REPUBLIC OF TÜRKİYE
MINISTRY of HEALTH

TÜRKİYE MEDICINES AND
MEDICAL DEVICES AGENCY

# GUIDELINE FOR SAMPLING PROCEDURES AND PRINCIPLES

**DEPARTMENT OF MEDICINE INSPECTION**

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## 1.INTRODUCTION

### 1.1. Purpose

The purpose of this guideline is to guide the Provincial Directorates of Health and related parties about the quality issue complaints received by the Turkish Medicines and Medical Devices Agency from various sources such as citizens, pharmacies, hospitals and physicians regarding medicinal products for human use and their active agents, as well as dietary products for special medical purposes, and procedures and principles of sampling from the market as part of annual market inspection activities

This guideline also provides, if deemed necessary in line with the Recall Implementing Regulation, the procedures and principles for obtaining product and active agent samples from the manufacturer or the market.

### 1.2. Scope

The procedures for collecting product and active agent samples from the market by the Provincial Directorates of Health as part of the annual market inspection activities regarding the products that have permit/marketing authorization granted by the Turkish Medicines and Medical Devices Agency are entailed in this guideline, as well as complaints and applications regarding product and active agent quality issues communicated to the Turkish Medicines and Medical Devices Agency.

### 1.3. Basis

This guideline is based on the following rules and provisions:

- **a)** Article 10 of the Pharmaceuticals and Medical Preparations Law No. 1262 published in the Official Gazette dated 26.5.1928 and no. 898,
- **b)** Article 506 of the Thirty-sixth Section of the Presidential Decree No. 4 published in the Official Gazette dated 15.07.2018 and no. 30479,
- **c)** Subparagraph (ğ) of the 1st paragraph of Article 508 of the Thirty-sixth Section of the Presidential Decree No. 4 published in the Official Gazette dated15.07.2018 and no. 30479,
- **ç)** Implementing Recall Regulation published in the Official Gazette with date 19.11.2015 and no. 29537,
- **d)** Subparagraph n of the first paragraph of article 5 of the Implementing Regulation on the Labeling, Package Leaflet and Tracing of Human Medicinal Products published in the Official Gazette dated 25.04.2017 and number 30048,

### 1.4. Definitions and Abbreviations

**Medicinal Products For Human Use:** A mixture of active agents or agents with natural or synthetic origin that are administered to people to treat, prevent, or diagnose illness, or to

regulate or alter a physiological function

**Unit:** Pharmaceutical Market Inspection and Consumer Issues Unit,

**Active Agent:** Pharmacological active agents used in medicinal products for human use

**Recall**: Collection of the faulty or suspected faulty product from the distribution chains by the marketing authorization holder company depending on the level of such fault

**PTS:** Pharmaceutical Tracking System

**Agency:** Turkish Medicines and Medical Devices Agency

**Laboratories:** Laboratories of Turkish Medicines and Medical Devices Agency, Vice Presidency of Economic Assessment and Laboratory Services, and Department of Analysis and Control Laboratories

**Sample:** The sample of the material taken for market inspection and in response to a complaint

**Dietary products for special medical purposes:** Foods made or formulated especially for patients' diets to meet their specific nutritional needs and to be used under medical supervision

**Batch (Lot):** The defined amount, if considered as homogeneous, of a raw material, packaging material or the defined quantity of a product obtained after a process or series of processes

**Reference sample:** The stored sample obtained from the starting materials, packaging material, product in primary packaging or finished products of a batch so that it can be analyzed when needed

**Storage conditions:** Room temperature: 15-25 ºC, cold chain: 2-8 ºC,

**Witness sample:** The sample, which has the same batch number as the sample retrieved from the market for market inspection, kept at the site where the sample was taken, sealed, and made available upon request

**Product:** Medicinal product for human use or dietary product for special medical purposes

**Product complaint:** Any request received via written, electronic, or verbal communication about alleged or potential flaws in the product's quality which is on the market for patients use (including product identity, durability, reliability, safety, efficacy and performance)

**TITCK:** Turkish Medicines and Medical Devices Agency.

**TÜFAM:** Turkish Pharmacovigilance Center.

## 2. SAMPLING

### 2.1. Sampling as Part of Complaints and Applications Regarding Product Quality Issues

- Complaints about product quality problems coming from various sources (citizens, pharmacies, hospitals, physicians etc.), SABİM, CIMER, TÜFAM, Provincial Directorate of Health, Agency Public Relations Unit etc. shall be made to the Department of Medicine Inspection, Pharmaceutical Market Inspection and Consumer Issues Unit
- The unit shall evaluate the application, and the relevant Provincial Directorate/Directorates of Health shall be notified about the market sample to be taken in accordance with the application content.

- The sample request letters for the samples that the Unit will request from the Provincial Directorate/Directorates of Health must include information on the Product Name, Marketing Authorization Holder, Product Batch Number, and Product Expiry Date information.

- Provincial Directorates of Health shall obtain and send an adequate number of samples to the Agency together with the minutes under Annex-1, in accordance with the PTS (Pharmaceutical Tracking System) data of the pertinent sample included in the annex of the sample request letter sent by the Unit. The samples shall be returned in the event that the sampling minutes is not enclosed with them.

- In the sampling minutes, two signatures should be of the Provincial Directorate of Health officials and one signature should be of the responsible manager of the pharmacy, hospital, pharmacy warehouse, or final product manufacturer. One copy of the minutes shall be delivered to the Agency along with the samples.

- The Provincial Directorate of Health shall collect samples over the channels included in the PTS data.

- The Provincial Directorate of Health shall send a sample they have taken from the lot number specified in the PTS data in the cover letter and its annex. Samples shall be returned in case they come from a different batch number than what was requested.

- Unless the unit specifies a number, Provincial Directorates of Health shall collect samples in accordance with the number stated in the PR10/KYB Sample Acceptance Criteria Procedure, published on the www.titck.gov.tr website, given that they have sufficient number of samples. If the number of samples specified in the procedure may not be provided, then the samples that could be obtained shall be sent to the Agency. It should be ensured that the samples are sent in compliance with the storage conditions, are unopened, and have intact packaging.

- In the event that a sample cannot be collected, the Provincial Directorate of Health shall fill in the report under Annex-2, explaining that the sample was not present in any of the locations mentioned in the RTS data and send it together with a cover letter to the Agency.

- In cases where the requested sample must be transported by using Cold Chain Transportation, a sample shall be taken by the Provincial Directorate of Health, by complying with the transport conditions determined for the samples requiring cold chain transportation and in line with the PR10/KYB Sample Acceptance Criteria Procedure (There are two working dataloggers in each box and the datalogger software is available for the purpose of outputting and/or data transfer of the mentioned datalogger data, or the portable/laptop computer on which the software is installed in order to receive the datalogger data, etc. ) and it must be delivered to the marketing authorization holder to be delivered to the Department of Analysis and Control Laboratories following cold chain transportation rules regarding the product. The Department of Analysis and Control Laboratories shall be informed about the samples to be delivered by the Marketing Authorization Holder by the Unit.

- In the event that product samples are sent by use of cold chain transportation to our Agency, it is important that the Unit is contacted by the relevant stakeholders (company, Provincial Directorate of Health officials, etc.) and that they act according to the instructions to be received. In case it is discovered that the cold chain transportation conditions are not followed, the samples shall be returned by the Department of Analysis and Control Laboratories as they cannot be analyzed due to acceptance conditions being not met.

### 2.2. Sampling as Part of Recalling Activities

If deemed necessary by the Recall Regulation, samples shall be taken from the market or from the manufacturer following the aspects specified in Article 2.1 and analyzed. Procedures shall be carried out in accordance with the Implementing Recall Regulation and the Recall Guidelines.

### 2.3. Product Sampling as Part of Market Inspection Activities

As is common knowledge, analyses of products with marketing authorization/permit and active agents in our country are carried out within the scope of the defined market inspections.

- The Pharmaceutical Market Control and Consumer Issues Unit, which is affiliated with the Department of Medicine Inspection shall plan the market inspection program for products periodically by using a risk-based approach.

- The list produced by the unit as a result of the risk-based assessment includes provincial

health directorates, product names, and required sample quantities.

- Within the specified time period, the relevant Provincial Directorates of Health shall be notified and the samples shall be requested for products included in the market inspection program.

- The RTS data of the products covered in the market inspection program shall be organized according to the Provincial Directorates of Health and distributed to all Provincial Health Directorates.

- The product barcode number, name, province, district, stakeholder name, number of products, and type of the stakeholder shall be included in RTS data for allowing the supply of such product: (center where it will be used, manufacturer company, pharmacy warehouse, pharmacy).

- The Provincial Directorate of Health shall provide the required sample quantity in accordance with the RTS data, and the package shall be sent to the Agency intact with the report under Annex-1. The sample batch number and the batch number indicated in the sampling minutes must match. Otherwise, the samples shall be returned.

- According to the statement "Samples sent for analysis regarding market inspection should have a minimum of 6 months until their expiration date" in the Sample Acceptance Criteria Procedure published by the Department of Analysis and Control, when carrying out the sampling processes, samples with the longest expiration date should be chosen.

- The samples that are to be collected within the scope of market inspection activities must come from the same batch number. Otherwise, the samples shall be returned and samples with the same batch number shall be requested. It should be ensured that the samples are sent in compliance with the storage conditions, are unopened, and have intact packaging.

- The number of samples collected from the market by the Provincial Directorates of Health should be adequate for analysis. The Required quantity of samples shall be included in the product list sent by the Unit. There shall be no requirement to look further in cases where the RTS data are evaluated and the number of samples needed for analysis can be collected at one site. To collect the necessary quantity of samples, other locations shall be looked into if not enough samples can be collected at one site. In these cases, samples can be collected from different places until a sufficient number is reached, provided that they have the same batch number.

- An adequate number of samples with the same serial number shall be taken by leaving a witness sample and specified in the sampling report under Annex-1.

- In the sampling minutes, two signatures should be of the Provincial Directorate of

Health officials and one signature should be of the responsible manager of the pharmacy, hospital, or pharmacy warehouse. One copy of the minutes shall be delivered to the Agency along with the samples.

- It is important to appropriately record the product's batch number on the sampling report and avoid mistaking it for the barcode number.

- If no sample can be obtained as a result of the investigations, the "Minutes to be Filled Out for Product Samples Not Able To Be Obtained" in Annex-2, indicating that no samples could be obtained from any of the relevant places, should be prepared with stamp and signature, and the Unit should be informed together with the information letter.

- In the event that a product on the product list requires cold chain transportation, the samples to be taken by the Provincial Directorate of Health, as explained in detail in 2.1, shall be delivered to the Department of Analysis and Control Laboratories of our Agency under appropriate conditions by the marketing authorization holder. In the event that product samples are sent by use of cold chain transportation to our Agency, it is important that the Unit is contacted by the relevant stakeholders (company, Provincial Directorate of Health officials, etc.) and that they act according to the instructions to be received. In case it is discovered that the cold chain transportation conditions are not complied with/provided for, the samples shall be returned by the Department of Analysis and Control Laboratories as they cannot be analyzed due to acceptance conditions being not met.

## 2.4. 2.4. Active Agent Sampling of Medicinal Product for Human Use as Part of Market Inspections

- The Pharmaceutical Market Control and Consumer Issues Unit, which is affiliated with the Department of Medicine Inspection shall plan the market inspection program for the active agent of medicinal products for human use periodically using a risk-based approach.

- The Provincial Directorates of Health shall be provided with the list of active agents for market inspection, obtained from the manufacturers. The active agent's name, dosage, and manufacturer shall be listed on the list.

- Provincial Directorates of Health shall obtain the necessary sample quantity in line with the list and send a witness sample to the Agency together with the sampling report.

- In the sampling minutes, two signatures should be of the Provincial Directorate of Health officials and one signature should be of the responsible manager of the manufacturing site. One copy of the minutes shall be delivered to Agency along with the samples.

## 3.Miscellaneous Considerations

- When necessary, product samples can be collected by the Inspectors and Product Inspectors of our Agency following the relevant legislation.

- If deemed necessary in the context of product quality issues, the Agency may request that the products be checked on-site without taking samples from the Provincial Health Directorate. Provincial Directorate of Health officials should go to the manufacturing site, where products are stored, and carry out inspections in line with the RTS data regarding the issues specified in the instruction. The Agency should be notified by filling out the form in Annex-3 together with the cover letter on the subject.

- If deemed necessary by the Agency in the context of product quality issues (in cases where the quantity of products in the RTS data is low/absent etc.), product reference samples can be requested from the manufacturing site by the Provincial Health Directorates.

- The Unit shall deliver the samples that were sent by the Provincial Directorates of Health to the Department of Analysis and Control. The Department of Analysis and Control Laboratories shall conduct the necessary examinations and analyses, and an analysis report shall be prepared. The analysis reports sent to the unit shall be evaluated and the relevant authorities shall be informed about the compliance/non-compliance of the report.

## 4.References

- Procedure on Consumer Complaints *(Effective Date: 28.08.2015, Revision Date/No:14.08.2015/R.02)*

- İDD-SOP-05 Annual Market Control Activities Procedure *(Effective Date: 28.08.2015, Revision date/No. 14.08.2015 / R.02)* Procedure regarding Sample Acceptance Criteria prepared by the Department of Analysis and Control Laboratories of the Vice Presidency of Medicines and Pharmacy *(Published on: 31.05.2019/04, Revision date:11.10.2019/01)*

- Implementing Regulation on Health Inspectors published in the Official Gazette dated 30 May 2013 and no. 28662

- Implementing Regulation on Product Inspectors published in the Official Gazette dated 30 April 2013 and no. 28633

- Implementing Recall Regulation published in the Official Gazette dated 19.11.2015 and no. 29537

**5. Annexes:**

**Annex1: Sampling Minutes**

**Annex 2: Minutes to be Filled Out for Product Samples Not Able To Be Obtained**

**Annex 3: Minutes To Be Filled Within The Scope of the Physical Inspection of The Product**

**Annex1: Sampling Minutes**

.....Provincial Directorate of Health

**SAMPLING MINUTES**

Reason for Sampling ☐ Market Inspection ☐ Complaint/Quality Issue

Product Name :
Batch No. :
Expiration Date :
Packaging Type :
Storage Conditions: :
Pcs. :
Marketing Authorization Holder :
Manufacturing Site: :
Place of Collection: :
Date of Collection: :

This constitutes the minutes prepared to demonstrate that we have received the product, of which name and qualities are specified above, for market inspection.

Delivered By:
Received By:

**Signature** **Signature** **Signature**

**Note:** This minute shall be filled in as 4 copies. The first copy shall be sent to our Agency as an annex of the cover letter, the second copy shall be sent to our Agency in the sample package, the third copy shall be preserved at the Provincial Directorate of Health, and the fourth copy shall be preserved at the site where the medicinal product sample was collected.

**Annex2: Minutes to be Filled Out for Product Samples Not Able To Be Obtained**

Reason for Sampling Issue ☐ Market Inspection ☐ Complaint/Quality

.....Provincial Directorate of Health

| **The form to be filled for product samples that will not be inspected within the scope of the Market Inspection Program/Complaint-Quality Issue.** | | | |
|---|---|---|---|
| **Product Name** | **Batch No.** | **Expiration Date** | **Name Of The Marketing Authorization Holder** |
| | * | * | |
| | (* Batch No. and Expiration Date | | |

| | **Name of the Pharmacy/the Pharmacy Warehouse** | **Date** | **Stamp/Signature** |
|---|---|---|---|
| **Pharmacy** | | | |
| **Pharmacy** | | | |
| **Pharmacy** | | | |
| **Pharmacy** | | | |
| **Pharmacy** | | | |
| **Pharmacy** | | | |
| **Pharmacy** | | | |

**Note:** This form can be copied and used as much as needed. A form shall be filled out per each product not able to be obtained.

| | Name of the Pharmacy/the Pharmacy Warehouse | Date | Stamp/Signature |
|---|---|---|---|
| **Pharmacy** | | | |
| **Pharmacy** | | | |
| **Hospital** | | | |
| **Hospital** | | | |
| **Pharmacy** | | | |
| **Pharmacy** | | | |

**Note:** This form can be copied and used as much as needed. A form shall be filled for each product not able to be obtained.

**Annex3: Minutes to be Filled Out As Part of Physical Product Inspection**

**.....Provincial Directorate of Health**

**Product Name :**

**Batch no :**

**Expiration Date :**

**Marketing Authorization Holder :**

**Place of Inspection: :**

**Date of Inspection:**

**Result of Inspection: :**

**Signature** **Signature** **Signature**