WHO Prequalification of in vitro diagnostics: Manufacturing site(s) inspections

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Requirements for Inspections

- Fully implemented quality management system (design & development, manufacturing including quality control, storage, distribution)
- Risk management to meet ISO 14971:2007
- Product stable to meet "harsh" conditions (hot, wet, dry, dusty)
- Products undergoing prequalification have to be in routine manufacturing
- Sufficient capacity to ensure reliable delivery

Quality Management System

- Fully implemented quality management system (design & development, manufacturing including quality control, storage, distribution)
  - Meets ISO 13485:2003 requirements (note: user requirements in areas of interest)
  - Competence of personnel
  - Work environment (determined and established)
  - Quality control processes follow risk management results, quality control plan established, performance tested according to claims in instruction for use
  - Storage conditions, temperature and humidity, validated for intermediates, components and kit, real time data required

Risk Management

Risk management to meet ISO 14971:2007

- > Risk management for product realisation (design, manufacturing, storage, transportation), user and patient
- > Risk management file
- > Risk management plan
- > Risk analysis
- > Risk evaluation and control
- > Residual risk acceptable?

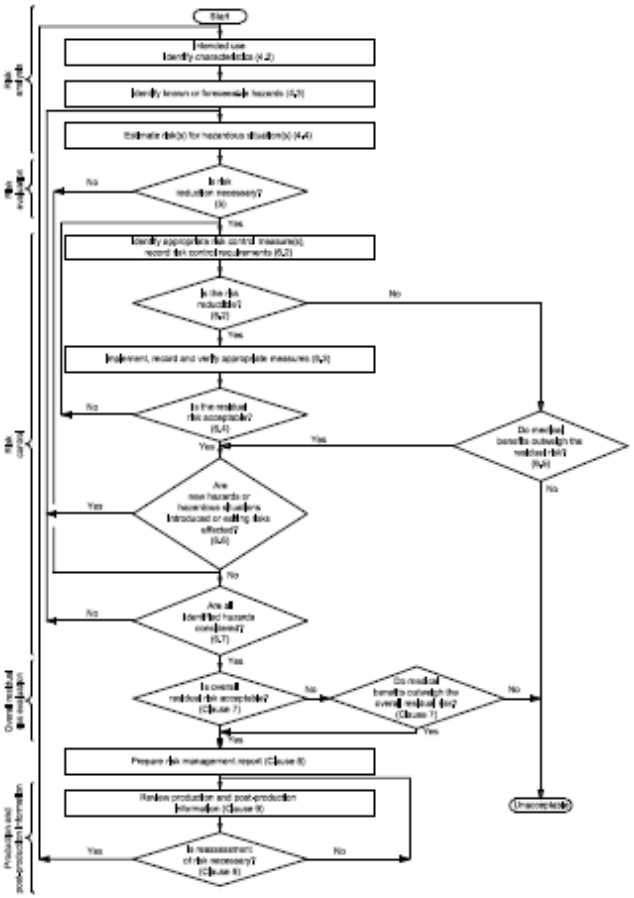

Figure B.1 — Overview of risk management activities as applied to medical devices

Product Stability

Product stable to meet "harsh" conditions (hot, wet, dry, dusty)

- Transportation studies (simulate "worst" conditions)
- Long term stability at limiting conditions
- In-use stability studies (open vial)
- Data to support all claims available on-site
- Note: product labelling (component, kit and shipping box)

Routine Manufacturing

- Transfer from R&D to production completed
- Established and evaluated suppliers
- Validated processes (acceptance ranges determined, in-process controls established)
- Trained personnel (requirements determined, training plan, records)
- Standard batch sizes
- Established "out-of-specification" process
- Batch manufacturing records established (include all manufacturing information, full traceability of material and equipment)

Guidance Documents

WHO Guidance

- Overview of the prequalification of diagnostics assessment process (PQDx_007)
- **Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics (PQDx_014)**
- Abbreviated prequalification assessment (PQDx_173)

International Guidance

- GHTF.SG4.(99)28 Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 1: General Requirements (including supplements 1,2, 4 and 6). Note: 10.2.1 and 10.2.3 in this document further describe audit team competency criteria
- GHTF/SG4/N30R20:2006 Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 2: Regulatory Auditing Strategy

Guidance Documents

International Guidance

- GHTF/SG4(pd1)/N33R16:2007 Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 3: Regulatory Audit Reports
- GHTF/SG3/N17:2008 Quality Management System – Medical Devices – Guidance on the Control of Products and Services Obtained from Suppliers
- **GHTF/SG3/N19:2012 Quality management system – Medical devices - Nonconformity Grading System for Regulatory Purposes and Information Exchange**
- GHTF/SG3/N15R8:2005 Implementation of risk management principles and activities within a Quality Management System.

Guidance Documents

- **IMDRF guidance**
- WHO PQDX is an official observer to the MDSAP
- Guidance for Regulatory Authority Assessors on the Method of Assessment for MDSAP Auditing Organizations
- Medical Device Regulatory Audit Reports
- MDSAP Assessment and Decision Process for the Recognition of an Auditing Organization
- Requirements for Medical Device Auditing Organizations for Regulatory Authority Recognition
- Competence and Training Requirements for Auditing Organizations
- Regulatory Authority Assessment Method for the Recognition and Monitoring of Medical Device Auditing Organizations
- Clarification of the Term “Legal Entity” for MDSAP Recognition Purposes
- MDSAP: Overview of Auditing Organization Assessment and Recognition Decision Related Processes

International Standards

- ISO 13485:2003 Medical devices - Quality management systems - Requirements for regulatory purposes
- ISO 14969:2004 Medical devices - Quality management systems - Guidance on the application of ISO 13485:2003
- ISO 19011:2011 Guidelines for quality and/or environmental management systems auditing.
- ISO 14971:2007 Medical devices - Application of risk management to medical devices
- Note: EN ISO 14971:2012 applies only to manufacturers placing devices on the market in Europe and contains useful annexes; the body of the standard is identical to ISO 14971:2007 ISO 9000:2005 Quality management systems - Fundamentals and vocabulary

International Standards

- ISO 15223-1:2012 Symbols to be used with medical device labels, labelling and information supplied—Part 1 General requirements
- ISO 2859-10:2006 Sampling procedures for inspection by attributes — Part 10: Introduction to the ISO 2859 series of standards for sampling for inspection by attributes
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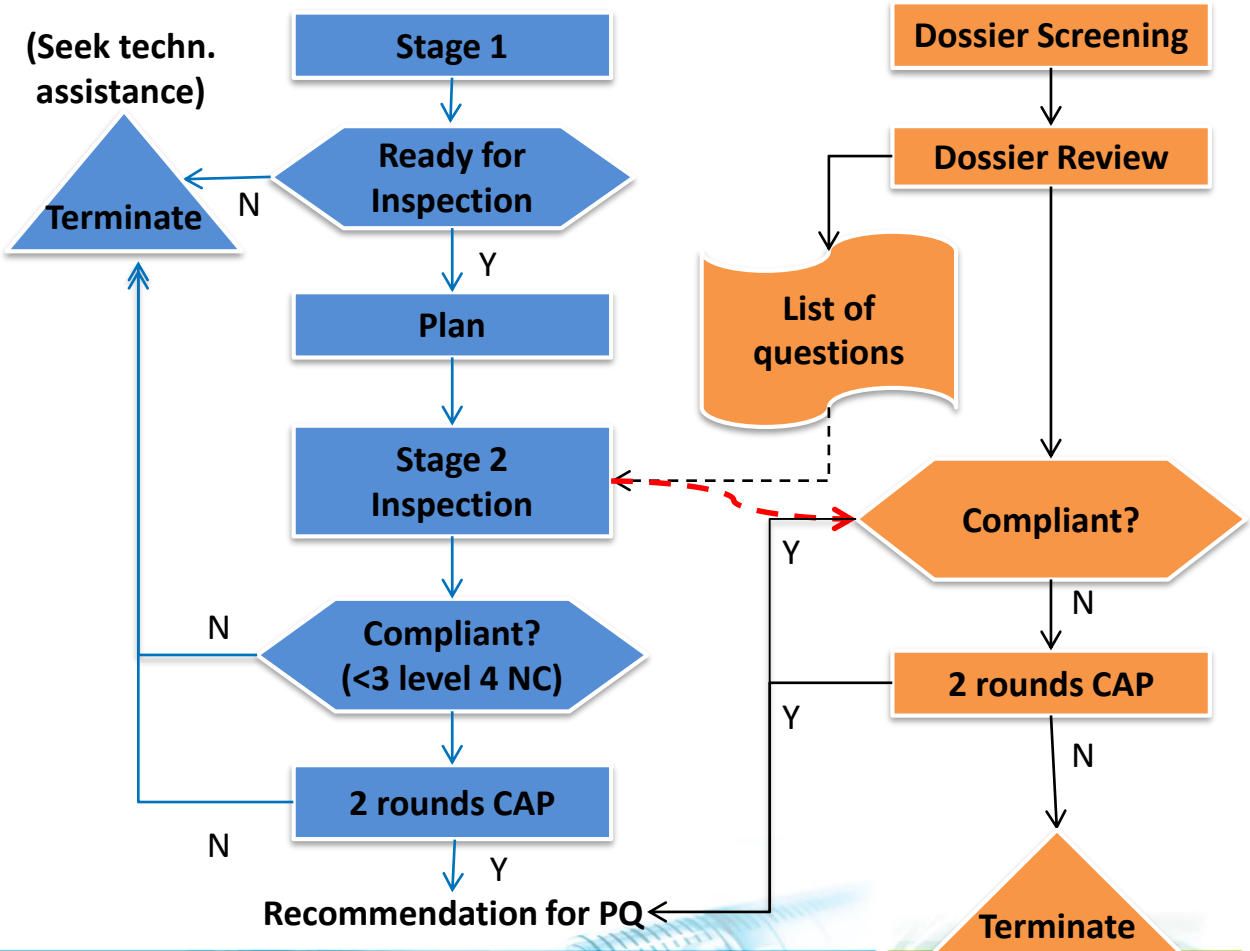
Inspections process



Onsite Inspections

Application (Pre-submission form)

Dossier review (QM documentation part)

Inspection Cycle:

- **Evaluation of readiness for inspection (stage 1)**
  - Desktop of additional documentation (Certificates, recent audit reports, quality procedures, SOP, summary of sold product...)
  - Stage 1 inspection (1 inspector day to inspect state of QMS implementation, facility, competence of staff, critical suppliers incl. outsourced activities, internal audit and management committment / review)
- **Initial (Stage 2) Inspection**
- **Follow up (confirm implementation of CAP); onsite inspection, if required**
- **Re-Inspection (risk based, after 3-5 years)**

Спасибо!

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