Post-prequalification activities: changes notifications and post-market surveillance

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What happens after PQ

- Post-qualification also includes **mandatory manufacturer notification of change**s to the product or the quality management system.

- **Post-market surveillance** is a WHO post-qualification activity which includes reactive and proactive measures, through complaint reporting and post-shipment/pre-distribution lot testing.

Changes to a Prequalified IVD

- As part of the life cycle of an IVD, changes to a product, its manufacture and the QMS under which it is produced may become necessary

- A critical part of a manufacturer's QMS is a system to design, validate and implement changes, and to determine their potential to impact on the product quality, safety and/or performance

- Changes applied to an IVD must be made in compliance with the requirements for control of design change according to ISO 13485

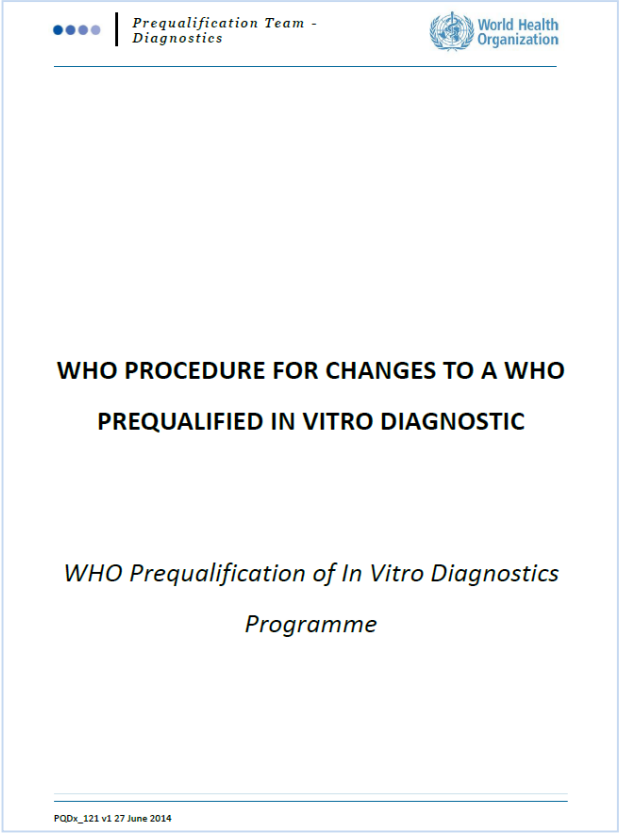
Changes to a Prequalified IVD

- **Guidance for manufacturers for reporting changes to a prequalified IVD:**

✓ Changes to the prequalified product or the manufacturing process

✓ Changes to the Quality Management System (QMS)

✓ And/or other reportable administrative changes



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WHO PROCEDURE FOR CHANGES TO A WHO PREQUALIFIED IN VITRO DIAGNOSTIC

WHO Prequalification of In Vitro Diagnostics Programme

PQDx_121 v1 27 June 2014

Determining the impact of a change

Cause of the change!

- Actions taken related to concerns arising from post market surveillance, including adverse events, recalls or complaints
- Development of state of the art
- Changes to a manufacturing process, facility or equipment
- Changes to the design or composition of the prequalified IVD
- Changes to the organization of the manufacturer
- Changes to the intended use and/or test procedure
- Changes necessitating new clinical and/or analytical data that raise new issues of safety and performance

Determining the impact of a change

Impact of the change!

- Introduces new hazards that have not been previously addressed
- Adversely affects the risk associated with existing hazards
- Alters the details of any of the information submitted for prequalification (related to dossier, manufacturing site(s) inspection, or laboratory evaluation), such as the intended use and/or compliance with the Essential Principles
- Affects the continued compliance of the QMS with the relevant standards

Process for reporting a change

- **Reporting to WHO:**
  Let us know in advance!

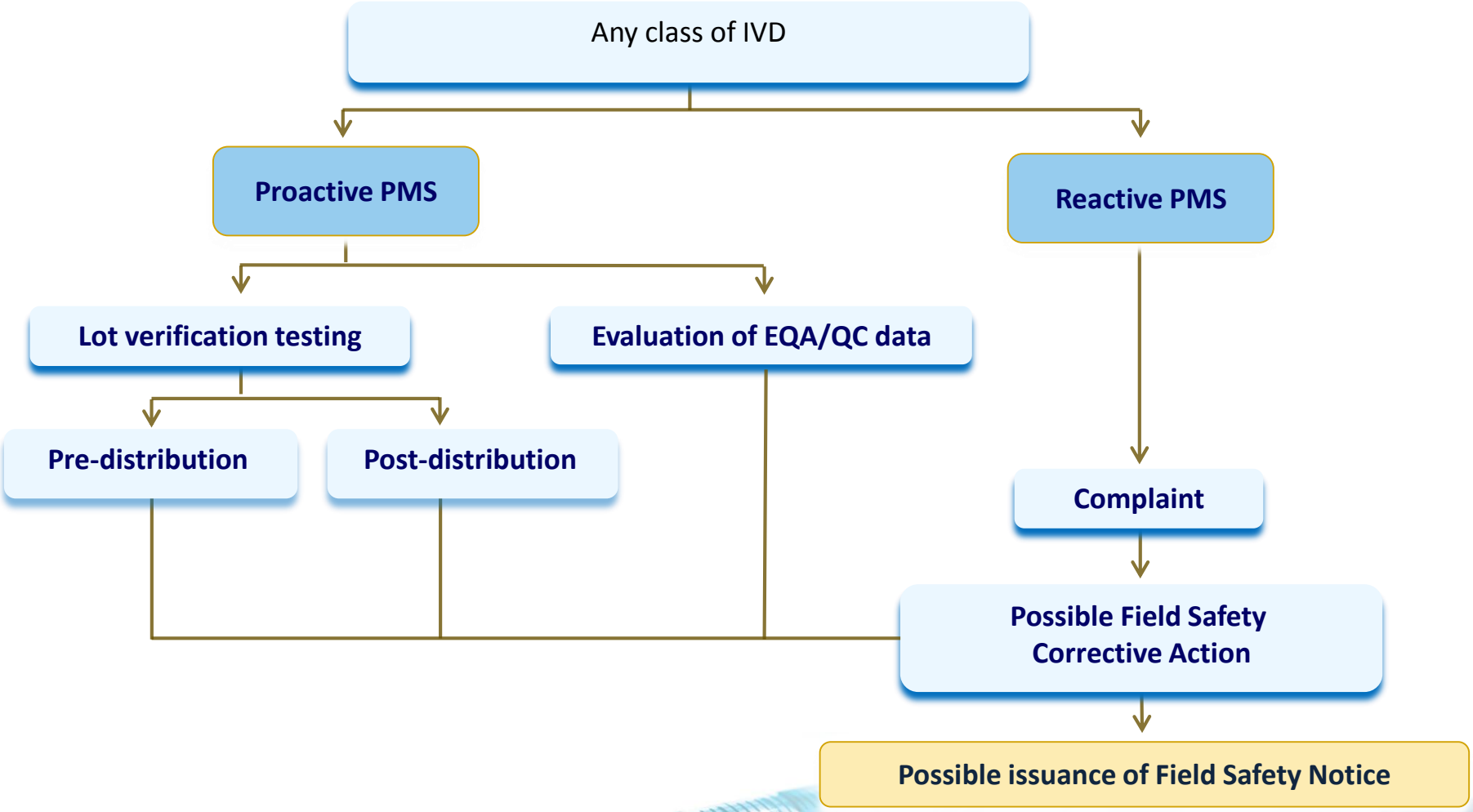
- **Assessment of submitted PQDx Change Report Forms and documentation:**
  Information undergoes full technical review

- **Outcome of assessment of the change report:**
  Outcome of the assessment is communicated to the manufacturer and where a change is accepted by WHO, the manufacturer can implement the change

Post-market surveillance

(complaint reporting)

WHO post-market surveillance of IVDs



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What end-users should look for

- When test result was incorrect
  - ✓ Recently diagnosed HIV+ individual is re-tested & found to be HIV-
  - ✓ EQA data shows incorrect test result across multiple testing sites for the same assay

- Intuition! When something doesn't seem right
  - ✓ Any differences in the product, e.g. changes to the IFU, packaging looks damaged
  - ✓ For RDTs

    Slow migration, incomplete migration, streaks, high background
  - ✓ Running out of test devices or buffer more quickly than usual

Examples of complaints related to IVDs

Serious
An individual is diagnosed as HIV+ after transfusion of a blood product. The blood donation was screened as negative by an HIV-1/2 RDT.
A HIV+ individual reporting for ART initiation was re-tested to confirm their HIV diagnosis. The re-testing results are HIV negative.
A healthcare worker operating a small instrument-based test at POC couldn't remove a cartridge and inserted a knife into the instrument and was electrocuted, resulting in death.

Examples of complaints related to IVDs

Moderate
The invalid rate for an RDT exceeds 5%, for any reason.
Higher than usual background which may or may not obscure reading window and prevent reading of results.
Greater than expected discrepant rate between assay 1 and assay 2, suspected reduced specificity of assay 2.

Examples of complaints related to IVDs

Mild
The packaging of a single use device is labelled with the caution 'do not use if the packaging is opened or damaged'. Prior to use, obvious damage is observed and the device is not used.
A component labelled as lyophilized is found to be fluid, this is discovered by the user prior to use. Entire test kit must be discarded
Control line does not appear, test result is invalid and new device is used.
Desiccant has changed colour/density. Device is discarded and a new device used.

Complaints: how to document

- **Usual records kept at testing sites**
  - Assay name
  - Lot number, expiry date
  - Version number and language of IFU
  - Operator
- **Any additional testing results to support the investigation**

> Accurate denominator data
  - How many tests performed per assay per site in total
  - How many invalid test results per assay per site

> What type of invalid results
  - Absence of control line
  - High background
  - Incomplete migration
  - Lack of buffer

Complaints: how to report

- **Verify**
- Storage conditions
- Any breaches of packaging
- Changes to desiccant
- IFU matches SOP/training

- **Send**
- To manufacturer for **all categories** of complaints
- To WHO and your NRA, for any serious or moderate adverse event

ANNEX 3 – IVD COMPLAINT REPORTING FORM

USER COMPLAINT FORM FOR REPORTING COMPLAINTS AND/OR ADVERSE EVENTS RELATED TO IN VITRO DIAGNOSTICS

Send to: Manufacturer
If serious or moderate adverse event, report to the relevant National Regulatory Authority and WHO Prequalification of In Vitro Diagnostics Programme
Email: diagnostics@who.int

Report Number:	Date received:

1. Contact details of the reporting person/organization

Name of person/organization:	Street Name and No.:
City and postcode:	Country:
Telephone:	Fax:
Name and position of contact person:	Email of contact person:

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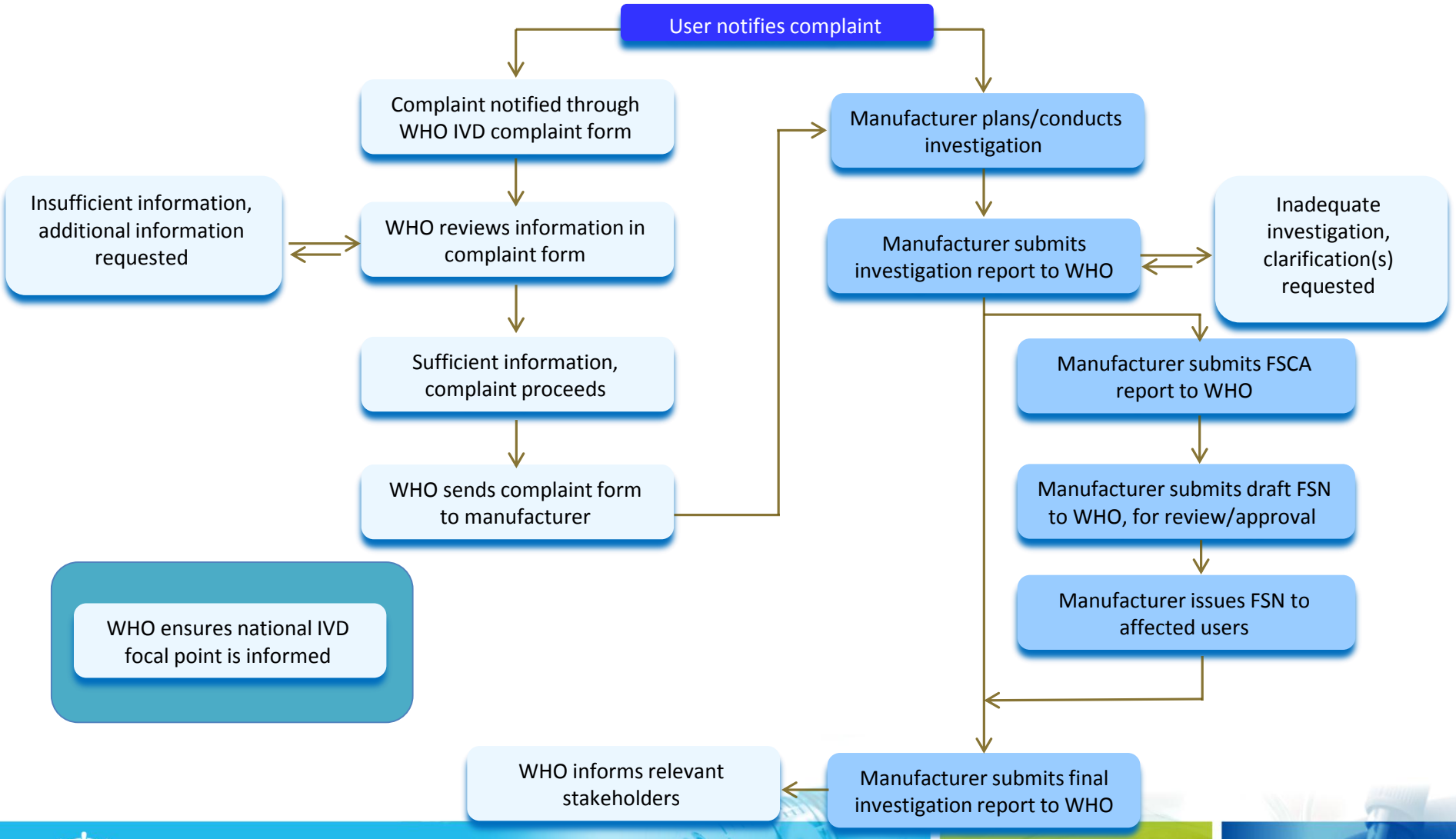
For complaints reported to WHO

- **Expect manufacturer to submit an initial investigation report within 15 days to WHO**

- **WHO will review**

- Processes for
  - ✓ Dealing with nonconforming product (e.g. root cause analysis);
  - ✓ Corrective actions taken; and
  - ✓ Application of risk management principles.
- What contributed to this nonconformance (product failure)?
- Was the complaint handling procedure adequate?
- Were the appropriate personnel involved?

Procedure for complaint handling



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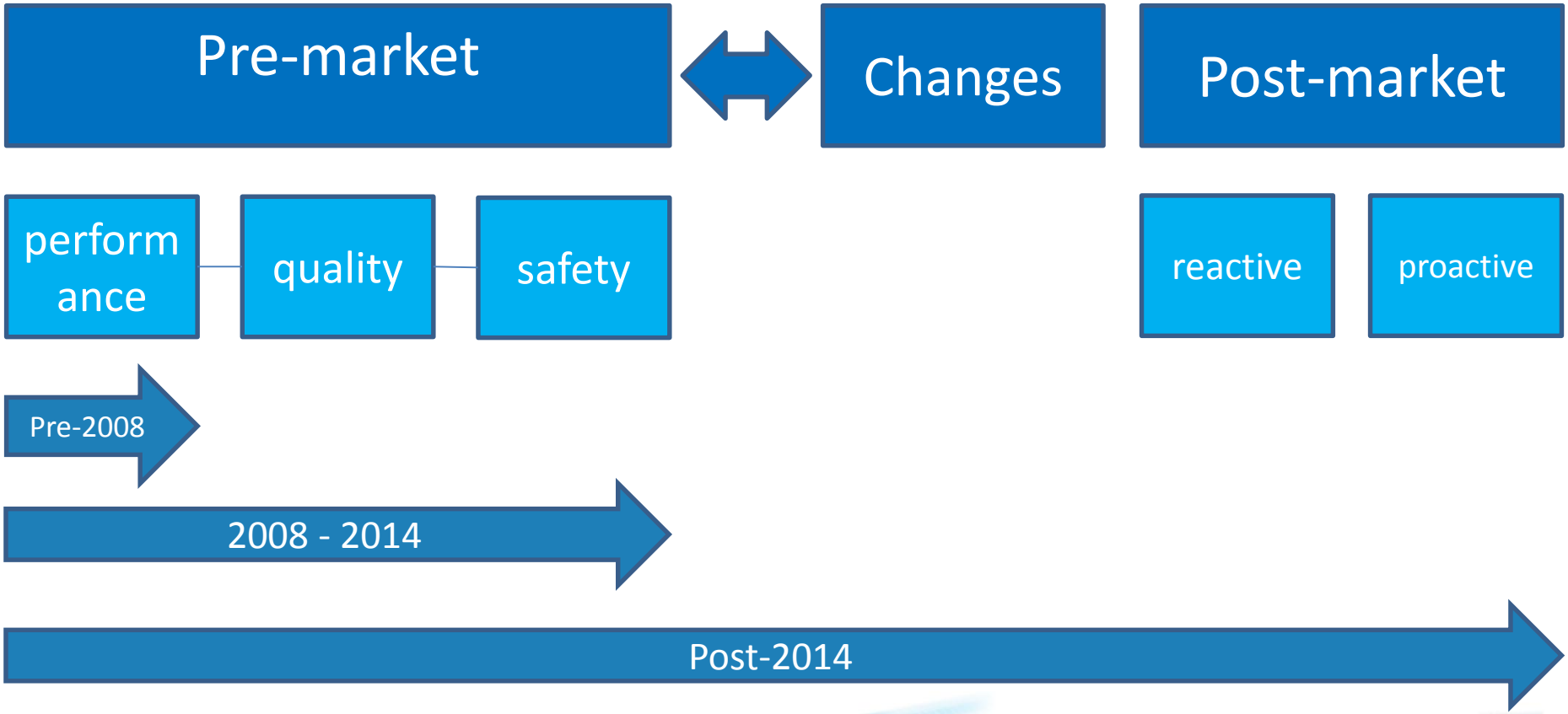
PQ in a regulatory framework



Спасибо!

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