trend analysis – considerations

- Quantity of potentially affected devices that remain in service often difficult to determine
- For many devices, longitudinal data not available
- “Similarity” of events, root causes, devices potentially affected
- Significance and risk of an apparent trend
- Trend analysis methods must be adapted to suit specific device categories

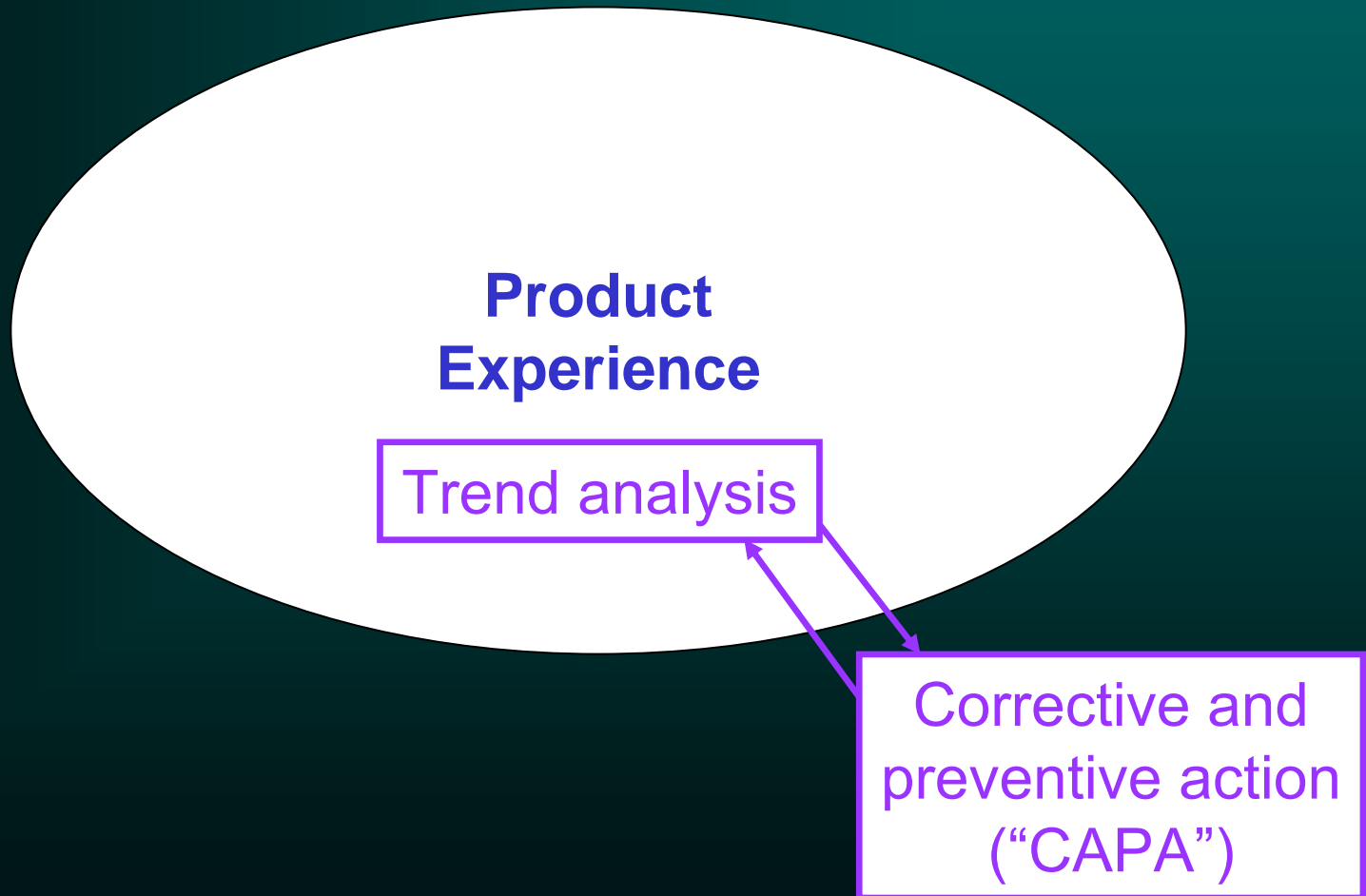


Medical device performance trend analysis – considerations

- How to define “failure”?
- How to account for differences in clinical practice?
- Appropriate “trigger” for corrective and preventive action
- How does trigger point vary?
 - Alternatives?
 - Maturity of technology?
 - Vulnerability of target population?
 - Etc



Uses of post-marketing experience data



Corrective and preventive actions

- Based on risk assessments
- Some measures prospective, some retrospective
- May include
 - Design changes
 - Process changes
 - Testing, verification, and validation changes
 - QMS changes
 - Labeling, training updates
 - Field safety corrective actions / recalls
 - Communication (whether, when, what, how, to whom?)



Uses of post-marketing experience data – risk management

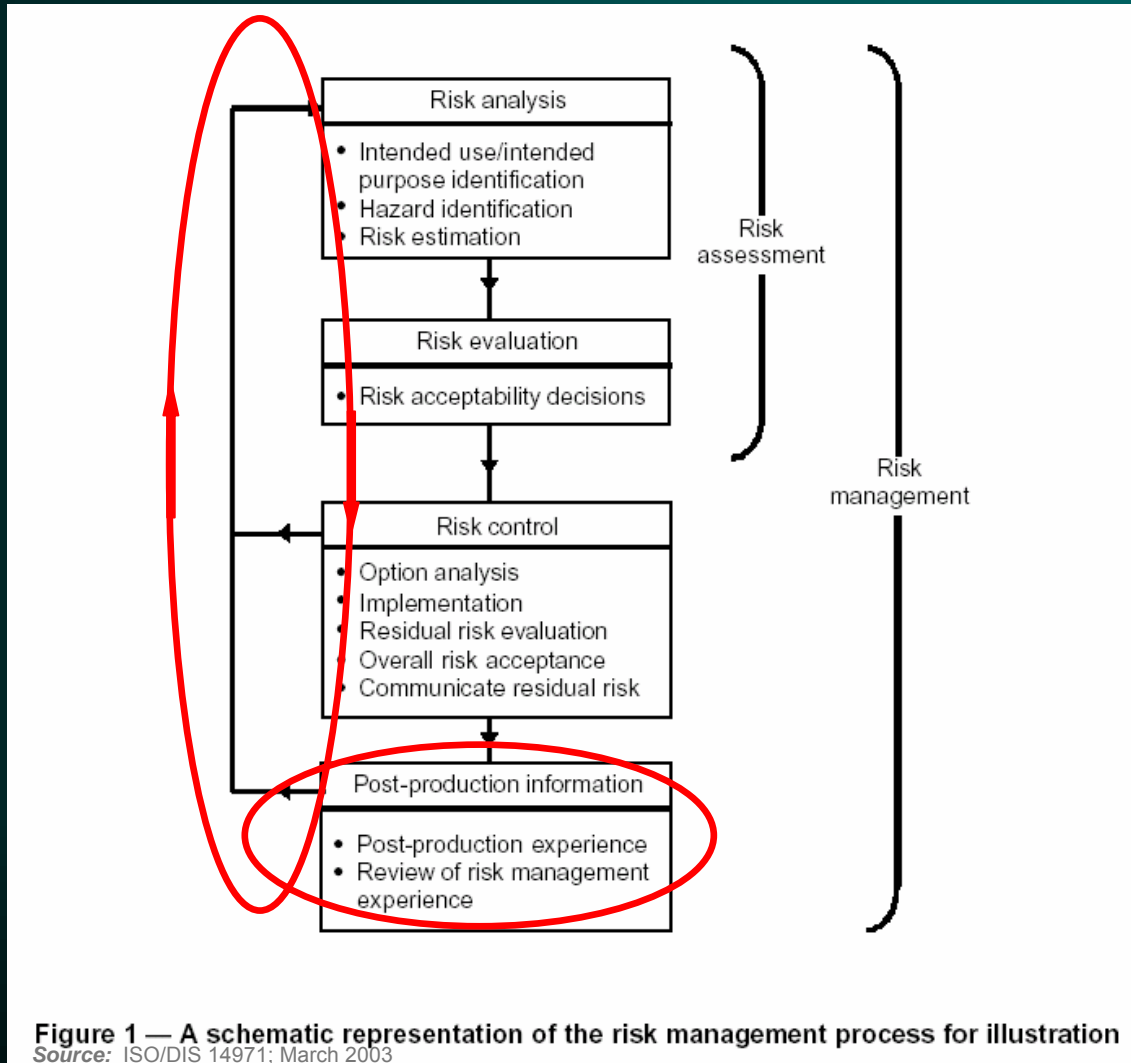
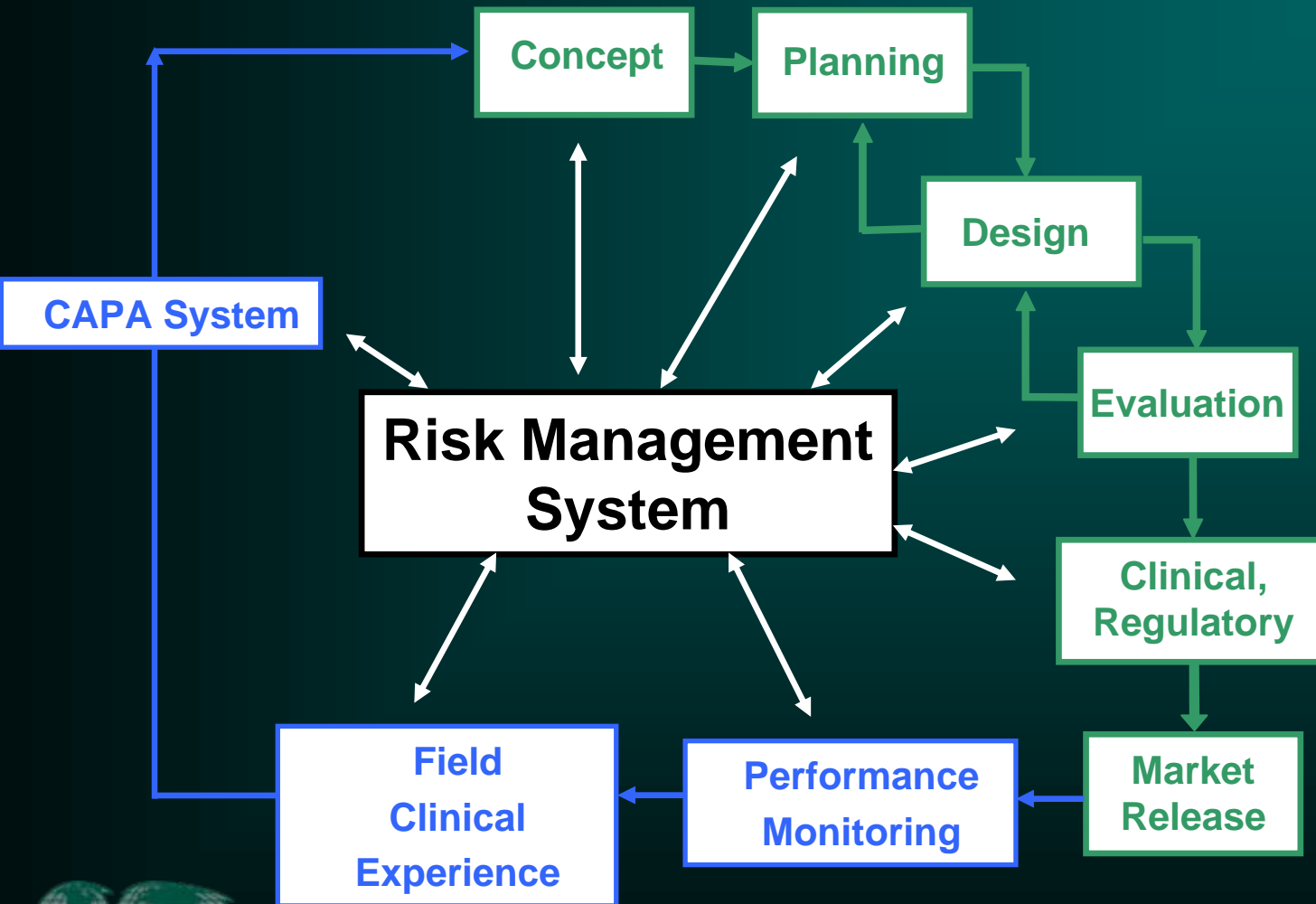


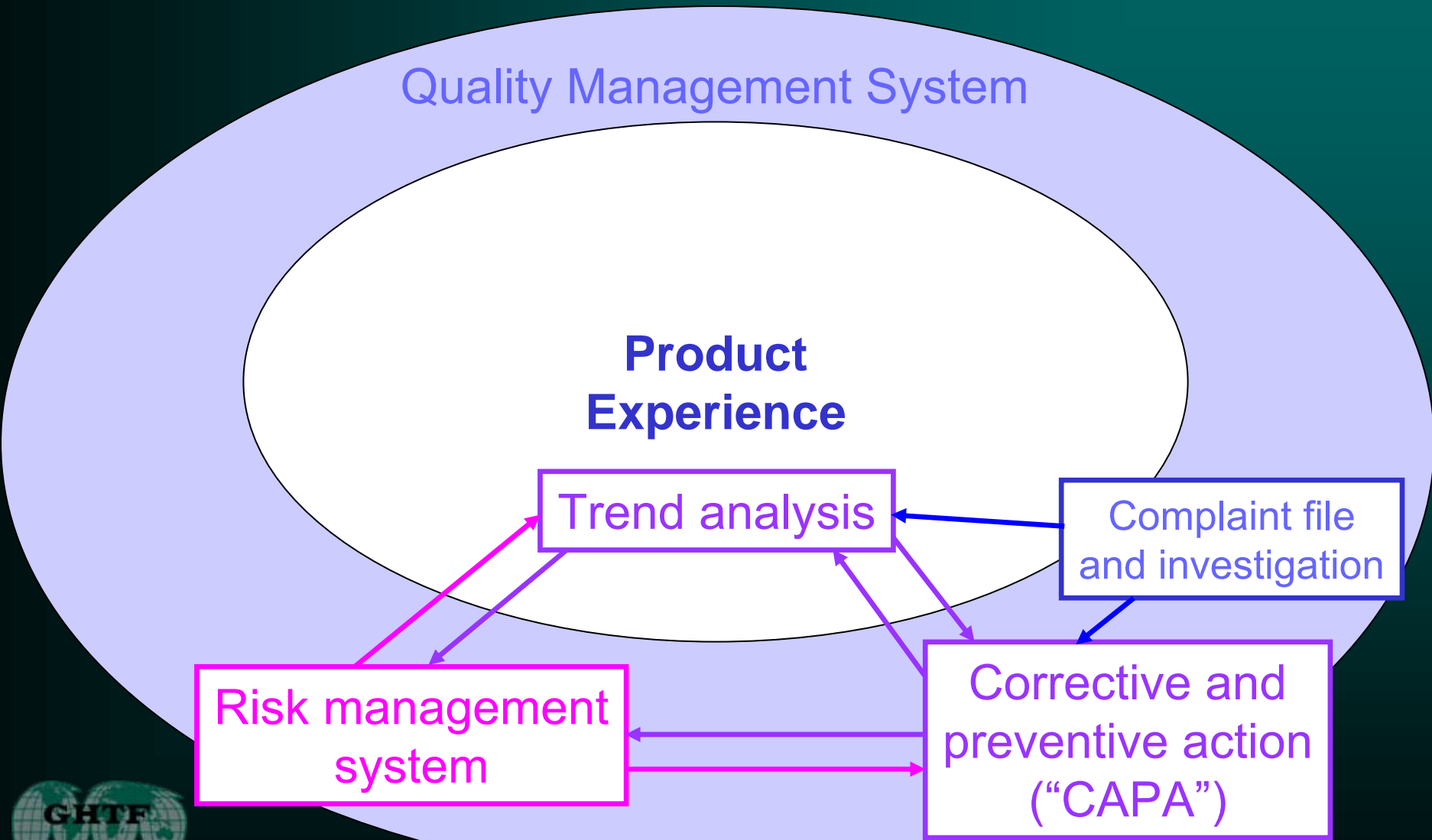
Figure 1 — A schematic representation of the risk management process for illustration

Source: ISO/DIS 14971; March 2003

Product development life cycle (representative)



Uses of post-marketing experience data

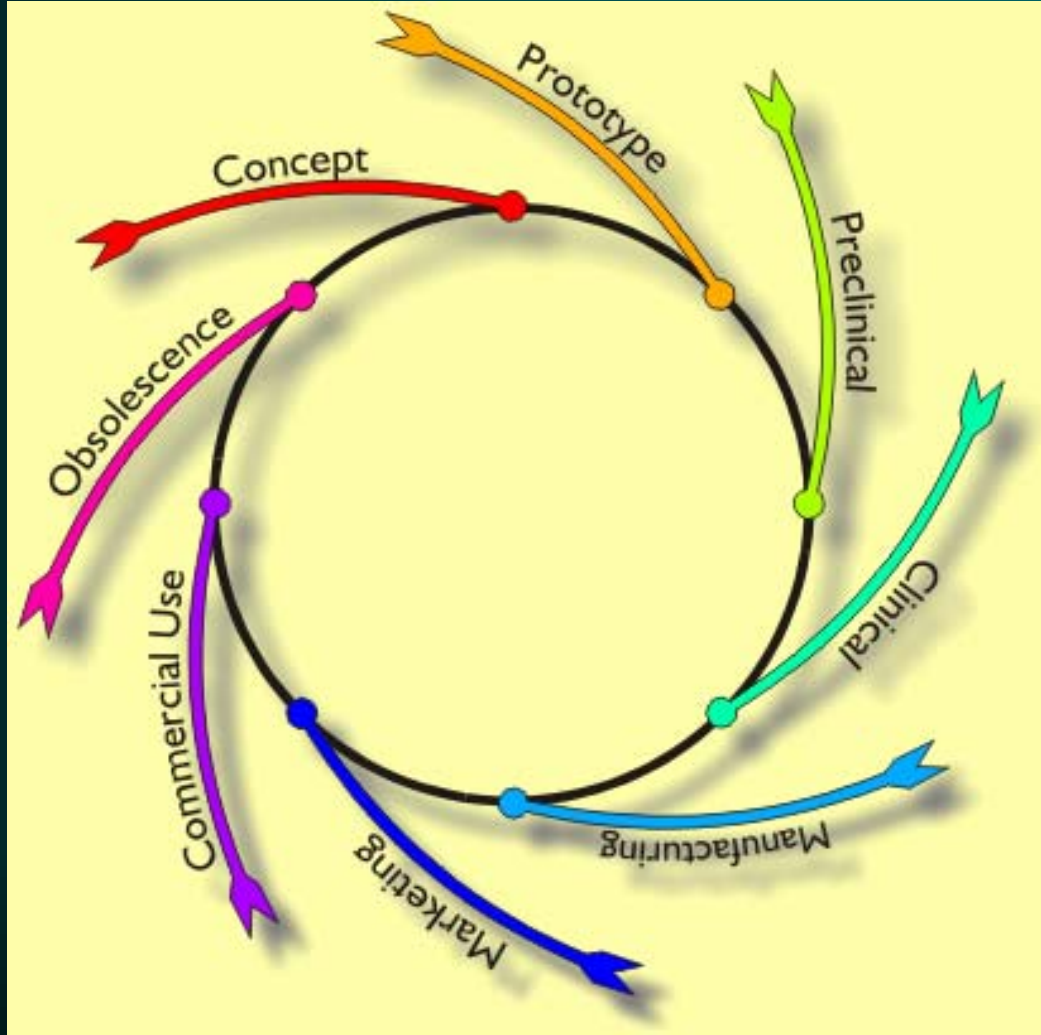


Corrective and preventive actions – regulatory policy

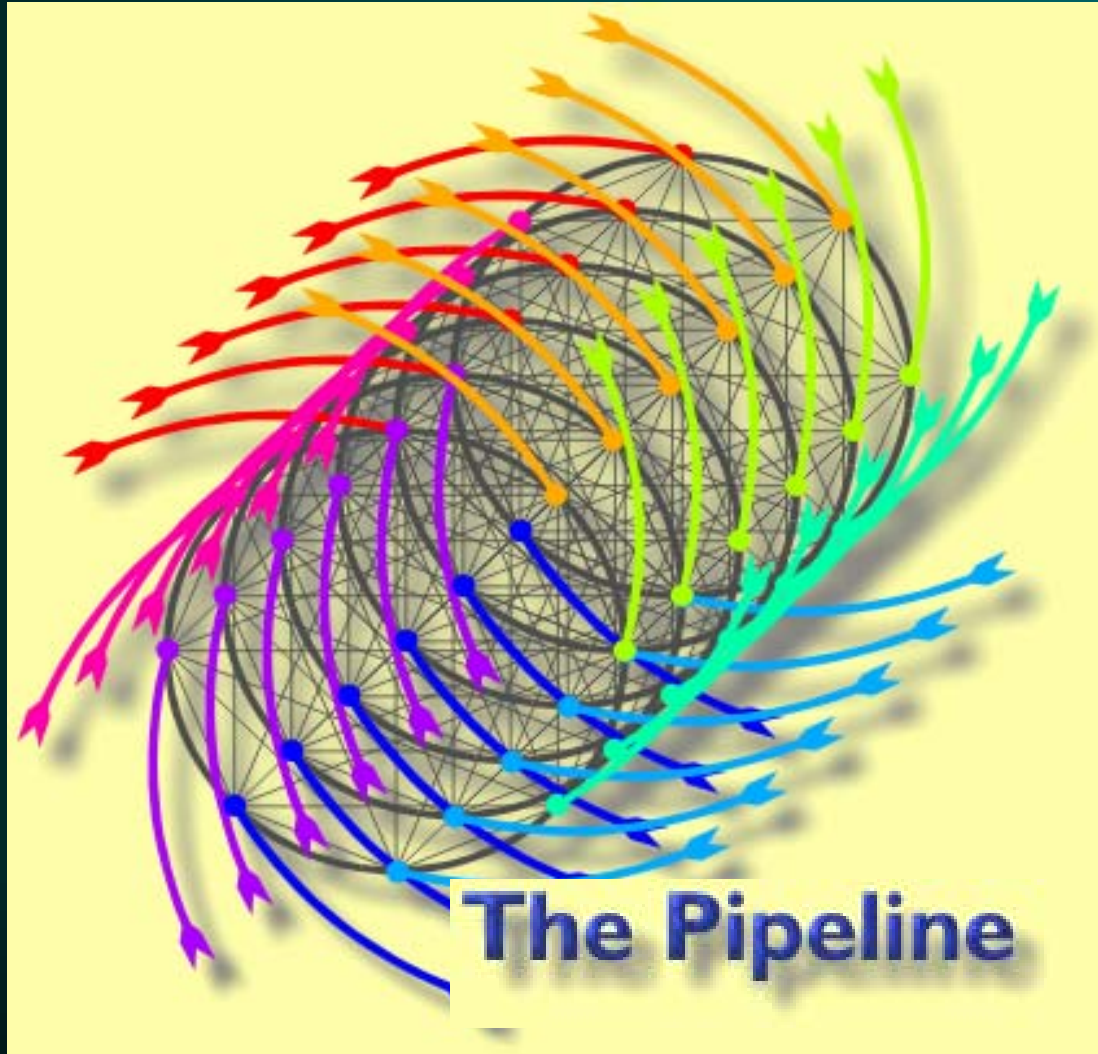
- Do regulatory requirements encourage or discourage operation of the CAPA system and continual improvement?
- Threshold for change notifications
 - Opportunity for international harmonization of guidance?
- Forms of change notification
- Review time
- How do regulators react to vigilance reports?
- How does post-market data inform pre-market review?



Post-marketing surveillance or life cycle surveillance?

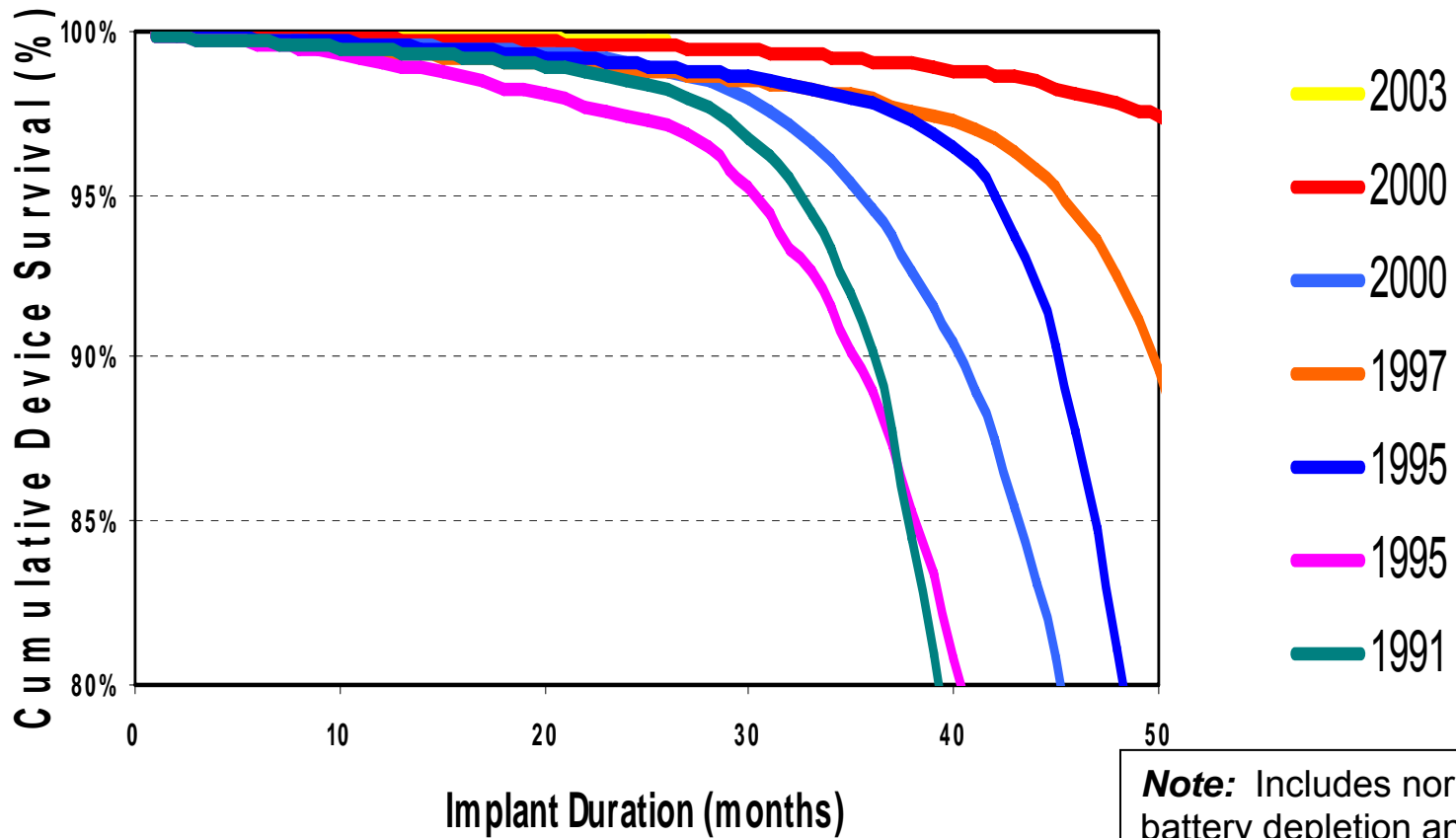


Generation – to - generation continual improvement



Source: US Food and Drug Administration, Center for Devices and Radiological Health, Strategic Plan 2001

Generation – to - generation continual improvement Implantable Cardioverter Defibrillator longevity



Note: Includes normal battery depletion and all failure modes



Generation – to – generation continual improvement

- Safety, performance, utility, and effectiveness have many dimensions
- Improvement in one may result in degradation in others
- How to find the optimum balance point?



GHTF Essential Principles

“Medical devices should be designed and manufactured in such a way that, 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.**”

- “Acceptable” as compared to what?
- “High level” as compared to what?



GHTF Essential Principles

“The solutions adopted by the manufacturer for the design and manufacture of the devices should conform to safety principles, taking account of the **generally acknowledged state of the art.**”

- How do we determine the current “state of the art”?
- How does the state of the art change over time?
- How does post-market surveillance help establish the state of the art?



GHTF Essential Principles

- Does the availability of an “improved” device mean that an earlier device is no longer “safe?”
- How much evidence is required to determine that an “improvement” really is an improvement?
- How to update assessments as the evidence shifts?



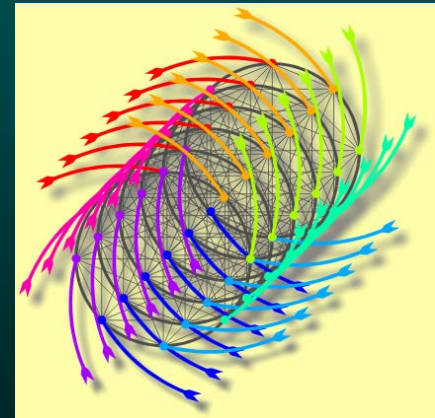
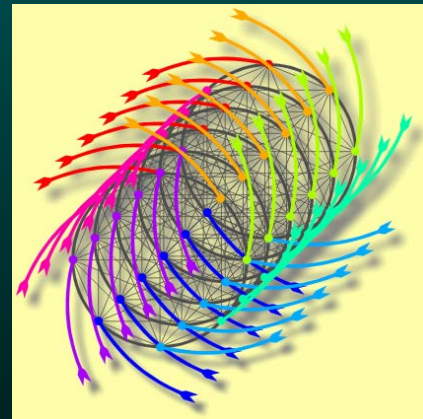
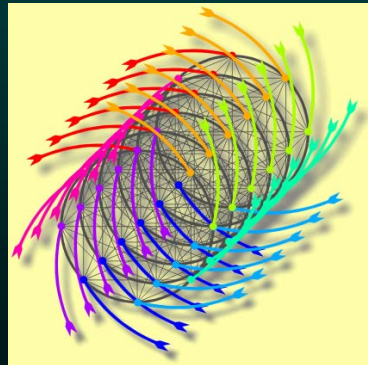
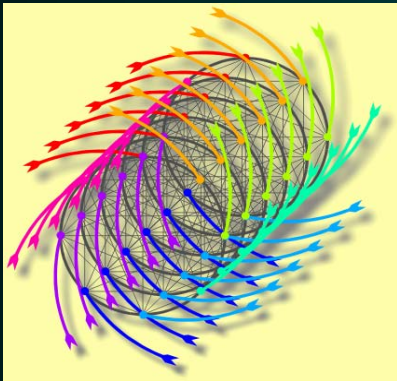
Generation – to -- generation continual improvement

- Ongoing innovation helps determine “state of the art”
- Competition stimulates ongoing innovation
- Regulatory policies and practices shape competition and barriers to entry
- Do cost vs. benefit analyses account for innovation foregone?



Generation – to -- generation continual improvement

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Risk assessment

Regulator
evaluates
benefits/risks
for the population



Provider
evaluates
benefits/risks
for a patient



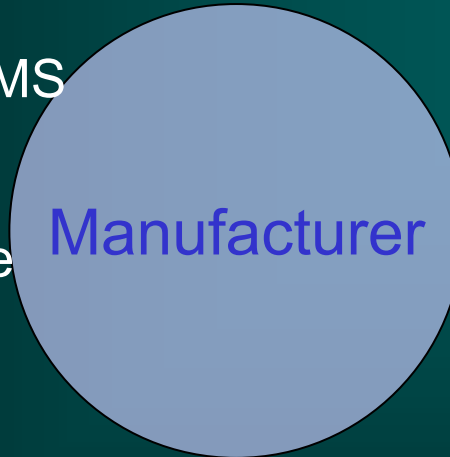
Patient
evaluates
benefits/risks
in terms of
personal values



Bodies of post-marketing experience data

Manufacturers typically “know”

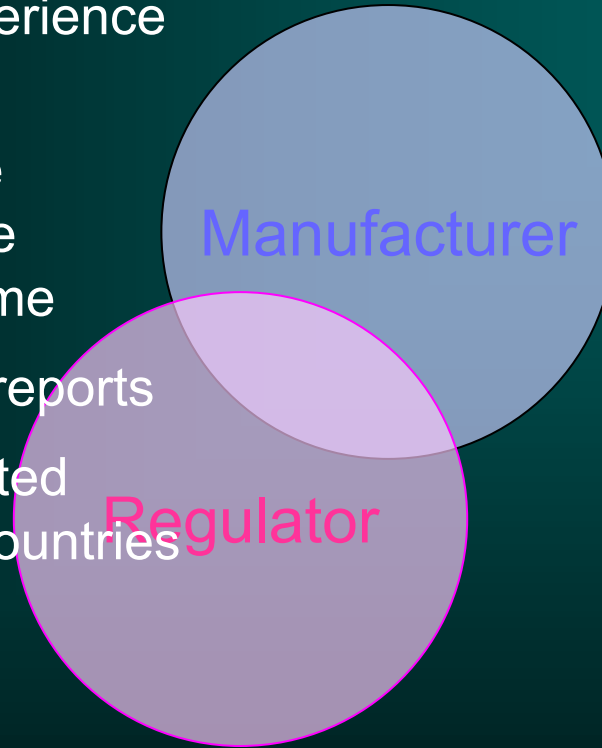
- technical details of product design and manufacture, QMS
- risk management data
- reported product experience
- location of original sale
- sales volumes (“numerator/denominator”)
- comparative performance across markets and between generations of own products
- anecdotal information on competitive products



Bodies of post-marketing experience data

Regulators typically “know”

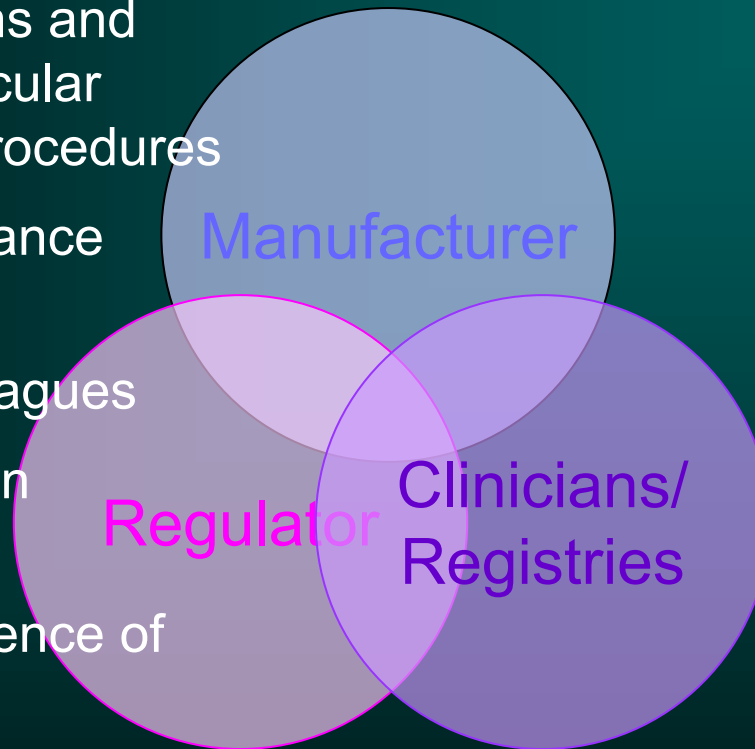
- reported product experience across many fields
- reported comparative performance for some product areas over time
- in some cases, user reports
- in some cases, reported experience in other countries



Bodies of post-marketing experience data

Clinicians typically “know”

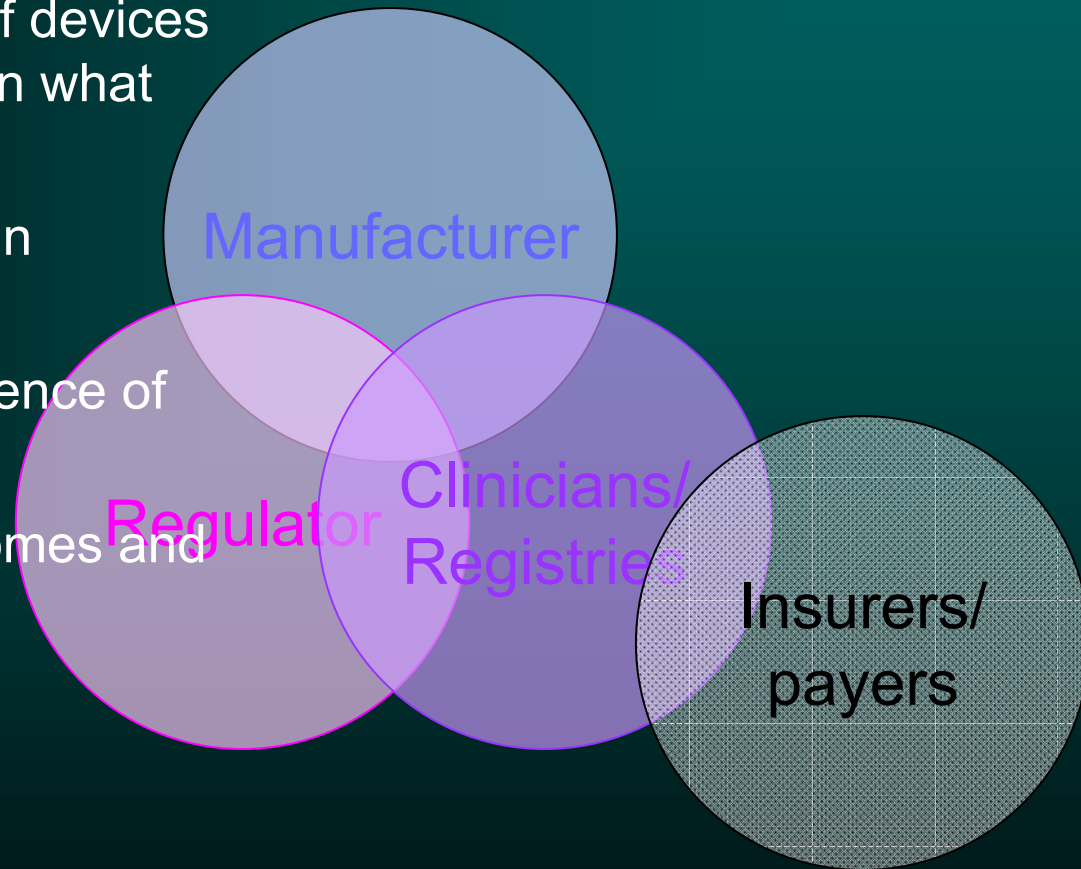
- their own observations and experience with particular technology/ies and procedures
- comparative performance in their practice
- anecdotes from colleagues
- experience reported in literature/registries
- incidence and prevalence of certain conditions



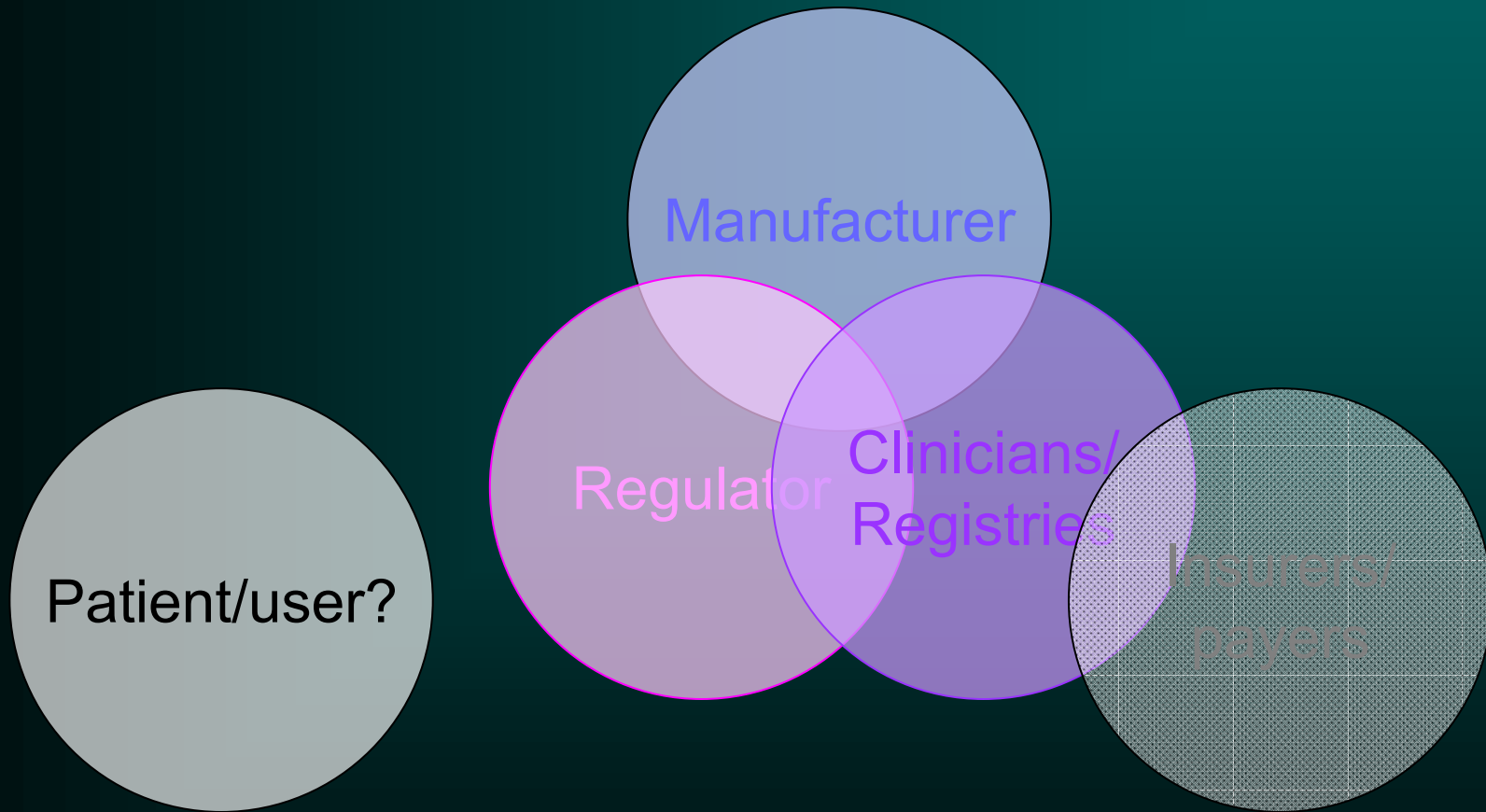
Bodies of post-marketing experience data

Insurers/payers typically “know”

- numbers and types of devices used by their clients in what clinical procedures
- experience reported in literature/registries
- incidence and prevalence of certain conditions
- in some cases, outcomes and re-interventions



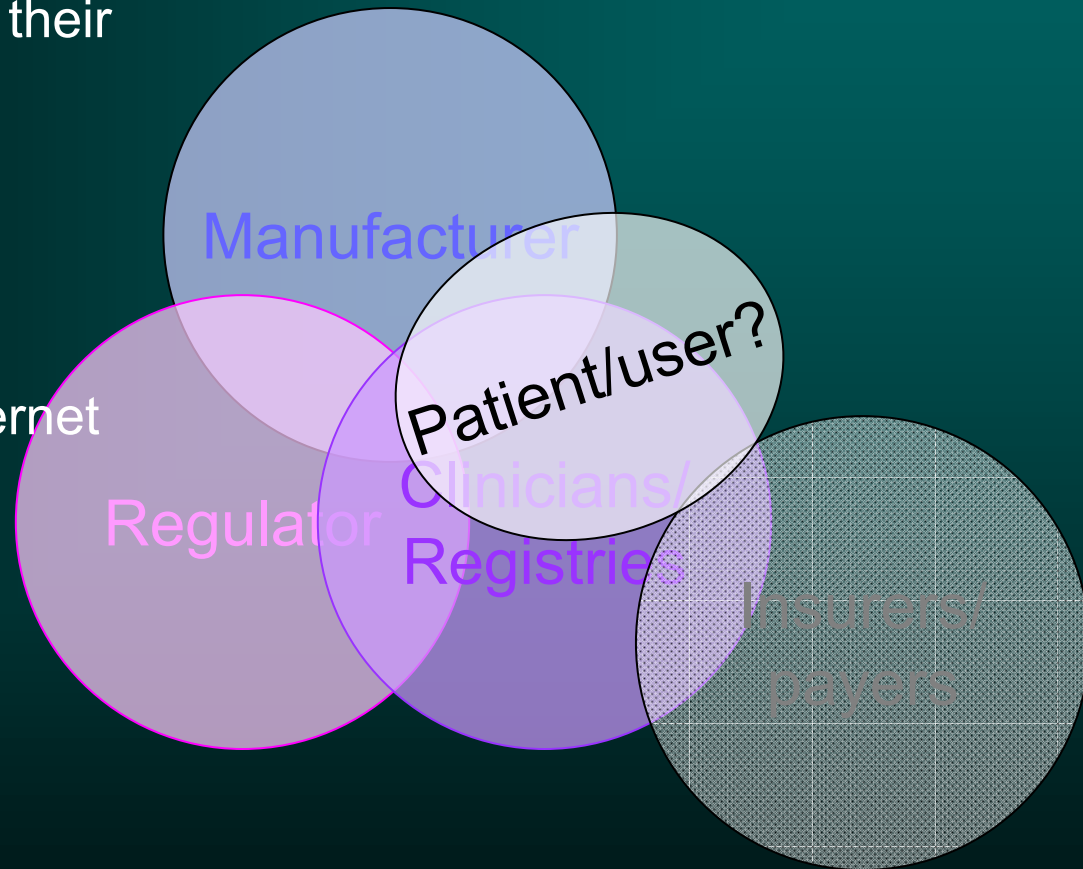
Bodies of post-marketing experience data



Bodies of post-marketing experience data

Patients typically “know”

- what they are told by their clinician
- device labeling (?)
- what their insurance/payer tells them (?)
- what they find on Internet



Bodies of post-marketing experience data

- Trend of growing demand for patient/public access to information on product conformity assessment and clinical evidence
- Growing awareness of, and demand for, patient access to technologies
- Patient choice of therapies and diagnostic tests



Conclusions and challenges

- Pace of innovation may overcome rate at which information becomes available
- Data \neq information \rightarrow how to improve?
- Need to acknowledge uncertainty and limitations \rightarrow what would it cost to reduce?
- No one party has access to all relevant information
- No single model for assessing safety and performance applies to all devices or all interventions/tests
 - Who decides?

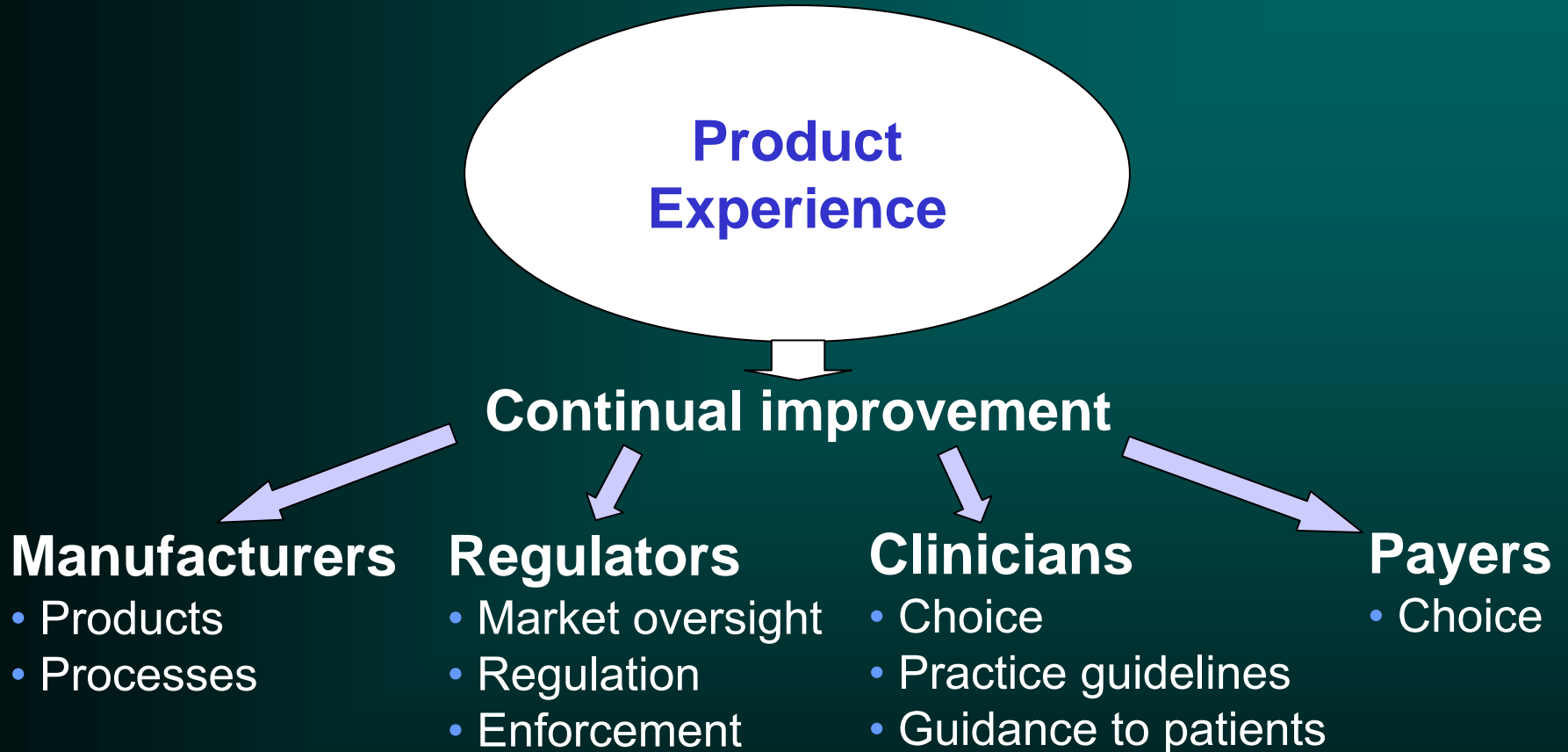


Conclusions and challenges

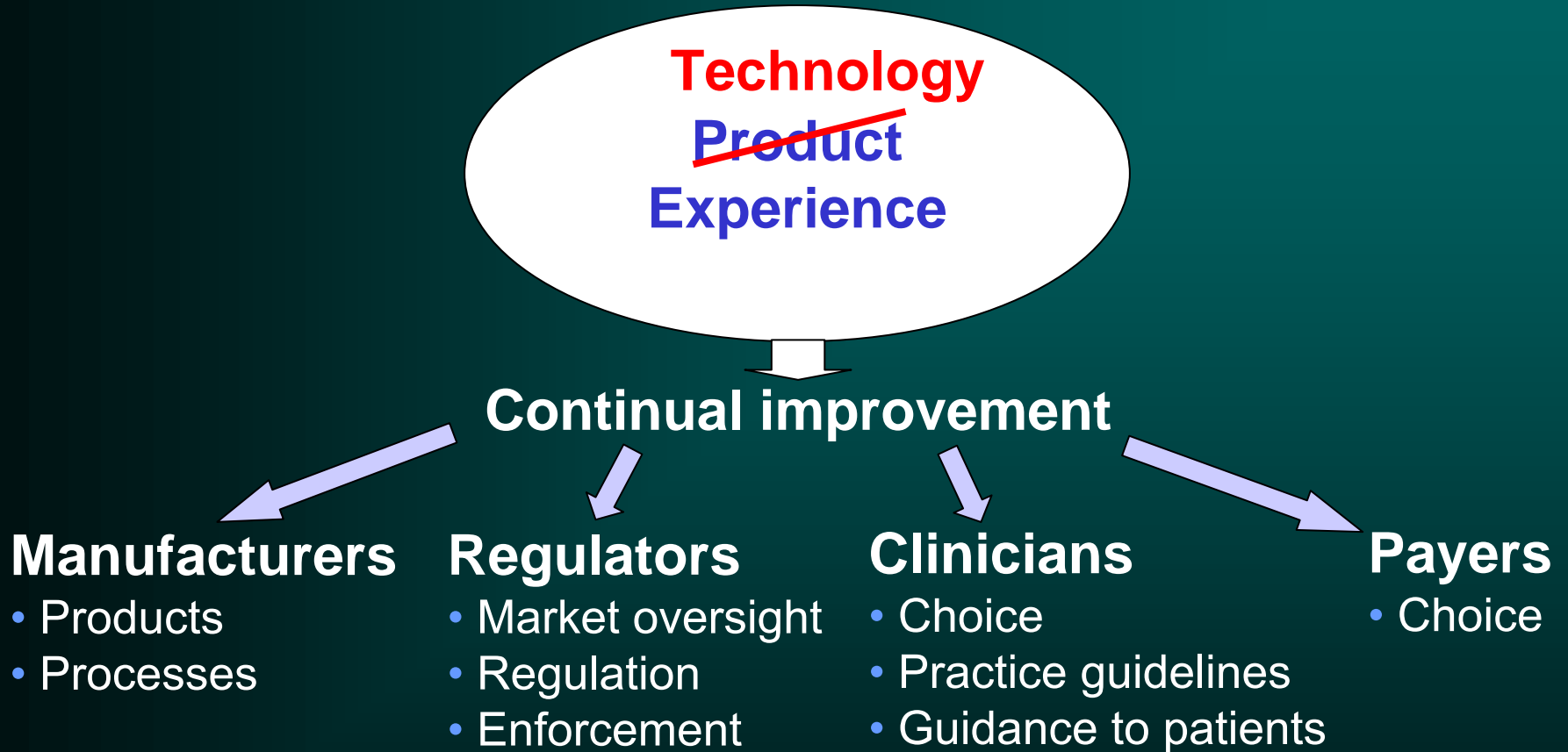
- Device safety and performance cannot be looked at in isolation
- Life cycle surveillance implies ongoing mechanism for post-marketing clinical follow-up and risk assessment
- How do regulatory policies affect continual improvement and innovation?
- Growing demand for greater public transparency
- Advent of new technologies will require new life cycle surveillance systems



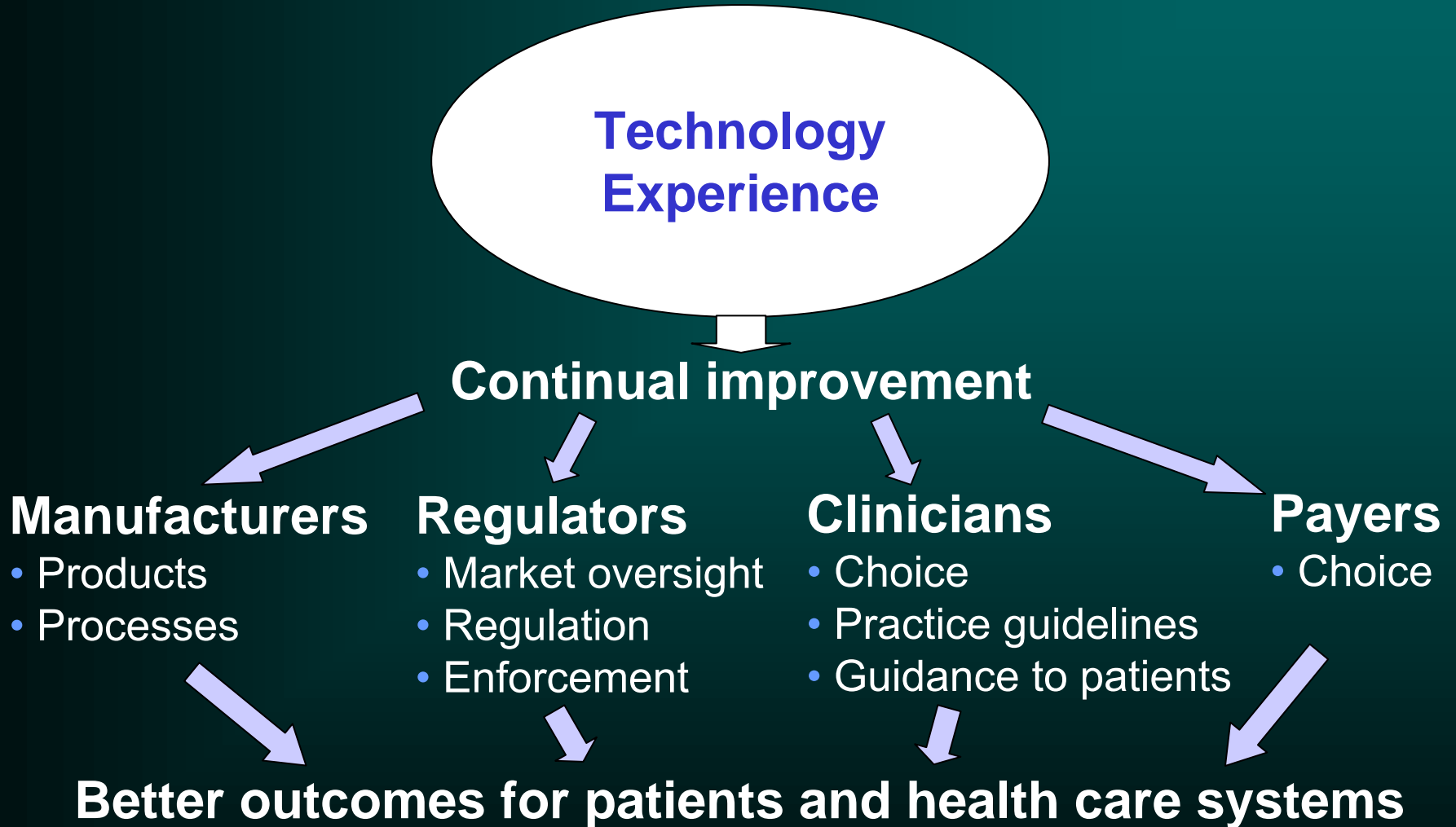
Uses of medical technology life cycle experience data



Uses of medical technology life cycle experience data



Uses of medical technology life cycle experience data



GHTF Vision

**Enhancing the health of the public worldwide
and facilitating innovation by harmonising the
global regulatory environment**

