

Regulatory and safety considerations: Premarket approvals and safety monitoring

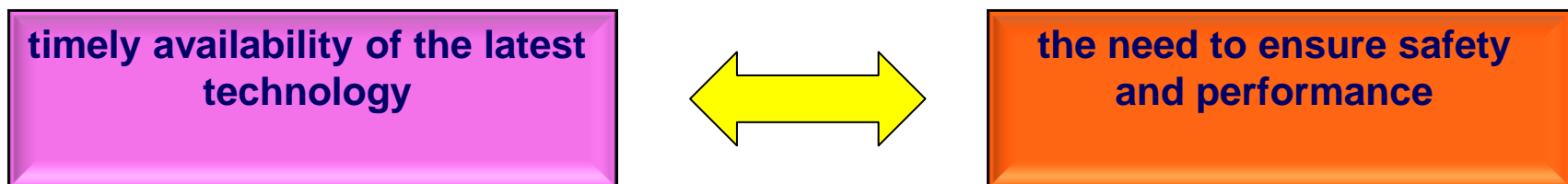
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**World Health
Organization**

Global MD regulatory landscape

- MD regulation is relatively new for many jurisdictions and the degree of harmonization is suboptimal, although improving
- In the rapidly evolving world of technology, the rate of change in MD design and development is high, and this provides a major challenge in maintaining a balance between



- Another issue is the number of products available, with the large number of variations within a product range

The GHTF

- 1993: senior regulatory officials and industry representatives from the EU, USA, Canada, Japan and Australia established a global consultative partnership aimed at harmonizing medical device regulatory practices: **GHTF**
- The GHTF was a voluntary group of representatives from national medical device regulatory authorities and the regulated industry
- The purpose of the GHTF was to encourage convergence in regulatory practices related to ensuring the safety, effectiveness/performance and quality of MD, promoting technological innovation and facilitating international trade.
- The primary way in which this was accomplished was via the publication and dissemination of **harmonized guidance documents** on basic regulatory practices.
- Guidance principles can be adopted/implemented by NRAs.



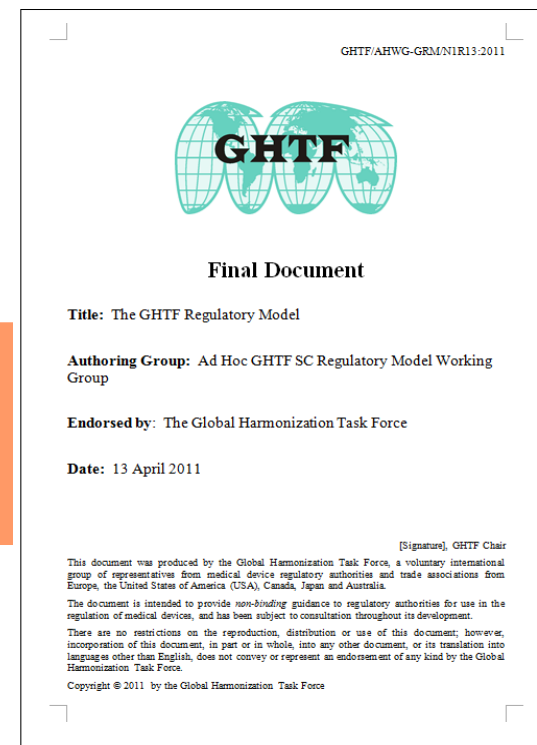
The GHTF

5 GHTF Study Groups

- Study Group 1 - Premarket Evaluation
- Study Group 2 - Post-Market Surveillance/Vigilance
- Study Group 3 - Quality Systems
- Study Group 4 - Auditing
- Study Group 5 - Clinical Safety/Performance

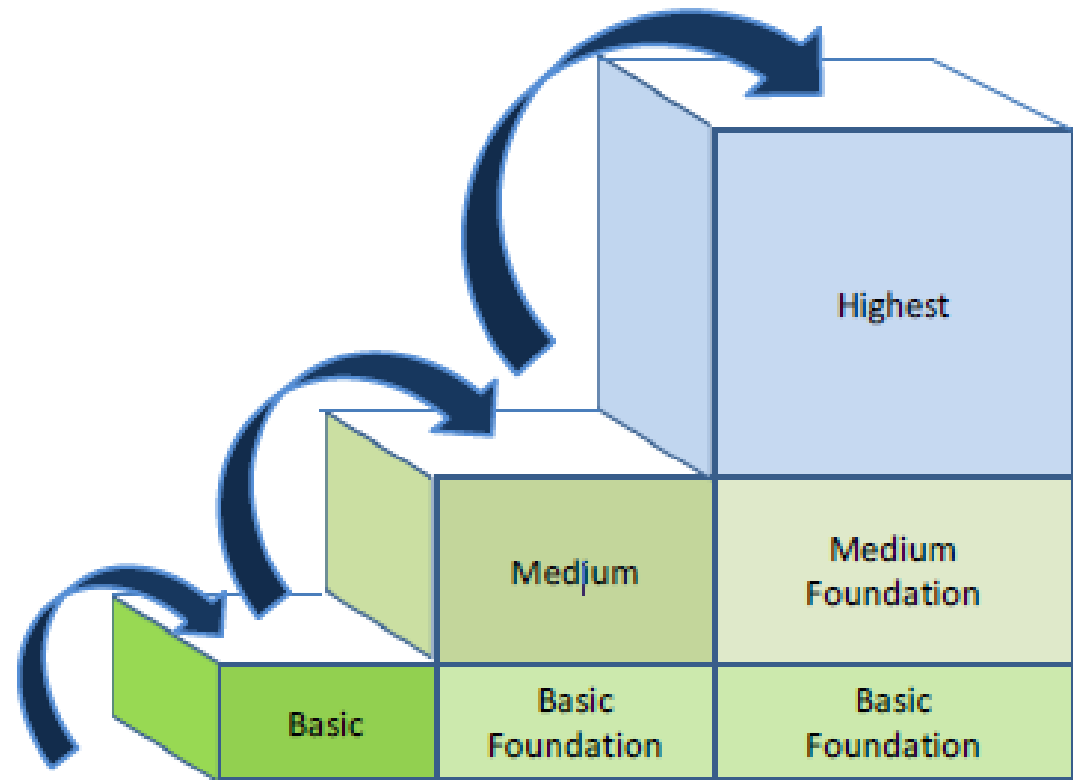
The GHTF regulatory model

- the core and basic elements
- supported by GHTF guidance documents

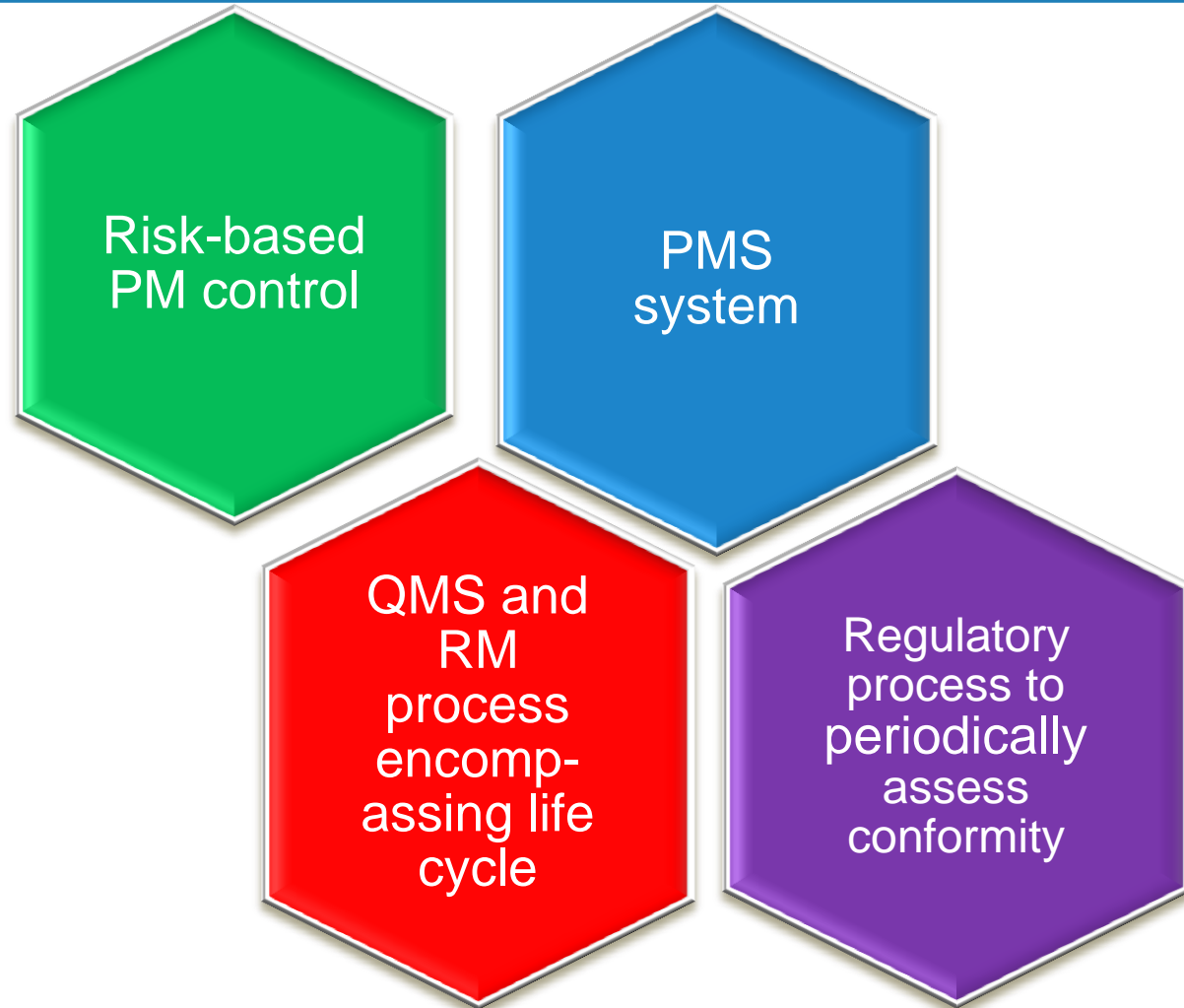


GHTF regulatory model

- The GHTF has developed a **risk-based** regulatory framework which covers all MD and is **flexible** enough to allow for technological development in the medical device field, so that legislation does not quickly become out-dated. (This was a problem with some of the earlier regulatory approaches, which regulated devices based on a list of those considered to be high risk.)
- The system also allows for **implementation in a staged approach**, in a manner most appropriate to the resources available to a regulatory authority.



GHTF regulatory model: key subsystems



These elements are interrelated and mutually interdependent.

Elements

All of these elements are complementary, and interlock closely with each other, to give strength to the regulatory framework

a clear definition of a medical device;

a set of EP of safety and performance, which constitute the basis of the regulatory system;

rules for the classification of a MD, based on risk, where Class D is highest risk, and Class A lowest risk;

implementation of appropriate QMS for the development and manufacture of MD;

procedures for conformity assessment of the manufacturer and the MD;

assessment by a National Regulatory Authority/Conformity Assessment Body;

registration of manufacturers and their MD; and

post-market monitoring once a device is placed on the market.

Roles and responsibilities

Regulator

- Licensing of Mx and distributors; listing of MD; requirements for placing on the market and compliance assessment; vigilance

Manufacturer

- Implement QMS; ensure compliance with Q, safety and performance requirements; establish procedures for post-market monitoring

Importer/ distributor

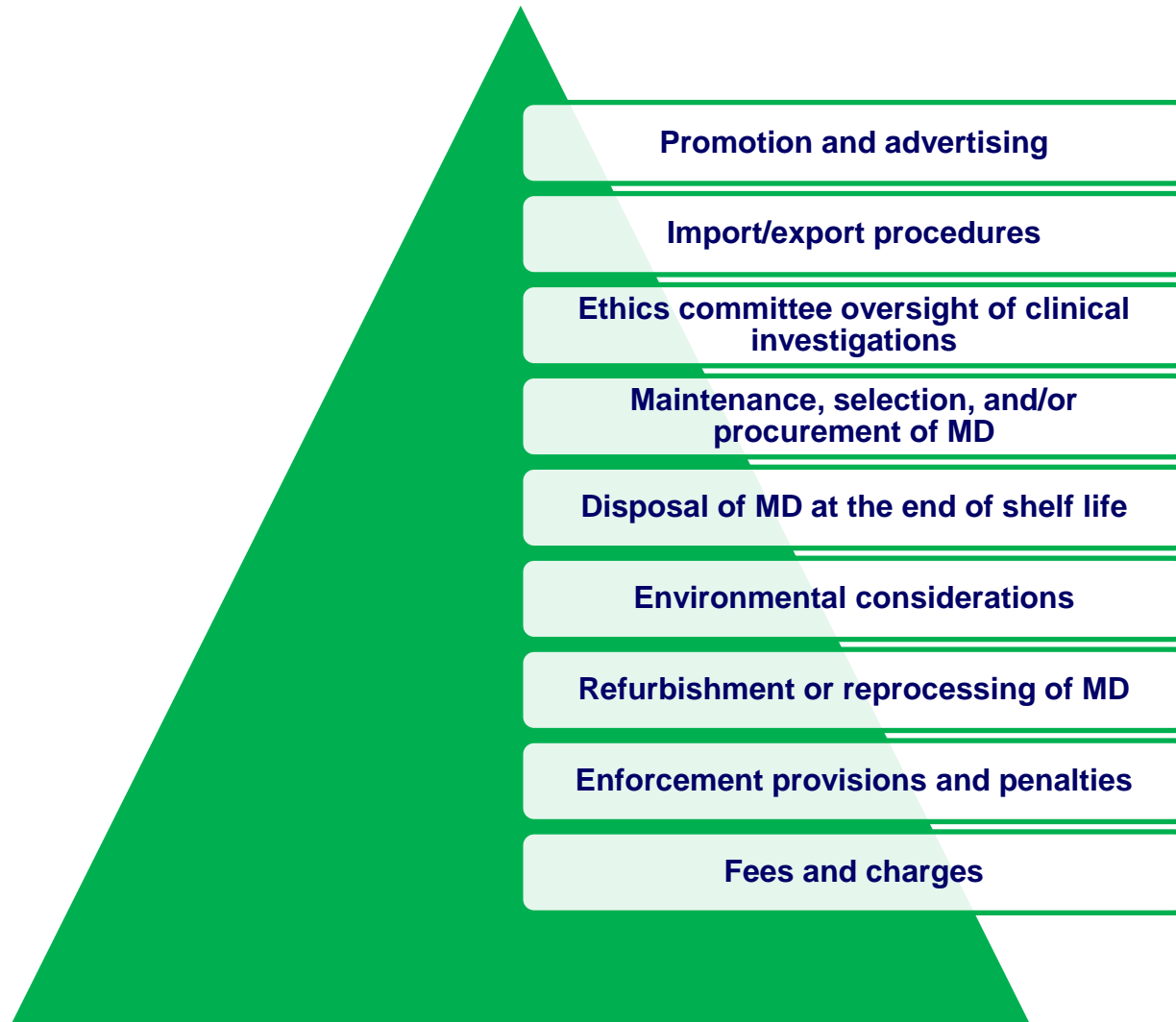
- Storage and transport; distribution records; interaction with NRA; vigilance

User

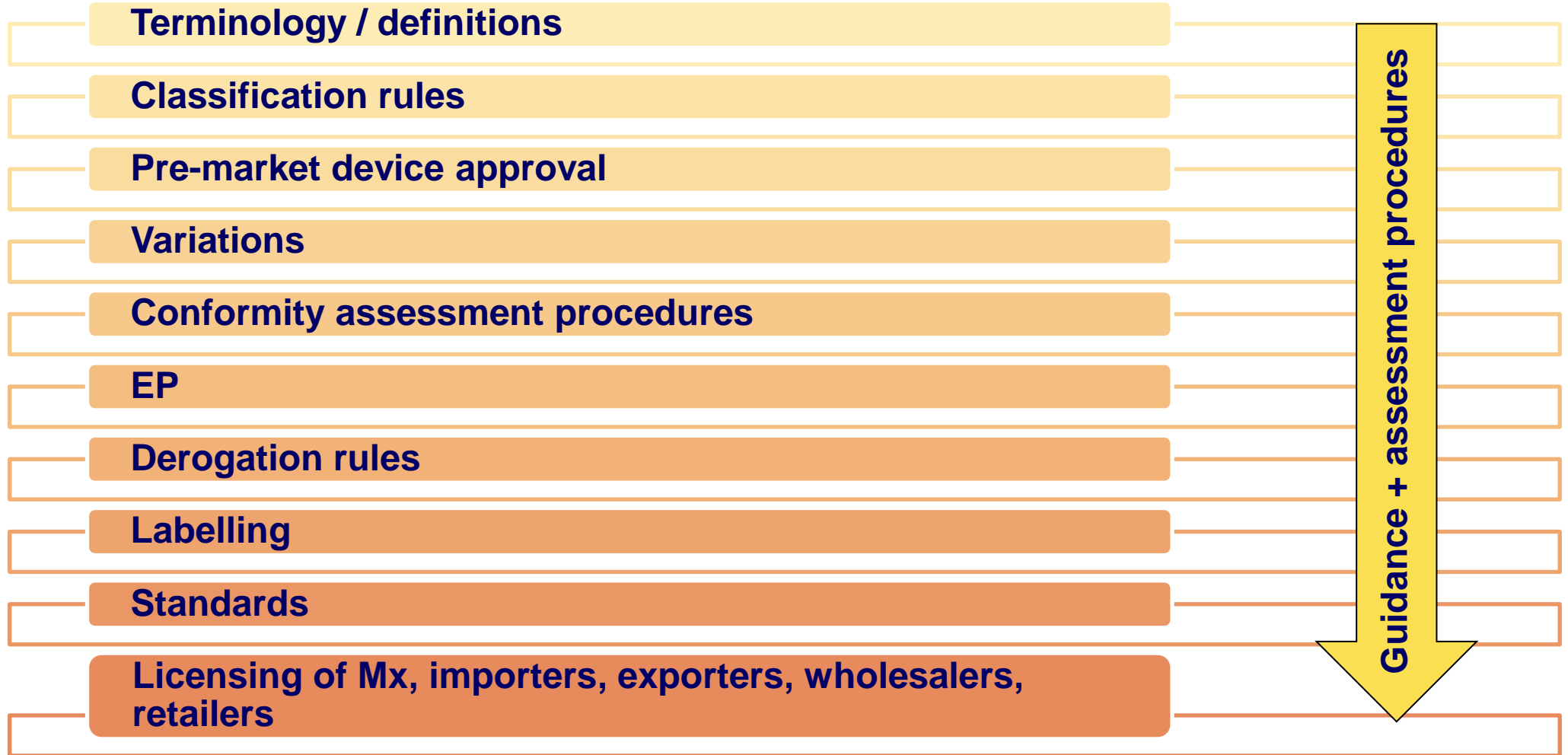
- Use according to intended use; inform the patient; vigilance



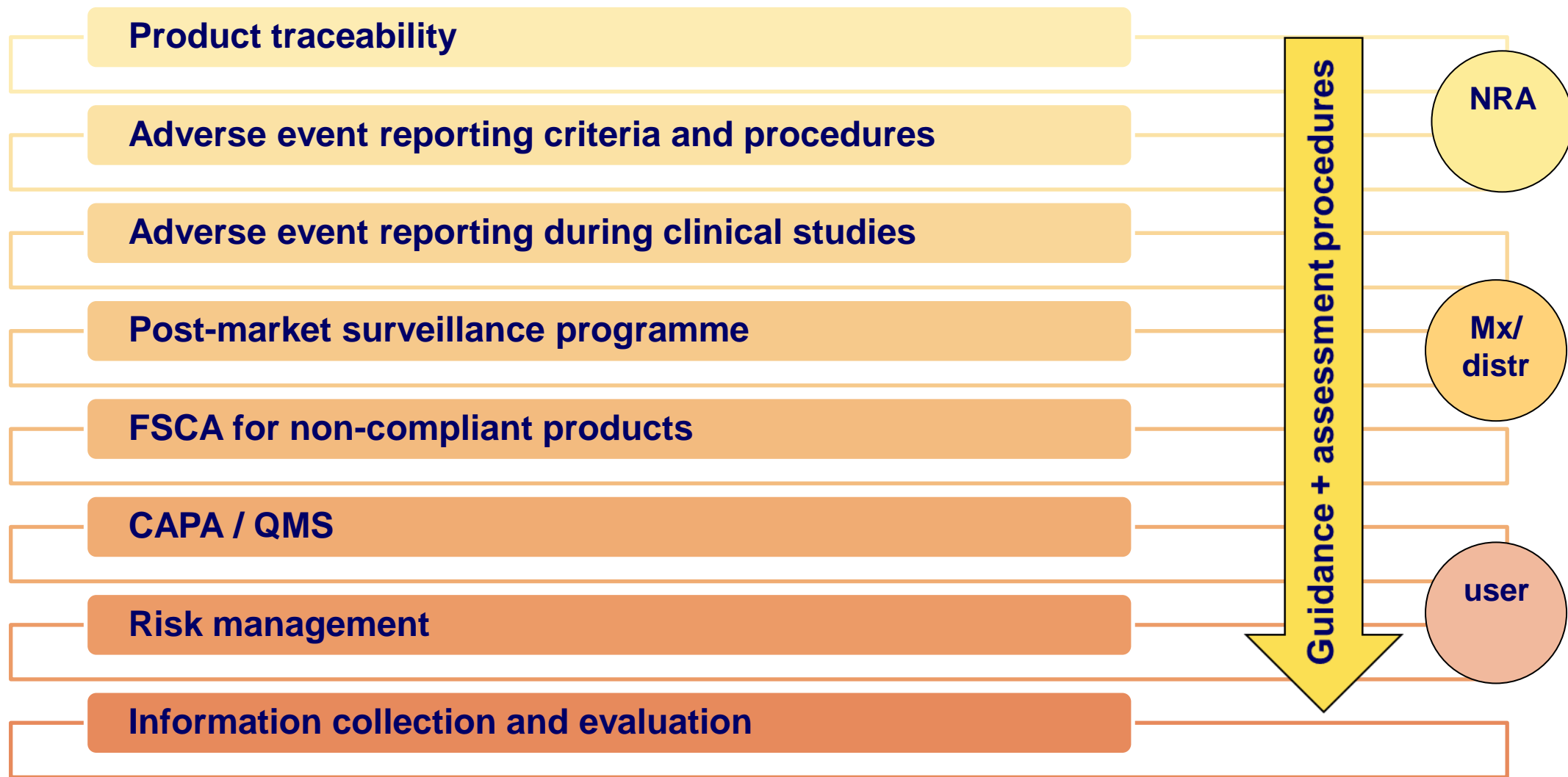
Other elements



Pre-market regulations: elements



Post-market regulations: elements



Post-market surveillance

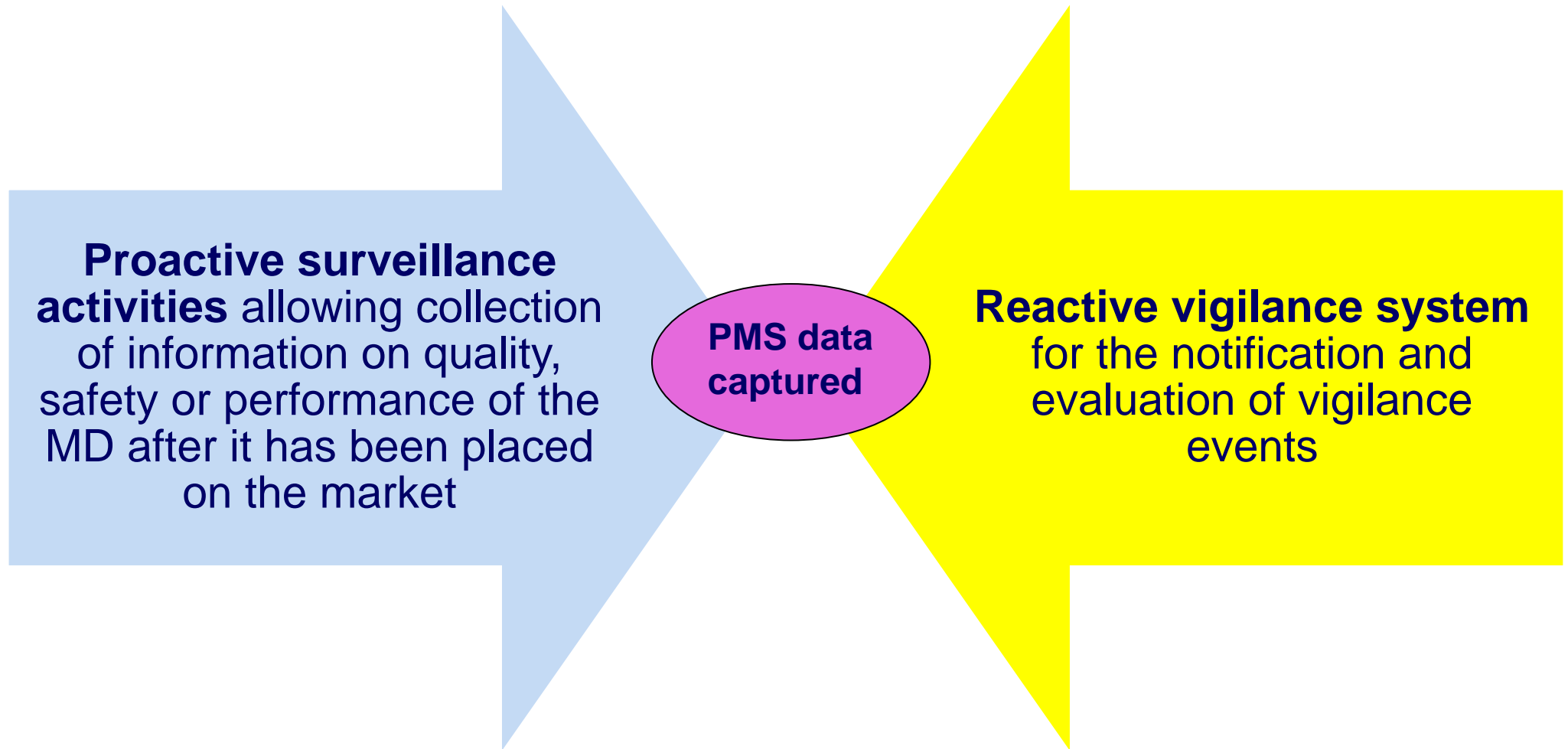
- The concept of an implemented and maintained PMS is embraced by several **internationally recognized standards like ISO** Quality Management and Risk Management Standards
 - ISO 9001:2000 , ISO 13485:2003 and ISO 14971:2000 comprise requirements on MD post-market activities to be performed by Mx

PMS provides **continuous feedback** on the products placed on the market and help the Mx to **maintain a high standard of product quality and customer satisfaction**

- By helping the Mx to obtain an understanding of the performance of the product placed on the market it also allows to **minimize exposure arising from incidents or potential incidents** through effective warning and product FSCA process and procedures
- As MD is placed on the market it is necessary to make sure that it **continues to meet all the safety and performance requirements and standards that were required for the PM approval.**
 - This is in addition to ensuring that any problems with the product are dealt with and reported through appropriate channels. This post-market phase of a MD is as important as the assessment and evaluation performed within the PM process.



Post-market surveillance: elements



Post-market surveillance: definitions

- **Abnormal use:** act or omission of an act by the operator or user of a medical device as a result of conduct that is beyond any reasonable means of risk control by the manufacturer.
- **Adverse event:** any event which meets all of the three basic reporting criteria as of IEC 60601-1-6:2004³.
- **Field safety corrective action:** an action taken by the manufacturer to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market. This may include
 - The return of a medical device to the manufacturer or its representative.
 - Device modification.
 - Device exchange.
 - Device destruction.
 - Advice given by the manufacturer regarding the use of the device (e.g. where the device is no longer on the market or has been withdrawn but could still possibly be in use).
- **Incident,:** any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or the instructions for use which, directly or indirectly, might lead or might have led to the death of a patient, or user or of other persons or to a serious deterioration in their state of health.
- **Use error:** act, or omission of an act, that has a different result to that intended by the manufacturer or expected by the operator.



Vigilance

- Vigilance programs are a range of activities undertaken by Mx, users and NRAs after any party becomes aware of adverse events, malfunctions, results of testing or other relevant vigilance information about a MD.
- Notification and evaluation of adverse events is known as the medical devices vigilance system. This system is based on a cooperative and effective exchange of information between all the parties involved.



Vigilance mechanisms

Mx' or users' submissions of vigilance reports to NRAs

Evaluation of reported adverse events

Dissemination of information, where appropriate, that could be used to prevent such repetitions, or to alleviate the consequences of such incidents

Modifications, where appropriate, of the MD or its removal from the market.

Reporting criteria

1. An event has occurred

- A malfunction or deterioration in the characteristics or performance.
- An incorrect or out of specification test result.
- The discovery of a design flaw during design review.
- An inaccuracy in the labelling, instructions for use and/or promotional materials.
- The discovery of a serious public health threat.
This can include an event that is of significant and unexpected nature such that it becomes alarming as a potential public health hazard, e.g. human immunodeficiency virus (HIV).
- Use error.
- Any other information that becomes available.



Reporting criteria

2. The manufacturer's device is associated with the event

3. The event led to one of the following outcomes:

Death of a patient, user or other person

Serious injury of a patient, user or other person

No death or serious injury occurred but the event might lead to death or serious injury of a patient, user or other person if the event recurs.

Exemption rules

- Whenever exemption rules are met, the adverse event does not need to be reported to the NRA by the Mx.
- Whenever certain rules* are met, the Mx will need to submit **periodic or summary reports** instead of individual adverse event reports.
- Those adverse events which are subjected to an exemption become reportable to NRAs if a change in trend (usually an increase in frequency) or pattern is identified.
 - Deficiency of a device found by the user prior to patient use
 - Adverse event caused by patient conditions
 - Service life or shelf life of the device
 - Malfunction protection operated correctly
 - Negligible likelihood of occurrence of death or serious injury
 - Expected and foreseeable side effects
 - Adverse events described in an advisory notice*



User error and abnormal use

- All potential use error events and potential abnormal use events should be evaluated by the Mx. The evaluation is governed by risk management, usability engineering, design validation, and CAPA processes. Results should be available, upon request, to NRAs.
- Use error which did result in death or serious injury or serious public health threat, should be reported
- Use error which did not result in death or serious injury or serious public health threat, need not be reported
- Use errors become reportable when a manufacturer:
 - Notes a change in trend (usually an increase in frequency), or a change in pattern of an issue that can potentially lead to death or serious injury or public health concern.
 - Initiates corrective action, to prevent death or serious injury or serious public health threat.

Other aspects for consideration

Reporting timelines

Reporting forms and guidance documents

Manufacturer' investigation of incidents

FSCA and FSN

CAPA

Information exchange

NRA assessment and monitoring

Thank you for your attention

Questions?

