Annex 9

Guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions

Background

In recent years both formal and informal collaboration among national regulatory authorities (NRAs) has significantly improved. This, in turn, has strengthened medicines regulatory systems, thereby improving the availability of good quality, safe and effective medical products for patients. A number of regional and supraregional groupings of NRAs are developing, which will facilitate collaboration.

During a World Health Organization (WHO) training symposium on the subject of collaborative registration procedures for national medicines regulatory authorities held in Kenya in September 2016, delegates recommended that the gap in common guidance on best practice for performing desk assessment should be filled. It was proposed that WHO, in collaboration with regulators from Member States, develop guidance that NRAs might leverage in their national regulatory practice and decision-making.

Up to now, there has been no general guidance on approaches and best practices for desk assessment. Desk assessments are conducted in order to verify and confirm compliance with good manufacturing practices (GMP), good laboratory practices (GLP) and good clinical practices (GCP) of foreign facilities for manufacture of finished pharmaceutical products (FPPs) and active pharmaceutical ingredients (APIs), quality control laboratories (QCLs), contract research organizations (CROs) and clinical trial sites.

1. Introduction

NRAs worldwide use systems for the authorization and post-marketing surveillance of medical products that depend upon the assessment of submitted dossiers, variations files and the inspection of FPP and API manufacturers, QCLs and CROs involved in the development, manufacture and distribution of a medical product. Inspections are performed to verify dossier data and to provide evidence that the FPP and API manufacturers, QCLs, CROs and clinical trial sites comply with the relevant good practice (GxP) guidelines and requirements. Thereafter, routine inspections may be conducted depending on the risk rating of the facility.

The performance of on-site inspection of manufacturing, testing and clinical trials as well as the supply and distribution chain outside the NRA's domestic territory is a resource-intensive activity and one that often lies on the critical path to regulatory decision-making. Furthermore, the hosting of multiple regulatory inspections and audits is also a significant overhead for the sites inspected, which adds to the cost of producing the products. Even the best-resourced NRAs face certain limitations and therefore it is regulatory best

practice to use quality risk management when prioritizing inspection activities. To make the best use of the limited inspection resources and minimize the need for repeated inspections, it is good practice for national authorities to leverage available and reliable evidence of compliance and noncompliance with good practice requirements as part of their risk-based inspection planning process, such that there is no on-site inspection without good cause.

Verification and confirmation of compliance with GMP by a manufacturer of an FPP or API in a foreign country may be based on the assessment of evidence that includes the report of a recent inspection of the manufacturer by a competent regulatory authority or another internationally recognized organization.

One element of this risk-based approach is the desk assessment of inspection information from reliable and trusted sources by national or regional authorities in order to decide whether to perform a further inspection before reaching a final decision on marketing authorization, renewal of marketing authorization or another regulatory action. Whereas a desk assessment for GMP and GCP verification and confirmation has been a method used by some organizations and agencies like the WHO Prequalification Team (*1*), European Member States Agencies (coordinated by the European Medicines Agency (EMA) for centralized marketing authorizations) *(2)* and the Australian Therapeutic Goods Administration (TGA) (*3*) for some years, for others it is emerging as an option to be considered.

Such agencies have relied on regulatory decisions made by other agencies, based on bilateral or multilateral agreements depending on the decisions made independently by each individual authority. While not a prerequisite, a range of international and regional formal agreements may be utilized to facilitate the effective management of regulatory decisions in order to increase access to good quality, safe and effective products on the market. These include mutual recognition agreements (MRAs), cooperation agreements (CAs) and memoranda of understanding (MoUs).

Mutual recognition works well if there are common technical standards (including documentation), good regulatory practices; clear procedural legislation in the form of agreement-tracking tools to support the process, trust and political will, with no interference in technical decisions. On the other hand, CAs or MoUs are an option where there is minimal legal obligation. It is also possible to perform desk assessments without a formal agreement.

A desk assessment may be used by an NRA to assess compliance with GMP, GLP and GCP by facilities that manufacture FPPs and APIs. It can also be used to assess CROs, clinical trial sites and outsourced QCLs, where there is an established MRA, CA or MoU, or recognition of a decision made by a competent regulatory authority; Pharmaceutical Inspection Co-operation Scheme (PIC/S) member; or through a WHO prequalification process.

The procedure for the desk assessment will depend on whether the facility was previously inspected by a competent regulatory authority, PIC/S member or under the WHO prequalification scheme, or if an MRA, CA or MoU exists.

The desk assessment process involves submission of documentary evidence by the applicant, usually a manufacturer or representative, to the NRA to demonstrate the conformity of all sites involved in FPP or API manufacturing, or of an outsourced QCL, CRO or clinical trial site to GMP (the reference is added in the relevant citation), GLP or GCP, respectively. The evidence provided is assessed to determine the level of compliance based on the accepted standards and the scope of the application. The outcome of the assessment process is used as the basis for a regulatory decision that serves as a prerequisite for granting the marketing authorization for a medical product.

Acceptance of data from clinical trial(s) to support a marketing authorization application will rely upon conformance with GCP, including review and approval by an institutional ethics committee where the study was conducted and on obtaining and documenting informed consent of the study subjects if applicable (*4*).

The option to undertake a desk assessment does not preclude an on-site inspection if the outcome of the assessment does not confirm compliance with the stipulated practices. The confirmation may be granted for a specified period and the process may be subject to recovery of costs. It is important to determine the number of times a desk assessment may be performed before it becomes necessary to conduct a physical inspection, taking into consideration the outcome of the desk assessment, i.e. the number, nature and impact of observations and the integrity of the data provided.

2. Aim and objectives of the guidance

This guidance aims at providing an approach for use by NRAs for assessing compliance with GMP, GLP or GCP using documentation issued by other NRAs in lieu of conducting an inspection of a specific site.

The use of the desk assessment as described in this guidance is intended to provide a way to reduce the necessity for duplication and the frequency of inspections while relying on authentic and reliable documentary evidence from other regulatory authorities. Desk assessment should also reduce the inspection resources needed by both the manufacturing site and the NRAs and result in broader availability of high-quality medicinal products to patients globally. It may also be used by NRAs for continuous evidence-based regulatory decisions and follow-up on quality assurance issues that go beyond marketing authorization.

The guidance also lists the key documents to be submitted by other regulatory authorities and/or manufacturers that provide reliable information about the status of compliance with good practices in manufacturing, quality control and clinical trials of a specified medical product. The essential information and documents that need to be available to conduct the desk assessment in relation to the most relevant GxPs, in this context GMP, GLP and GCP, are described.

The objective of this guidance is to:

- ensure that a standardized procedure is followed for desk assessment of inspection documentation and reports issued by trusted, competent regulatory authorities and of records of corrective actions from inspected sites;
- facilitate a convergent approach and model for exchange and use of inspection information in national and regional decision-making concerning the necessity to perform preapproval and surveillance inspections.

3. Scope of the guidance

This guidance applies to all FPP and API manufacturers (including biologicals and vaccines manufacturers, all sites where APIs are being imported, repackaged or relabelled, and investigational medical product manufacturers), outsourced QCLs, CROs and clinical trial sites that are subjected to GxP inspections in foreign countries. However, the NRA may use desk assessments to set up risk-based inspection plans without loss of regulatory oversight through physical inspections.

The guidance has general geographical applicability for regulatory authorities and United Nations agencies in order to support ongoing harmonization initiatives and optimum use of limited resources. It covers the information and evidence required to undertake a desk assessment process, but not the procedure for on-site inspection, except the process of tracking and review of completion of corrective and preventive action (CAPA). On-site inspection is covered in a separate WHO guidance document (*5*, *6*).

Desk assessment procedures can be used for preapproval, renewal and surveillance inspections. Caution is needed when assessing sites that have failed to meet the specified standard after GxP inspections. However, desk assessments may be appropriate for a site that has failed an inspection, in order to confirm the failure and thus avoid the need for a physical inspection. The NRA takes the ultimate decision on whether it is appropriate to perform a desk review or whether an on-site inspection would be needed.

4. Glossary

The definitions given below apply to the terms used in this guidance. They may have different meanings in other contexts.

active pharmaceutical ingredient. Any substance or mixture of substances intended to be used in the manufacture of a pharmaceutical dosage form and that, when so used, becomes an active ingredient of that pharmaceutical dosage form. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease or to affect the structure and function of the body.

agent or local technical representative. Every applicant who is not resident in the country of the national regulatory authority (NRA) should appoint a person in that country to be an agent (local technical representative). The appointment should be notified to the NRA by submitting a letter of appointment supported by powers of attorney duly notarized in the country of origin, and registered with the registrar of companies in the country of the NRA.

applicant. A person who applies for marketing authorization of a medical product to the national regulatory authority, who must be the owner of the product. The applicant may be a manufacturer or the party applying for a product certificate. After the product is registered, the applicant becomes the marketing authorization holder.

bioequivalence. Two medical products are bioequivalent if they are pharmaceutically equivalent or pharmaceutical alternatives, and their bioavailability, in terms of rate (C_{max} and t_{max}) and extent of absorption (area under the curve), after administration of the same molar dose under the same conditions, are similar to such a degree that their effects can be expected to be essentially the same.

clinical trial (or clinical study). Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamics effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.

competent regulatory authority. Any organization that has a legal authority or power to perform a designated regulatory function for authorization of a medical product: the national regulatory authority in the Member State.

cooperation agreement. A formal business document outlining the basic terms of an agreement with another individual, group or entity. It is one of the first steps towards a more detailed contract. Alternative names include, but are not limited to, memorandum of understanding, cooperation contract or collaboration agreement.

desk assessment. The evaluation of documentary evidence by a competent regulatory authority recognized by the national regulatory authority, for compliance with the required good practices (good manufacturing practices (GMP), good laboratory practices and good clinical practices) in support of marketing authorization and other regulatory decisions. Desk assessment may be performed in support of a new marketing authorization, or for routine GMP inspection (including in the frame of specified product(s) life-cycle management as required).

finished pharmaceutical product. A finished dosage form of a pharmaceutical product that has undergone all stages of manufacture, including packaging in its final container and labelling.

good clinical practices. In this context the term means a standard for design, conduct, performance, monitoring, auditing, recording, analysis and reporting of clinical trials in a way that provides assurance that the data and reported results are credible, accurate and that the rights, safety and well-being of trial subjects are protected.

good laboratory practices. A quality system concerned with the organizational process and the conditions under which nonclinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.

good manufacturing practices (GMP). That part of quality management which ensures that products are consistently produced and controlled according to the quality standards appropriate to their intended use and as required by the marketing authorization, clinical trial authorization or product specification. GMP are concerned with both production and quality control. GMP are aimed primarily at managing and minimizing the risks inherent in pharmaceutical manufacture to ensure the quality, safety and efficacy of products.

information sharing. An exchange of data between individuals or entities outside the traditional organizational boundaries, to achieve a common goal in terms of better policies and to deliver better services. This may mean that one party is disclosing information while the other is collecting the information or both parties are mutually disclosing and collecting information.

manufacture. All operations of purchase of materials and products, production, quality control, release, storage, distribution of medical products and the related controls.

manufacturer. A manufacturer is a natural or legal person who holds a manufacturing authorization and has responsibility for manufacturing of a medical product or active pharmaceutical ingredient.

marketing authorization (product licence, registration certificate). A legal document issued by the competent regulatory authority that establishes the detailed composition and formulation of the product and the pharmacopoeial or

other recognized specifications of its ingredients and of the final product itself and includes details of packaging, labelling and shelf life.

medical product. A term that includes medicines, vaccines, diagnostics and medical devices.

memorandum of understanding (MoU). A formal agreement between two or more parties. Companies and organizations can use MoUs to establish official partnerships. MoUs are not legally binding but they carry a degree of seriousness and mutual respect, stronger than a gentlemen's agreement.

mutual recognition agreement. This is defined as the reciprocal adoption or acceptance of regulatory decisions or outcomes in other partner states in form of a legal agreement. It is stronger than a gentlemen's agreement and is usually binding.

Pharmaceutical Inspection Co-operation Scheme (PIC/S). This is a non-binding, informal cooperative arrangement between regulatory authorities in the field of good manufacturing practices of medical products for human or veterinary use.

pharmaceutical product. Any substance or combination of substances marketed or manufactured to be marketed for treating or preventing disease in human beings, or with a view to making a medical diagnosis in human beings, or to restoring, correcting or modifying physiological functions in human beings.

quality control. All measures taken, including the setting of specifications, sampling, testing and analytical clearance, to ensure that raw materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics

quality management system. An appropriate infrastructure, encompassing the organizational structure, procedures, processes and resources, and systematic actions necessary to ensure adequate confidence that a product or service will satisfy given requirements for quality.

quality system. The sum of all features that are necessary to implement an organization's quality policy and meet quality objectives. It includes organizational structure, responsibilities, procedures, systems, processes and resources. Typically these features will be addressed in different kinds of documents, such as the quality manual and documented procedures.

5. Essential elements of desk assessment

5.1 High-level support and cooperation

Interagency communication can facilitate greater regulatory convergence. This in turn can increase the efficiency and quality of medical product development

and the NRA review processes as well as improving patients' access to quality medical products. This not only entails accessing information from the public websites of other NRAs, such as guidelines, decisions and product recalls, but also actively sharing information between NRAs, in particular with respect to inspection findings during application review and for decision-making.

The legal framework and governance structure of the NRA should include provisions on support and collaboration with other agencies in making regulatory decisions. Legal provisions (laws and regulations) that allow reliance on foreign NRA inspections and enforcement actions based on well-defined criteria should be established and implemented. Such recognition can take the form of MRAs, CAs or MoUs between collaborating inspectorates and could entail agreements that would enable bilateral or multilateral commitment and exchange of information on specified sites.

MRAs are usually binding and may require inspectorates at the same level of development with the appropriate organization and funding to fulfil the responsibility of protecting and promoting public health. Where such recognition exists, fewer requirements are needed to determine compliance with GMP, GLP and GCP of foreign manufacturing sites, CROs and outsourced QCLs, given the level of cooperation and trust established.

5.2 Commonality of quality management systems in inspectorates

There should be a quality system in place based on recognized international standards, namely the WHO quality management system (QMS) or International Organization for Standardization (ISO) QMS standards. The QMS should be established, implemented and maintained throughout the period of recognition or reliance. The primary purpose of a QMS is to ensure that adequate quality standards are maintained.

Adopting common standards for quality system requirements (within GMP, GLP or GCP of the NRA) helps to achieve consistency in inspection standards between inspectorates and thus facilitates mutual recognition and reliance.

5.3 Convergent standards of good practices

WHO has published standard requirements for compliance with GMP (*7*) and other good practices including *Good practices for pharmaceutical quality control laboratories* (*8*) and GCP (*4*, *9*). These serve as a measure of the standards established by the manufacturers in order to deliver and supply a good quality and safe product. The NRA should have similar standards of GxP in order to facilitate uniform desk assessment.

5.4 Reliability and accuracy of information

Applicants are responsible for ensuring that information provided for desk assessment is reliable and not false or misleading.

Mechanisms and controls should be established to ensure that the information provided by the applicant is authentic, legible, current and accurate. There should be strong confidence that the information provided relates to the same strength and specifications of the product and to the same site, workshop or production line (use of unique facility identifiers should be considered); and should accurately relate to the product under assessment, without any false information.

Controls should be established and documented by the NRA to ensure that the information provided by the applicant is secured and remains confidential.

5.5 Management tools to support consistent and objective assessment

Well-structured and up-to-date assessment tools and procedures should be adopted to enable uniform and consistently objective assessment of the documents provided. Personnel involved in the assessment process should have an acceptable level of training and experience with GMP, GLP or GCP. They should also be trained to use the assessment tools and procedures consistently without bias, and to be able to detect inconsistent and inaccurate information regarding the product under assessment. Validated electronic assessment tools (software applications) may be used to perform the desk assessments. Although paper-based systems may also be used, electronic tools are preferred.

5.6 Risk-based assessment of available information

Even the best-resourced NRAs are subject to limitations in terms of time, funding and personnel, and therefore it is regulatory best practice to apply quality risk management as defined and outlined in ICH Q9: Quality risk management, in prioritizing inspection activities (*10*, *11*). The aim of the desk assessment process should be to provide to the NRA, in a timely manner, the required assurance that the site in question demonstrates an acceptable level of GxP for the FPP, API or trial under assessment.

The assessment should take into consideration and focus on the critical products and critical processes in the manufacture of a specified product in relation to patient risk, based on the knowledge that other competent and trusted inspectorates have inspected and approved the site of manufacture.

Key factors to consider include the origin of the information and its authenticity, the location of the site of manufacture, complexity and type of the product (whether sterile or biological) and the risk to the patient (*12*).

5.7 Mutual trust and confidence among inspectorates

Joint inspections may be conducted by countries within the same region or countries that are party to a relevant agreement. Through such interactions, regulators may be able to build confidence, share information and experiences in order to be able to rely on others' inspection outcomes and regulatory decisions. Joint inspections also serve as a basis for desk assessments through building mutual trust and identifying barriers to reliance on other regulators' inspection outcomes and devising solutions to overcome them. Building mutual trust and confidence involves exchange of information, identifying areas of collaboration, work sharing and eventually binding through a legal agreement between collaborating NRAs.

Some competent NRAs are already using these models successfully. Examples include the United States of America (USA) Food and Drug Administration's MRA with the European Union, Health Canada's MRA with the European Union, and the TGA's risk-based desktop assessment process. The TGA's process comprises MRA and compliance verification pathways, which are essentially desk reviews. Those two pathways can result in cost savings for both the manufacturer, who does not have to bear the cost of hosting another inspection, and the regulator, who saves on personnel time and other resources.

5.8 Quality assurance of the desk assessment process

Quality assurance of the desk assessment process involves inspiring confidence that the requirements of the assessment process will be fulfilled. This would require documented evidence of compliance of the inspectorate function with a QMS[1] over a period of three to five years.

NRAs should create a cycle for the process of reviewing desk assessments, including timelines for applicants' responses.

5.9 Communication of assessment outcomes

Communication of the outcome of the desk assessment process should be transparent and timely. Communication should focus on the quality of the product and the regulatory decisions between the authorities in the importing country and exporting country, the manufacturers and any other relevant third party, such as procurement agencies. The outcome of the desk assessment should be communicated to the applicant whether the result is an approval, a deferment or a rejection of an application for GxP assessment, and to the responsible NRA.

[1] For example, ISO/International Electrotechnical Commission (IEC) 17020 *Conformity assessment – requirements for the operation of various types of bodies performing inspection*, PIC/S *Quality management system for inspectorates* or ICH Q9 *Quality risk management*.

If a rejection leads to a regulatory decision to conduct an on-site inspection, a statement of the reasons should be provided, with details of the documents, information and regulatory requirements taken into account in reaching the decision. An appeal mechanism, including a time frame within which applicants may lodge an appeal, should also be in place. The NRA should reserve the right to conduct an inspection of any site.

6. Sources of good information and related challenges

Trusted sources of information are available either in the public domain or from the NRAs. The amount of detail provided in the information may vary depending on applicable restrictions and rights of the owners. Websites of NRAs may provide information on non-compliant facilities, market complaints and product recalls, among others.

Certificates, reports or other documents issued by competent regulatory authorities also provide information about a specified manufacturer, outsourced QCL, CRO or clinical trial site.

6.1 Official websites with databases

NRAs and organizations such as WHO and EMA have websites where information on facilities' compliance and noncompliance with GxP is available. Some websites provide GMP certificates and inspection reports together with other information about medicines, pharmaceutical manufacturing facilities, QCLs and clinical trials. Information may also be obtained on medicine sampling and results of the testing, including samples that failed analysis, product recalls and rapid alerts. The website consulted should be current and regularly updated. Certificates presented by applicants for marketing authorization should be verified using the information available on the websites of NRAs or by contacting the relevant NRA directly. The NRA is responsible for checking that information is current and complete.

6.2 Authenticity of documents

It is important that documentary evidence provided by the applicant as the basis for granting approval for GMP, GLP or GCP be current, accurate and authentic. It is the responsibility of the applicant to ensure this. The applicant should include a cover letter with the application stating that all the documents submitted are authentic and correct. NRAs may request that information such as inspection reports and certificates granted by NRAs be notarized or certified.

Submission of inaccurate or false information may result in declaration of the manufacturer, QCL or CRO as noncompliant.

6.3 Failure to submit documentary evidence

If the applicant is unable to provide adequate documentary evidence, including information on current compliance, or to submit the documents before a specified deadline, or fails to submit documents as required, the application for desk assessment may be rejected, leading to a decision to conduct an on-site inspection. In such circumstances, approval of GMP, GLP or GCP should only be granted after the on-site inspection has been conducted, and the manufacturer, CRO, clinical trial site or outsourced QCL has been found compliant.

7. Submission and assessment of documentary evidence and information

7.1 Submission of application for desk assessment and documentary evidence

Prior to assessment, an application for desk assessment for each site should be submitted by the applicant to the NRA. Applications may be required for preapproval, renewals and surveillance inspections, as specified by the NRAs in the respective inspection guidelines and procedures.

7.2 Assessment of documentary evidence and information

Desk assessment involves a detailed evaluation of the specified documentary evidence supplied by the applicant. It will include an assessment of reports of recent inspections of the relevant manufacturing site undertaken by a competent regulatory authority, together with other available regulatory information. Desk assessment for compliance of facilities manufacturing FPPs and APIs with GMP, GLP or GCP can be used where the NRA has an agreement or understanding on exchange of information, such as an MRA, CA or MoU.

In accordance with international agreements with certain countries, the NRA may accept compliance of a foreign site with GMP, GLP or GCP requirements based on a current certificate or approval letter issued by the regulatory agency of the other party to the MRA.

Marketing authorization may be granted by the NRA on the basis of a current certificate or approval letter issued within the scope of an MRA. The scope of the manufacturing activities indicated in the application should be within the scope of the activities covered by the certificate or approval letter.

Generally, where an MRA has been established:

a. a copy of the manufacturing authorization granted by national authorities together with a certified translation, where this is not in English, may suffice.

Where a CA or other bilateral or multilateral arrangement has been established, the document specified in a. above should be provided in addition to the following essential documents:

b. a site master file (*13*) whose approval date was not more than one year ago, and any forecast modifications, together with legible colour printouts of water treatment and air-handling systems, including pipeline and instrumentation drawings in A3 or A2 format;
c. a list of all the products and dosage forms manufactured on-site. The list should include proprietary names and International Nonproprietary Names (INN);
d. a copy of the last inspection report issued by the NRA with a certified translated copy where this is not in English, and GMP, GLP or GCP certificates or an approval letter with a certified translated copy where this is not in English (production-line specific);
e. current full inspection report(s) for inspections performed by a competent regulatory authority in the past three to five years, with a certified translated copy where this is not in English;
f. proof of CAPA implementation and final decision by the NRA related to observations or deficiencies noted in the latest inspection report or any warning letter or equivalent regulatory action (production-line specific);
g. the most recent product quality review(s) (PQR)(s) of the concerned product(s); PQR(s) (*4*) or equivalent documentation covering all required subsections and trend results should be presented; proprietary information for vaccines is not required;
h. the completed batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant product(s);
i. a list of any recalls in the past three years related to products with quality defects.

The following documents may be evaluated while performing desk assessments:

- a confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the product(s) has been performed and all matters dealt with;
- master batch manufacturing and packaging record(s) of the product(s) of interest;

- a copy of any warning letter, or equivalent regulatory action, issued by any authority to which the site provides or has applied to provide the product;
- out-of-stock situations.

The evidence lists required for desk assessment of compliance with GMP, GLP or GCP for each type of facility and collaborative arrangement are listed in Table A9.1 and the specific documentary evidence required is presented in Table A9.2.

Table A9.1
Type of facility and evidence documents required for desk assessment[a]

Type of facility	Where an MRA exists	Where a CA or MoU exists; or member of PIC/S; or competent NRA regulator; or WHO prequalification scheme	Where no MRA, CA or MoU exists; or non-member of PIC/S; or WHO prequalification scheme
Nonsterile products facilities • FPP • API	Evidence list A	Evidence list B	On-site GMP inspection
Sterile products facilities • FPP • API	Evidence list A and certification to relevant ISO standards for sterilization facility[b]	Evidence lists B and C	On-site GMP inspection
Outsourced (contract) testing laboratory; and outsourced sterilization	Evidence list A	Evidence list D	On-site laboratory inspection On-site GMP inspection

Table A9.1 *continued*

Type of facility	Where an MRA exists	Where a CA or MoU exists; or member of PIC/S; or competent NRA regulator; or WHO prequalification scheme	Where no MRA, CA or MoU exists; or non-member of PIC/S; or WHO prequalification scheme
CRO or clinical trial site • clinical facility • clinical laboratory • bioanalytical laboratory • company performing pharmacokinetics statistical analysis	Evidence list E	Evidence lists E and F	On-site GLP or GCP inspection

API: active pharmaceutical ingredient; CA: cooperation agreement; CRO: contract research organization; FPP: finished pharmaceutical product; GCP: good clinical practices; GLP: good laboratory practices; GMP: good manufacturing practices; ISO: International Organization for Standardization; MoU: memorandum of understanding; MRA: mutual recognition agreement; NRA: national regulatory authority; PIC/S: Pharmaceutical Inspection Co-operation Scheme.

[a] Explanations of the evidence lists are provided in Table A9.2.

[b] If applicable to the manufacturing facility or activity.

A list of the documents that should be provided for desk assessment is given in Table A9.2. The documents required for desk assessment of manufacturing sites are indicated in evidence lists A, B, C and D; for outsourced QCL, they are indicated in evidence lists A and D and for CROs and clinical trial sites, they are indicated in evidence lists E and F.

Table A9.2
Documentary evidence requirements for desk assessment

	Required evidence	Comments and exceptions
Evidence list A	Current GMP certificate or approval letter GLP or ISO/IEC 17025 certification for outsourced laboratory	Certificates must be sufficient to cover the scope of the GMP compliance application

Table A9.2 *continued*

	Required evidence	Comments and exceptions
Evidence list B	Current GMP certificate or approval letter	GMP agreements may be requested if the foreign manufacturer performs the release for supply function
	Current manufacturing licence	The manufacturing licence should show the scope of products and activities approved by the NRA
	Regulatory inspections conducted within the past three years and a copy of the most recent inspection report issued by the competent regulatory authorities as stated in Table A9.1	A list of all inspection reports applicable to the scope of the application is required. These may be sent to the NRA directly from the manufacturer CAPA evaluation for the recent inspection report should be provided
	Market complaints register	For the previous three years, including one investigation report for one of the complaints classified as high risk to public health The complaint register should be applicable to the products named in the application
	Details of any regulatory actions in the past three years	For example, product alerts, warning letters, import alerts, recalls due to defects
	Site master file, quality manual or equivalent	Site master file[a] Site master file is not required if the scope of the application is only for the step of release for supply
	List of products intended for supply in the recipient country	

Table A9.2 *continued*

	Required evidence	Comments and exceptions
	• PQR report; • process validation report; and • batch records (batch manufacturing, packaging andtesting) for each product for which marketing authorization is being applied	The PQR reports should be provided for each product. If there are multiple products, one PQR report is required for each FPP dosage form for which an application is being made The batch records of a product for each FPP dosage form manufactured in the past 6 to 12 months; and the corresponding process validation reports and annual product quality review reports
	List of reprocessed or reworked product batches in last year (or last two years)	
Evidence list C	Validation master plan	Not required if the scope of the application is only for the step of release for supply
	Aseptic processing and filling validation reports if applicable	Required if the application concerns products that are not terminally sterilized
Evidence list D	Current GMP certificate, or ISO/IEC accreditation certificate or WHO prequalification	For outsourced testing laboratories, a GLP certificate issued by a recognized regulatory authority or a current ISO/IEC 17025 accreditation certificate or prequalification of the laboratory by WHO is required For outsourced sterilization facilities, certification to applicable ISO sterilization standards (e.g. ISO 11137, ISO 11135) is necessary

Table A9.2 *continued*

	Required evidence	Comments and exceptions
	Quality manual, laboratory manual or equivalent	The quality manual or laboratory manual should be written in accordance with the principles of *WHO good practices for pharmaceutical quality control laboratories* (*8*), or as per the ISO/IEC 17025 *General requirements for the competence of testing and calibration laboratories* (*14*).
	Contract or agreement between the FPP or API manufacturer and the outsourced testing laboratory or sterilization institution	A copy of the contract or agreement clearly describing the roles and responsibilities of the manufacturer and the testing laboratory or sterilization institution should be submitted
	A list of tests a laboratory is authorized to perform as per the scope of its accreditation according to the ISO/IEC 17025 or WHO prequalification For botanical ingredients, evidence that authenticated standard reference materials are used	The scope of activities of the outsourced laboratory should include the type, range and volume of testing and/or calibration, validation and verification activities it undertakes
	Out-of-specifications (OOS) procedure	Records of three OOS including at least one assigned to a laboratory error
Evidence list E	Current GCP or GLP certificate or approval letter	GCP/GLP certificate or approval letter issued by the NRA; non-use of disbarred investigators or firms

Table A9.2 *continued*

	Required evidence	Comments and exceptions
Evidence list F	Clinical trial approval by the NRA	Provide a list summarizing the approved trials and their outcome Provide complete study report if no application has been submitted for marketing authorization of a product Where applicable, reports from a data safety monitoring board or independent safety monitors should be provided
	Copy of IRB/IEC clinical trial approval	Provide approved protocol, amended protocol and consent form Provide a list of committee members of the IRB/IEC
	Clinical trial master file	Responsibilities of the sponsor and clinical investigator should be reported Records of management and assessment of subcontracted vendors should be provided Deviation management and procedures for handling the investigational product should be made available
	Inspections conducted within the past three years and a copy of the most recent inspection report issued by the competent regulatory authority as stated in Table A9.1	A list of all inspection reports applicable to the scope of the application is required. These may be sent to the NRA directly from the manufacturer or CRO Provide the following reports: • reports by the NRA; • clinical monitoring reports by the sponsor or the CRO (if monitoring tasks were outsourced to a CRO)

Table A9.2 *continued*

	Required evidence	Comments and exceptions
	Concerns or alerts raised by the NRA and any other responsible authority	Provide details of investigation of any instances of noncompliance and how they were addressed

API: active pharmaceutical ingredient; CAPA: corrective and preventive action; CRO: contract research organization; FPP: finished pharmaceutical product; GLP: good laboratory practices; GMP: good manufacturing practices; IEC: independent ethics committee; IRB: institutional review board; ISO: International Organization for Standardization; NRA: national regulatory authority; PQR: product quality review.

[a] Refer to WHO Technical Report Series, No. 961, Annex 14 , for guidelines on compiling a site master file (*13*).

7.3 General requirements for documents

Documents to be submitted to NRAs as evidence of compliance should adhere to the following general requirements.

- All certificates and other supporting documents should be in English or in a nationally accepted language.
- Where the document is not in English or a nationally accepted language, it should be submitted with a certified translation.
- Translated documents must be accompanied by a signed and dated statement by the certified translator, stating that each is a true and accurate translation of the original document.
- Submitted documents should be the most recent and reflect current activities and practices, and dated (expired or superseded documentation cannot be used).
- Documents must provide sufficient information to cover the scope of activities for which confirmation of GxP compliance is sought.

All documents, whether the original format is paper or electronic, are to be submitted electronically (for example as DVDs CDs, etc.) and are not required to be certified as original copies unless requested by the NRA. Certification of a document may be requested if, for example, there is concern over the validity of the supplied documents. The NRA can request certified copies of original documents at any time. Certified copies must be legible and authenticated as true copies by either:

- an official of the regulatory agency of a country that is a party to an MRA, or a partner to an MoU or a CA, WHO prequalification, stringent regulatory authority, regulator; or

– a public notary (who must include details of the relevant practice certificate or licence number).

Figure A9.1
Model declaration form for the front page of a certified document

Declaration of authenticity

I, the undersigned, as a _____ for the state of _____ , country _____
declare that the attached copy of the document issued by _____ and certified by me, is a true and accurate copy of an original document presented to me for certification.

_____ Date: _____ /_____ /_____
Full names [signature] day/month/year

8. Regulatory actions and reporting of serious instances of noncompliance

Regulatory actions should be taken by NRAs in response to the reporting of serious instances of noncompliance, such as a variation from the registered product that has a direct impact on the safety of a patient or subject, and follow applicable procedures for appropriate investigations.

The impact of the noncompliance should be assessed by the NRA to ascertain the potential risk to public health, supply and availability of affected medicines. This assessment should take into consideration the risk of exposure to national shortages having undesirable safety and financial implications.

The following are some of the actions that can be taken by the NRA in response to confirmed reports of serious noncompliance:

– issuance of a rapid public alert to collaborating partners;
– issuance of a noncompliance letter;
– suspension, revocation, withdrawal or cancellation of GMP, GLP or GCP certificate;
– suspension of certificate of suitability;
– institution of a recall;
– suspension of supply or importation;
– prosecution.

8.1 Communication and information exchange

There should be a mechanism for exchange of information among inspectorates, for example, a shared web-based portal for communication of serious instances of noncompliance in a timely and secure manner. The NRA should have a process for information exchange and use of identifiers for tracking enquiries and applicants' responses.

If facilities are found to have serious issues of noncompliance with GMP, GLP or GCP guidelines, this should be communicated to stakeholders and partners. The regulatory decision and action taken should be explained to the stakeholders, including the analysis of the risk and threats to the patient.

9. Responsibilities of the applicant

The main responsibilities of an applicant for GMP, GLP or GCP desk assessment are summarized below.

- Ensuring that all required evidence documents are submitted with applications for GMP, GLP or GCP desk assessment. Incomplete applications may be rejected.
- Remitting all application fees at the time of lodging an application for GMP, GLP or GCP desk assessment.
- Submitting applications for renewal of a GMP, GLP or GCP certificate prior to the expiry of the current certificate, according to a deadline specified by the NRA.
- Promptly submitting any additional information that may be requested by the NRA during an assessment. Failure to provide required documents in time may result in the application being rejected.

References and further reading

References

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2. Compilation of community procedures on inspections and exchange of information EMA/572454/2014 Rev 17 compliance and inspection. London: European Medicines Agency; 2014.
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4. Guidelines for good clinical practice for trials on pharmaceutical products. In: WHO Expert Committee on the Selection and Use of Essential Medicines: sixth report. Geneva: World Health Organization; 1995: Annex 3 (WHO Technical Report Series, No. 850).

5. Guidelines on pre-approval inspections. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fourth report. Geneva: World Health Organization; 2002: Annex 7 (WHO Technical Report Series, No. 902).

6. Provisional guidelines on the inspection of pharmaceutical manufacturers. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-second report. Geneva: World Health Organization; 1992: Annex 2 (WHO Technical Report Series, No. 823).

7. WHO good manufacturing practices for pharmaceutical products: main principles. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-eighth report. Geneva: World Health Organization; 2014: Annex 2 (WHO Technical Report Series, No. 986).

8. WHO good practices for pharmaceutical quality control laboratories. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-fourth report. Geneva: World Health Organization; 2010: Annex 1 (WHO Technical Report Series, No. 957).

9. Guidance for organizations performing in vivo bioequivalence studies. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fiftieth report. Geneva: World Health Organization; 2016: Annex 9 (WHO Technical Report Series, No. 996).

10. ICH Q9 quality risk management. Geneva: The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q9/Step4/Q9_Guideline.pdf).

11. Guidelines on quality risk management. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-seventh report. Geneva: World Health Organization; 2013: Annex 2 (WHO Technical Report Series, No. 981).

12. Guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-eighth report. Geneva: World Health Organization; 2014: Annex 5 (WHO Technical Report Series, No. 986).

13. Guidance for site master file. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-fifth report. Geneva: World Health Organization; 2011: Annex 14 (WHO Technical Report Series, No. 961).

14. ISO/IEC 17025:2005, General requirements for the competence of testing and calibration laboratories. Geneva: International Organization for Standardization/International Electrotechnical Commission; 2005.

Further reading

ICH efficacy guidelines (R2). Geneva: The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html).

Inspection of pharmaceutical manufacturers, Annex 2, WHO Technical Report Series 823, 1992.

ISO 11135:2014. Sterilization of healthcare products – ethylene oxide – requirements for the development, validation and routine control of a sterilization process for medical devices. Geneva: International Organization for Standardization; 2014.

ISO 11137-1:2006. Sterilization of healthcare products – radiation – part 1: Requirements for development, validation and routine control of sterilization process for medical devices. Geneva: International Organization for Standardization; 2006.

ISO 11137-2:2013, Sterilization of healthcare products – radiation – part 2: Establishing the sterilization dose. Geneva: International Organization for Standardization; 2013.

ISO 9001:2015. Quality Management Systems – Requirements. Geneva: International Organization for Standardization; 2015.

ISO/IEC 17020:2012. Conformity assessment – Requirements for the operation of various types of bodies performing inspection. Geneva: International Organization for Standardization/International Electrotechnical Commission; 2012.

Outline of a procedure for coordinating the verification for the GMP status of manufacturers in third countries. London: European Medicines Agency; 2005.

PIC/S. Recommendation on quality system requirements for pharmaceutical inspectorates PE 009-13 (Annexes). Geneva: Pharmaceutical Inspection Co-operation Scheme; 2017.

PIC/S. Recommendation on quality system requirements for pharmaceutical inspectorates, PI 002-3. Geneva: Pharmaceutical Inspection Co-operation Scheme; 2007.

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WHO Guidelines on variations to a prequalified product. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-seventh report. Geneva: World Health Organization; 2013: Annex 3 (WHO Technical Report Series, No. 981).

Appendix 1

Model report format for desk assessment for finished pharmaceutical products and active pharmaceutical ingredient manufacturers

Part 1. General information		
a)	Particulars of the applicant	Name of applicant, physical address, postal address of applicant (if different from physical address), 24-hour telephone numbers, fax, email address
b)	Particulars of the manufacturer	Name of manufacturer, physical address of manufacturer including the block and/or unit number, postal address of manufacturer (if different from physical address), 24-hour telephone number(s), fax, email address, contact person
c)	Activities performed on the site	For example, manufacture of APIs, manufacture of FPPs, intermediates or bulk packaging, laboratory testing, batch release, warehousing, primary and secondary packaging
d)	Date of last inspection by the NRA	Date when the last inspection was carried out, name of the national medicines regulatory authority that carried out the inspection
e)	Production and packaging lines applied for	For FPP: dosage form line, category: beta lactam, non-beta lactam, biologicals, vaccines, hormones, cytotoxic products For API: name of API
f)	Authorized representative of marketing authorization holder in the recipient country	For example, representative, agent

Table *continued*

Part 2. Documentary evidence (comment on adequacy of information provided)		
a)	Current site master file	Comment on date, completeness and adequacy in accordance with WHO or PIC/S guidelines for writing site master file
b)	List of all regulatory inspections carried out in the past three years	Name of all the regulatory authorities that carried out the inspection, dates when the inspection was carried out, inspection outcome
c)	Copy of valid manufacturing licence granted by the NRA together with a certified translation, if not in English	Number of manufacturing licence, name of regulatory authority that granted the licence, validity of the manufacturing licence and scope
d)	Copy of valid GMP certificate granted by the national medicines regulatory authority together with a certified translation, if not in English	Number of GMP certificate, name of NRA that granted the certificate, validity of the GMP certificate and scope
e)	List of products manufactured at the site and those to be exported to the country of import	List of products, dosage form (where applicable), list of registered products and those to be registered
f)	Notarized copy of inspection report(s) from the national medicines regulatory authority and/or that from WHO prequalification (whichever is applicable) carried out within the past three to five years	• Name of the regulatory authority that carried out the inspection, dates of the inspection, scope of inspection, findings and recommendations, list of findings of noncompliance, conclusion • CAPA reports submitted and found satisfactory for the most recent inspection (adequacy of CAPA, timelines)
g)	Performance of the company's products on the market over the past three years	Any product alerts, warning letters, market complaints, product failure, product recall or any unacceptable findings for the product(s) in scope Any product alerts, warning letters, market complaints, product failure, product recall, or any unacceptable findings for the product(s) in scope

Table *continued*

h)	Reports of product quality review	For products for which marketing authorization is being sought or renewed: assess the consistency of the processes, trends, specifications, process changes, recalls, returns, market complaints, deviations from critical parameters, in-process controls, quality control tests, stability study data (select product of interest)
i)	Validation master plan	Validation policy, utilities qualification, equipment qualification, procedures, protocols, reports, cleaning, personnel qualification, process validation, analytical method validation, computer validation, revalidation, requalification, validation matrix
j)	Process validation for one of the products marketed or to be registered in the country of import	Comment on adequacy
k)	One batch manufacturing record (BMR) for each product together with the master batch record including the packing and analytical part (with a certified translation of the original BMR where applicable); BMR should refer to a product marketed or to be registered in the country of import	Comment on adequacy
l)	Out-of-specification (OOS) procedure: records of three OOS including at least one assigned to a laboratory error	
m)	List of reprocessed or reworked product batches in the past two years	

Table *continued*

Part 3. Recommendation
1. Recommended for a GMP compliance approval? *(Provide recommendation based on the results of the assessment done in Parts 1 and 2)*
2. If Yes, list production lines, product, pharmaceutical active ingredient recommended:
3. If No, state reasons and the relevant sections of the guideline(s) below:

Part 4. Evaluation team
First assessor Signed: _____ Date: _____ Name: _____ Position: _____ (BLOCK CAPITALS)
Second assessor Signed: _____ Date: _____ Name: _____ Position: _____ (BLOCK CAPITALS)

API: active pharmaceutical ingredient; CAPA: corrective and preventive action; FPP: finished pharmaceutical product; GMP: good manufacturing practices; NRA: national regulatory authority; PIC/S: Pharmaceutical Inspection Co-operation Scheme.

Appendix 2

Model report format for desk assessment of quality control laboratories

Part 1. General information		
a)	Particulars of the applicant	Name of applicant, physical address, postal address of applicant (if different from physical address), 24-hour telephone numbers, email address
b)	Particulars of the quality control laboratory (QCL)	Name of QCL, physical address of QCL, postal address of the laboratory (if different from physical address), 24-hour telephone number(s), email address, contact person
c)	Date of last inspection by SRA, WHO or accreditation body for ISO/IEC 17025	Name of NRA or accreditation body that carried out the inspection, dates when the inspection was carried out and the inspection outcome
Part 2. Documentary evidence (comment on adequacy of information provided)		
a)	Copy of appropriate certificate or approval granted by a recognized regulatory authority or accreditation certificate granted by accreditation body for ISO/IEC 17025 together with a certified translation, if not in English	Number/reference of appropriate certificate or approval or ISO/IEC 17025 certificate, name of regulatory authority that granted the certificate and validity of the certificate
b)	Scope of accreditation	Indicate the analytical methods and techniques
c)	Current quality manual, laboratory manual or equivalent	Comment on adequacy[a]
d)	Contract between the manufacturer and contract laboratory and its subcontractors if applicable (where testing is outsourced)	Comment on adequacy of the agreement stating responsibilities of the parties

Table *continued*

e)	List of all inspections carried out in the past three years by a regulatory authority or accreditation body	Provide the list of regulatory authority or accreditation body indicating the name, date of inspection and outcome in the inspection
f)	Copy of inspection report(s) from regulatory authority or accreditation body and/or from WHO prequalification (whichever is applicable) carried out within the past three to five years	Name of the regulatory authority or accreditation body that carried out the inspection, dates of the inspection, scope of inspection, findings and recommendations, list of instances of noncompliance, conclusion
g)	CAPA reports submitted and found satisfactory for the most recent inspection	Comment on adequacy
h)	Register of OOS, OOS procedure and investigation reports of at least three OOS assigned to laboratory error in past one year handled	Comment on adequacy
Part 3. Recommendation		
1.	Recommended for a GMP compliance approval? *(Provide recommendation based on the results of the assessment done in Parts 1 and 2)*	
2.	If Yes, state laboratory testing activities/product analysed:	
3.	If No, state reasons and the relevant sections of the guideline(s) below:	

Table *continued*

Part 4. Evaluation team

First assessor

Signed: _____ Date: _____

Name: _____ Position: _____
(BLOCK CAPITALS)

Second assessor

Signed: _____ Date: _____

Name: _____ Position: _____
(BLOCK CAPITALS)

CAPA: corrective and preventive action; ISO/IEC: International Organization for Standardization/International Electrotechnical Commission; NRA: national regulatory authority; OOS: out of specification; SRA: stringent regulatory authority.

[a] Refer to WHO good practice for pharmaceutical quality control laboratories. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-fourth report. Geneva: World Health Organization; 2010: Annex 1 (WHO Technical Report Series, No. 957).

Appendix 3

Model report format for desk assessment for contract research organizations and clinical trial sites

Part 1(i). General information – study		
a)	Particulars of the applicant	Name of applicant, physical address, postal address of applicant (if different from physical address), 24-hour telephone numbers, email address
b)	Particulars of the organization	Name of research organization, physical address, postal address (if different from physical address), 24-hour telephone number(s), fax, email address
c)	Title of the study	
d)	Particulars of the bioanalytical laboratory	Name of bioanalytical laboratory, physical address of bioanalytical laboratory, postal address of the laboratory (if different from physical address), 24-hour telephone number(s), fax, email address
e)	Particulars of the sponsor	Name of sponsor, 24-hour telephone number(s), fax, email address, contact person
Part 1(ii). General information – site quality management system		
a)	Date of last inspection by NRA (if applicable)	Dates when the last inspection was carried out; name of the national medicines regulatory authority that carried out the inspection
b)	Particulars of the investigator's current curriculum vitae and/ or qualifications	

Table *continued*

Part 2(i). Documentary evidence – study		
a)	Copy of institutional review board (IRB)/independent ethics committee clinical trial/ bioequivalence (BE) study approval	For multicentre trials, only the study approval issued by the IRB/IEC of the coordinating investigator of the trial is required
b)	Copy of clinical trial/BE approval granted by a competent national medicines regulatory authority with a certified translation, if not in English	Name of the approving authority, validity of approval (study)
c)	Copy of clinical trial/BE/ bioavailability study protocol and any amendments[b]	Comment on the trial design, selection and withdrawal of subjects, treatment of subjects, assessment of efficacy, assessment of safety, statistics, data handling and record-keeping, ethics, financing and insurance, quality control and quality assurance, and publication policy
d)	Copy of investigator's brochure	Confidentiality statement, physical chemical and pharmaceutical properties and formulation, nonclinical studies, effects in humans, summary of data and guidance for the investigator
e)	Copy of current clinical trial/ BE reports including safety reports	Comment on adequacy and compliance with the protocol (study)
f)	Copy of clinical trial monitoring report by the sponsor or contract research organization (CRO)	
Part 2 (ii). Documentary evidence – site quality management system		
a)	Copy of current GCP/GLP certificate or regulatory approval	
b)	Number of clinical trials/BE study approvals granted by a national medicines regulatory authority in the past five years, with a certified translation, if not in English	State number of approved clinical trials/ BE studies and their outcomes, name of the approving authority, validity of approval

Table *continued*

c)	Copy of current clinical trial master file[a] (make reference to the quality assurance mechanism for CRO) Documentation on the responsibilities of the sponsor and clinical investigator, management and assessment of subcontracted vendors should be provided.	Comment on adequacy of deviation management and procedures for handling the investigational product
d)	List of all inspections carried out in the past three years	Clinical monitoring reports by the sponsor or the CRO (if monitoring tasks were outsourced to a CRO)
e)	Copy of inspection report(s) from national medicines regulatory authority and/or that from WHO prequalification (whichever is applicable) carried out within the past three to five years	Including bioanalytical method validation and compliance with GLP
f)	Provide evidence of NRA oversight including concerns raised and alerts, if any	
g)	Copy of study monitoring report by the sponsor or CRO (where applicable)	
Part 3: Recommendation		
1.	Recommended for a GCP compliance approval? *(Provide recommendation based on the results of the assessment done in Parts 1 and 2)*	
2.	If Yes, study/clinical trial site recommended:	
3.	If No, state reasons and the relevant sections of the guideline(s) below:	

Table *continued*

Part 4. Evaluation team	
First assessor	
Signed: _____	Date: _____
Name: _____ (BLOCK CAPITALS)	Position: _____
Second assessor	
Signed: _____	Date: _____
Name: _____ (BLOCK CAPITALS)	Position: _____

GCP: good clinical practices; GLP: good laboratory practices; NRA: national regulatory authority.

[a] Guidelines for good clinical practice E6 (R1), Current Step 4 Version, 10 June 1996. Geneva: International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf).

[b] Guidance for organizations performing in vivo bioequivalence studies (revision). In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fiftieth report. Geneva: World Health Organization; 2016: Annex 9 (WHO Technical Report Series, No. 996).