Bulk sampling

1) The drug factories inspector receive the approved invoice from custom release department
2) The inspector review the following documents in the company, And compare it with the data on the bulk container:
   a) Supplier certificate of analysis
   b) Bill of landing
   c) The invoice
3) The inspector make a (فحص مشمول) report for all bulk imported by the company and the company shouldn't open any of the containers before this report is written by the inspector.
4) In case of strips, ampoules, bottles, cream tubes:
   a) The first three consecutive batches should be sampled in case of reference countries and seven consecutive batches in case of non-reference companies and the batch should be kept hold till the release certificate is issued from NODCAR
   b) Relay on the supplier certificate of analysis
5) In case of capsules and tablets:
   a) The first three consecutive batches should be sampled in case of reference countries and seven consecutive batches in case of non-reference companies and the batch should be kept hold till the release certificate is issued from NODCAR
   b) The company should analyses the bulk products
   c) In case that the company doesn't have the ability to analyses the bulk it should make contract with another company for analysis if there isn't any way to analyses the bulk, the product should be sampled for every bulk supplied to the company
6) The inspector take sample for analysis and another sample as retained sample to be used in case of any non-conformance or re analysis is needed by NODCAR
7) The inspector reviews the final registration license and the approved documents (the pack, the pamphlets) and writes sampling report and sampling form accompanied by certificate of analysis and copy of registration license.

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8) **Release In case of first three batches:**
   a) **After the conformity report is issued from NODCAR, the inspector release the products**
9) **In case of random samples:**
   a) **The inspector delivers the conformity report to the company and writes a conformity report delivering report**
10) **In case of non-conformance for any of the three batches the rules of non-conformance is applied and another three consecutive batches just after the non-conformance batch should be sampled**
11) **If another bulk having the same batch no. that has been sampled delivered to the company, another sample should be taken with clarifying in the sampling form that it is sampled due to (different transportation conditions) and this sample will not be considered as one of the first three batches**

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Destruction

1) The inspector Attend destruction committee in the following cases:
   a) expired finished products
   b) recall for the product
   c) damaged drugs
   d) new warning
2) The drug factories inform the factory inspection department for its need for destructing damaged or expired drug products through a request letter containing (the list of name of the product, quantities, batch number s ,the reason for destruction ,approval of ministry of environment for way& place of destruction)
3) After approval from the factory inspection department the inspector attend the destruction in the presence of the destruction committee which consist of (the CAPA inspector, the responsible security of the factory, quality control, ware house, financial department, the responsible pharmacist for CAPA in the company) &count the products that should be destructed& compare it with the approved request &list from CAPA.
4) Destruction take place due to the request of the company without any responsibility on the central ADMINISTRATION OF PHARMACEUTICAL AFFAIR & according to the way &in the place previously approved on &in the presence of all the destruction committee
5) After insuring that all products have been destructed the report is written &signed from all the destruction committee and stamped by the inspector

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stamp &the original report left for the company and it should be authorized from the central administration of pharmaceutical affairs and stamped by the official stamp (ختم النسر)&copy taken to CAPA

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Finished products sampling

1) The Drug Factories Inspector has the authority to sample any batch produced in the factories
2) The inspector withdraw the sample from the company store
3) The inspector take a sample of 10 packs from the sampled batch and another 10 packs as retained sample and this sample should retain in the factory in case of non- conformance or any further analysis needed by NODCAR
4) Review the factory analysis certificate of every sampled batch & review the batch record
5) In case of toll manufacturing the inspector reviews the toll manufacturing contract.
6) The collected sample should be stamped with an authorized inspector stamp from three different sides
7) Sample should be combined with the sample sending form, the factory analysis certificate and the raw material certificate
8) The inspector writes a sampling report
9) The responsible person should sign the sampling report
10) **Random sample:**
    a) In case of random sampling keep the sampled batches hold in the factory until the release.
11) **Sampling of tender drugs:**
    a) Every batch produced for the tender purpose should be sampled
12) **Sampling of antibiotics:**
    a) 30% of batches produced annually should be sampled

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13) Sampling of large volume parenteral:

a) Sample 100% of large volume parenteral

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First three batches:

1) The inspector review the following document:
   a) Master formula & compare with the batch record.
   b) Batch record

      N.B: the size of 1st 3 batches should be 90% ± 10% of size of subsequent commercial batches

   c) Supplier of raw materials used in production is the same supplier stated in the regestration license
   d) NODCAR conformity report for the used raw materials.
2) The inspector takes samples for analysis in the company QC lab.
3) After submission of the company certificate of analysis the inspector takes the following sample (4 samples):
   a) Sample for analysis in NODCAR
   b) Retained sample remain in the company
   c) Sample for accelerated stability study and begin real time stability study.
   d) Sample for bioequivalence study or comparative in vitro dissolution (if required) from the first batch only.
4) Minute for sampling should be written clarify no. of samples taken for each purpose listed before and the remaining quantity in the company.
5) The batch should be kept hold in the factory until release from NODCAR is issued, Submission of bioequivalence study, or comparative in vitro dissolution (if required) to be approved from registration department of CAPA The company writes commitment to submit the accelerated stability study within 8 month.
6) The 2nd & 3rd batches reviewed as the first batch and sampled.
7) After wise this product if not for tender purpose or not antibiotic, will be sampled randomly.

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Non-conformity

1) In case of receiving non-conformity report from NODCAR:

2) The inspector visits the concerned company to writes none conformity minute Clarifying the following:

   a) name of product
   b) batch number
   c) batch size
   d) the remaining Quantity of batch in company store, it should be kept hold in the factory
   e) Name of production Pharmacist.
   f) Name of analyste Pharmacist.
   g) number of NODCAR non-conformity report
   h) reason for non-conformity in NODCAR report
   i) The responsible person opinion about the reason of the non-conformity with the commitment of keeping the batch holds in the company.

3) Upon the company request a 2nd sample from the non-conform batch is withdrawn for reanalysis in NODCAR.

   a) if the 2nd sample not conforms : the CAPA initiate recall process according to ministerial decree no. 540 for year 2007, in exception cases a third sample could be withdrawn after approval of NODCAR manager and the division head

   b) **if the 2nd sample conforms:** take 3rd sample

      i) if the 3rd sample conform: the batch is released

      ii) if the 3rd sample not conform (3 non-conformance): the CAPA initiate recall process according to ministerial decree no. 540 for year 2007

Note:

The inspector inspects the line on which the non-conform product was manufactured and write a report.

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Pilot batches

1) Review the patch record and confirm that the patch has been produced in manufacturing line not in the company labs and confirm that the batch size is not less than 10% from the commercial batch size
2) Review the company certificate of analysis
3) The inspector doesn't take samples unless there is an approved formula and an approved supplier for the raw material and one of these documents:
   a) Final registration license
   b) Primary registration license
   c) Approval for ongoing on the registration procedure
   d) Or a formula approved from the stability committee
4) Take sample for the bioequivalence or comparative in vitro dissolution study accompanied by the formula in the product in the presence of:
   a) Contract with a bioequivalence center authorized from central administration of pharmaceutical affairs
   b) Authorization from the a bioequivalence center to one of the factory members or presence of the a bioequivalence center member by himself to receive the sample
   c) The comparative in vitro dissolution study could be done either rin the company or in authorized center
5) The inspector write a sampling report clarifying the sample information and the receiver information (sample for the bioequivalence or comparative in vitro dissolution study will not be stamped)
6) The inspector take a sample of 10 packs from the sampled batch and another 10 packs as retained sample and this sample should retain in the factory in case of non- conformance or any further analysis needed by NODCAR
7) The inspector writes a sampling report
8) The responsible person should sign the sampling report
9) The collected sample should be stamped with an authorized inspector stamp from three different sides

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10) Sample should be combined with the sample sending form, the factory analysis certificate and the raw material certificate

This batch will never be marketed.

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Raw materials sampling

1) Active raw materials:
   a) If the company has a stable and approved supplier and the company and NODCAR have released five consecutives lots or more from the same supplier this supplier is considered as approved supplier and random samples is taken from this material after wise after (فض المشمول)
   b) If the supplier of the raw material has been changed the company should do the following studies
      i) Stability studies
      ii) Re validation studies
   c) And another five consecutives batches from the same supplier should be sampled and the first batch should be kept hold in the company until the conformity report is issued from NODCAR
2) Non-active raw materials
   a) This case is the company responsibility
3) The inspector make a (فض مشمول) report for all raw materials imported by the company and the company shouldn't open any of the containers before the (فض المشمول) report is written by the inspector.
4) Rules for (فض مشمول الرسالة)
   a) Review the shipment invoice with the actual containers in terms of quantities, lot no. and manufacturing and expiration dates
   b) Review the supplier certificate of analysis with the actual containers in terms of lot no. , manufacturing and expiration dates and presence of the same logo
   c) Make a (فض مشمول) report
   d) If there is any conflict between the invoice or the certificate of analysis and the actual containers the inspector make a report clarifying the situation and the a (فض المشمول) is delayed until the case is solved
5) The inspector sample the raw materials used in producing the first three batches
6) The company is allowed to use the raw material after sampling and a commitment should be made by the responsible pharmacist that the finished

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product shouldn't be released unless the conformity report is issued from NODCAR for the sampled raw material used in this product.

7) In case of non-conformity report is issued from NODCAR for any of the first five lots or the random sample ,another five consecutive lots should be sampled until five conformity reports is issued from NODCAR

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Rules for recall process

1) The decision of recall is taken in the following cases:
   a) If non-conformity certificate is issued from NODCAR
   b) If a new regulation from international organization is issued prohibiting the use of the drug product or the raw material used in manufacturing the product
   c) If any harm or side effect occurred upon taking the drug and not mentioned in the pamphlet.
2) The decision of recall is taken by the inspection department general manager and approved by undersecretary of pharmaceutical affairs
3) the recall process is done according to the procedure mentioned in the ministerial decree no. 540 (Refer to the attached copy)
4) The administrative department initiates the recall letter
5) The recall letter then distributed to the Provinces to monitor the recall process
6) A copy of the recall letter is sent to the manufacturer.
7) The manufacturer is committed to withdraw the non-conform product from the market on its own expenses in period not more than one month from issuing the recall letter under the supervision of the drug factories inspection
8) The recalled quantities should be discriminated in the presence of the drug factories inspector

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