

Collaborative Procedure between World Health Organization (WHO) and Selected National Medicines Regulatory Authorities (NMRAs) in Inspection Activities

1. TITLE

Collaborative procedure between World Health Organization Prequalification Team: medicines (PQTm) and selected national medicines regulatory authorities (NMRAs) in inspection activities.

2. OBJECTIVE

This procedure includes a more targeted involvement of inspectors from NMRAs of developing countries and other interested member states in inspections organized by the PQT (including joint inspections) and better sharing of inspections related information. This has the following objectives:

- Efficient use of inspection resources while maintaining the international character on the programme for wide application.
- Capacity building of inspectors from NMRAs of developing countries and other interested WHO Member States.
- Facilitating use of PQT inspection results in the national regulatory environment for information and decision-making.
- Facilitation of harmonization through joint inspections and sharing of outcomes.

To provide guidance for the administrative arrangements and selection of inspectors invited as observers to participate in the PQT inspections, as part of the capacity building objective of PQT. This will also assist in exposing the inspector to the manner in which inspections are performed to assess compliance with WHO Good Manufacturing Practices (GMP). It is anticipated that this will also facilitate national regulatory approval (registration) of prequalified drugs.

3. RESPONSIBILITY

WHO will coordinate the inspections and shall have final responsibility for the inspection under the collaborative procedure. This shall be under the supervision of the Coordinator of PQT but shall be directly coordinated by the Group Lead of Inspection services or a designated inspector.

Heads of NMRAs shall be responsible for applying for participation in the collaborative procedure and nominating the focal person to manage participation of the NMRA in the procedure. The NMRAs will nominate inspectors for participation according to their internal procedures but should involve the focal person.

4. COLLABORATIVE PROCEDURE

The collaborative procedure is a targeted involvement of inspectors from NMRAs of developing countries and other interested Member States in inspections organized by the PQT (including joint inspections) and better sharing of inspections-related information.

This will be done in a collaborative manner where nominated inspectors from NMRAs of developing countries and other interested member states will be invited to participate in PQT-organized inspections and in turn, the NMRAs will be given appropriate access to outcomes of these inspections.

NMRAs of WHO member states shall be notified (**Annex A**), through the respective WHO Regional and Country offices, about the collaborative procedure and invited to submit, in the prescribed format, an expression of interest to participate (**Annex B**). The procedure is open to all NMRAs of member countries and those from developing countries are particularly encouraged to participate. This will be piloted in one of the regional groupings of developing countries which have initiated harmonization activities. Priority shall be given to a groups of countries committed to harmonization of their regulation procedures and to use of PQT evaluation (dossier assessment and site inspection) outcomes to facilitate national or regional regulatory decisions. Well-resourced NMRAs are also welcome to express their interest to join the collaborative procedure, especially if they are contributing to PQT by providing their inspectors and commonalities exist between national and PQT inspection targets.

Each participating NMRA will be requested to nominate a focal person for inspections who will also moderate access and postings to a secure web-based shared point specially created within the WHO website for the purpose. NMRAs will share their inspection plans (*by posting onto the secure website: see format in Annex C*) and nominate inspectors to participate as observers or co-inspectors in PQT inspections and other joint inspections arranged between participating countries (**Annexes D and E**).

A nominated inspector shall be a person already appointed as an inspector in the NMRA; should:

- have appropriate qualifications and basic experience in inspection
- have good knowledge of WHO GMP, Good Clinical Practice (GCP), Good Laboratory Practice (GLP) and related norms and standards as appropriate for the intended inspection
- have a good command of English and be able to follow the inspection in English
- have good interpersonal skills
- have no conflict of interest and shall sign a confidentiality agreement
- be willing and able to travel in foreign countries
- be able and in position to share the acquired skills with colleague inspectors in the NMRA and/or region.

All PQT members of staff are bound by confidentiality agreements. Appointed experts (*inspectors and observers*) also have to treat all information submitted and observed during site inspections as strictly confidential and proprietary to WHO, or parties collaborating with WHO, in accordance with the terms contained in an agreement. The nominated focal person and each nominated observer or co-inspector shall be invited to sign a confidentiality agreement and declaration of interest form as an expert adviser to WHO, (**Annex F**).

PQT shall allocate the nominated inspectors to the scheduled inspections considering their qualifications, experience and expressed interest in the site as indicated in the shared NMRA inspection plan. Consideration shall be given to inspectors who may represent several countries through harmonization initiatives, but equal opportunity shall be accorded to the participating NMRAs/countries.

Inspection plans are dynamic and shall be updated as appropriate. Participating partners shall be notified of the updates via the website and/or email.

WHO norms and standards for GMP, GCP and GLP shall be the basis for inspection together with other relevant international guidelines (such as those from the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use). PQT inspection procedures shall be used in arranging inspections in a manner which enables involvement of nominated inspectors from concerned countries. WHO will coordinate these inspections and shall have final responsibility for the inspection under the collaborative procedure.

The preparation of the inspection report, assessment of responses from the inspected site for corrective and preventive actions (CAPAs), preparation of the inspection closing letter, WHO Public Inspection Report (WHOPIR) and Notice of Concern (NOC), as the case may be, shall be done by PQT with involvement of the or co-inspector(s) and participating observer(s).

Participating resource-limited NMRAs will be expected to show commitment to establish or strengthen their quality systems for their inspectorates based on WHO guidelines, norms and standards. (See: [Quality systems requirements for national good manufacturing practice inspectorates. WHO Technical Report Series, No. 902, Annex 8, 2002.](#))

If an NMRA does not actively cooperate with the collaborating partners or does not show commitment to use the information and build capacity, it may be suspended from the collaboration.

5. HOW TO JOIN THE PROCEDURE

Any NMRA wanting to participate in the collaborative procedure should provide WHO with:

1. **A letter** expressing interest in participating in the WHO Collaborative Procedure for inspections and confirming that the submitted information is complete and correct.
2. **Information on the NMRA**, compiled in the prescribed format.
 - a. Name and contact address of the head of the NMRA.
 - b. Name and contact details of the focal person for inspections.
 - c. Names, qualifications (*basic specialized training in GMP*) and experience [years, numbers and categories (*oral solid dosage forms, oral and external liquids and mixtures, sterile injectables, contact research organizations*) inspected] of NMRA inspectors.
 - d. Inspection schedule in the prescribed format.
 - e. If the inspectorate of the NMRA has documented its quality system as a quality manual this can be submitted.

All of the above-mentioned information should be submitted in English. Submissions that are not made in English must be accompanied by a certified English translation.

The submissions containing the covering letter and the completed expression of interest form and should be sent to:

Inspection services
Prequalification Team
World Health Organization
HIS/EMP/RHT/PQT
20 Avenue Appia
1211 Geneva 27
Switzerland

Any NMRA can express an interest in collaborating with PQT in inspection activities; participation in the prequalification procedure is voluntary. This invitation is not limited to NMRA from a specific region. However, PQT reserves the right to prioritize collaboration with:

- NMRAs which have an urgent need and commitment for capacity building, and
- NMRAs in regions pursuing harmonization of their regulatory activities.
- NMRAs (belonging to the Pharmaceutical Inspection Convention/Scheme) that provide substantial help to PQT in terms of making their inspectors available for WHO as co-inspectors.

6. CRITERIA FOR NOMINATING AN INSPECTOR TO PARTICIPATE IN THE PROCEDURE AS AN OBSERVER

A nominated inspector should:

- be a person already appointed as an inspector in the NMRA
- have appropriate qualifications and basic experience in inspection
- have good knowledge of WHO GMP, GCP, GLP and related norms and standards as appropriate for the intended inspection
- have a good command of English and be able to follow the inspection in English.
- have no conflict of interest and be willing to sign a confidentiality agreement
- be willing and able to travel in foreign countries, and
- should be able and in position to share the acquired skills with colleague inspectors in the NMRA and/or region.

7. EXPECTED OUTCOMES

It is hoped that this collaborative procedure will have many benefits, including capacity building of inspectorates of NMRAs of developing countries, and other interested Member States, through "*hands-on*" training in inspection, and practical interpretation and application of international norms and standards. Participating inspectors are likely to develop similar skill levels, similar approaches to inspection and practical experience in multi-agency collaboration which will in turn facilitate harmonization of regulatory practices in the region. This will in turn lead to faster access to good-quality essential medicines, including those prequalified by WHO.

The approach and skills could be used to facilitate harmonized inspections among regional NMRAs even in product categories outside the focus of WHO prequalification.

8. INDICATORS

- Number of inspectors participation in WHO arranged inspections
- Number of countries represented by observers or co-inspectors
- Positive feedback in relation to capacity building

9. DOCUMENTS

Annex A: Invitation to submit expression of interest in participating in the collaborative procedure

Annex B: Format for submission of expression of interest

Annex C: Format for submission of inspection schedules

Annex D: Form for nomination of an observer or co-inspector

Annex E: Observer/co-inspector details

Annex F: Confidentiality and declaration of interest form

Annex G: Appointment of observer or co-inspector : template letter

Annex H: Appointment of observer or co-inspector: template letter to supervisor