The United Republic of Tanzania
Ministry of Health, Community Development, Gender, Elderly and Children

Standard Operating Procedure

When and how to conduct the Shake Test

TANZANIA
USAID FROM THE AMERICAN PEOPLE
unicef
World Health Organization
CLINTON HEALTH ACCESS INITIATIVE

Approvals	Name	Date	Signature
Authorized by:			
Reviewed by:			
Revised by:			
Original author:			

Version history

No	Date	Description of change	Reason for change
1			
2			
3			

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Distribution

Distribute this SOP to the following:

Facility type	Position(s)
Central Vaccine Stores	**Logisticians**
Regional Vaccine Stores	**Immunization and vaccine officers**
District Vaccine Stores	**Immunization and vaccine officers**

1. Policy and objectives

1.1 Policy

The Shake Test is designed to determine whether aluminium adsorbed vaccines have been frozen. Whenever it is suspected that vaccine has been frozen, at least one member of the duty personnel in every facility that stores vaccine should know how to perform and interpret the test reliably and correctly. Vaccine, which fails the Shake Test, should not be distributed or administered.

1.2 Objectives

This SOP explains when to do the Shake Test and what to do if you find vaccine that has been damaged by freezing. The Shake Test protocol is attached as Annex 1 and **must not be altered** – there is only one correct way to conduct this test.

2. Responsibility

Logisticians, Region immunization vaccine officers and district immunization vaccine officers responsible for looking after vaccine and for checking its condition

3. Associated materials and equipment

Access to a refrigerator with freezing compartment, or a freezer is essential. The test cannot be carried out in facilities that are only equipped with a refrigerator without a freezing compartment.

4. Procedure

4.1 Contact details

All Logisticians, Immunization and vaccine officers responsible for looking after vaccine must be trained to conduct the Shake Test correctly.

4.2 Applicability

The Shake Test currently applies to freeze sensitive vaccines which are:

- DTP-HepB-Hib
- TT
- PCV13
- Hepatitis B
- HPV

After freezing, the bonds between the aluminium adsorbent and the antigen in a vaccine are broken. Separated adsorbent tends to form larger, heavier granules that gradually settle at the bottom of the vial when this is shaken. Sedimentation occurs faster in a vaccine vial, which has been frozen than, in a vaccine vial from the same manufacturer, which has never been frozen.

When carried out correctly the Shake Test has been shown to have 100% sensitivity and 100% specificity and 100% positive predictive value[1].

1 Kartoğlu, Ü, *et al. Validation of the shake test for detecting freeze damage to adsorbed vaccines.* Bulletin of the World Health Organization, 2010; 88:624-631 http://www.who.int/bulletin/volumes/88/8/08-056879/en

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4.3 When and how to do a Shake Test

If a freeze Tag or FRIDGE TAGS OR other temperature-monitoring device shows a freeze alarm, or if you suspect that freezing has occurred, then the shake test must be done to confirm the status of the vaccine. Follow the Shake Test Protocol exactly as described in **Annex 1**.

Individual batches of vaccine may behave differently from one another. Therefore the procedure should be repeated with *all* suspect batches. Follow the appropriate sampling methodology as set out in Section 4.4 to ensure that all of the damaged vaccine is identified and that none of this damaged vaccine is distributed or used.

The Shake Test need NOT be conducted under the following circumstances:

- When solid frozen vaccine vial(s) have been found.

4.4 Sampling methodologies

The method for selecting the *test sample* depends upon the number of vials you suspect have been frozen.

4.4.1 Sampling incoming shipments from the vaccine supplier

When vaccine arrives from the vaccine supplier it must be inspected and approved before it can be accepted into the country supply chain. International shipments arranged by UNICEF Supply Division will always have an electronic shipping indicator in each and every shipping container. Proceed as follows:

<u>CASE 1: When there is a shipping indicator in every container:</u>

a. Mark and isolate any shipping container(s) where the electronic shipping indicator shows a freeze alarm. Keep the shipping containers in the cold chain.

b. Inspect each suspect container individually following the sampling procedure described in **Annex 1.** Draw the correct number of sample vials from locations throughout the suspect container(s), including the middle of the container(s).

c. Remember to prepare a frozen control sample for each individual vaccine batch.

d. Send the shake test results to the vaccine supplier. In the case of UNICEF-procured or donated vaccine, supply the shake test results to UNICEF for a final decision on what to do with the consignment.

e. If the decision is taken to dispose of the vaccine, discard all vaccine in the affected container(s).

<u>CASE 2: When there are no shipping indicators in the shipment, or if shipping indicators are not supplied in every container:</u>

a. Mark and isolate the entire shipment but keep it in the cold chain.

b. Follow the sampling procedure described in **Annex 1** for all vaccine in the shipment**.** Draw the correct number of sample vials from locations throughout the suspect shipment, including the middle of the container(s). Remember to prepare a frozen control sample for each individual vaccine batch.

c. Send the shake test results to the vaccine supplier. In the case of UNICEF-procured or donated vaccine, supply the shake test results to UNICEF for a final decision on what to do with the consignment.

d. If the decision is taken to dispose of the vaccine, discard all vaccine in the shipment

4.4.2 Sampling vaccine that is already in the supply chain

a. *Small numbers, single batch:* If there are only a small number of vials to be tested, and these are all from the same batch, then you should test all the vials against the control sample. A typical example would be a single refrigerator or cold box where freezing is suspected. In this case, discard all vials that fail the test and keep those which pass the test.

b. *Small numbers, more than one batch:* If there are a small number of vials to be tested, but there is more than one batch or more than one type of freeze-sensitive vaccine, then you will need to repeat the shake test for each batch and for each vaccine. In this case, discard all vials that fail the test and keep those which pass the test. **Remember:** you must also prepare a frozen control sample for each batch and for each vaccine.

c. *Large numbers:* If there are a large number of suspect vials, for example, in a cold room or a large refrigerator, you should follow the sampling procedure described in annex 2. Draw the correct number of sample vials from locations evenly distributed throughout the suspect load.

d. If any vials in the sample fail the Shake Test, all the suspect vials must be discarded, including those that have not been tested.

4.5 Disposal of freeze-damaged vaccine and frozen control samples

After you have completed the test(s) described above, discard all freeze-damaged vials and all control samples as described in TAN-EVM-SOP-E6-04: *Safe disposal of damaged or expired vaccine*.

You should never issue a vaccine vial that has deliberately been frozen as a *control sample* for a Shake Test; these vials must always be kept separated from the general stock. There are two cases to consider.

CASE 1: You may want to keep the control sample and use it for further tests. This only applies while you still hold stocks of the same batch of the same vaccine.

CASE 2: If the control sample batch has all been issued, the sample must be disposed of.

Proceed as follows:

a. Use the stock control system to 'issue' the control sample(s) for the shake test. This ensures that the vials are properly accounted for.

b. *If the control sample is to be kept for further tests*: Place the control sample in a closed plastic container in a cold room or vaccine refrigerator, clearly marked: 'CURRENT SHAKE TEST CONTROL SAMPLES'.

c. *If the control sample batch has all been issued:* Place the control sample in a closed plastic container outside the cold room, clearly marked: 'SHAKE TEST CONTROL SAMPLES FOR DISPOSAL– DO NOT USE''.

5. Related documents and SOPs

- TAN-EVM-SOP-E6-04: *Safe disposal of damaged or expired vaccine.*

Annex 1: Shake test protocol

<table>
<tr><td colspan="2">NOTES:
1. This protocol must not be altered. There is only one correct way to conduct a Shake Test.
2. The test procedure described below should be repeated with all suspect batches. In the case of international arrivals, the shake test should be conducted on a random sample of vaccine. However, if there is more than one lot in the shipment, the random sample must include a vial taken from each and every lot.</td></tr>
<tr><td colspan="2">1. Take a vial of vaccine of the same type and batch number as the vaccine you want to test, and made by the same manufacturer.</td></tr>
<tr><td colspan="2">2. Clearly mark the vial as “FROZEN.”</td></tr>
<tr><td colspan="2">3. Freeze the vial in a freezer or the freezing compartment of a refrigerator until the contents are completely solid.</td></tr>
<tr><td colspan="2">4. Let it thaw. Do <u>NOT</u> heat it!</td></tr>
<tr><td colspan="2">5. Take your “TEST” vial from the batch that you suspect has been frozen.</td></tr>
<tr><td colspan="2">6. Hold the “FROZEN” vial and the “TEST” vial together in one hand.</td></tr>
<tr><td colspan="2">7. Shake both vials vigorously for 10-15 seconds.</td></tr>
<tr><td colspan="2">8. Place both vials on a flat surface side-by-side and start continuous observation of the vials until test is finished.
(NOTE: If the vials have large labels, which conceal the vial contents, turn both vials upside down and observe sedimentation in the neck of the vial.)</td></tr>
<tr><td colspan="2">Use an adequate source of light to compare the sedimentation rates between vials.
IF,</td></tr>
<tr><td>9. The TEST vial sediments slower than the FROZEN vial,
THEN,</td><td>10. Sedimentation is similar in both vials
OR
The TEST vial sediments faster than the FROZEN vial
THEN,</td></tr>
<tr><td>11. Use the vaccine batch.</td><td>11. <u>Vaccine damaged</u>: Notify your supervisor. Set aside all affected vaccine in a container marked “DAMAGED VACCINE FOR DISPOSAL– DO NOT USE”</td></tr>
<tr><td rowspan="2"></td><td>12. Discard all affected vaccine once you have received permission to do so.</td></tr>
<tr><td>13. Fill in the Loss/Adjustment Form.</td></tr>
</table>

Annex 2: Sampling method

Any pharmaceutical system should have a quality control plan in place, which describes the sampling procedure to be used in cases such as the one given in the example below.

This annex shows how to use a quality control sampling system.

Example:

A batch of Hepatitis B Vaccine is held at the central store. The temperature records show that the vaccine may have been frozen during storage.

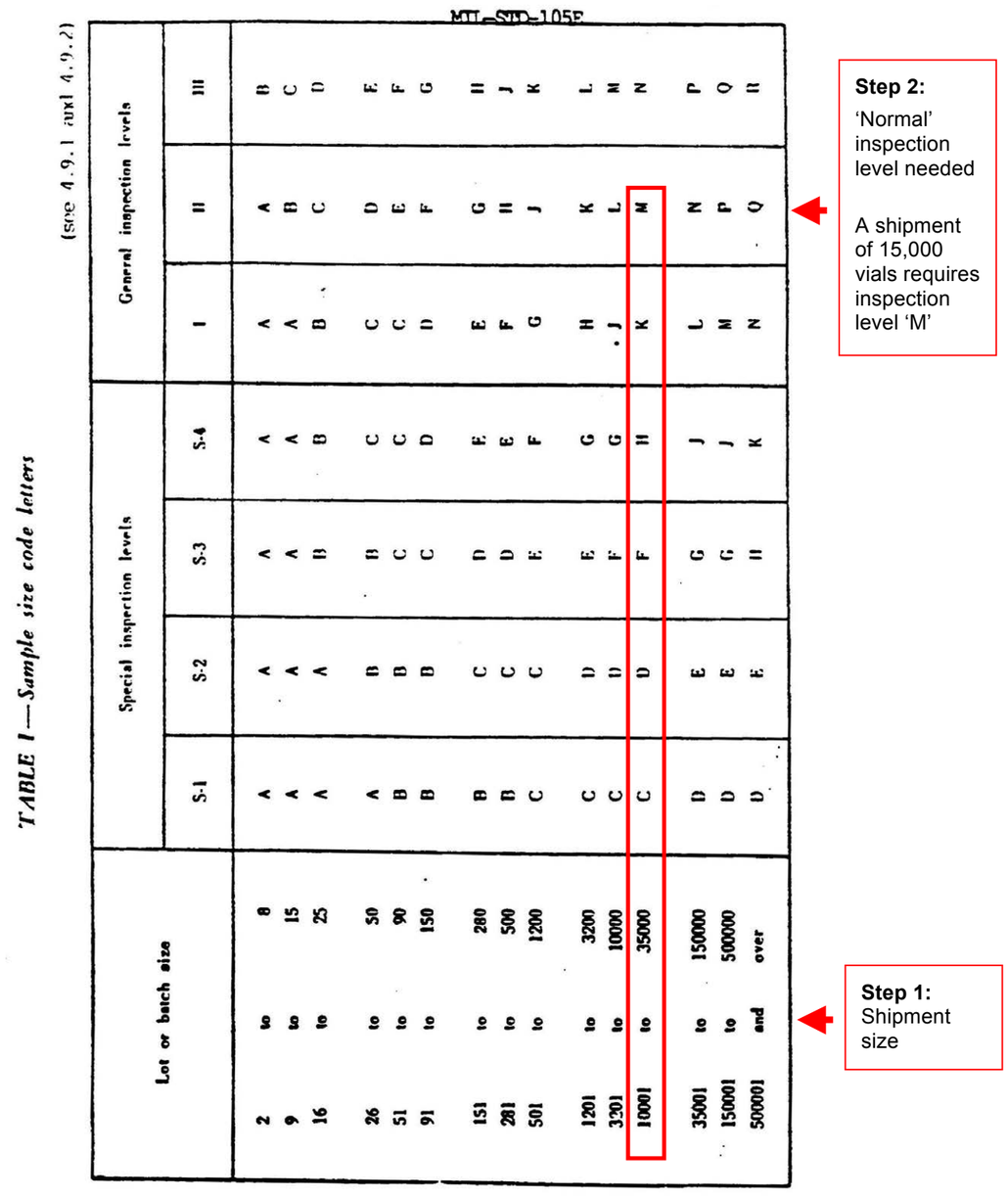
The batch consists of 15,000 vials. It is impossible to do the shake test on all the vials and a representative sample must therefore be tested. How many vials should be tested in order to indicate the status of the batch?

Notes on sampling:

1. It is assumed that a 'normal' inspection level will be adequate.
2. For freeze sensitive vaccines, freezing is a *critical defect* and therefore the acceptance/ rejection criteria will always be 0 and 1. This means that you can accept the shipment if zero vials in the sample fail the test, but you **must** reject the shipment if one or more vials in the sample fails.

Step 1: Refer to Table 1 on page 13 of the Standard. Find the appropriate size range for the shipment in the *Lot or batch size* column as shown in the example below.

Step 2: Find the matching sample size code in the *General Inspection Levels* column II as shown in the example.



Step 3: Use Table II-A on page 14 of the Standard to determine sample size and acceptance/ rejection criteria.

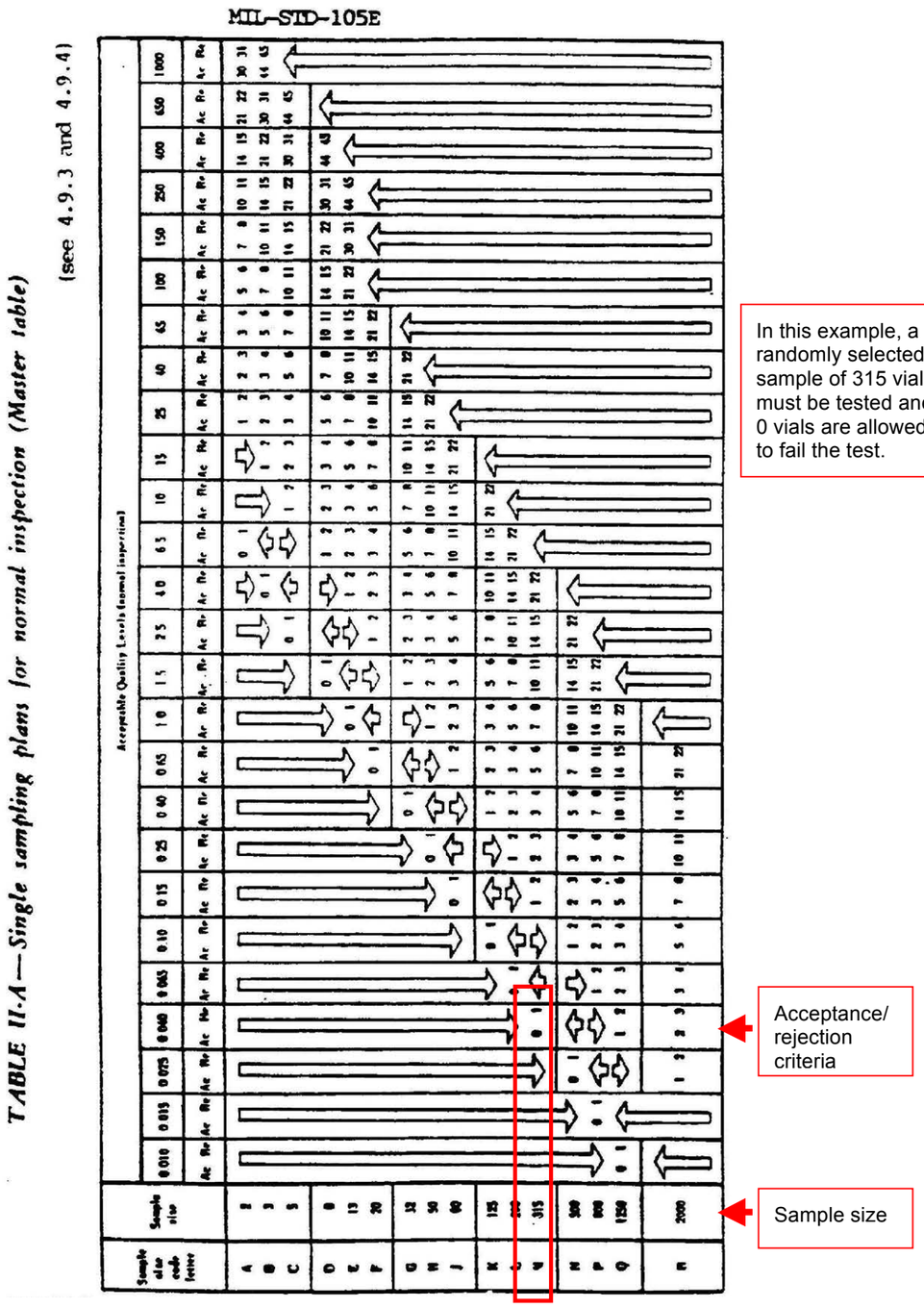


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TABLE II-A—Single sampling plans for normal inspection (Master table)

(see 4.9.3 and 4.9.4)

In this example, a randomly selected sample of 315 vials must be tested and 0 vials are allowed to fail the test.

Acceptance/ rejection criteria

Sample size

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