Appendix 11

Example of a standard operating procedure for performing an inspection

1. **Title**
   Performance of inspection

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<thead>
<tr>
<th>Signature</th>
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<tbody>
<tr>
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<td>1 July 2006</td>
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<tr>
<td>Authorized</td>
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</tbody>
</table>

2. **Policy and objective**
   2.1 Each manufacturer should be inspected by the procurement agency to assess compliance with good manufacturing practices.
   2.2 All inspectors should follow the SOP for performing inspections.
   2.3 The objective is to ensure that a standardized procedure is followed by all inspectors when performing inspections to prevent inspections being performed by different inspectors in different ways. This should ensure consistency in performance between inspectors.
   2.4 One of the objectives is to control and enforce the general standards of production for products that may be sourced as a result of the prequalification procedure.
   2.5 Through sequential examination of production and control activities of the manufacturer, the manufacturer of pharmaceutical products may be included on the prequalification list as a manufacturer of pharmaceutical products for possible supply of specified products to procurement agencies and other agencies.
   2.6 During inspections, the performance of manufacture of products and data submitted in the relevant product information files should be verified.

3. **Responsibility**
   Project Manager
   Inspectors
4. **Action**

All actions described here are taken from the details provided in the WHO publication *Quality Assurance of Pharmaceuticals*, Volume 2, Chapter 4: Inspection of pharmaceutical manufacturers and inspection of drug distribution channels. These guidelines or other similar systems operated by national drug regulatory authorities should be followed in detail.

4.1 Clarification and definitions

4.1.1 Different types of inspections are identified in the WHO text referred to above. These include:

— routine inspection;
— concise inspection;
— follow-up inspection;
— special inspection; and
— quality systems review.

4.2 The performance of the inspection is dependent on the type of inspection; however, in principle, the basic aspects of this procedure can be followed for performance of an inspection.

4.3 A routine inspection is a full review of all aspects and components of GMP within a facility. It is appropriate to perform a routine inspection under the following circumstances:

- When there is a new expression of interest (EOI) from a manufacturer or a newly established manufacturer.
- When the listing on the prequalification list is due for renewal.
- If there have been significant changes such as new products or new product lines; modification to manufacturing methods or processes; or changes in key personnel, premises and/or equipment.
- If an inspection has not been carried out within the past 3–5 years.

4.4 A concise inspection is the evaluation of limited aspects relating to GMP compliance within a facility. (It is known as an abbreviated inspection in some countries.) A limited number of GMP requirements are selected by the inspector to serve as indicators of overall GMP compliance by the manufacturer. The inspector also has to identify and evaluate any significant changes that could have been introduced by the manufacturer since the last inspection.

4.4.1 Collectively, the selected indicators and the changes identified indicate the manufacturer’s attitude towards GMP.

4.4.2 A concise inspection is appropriate under the following circumstances:

- Where a manufacturer has a consistent record of compliance with GMP through routine inspections in the past.
• Where a sample of aspects can be taken as a good indication of the overall level of compliance with GMP.

4.4.3 However, if the concise inspection uncovers evidence that the level of GMP compliance has fallen, a more comprehensive or full GMP inspection should be performed soon after the concise inspection.

4.5 A follow-up inspection is also referred to as a re-inspection or a reassessment of the manufacturer.

4.5.1 A follow-up inspection is performed specifically to monitor the result of corrective actions of the manufacturer following a previous inspection.

4.5.2 Depending on the nature of the defects and the work required, the follow-up inspection could be carried out between 6 weeks and 6 months after the original inspection took place.

4.5.3 The follow-up inspection is limited to specific GMP requirements that have not been observed or that have been inadequately implemented by the manufacturer.

4.6 There are a number of circumstances in which special visits or inspections may be necessary. A special inspection is undertaken to do spot checks. Spot checks could focus on one product, a group of related products, or specific operations e.g. mixing, or labelling. If there have been complaints about a specific product that suggest there may be defects, a special inspection could be performed to investigate the quality defects of the product. If there has been a product recall, this can also trigger an inspection, as would adverse drug reactions. In the above cases, the inspection would focus on the specific product or aspect of production that is suspect. A special inspection could also be performed to gather specific information, or to investigate specific operations of the manufacturer.

4.7 The purpose of a quality systems review is to review the manufacturer’s quality system and to ascertain whether it has been shown to operate satisfactorily.

4.8 Plan the inspection to ensure that all areas for assessment are covered in the allocated timeframe. The length of time needed for an inspection is determined by a number of factors, including the type of inspection to be performed, the number of inspectors, the size of the company and the purpose of the inspection or visit.

4.9 An inspection can be performed over a period of a few days to several weeks.

4.10 The time taken will also depend on the size of the inspection team. One or more inspectors can perform the inspection as part of an inspection team.
4.11 If necessary, appoint a specialist to accompany the team during the inspection, e.g. for particular dosage forms, chemistry or another aspect, e.g. the manufacture of biologicals.

5. **Addenda**

Addendum A: Inspection programme

Addendum B: Documentation required for verification during the inspection

6. **Distribution and retrieval**

The record of distribution and retrieval of the SOP should be entered in a table; see the model below.

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<tr>
<th>Distribution</th>
<th>Retrieval</th>
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<td>Date</td>
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7. **History**

The history of changes to the SOP should be entered in a table; see the model below.

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Addendum A: Inspection programme

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Inspectors

Day 1

08:30 Arrival
08:35 Opening meeting
08:45 Company presentation
09:00 Receiving area and stores
10:30 Tea
10:45 Sampling and weighing areas
11:15 Packaging material stores and control
12:30 Lunch
13:15 Manufacturing areas
15:30 Tea
15:45 Manufacturing (cont.)
16:30 Summary of findings, day 1

Day 2

08:30 Arrival
08:35 Manufacturing area (cont.)
10:30 Tea
10:45 Laboratories
12:30 Lunch
13:15 Laboratories (cont.)
15:30 Tea
15:45 Utilities
16:30 Summary of findings, day 2

Day 3

08:30 Arrival
08:35 Utilities (cont.)
10:30 Tea
10:45 Documentation
12:30 Lunch
13:15 Documentation (cont.)
15:30 Tea
15:45 Preparation for closing meeting
16:00 Closing meeting
Addendum B: Documentation required for verification during the inspection

1. Organigram
2. Job descriptions
3. Quality policy (e.g. quality manual)
4. Validation policy (e.g. validation master plan or programme)
5. Raw material specifications (for specific products)
6. Packaging material specifications
7. Manufacturing formula and method masters
8. Packing instructions master
9. Batch manufacturing records (verification against master documents)
10. SOP index
11. SOP: self inspection
12. SOP: recalls
13. SOP: complaints plus records
14. SOP: batch number allocation
15. SOP: planned preventive maintenance
16. SOP and record: planned preventive maintenance of specific equipment
17. SOP: training (plus record of personnel)
18. SOP: environmental monitoring plus records
19. SOP: water sampling and testing plus records
20. Validation protocol and report for specific products
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