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GDP inspection procedure

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1. Introduction

In accordance with Art 111 of Directive 2001/83/EC and 123 (1) of Regulation 2019/6 competent authorities are required to perform inspections of wholesale distributors and their premises and may also, for medicinal products for human use only, perform inspections of brokers. The purpose of this document is to provide guidance on the conduct of inspections to harmonise inspection procedures, frequency of inspections and follow-up procedures thus ensuring a consistent approach to assessment and decision-making by Competent Authorities.

2. Scope

This guideline defines the basic procedures to be followed by an inspector when preparing for and performing Good Distribution Practice inspections. It gives guidance on issuing an inspection report that should list and categorise all deficiencies found during the inspection. It describes the issue of a certificate when finalising the inspection. This document describes also how to establish the frequency of inspections.

3. General considerations on inspections

The primary role of the inspector is the protection of public and animal health in accordance with Union provisions. The function of the inspector is to ensure adherence by wholesale distributors and brokers to GDP principles and guidelines and compliance with legislation.

The primary goal for the inspector should be to determine whether the various elements within the quality management system are effective and suitable for achieving compliance with GDP principles.

Inspectors should strive to create a positive atmosphere during the inspection. The inspector should be aware of his/her influence in decision making processes. The inspector should always answer questions but avoid entering the role of a consultant.

Different types of inspection may be carried out according to the activities of the company. The conduct of an inspection may vary according to its objectives and may for example focus on the general level of GDP compliance, or on a particular activity covered by the wholesale distributor.

GDP inspections may be performed before granting or modifying a wholesale distribution authorisation. Routine GDP inspections cover the assessment of GDP compliance of a site. Non-routine inspection may be conducted to check specific aspects of GDP compliance, for example investigation of complaints, recalls, quality defects, previous non-compliance or suspected falsified products.

The wide diversity of facilities together with the variety of products supplied and handled by a site means that assessment by inspectors on site of the degree of compliance with GDP is essential. A consistent approach to the evaluation of the GDP standard is required.

Inspections may disturb the normal working patterns within a company and inspectors should therefore carry out their inspection in a careful and planned manner. Inspectors should be aware of the confidential nature of their work.

4. Inspection procedures

4.1 Planning of Inspections

The competent authority should plan inspections in advance and elaborate a programme. This programme should ensure that the frequency of inspection of individual wholesale distributors can be adhered to as planned. Sufficient and qualified resources must be determined and made available to ensure the designated programme of inspections can be carried out in an appropriate manner.

4.2 Preparation of Inspections

Prior to conducting an inspection, the inspector should familiarise him/herself with the company to be inspected according to the inspectorate's procedures. This may include the following:

Figure: 1. Review of documents requested prior to the inspection;

Figure: 2. Review of the activities conducted by the company and types of products authorised under the wholesale distribution authorisation of the company (may include internet search about the company);

Figure: 3. Review of reports from previous inspections and other records available;

Figure: 4. Review of responses (follow-up actions) as committed to by the company arising from deficiencies identified during previous inspections;

Figure: 5. Review of product recalls and suspected falsified medicinal products since the previous inspection;

Figure: 6. Review of any specific standards/guidelines associated with the site to be inspected (e.g. internal Inspectorate guidelines).

Plan the areas to be covered during the inspection and where considered appropriate, prepare a written plan. In the case of an inspection team, the lead inspector shall coordinate these activities, delegating the inspection preparation activities as he/she considers appropriate.

The inspection plan may include:

Figure: 7. The objectives and scope of the inspection in light of previous inspections;

Figure: 8. Identification of the inspection team members and their respective roles;

Figure: 9. Identification of the organisational units to be inspected;

Figure: 10. The expected time and duration for each major inspection activity (premises and equipment, personnel etc.);

Figure: 11. The schedule for the close-out meeting.

4.3 Announcement of inspection

Competent Authorities have the right to inspect at any time. Prior announcement of inspection may be given. By informing in advance the day(s) for the inspection to take place and the length of time the inspector expects to be on site, the objectives of the inspection will be known to the company and the relevant personnel and documentation can be made available.

4.4 The opening meeting

Request an opening meeting with the management and key personnel of the company to introduce yourself and any accompanying official(s) or specialist(s) and to discuss general details of the inspection plan. Immediate site tour upon arrival may be of value in some cases, particularly where the inspection is unannounced.

During the opening meeting the inspector should:

Figure: 12. outline the purpose and scope of the inspection;

Figure: 13. identify of any hazards on site;

Figure: 14. review previous inspection issues and outstanding corrective / preventative actions;

Figure: 15. identify the activities of the company including significant changes since the last inspection;

Figure: 16. inform the company of the documentation which may be required during the inspection;

Figure: 17. if considered appropriate to the inspection request a rapid initial site tour for familiarisation with the site.

During the opening meeting the company should:

Figure: 18. present the management structure and quality management within the company;

Figure: 19. explain significant changes in premises, equipment, products and personnel since the last inspection;

Figure: 20. identify personnel to accompany the inspector and allocate a room to review documentation if requested.

4.5 The inspection

During the inspection, always discuss observations as they arise to establish facts, indicate areas of concern and to assess the knowledge and competence of personnel.

A detailed plant tour may be performed to determine whether the facilities and equipment are of suitable lay-out and design and whether the way in which these are used suits the intended operations. Normally, for the first inspection of a site, the logical flow of products is followed.

It may be appropriate to concentrate effort in one department of the company if there are special problems or requirements.

The system of documentation, based on procedures and records covering the distribution operations should be checked by examining particular examples at different stages throughout the receipt, storage, assembly and dispatch process.

In order to assess compliance with the terms and conditions of the wholesale distribution authorisation the following documentation may be examined:

Quality management system related documentation:

Figure: 1. standard operating procedures (SOPs);

Figure: 2. job descriptions and personnel training records;

Figure: 3. supplier and customer qualification records;

Figure: 4. contract agreements for outsourced activities;

Figure: 5. system for handling a suspected falsified medicinal products;

Figure: 6. deviations from standard processes;

Figure: 7. suitability of premises.

Documentation of ongoing activities:

Figure: 1. review of actual operating activities and changes;

Figure: 2. review of supply chain;

Figure: 3. check of invoices correlating to supply chain;

Figure: 4. temperature and humidity monitoring of storage areas;

Figure: 5. verification of effectiveness of low temperature storage facilities;

Figure: 6. returned product log;

Figure: 7. records of product quality complaints;

Figure: 8. records of product recalls and mock recalls;

Figure: 9. self-inspection system and execution;

Figure: 10. review records related to transportation.

Wholesaler distributors may be inspected with regard to their capability to maintain the minimum stock of life saving medicinal products according to national law. Their internal procedures to be on stand-by in case of emergency should be critically reviewed.

Facts and objective evidence supporting the observations should preferably be agreed by the company. The company may if they so wish discuss initial proposals for remedial action but these discussions should not delay the progression of the inspection.

In the case where serious deficiencies leading to possible risk for the patient/animal and public or animal health are identified, immediate action should be taken. These actions may include requesting the company to complete any of the following:

Figure: 1. Voluntarily suspending the wholesale distribution activities/operations impacted (e.g. supply of products requiring low temperature storage);

Figure: 2. Quarantining and withholding from sale, supply or export any batches of medicinal products impacted;

Figure: 3. Initiating the recall of impacted batches of medicinal products that have already been sold, supplied or exported.

The inspector should ensure, where appropriate, that these restrictions have been implemented by the company prior to completing the inspection. This should include obtaining written statements to this effect from the appropriate personnel. This should also include commitment that the restrictions will remain in place, until the underlying deficiencies have been addressed to the satisfaction of the competent authority.

Throughout the inspection, review:

Figure: 1. The completeness of the inspection with respect to the original objectives;
Figure: 2. Conduct of the inspection with reference to the areas covered / not covered;

Figure: 3. Classification of deficiencies and inter-related deficiencies which may be indicative of a system failure rather than isolated incidents.

Ensure that deficiencies are discussed during the course of the inspection so that an inordinate amount of time is not taken up with discussion at the final close out meeting.

4.6 The close-out meeting

The close-out meeting is a significant part of the inspection. Summarise and classify the findings of the inspection in the close-out meeting with representatives of the company. Senior management of the company should be present, where appropriate. Discuss the deficiencies observed during the inspection and their classification. Where considered necessary, discuss deadlines for remedial actions.

As far as possible all relevant observations should be reported at this meeting so that the company can initiate the necessary corrective actions at the earliest possible date.

Assess the need for a follow-up inspection based on the nature of the deficiencies observed. The company should be informed at this stage of the possible need for a follow-up inspection. In certain cases, it may be appropriate to evaluate the responses received from the company before determining

if a follow up inspection is required.

In certain cases of critical non-compliance further actions may be taken against the authorisation holder or broker by the competent authority.

5. Inspection report

The contents of the initial inspection report should be sent to the company for its comments to enable the report to be finalised within the relevant timeframe of the inspection request and to enable, if applicable the issue of a GDP certificate within the statutory 90-day timeframe.

A response with proposed corrective actions should be requested to be returned by the company in due course. These corrective actions and proposed timelines for their implementation should be considered by the inspector and a decision made on whether the entity can be considered to be compliant with GDP.

The close out of the inspection should be completed within 90 days from the last day of inspection in order to issue a certificate of good distribution practices to the inspected entity if the outcome of the inspection shows that it complies with GDP. If the inspection outcome was negative, a statement of non-compliance should be issued and regulatory actions should be considered.

The GDP certificate or the non-compliance statement shall be entered in the Union database referred to in Article 111(6) of Directive 2001/83/EC and Article 91(3) of Regulation 2019/6..

Inspection reports should ideally be subject to a review process, which may include:

Figure: 1. extent and depth of inspection;

Figure: 2. classification and description of deficiencies;

Figure: 3. actions required and timelines proposed for completion;

Figure: 4. clarity and relevance of the content of the report.

6. Inspection frequency

Inspections should be carried out repeatedly to ensure compliance with GDP by the wholesale distributor and the authorised premises. The intervals between inspections should be set at a level that provides confidence that the wholesale distributor maintains continued compliance with GDP and its principles. The maximum period between inspections per site should not exceed 5 years as lack of continuity may give rise to lower awareness of current GDP or allow significant deficiencies to develop.

The activities of the individual company and its past record of GDP compliance should be taken into consideration when planning the frequency and duration of inspection. A risk based approach may be applied to establish the frequency of inspections.

Factors that could be taken into account to establish the interval between inspections might include:

Figure: 1. Size of site and number of staff;

Figure: 2. Number of customers / sales volume;

Figure: 3. Number of suppliers, type / category of supplier (special medicines);

Figure: 4. Parallel distribution/ parallel trade / import;

Figure: 5. Exporter to non-EU and complexity of the supply chain;

Figure: 6. Handling of products requiring low or high temperature storage;

Figure: 7. Contract activities;

Figure: 8. Categories of products - narcotics /non-authorised medicines in EEA / non-authorised

medicines in country of company;

Figure: 9. Previous inspection history and compliance with GDP;

Figure: 10. Number and relevance of any areas not covered at previous inspection;

Figure: 11. Number and type of deficiencies found on previous inspections;

Figure: 12. Company corrective actions proposed following previous inspections;

Figure: 13. Complaints history, number and criticality of complaints.

The risk based approach may be used to set an inspection frequency but the date of inspection should be reviewed if significant issues are reported to the competent authority. Such issues could be staff changes, complaints, recalls, quality defects, reports of suspected falsified medicines.

Inspections in the context of granting a Wholesale Distribution Authorisation should be determined on a case by case basis.

7. Inspection of brokers (medicinal products for human use only)

Inspections may also take place at the premises of brokers of medicinal products for human use. These inspections would usually be for-cause inspections to investigate a suspected non-compliance with legislation and the specific provisions for brokers in the Union Guidelines on GDP. The need for an inspection could for example be identified during inspections of wholesale distributors operations or could be triggered by the following:

Figure: 1. Suspicion of brokering of falsified medicinal products;

Figure: 2. Suspicion that the broker is not located in address to which it has registered;

Figure: 3. Suspicion that they may be conducting activities of a wholesale distributor;

Figure: 4. Suspicion of brokering between unauthorised suppliers / customers;

Figure: 5. Suspicion that paperwork conceals the true origin or destination of the product.

The inspection of a broker should be carried out in accordance with this procedure.