The Implementation of ICH Q12 in the EEA & the PQS Effectiveness Pilot Inspections Programme, March 2026-March 2027

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Please note that the statements, views and opinions expressed by KOD today are his own personal ones and should not be taken to be the views or opinions of the HPRA, EMA, PMDA or the EEA-GMDP Inspectors Working Group.

The Implementation of ICH Q12 in the EEA

While ICH Q12 was finalised by ICH in November 2019, it was only implemented in the EEA in January 2026.

- This was because changes had to be made to the EU variations framework, e.g., to introduce the concept of the PLCM (Product Lifecycle Management) document.
- The revised EU Variations Guidelines were published on September 22nd, 2025 - Official Journal of the EU - C/2025/5045
- The revised EU Variations Guidelines entered into force in the EU on January 15th, 2026.
  - All variation submissions from this date, for National, MRP, DCP and CAP Marketing Authorisations, should follow the revised guidelines.
  - Additional guidance and Q&As have been published by EMA to support implementation.

The Implementation of ICH Q12 in the EEA

The revised EU Variations Guidelines refer to the use of Additional Regulatory Tools:

- Design Space – this relates to ICH Q8/Q11/Q14
- Post-Approval Change Management Protocol (PACMP) - this relates to ICH Q12
- Product Lifecycle Management document (PLCM) - this also relates to ICH Q12

These tools rely on enhanced pharmaceutical development approaches (QbD) and increased product and process understanding.

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A core requirement for use of the ICH Q12 tools is the need for an effective Pharmaceutical Quality System (PQS) to be in place, especially in relation to change management.

- ICH Q12: "***An effective PQS*** as described in ICH Q10 and compliance with regional GMPs ***is necessary for implementation of this guideline***."
- ICH Q12: "In particular, management of manufacturing changes across the supply chain is an ***essential part of an effective change management*** system."
- ICH Q12: "An ***effective change management system*** supports the principles of this guideline."

The Implementation of ICH Q12 in the EEA

- **Note**: The use of the Product Lifecycle Management document (PLCM) in Marketing Authorisations is a key element of the implementation of ICH Q12 in the EEA:
- This should serve as a global tool for harmonised lifecycle management.
  - Its aim is not to reduce the number of post-approval changes/variations, but to facilitate a harmonised approach across regulators/regions.
  - The benefit of this for pharmaceutical companies is predictability & certainty – rather than a reduction in the number of variation submissions.

The Implementation of ICH Q12 in the EEA

In 2024, discussions started between the EMA, the GMP Inspectors and the Pharmaceutical & Biological Assessors in the EEA in relation to the **PQS Effectiveness** elements of ICH Q12:

- **Question**: How should PQS effectiveness be assessed, especially in relation to risk-based change management?
- **Question**: How and where should PQS effectiveness be documented?
- **Question**: How should PQS effectiveness be communicated between the GMP Inspectors and the Pharmaceutical & Biological Assessors?
- **Question**: How can it be assured that any solution for the above is low burden and relatively simple?

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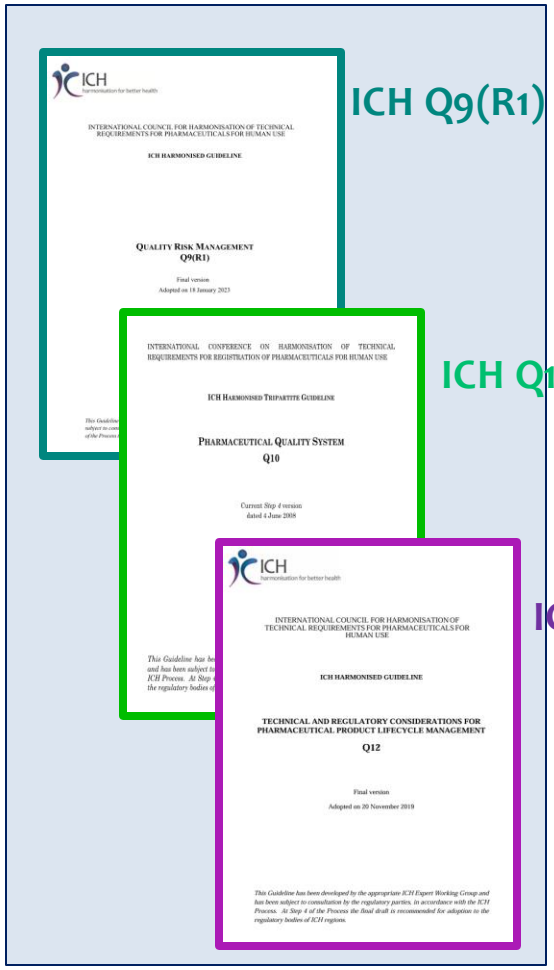
These issues were worked on by the GMDP-Inspectors Working Group in 2024-2025 and a **proposed solution** was developed for:

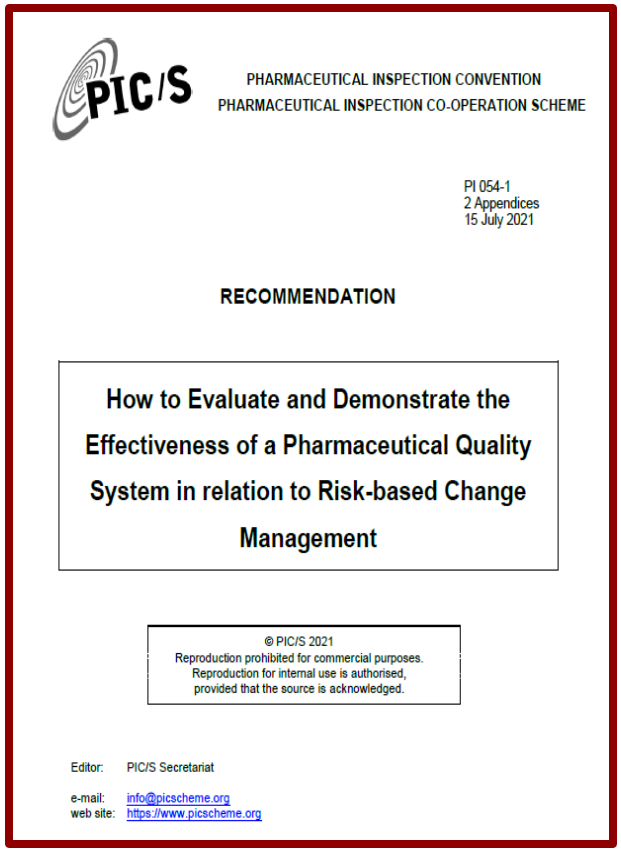
- a) The evaluation (by EEA GMP Inspectors) of manufacturing site PQS Effectiveness with regard to Risk-based Change Management, and
- B) the communication of PQS Effectiveness in this area by the GMP Inspectors to the Assessors in the EEA

A PIC/S paper from 2021 on PQS Effectiveness is at the core of the solution for implementing ICH Q12 in the EEA

The PIC/S Paper on PQS Effectiveness, July 2021

This paper builds upon the guidance in the EU & PIC/S GMPs, as well as in ICH Q9, Q10 & Q12, all of which stress the importance of PQS Effectiveness.





This PIC/S paper provides practical guidance on evaluating and demonstrating the effectiveness of a PQS in relation to risk-based change management.

This is in recognition of the fact that the EU and PIC/S GMP Guides require companies to demonstrate the effectiveness of their PQS and apply QRM principles to change control activities.

The PIC/S Paper on PQS Effectiveness
July 2021

'How to Evaluate and Demonstrate the Effectiveness of the Pharmaceutical Quality System with regard to Risk-based Change Management',

- The paper contains a tool (checklist) that GMP Inspectors can use when inspecting a site's change management activities

  …. and the industry can use it too, when seeking to make sure that their change management processes are mature and risk-based.

- The paper supports the implementation of ICH Q12, 'where **mature risk-based change management within an effective PQS is considered foundational** to enable greater regulatory flexibility in reporting of post-approval changes.'

- Application by a manufacturer of the PIC/S guidance '**will provide evidence of the effectiveness of their PQS** in relation to risk-based change management', where '**maturity** in change management may support… the **regulatory flexibilities** discussed in ICH Q12.'

- This should lead to **'the timely management of risk… continual improvement and innovation'.**

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These are fairly strong statements by regulators…

… and they show a clear way forward for companies seeking to use the regulatory tools offered by ICH Q12

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- This should lead to **'the timely management of risk… continual improvement and innovation'.**

The EEA Pilot Inspections Project on PQS Effectiveness

March 2026 - March 2027

The EEA's PQS Effectiveness Inspections Pilot Project

- This pilot is about **testing the proposed solution** for documenting and communicating (to Assessors) PQS effectiveness in relation to risk-based change management at manufacturing sites.
- This would provide Assessors with **evidence** to support the approval of the use of the ICH Q12 tools by companies, via their assessment of marketing authorisation variations.
- This proposed solution makes use of **two existing tools**:
  - *a) the EEA GMP Cert, and*
  - *b) the 2021 PIC/S paper on PQS Effectiveness.*
- The **pilot** involves performing a number of GMP inspections at pharmaceutical companies during 2026/27:
  - The Inspectors would inspect site **change control/change management** processes against the requirements of the EU Guide to GMP, using the PIC/S PQS paper as supportive guidance.

Goals of the Pilot Project

- **The goals of this pilot are twofold:**

  - to evaluate the usefulness of the PIC/S paper as a tool to be used in GMP inspections to demonstrate PQS effectiveness in relation to risk-based change management at manufacturing sites.

  - to confirm that the PIC/S paper, together with the EEA GMP Certificate, provides a solution for communicating the PQS effectiveness of the manufacturing sites to the Assessors who may be assessing ICH Q12-related marketing authorisation and variation applications.

How will the manufacturing sites be included in the pilot?

- **EU/EEA supervisory authorities can nominate sites for inclusion in the pilot**, and this can include routine inspections planned for 2026/27. (Note: the inclusion of routine GMP inspections is encouraged, as it helps ensure there is no bias introduced into the pilot).
- **Marketing Authorisation Holders or individual Manufacturers may nominate sites for inclusion in the pilot**, if there is a planned ICH-Q12 related variation for submission in the EEA from March 2026 onwards.
- **Marketing Authorisation Holders or individual Manufacturers may also nominate sites for inclusion in the pilot** that are not linked with any planned ICH-Q12 related variation.
  - *This is because PQS Effectiveness is a GMP requirement, regardless of any Marketing Variation submission.*
- **Note:** It is anticipated that, for the pilot, most manufacturing sites will be in the EEA; third country sites my also be included if they are in the inspection plan of an EEA authority for 2026/2027.

What kinds of manufacturing will sites be included in the pilot?

Sites to be included:

- Manufacturing sites producing sterile and/or non-sterile finished products.
- Biological API sites.
- Chemical API sites, QC-only sites and Batch Certification-only sites may also be proposed.
- **Note**: The pilot inspections will be performed at sites that manufacture EU/EEA-authorised medicinal products, or APIs which are supplied to the EU/EEA market.
- The medicinal products may have national, MRP, DCP or CAP marketing authorisations, and the manufacturing sites may be in the EEA or in third countries.

Sites to be excluded:

- ATMP manufacturing sites.
- Medicinal gas sites manufacturers.
- Radiopharmaceutical manufacturers.
- Sites that are under Compliance Management in the EEA.
- Sites that have Statements of Non-compliance and restricted GMP Certs issued by an EEA authority.

Areas to be inspected during the pilot inspections

- **The following areas should be inspected at least:**
  - The company's overall approach to Change Management.
  - How QRM is used in the company's approach to Change Management.
  - How Change Management (and QRM activities pertaining to changes) are documented within the site PQS.
  - Change Control procedure(s) and forms.
  - Specific Change Controls (regulatory impacting and non-regulatory impacting changes).
  - Risk Assessments and other QRM activities relating to change controls
  - How changes are reviewed in Product Quality Reviews (PQRs).
  - To what extent the site's approach to change management reflects the provisions of the PIC/S paper.

Use of the PIC/S Paper during the pilot inspections

- **In relation to how the PIC/S paper will be used during the pilot inspections:**
  - It is not the intention that all individual change controls would be reviewed during the pilot inspections against every single check-list item listed in section 5 of the PIC/S paper.
  - The intention is rather that the site change control process would be reviewed holistically against the four general areas listed in section 5 of the PIC/S paper, namely:
    - *Section 5.1: Change Proposals - Determination of when a change is needed*
    - *Section 5.2: Change Risk Assessments*
    - *Section 5.3: Change Planning and Implementation*
    - *Section 5.4: Change Review and Effectiveness*

Duration and No. of Inspectors per Pilot Inspection

It is anticipated that these may be relatively short inspections, lasting half a day or one day.

- They may just involve one GMP Inspector, and the relevant Inspectorate will decide whether or not a GMP certificate would be issued following the inspection.
- Routine GMP inspections, when included in the pilot, will (by definition) likely be longer in duration and will possibly have more Inspectors per inspection.
  - In these cases, GMP certs would be issued after those inspections, in cases where the manufacturers were found to have an acceptable level of GMP compliance.
- **Note:** Assessors may be invited by the relevant GMP Inspectorate to participate in pilot inspections.

Fees for the pilot inspections:

- The relevant Inspectorates will decide what fees to charge the sites, as per their own national procedures.

Post-inspection Questionnaire

- **A short, pilot-specific questionnaire will be completed by the lead Inspectorate of a pilot inspection and sent to a Pilot Coordinating Group; this will provide information such as:**
  - The type of site inspected, the scope of the inspection, whether it was a full or a partial inspection of the site.
  - The level of pre-inspection and post-inspection effort that was required.
  - A brief summary of any findings, observations and deficiencies.
  - A statement about whether PQS effectiveness with respect to risk-based change management was verified.
  - How the PIC/S paper was used during the inspection.
  - The views of the Inspector(s) in relation to using the PIC/S paper as useful guidance when doing future GMP inspections, post-pilot.
  - The views of the Inspector(s) in relation to whether the PIC/S paper should be incorporated in some way into the EU Compilation of Union Procedures.
  - The views of the Inspector(s) in relation to statements that could be added to GMP certs and inspection reports about site PQS effectiveness in the future.

Collaboration with other regulators…

The EMA and the Pilot Coordinating Group have had discussions with other regulatory authorities outside the EEA in relation to this pilot:

- The discussions involved MRA and ACCA partners, and were useful in that, in addition to discussing the EEA pilot, the following points were also addressed:
  - MRA/ACCA partners' approaches to PQS effectiveness evaluations and ICH Q12 implementation.
  - The potential for harmonised approaches to PQS effectiveness evaluation going forward.
  - How to deal with situations where a manufacturing site, located in an MRA/ACCA partner country, is involved in an EEA ICH Q12-related marketing authorization variation application.

Overall Learnings & Recommendations from the Pilot Project…

The Pilot Coordinating Group will:

- Document the learnings from the pilot inspections, for consideration by the GMDP-IWG. These also will include learnings from any routine GMP inspections that formed part of the pilot.
- Provide recommendations in relation to future PQS inspection design (e.g. in terms of their duration, no. of GMP inspectors, the level of effort needed to perform them, etc.).
- Provide recommendations in relation to using (or not using) statements on GMP certs and/or inspection reports about site PQS effectiveness.
- Provide recommendations in relation to the future use of the PIC/S paper in routine GMP inspections, post-pilot.
- Provide recommendations in relation to whether the PIC/S PQS paper should be incorporated into the EU Compilation of Union Procedures.
- **All of the above has implication for GMP inspections by EEA Inspectorates post-pilot… these implications will be considered by the GMDP-Inspectors' Working Group after the pilot.**

Next steps and points to be further discussed…

Next steps:

- The Pilot Coordinating Group will evaluate all nominations and applications for pilot inspections and discuss those with the relevant Supervisory Authorities in the EEA
- The pilot inspections will then begin
- Three companies have so far signaled their intent to volunteer for pilot inspections

Points to be further discussed:

- Potential statements regarding PQS effectiveness on GMP certificates and inspection reports.
- Inspection report format.
- How to handle cases whereby a site's PQS may not be deemed effective with respect to risk-based change management.

A few words of encouragement…

The industry is encouraged to participate in this pilot:

- The pilot is designed to test the proposed solution developed by the GMDP-IWG for the easy implementation of ICH Q12 in the EEA.
- This solution makes use of two existing tools: a) the EEA GMP Cert and b) the PIC/S paper on PQS Effectiveness with regard to Risk-based Change Management.
- The PIC/S paper serve as supportive guidance for the Inspectorates (and for the Industry) – and importantly, it does not introduce any new GMP requirements.
- This is intended to be a low-burden solution for all involved parties… the GMP Inspectorates, the Assessors, and Pharmaceutical Companies marketing medicinal products for human use in the EEA.
- Participating in the pilot project gives companies direct involvement in the proposed solution.

Thank you for your attention!

Questions? Discussion?