European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

Funded by the European Union and the Council of Europe

EUROPEAN UNION

COUNCIL OF EUROPE

CONSEIL DE L'EUROPE

Implemented by the Council of Europe

# General European OMCL Network (GEON)
# GENERAL DOCUMENT

## PA/PH/OMCL (06) 81 R8

## An "aide-mémoire" for the testing of suspected illegally traded and falsified medicines

| | |
|---|---|
| **Full document title and reference** | An "aide-mémoire" for the testing of suspected illegally traded and falsified medicines, PA/PH/OMCL (06) 81 R8 |
| **Document type** | Position Paper |
| **Legislative basis** | Council Directive 2001/83/EC and 2001/82/EC, as amended |
| **Date of first adoption** | February 2007 |
| **Date of original entry into force** | February 2007 |
| **Date of entry into force of revised document** | April 2019 |
| **Previous titles/other references / last valid version** | An "Aide Mémoire" for the Confirmation of Counterfeit Medicines, PA/PH/OMCL (06) 81 1R<br>An "aide-mémoire" for the testing of suspected illegal and counterfeit medicines, PA/PH/OMCL (06) 81 R6 |
| **Custodian Organisation** | The present document was elaborated by the OMCL Network / EDQM of the Council of Europe |
| **Concerned Network** | GEON |

# An "aide-memoire" for the testing of suspected illegally traded and falsified medicines

## Introduction

The illegal trade of medicines is well known and documented. The development of online networks and internet trade has facilitated the growth in illegally traded medicines across the globe. No single authority can combat the illegal trade of medicines alone. The fight against falsified and illegally traded medicines must therefore be carried out on several levels to be successful.

The role of the laboratories in the European OMCL Network is vital, since the testing data and evidence produced by OMCLs can confirm the status of samples under investigation and support the work of national enforcement and prosecuting authorities in taking appropriate actions proportionate to the risk to patients. It is expected that the continued sharing of practical experience between Network partners will allow individual OMCLs to continue to develop systems, expertise and processes to increase effectiveness and efficiency. Ultimately, this means the chances of the relevant Competent Authorities being successful in any forthcoming legal proceedings will be improved.

The person providing a sample will have knowledge of the background to the case and the OMCL should gather as much information as possible from the sample giver on receipt of the sample.

Documentary and evidence requirements for the courts system may differ from the usual OMCL quality system requirements. OMCLs should understand any differences or legal requirements and ensure these are followed when required. When there is any possibility of the data being needed for court proceedings, it is better to make sure that these requirements are met.

## 2. Illegally-traded or Falsified/Counterfeit Medicines?

There are many different definitions and opinions on what the terms "falsified", "substandard" "counterfeit" medicines mean.

A definition of "falsified medicinal product" was introduced in Directive 2011/62/EC, amending the directive 2001/83/EC regarding the prevention of the entry into the legal supply chain of falsified medicinal products.

This directive amended Article 1 of the directive 2001/83/EC to add:

"*33. Falsified medicinal product:*

- *Any medicinal product with a false representation of:*
- *(a) its identity, including its packaging and labelling, its name or its composition as regards any of the ingredients including excipients and the strength of those ingredients;*
- *(b) its source, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorisation holder; or*
- *(c) its history, including the records and documents relating to the distribution channels used.*

*This definition does not include unintentional quality defects and is without prejudice to infringements of intellectual property rights*."

OMCLs receive samples that are believed or suspected to be illegally traded. The testing applied will depend on the individual sample and what question(s) the Laboratory needs to answer.

For example, illegally traded and falsified medicines may include products:

- that do not claim to contain any active ingredients but, in practice, do ("medicines in disguise")
- which claim to contain drug substances that are not part of licensed medicinal products or legally authorised for sale or treatment or which are legally approved medicinal products from certain countries, traded illegally in markets where they are not approved ("unapproved products")
- that are manufactured to mimic a legally approved product ("falsified medicines")
- that are intended for supply to one market but are, in practice supplied to a different (usually more expensive) market outside of the authorised supply chain ("diverted products"). Depending on how these products are presented (in EU or other packaging) they may be treated as either "unapproved" or "falsified" products.

Such products may be:

- formulated with the correct active ingredients or excipients
- formulated with the wrong active ingredients or excipients
- formulated without any active ingredients
- formulated with the incorrect quantity of active ingredients or excipients
- with falsified packaging.

Any unusual or interesting results which would be informative to the GEON could be added into the Know-X database.

## 3. Product Receipt

Often an OMCL will have suspicions regarding the status of a suspect sample before starting any analysis. The product may have been provided for testing by a National Enforcement authority, the police, an Inspectorate or even a patient. Before starting any analysis it is vital that the analyst should be able to discuss any available intelligence/information available.

- What is the product?
- What is it used for?
- Where did it come from?
- Is it presented as a medicine? A food supplement? Are there any APIs declared?
- Has it (or similar-looking samples) been seen before?
- Is information available on the internet (e.g. on the homepage of the producer or is the product mentioned in internet chatrooms or discussion forums)?

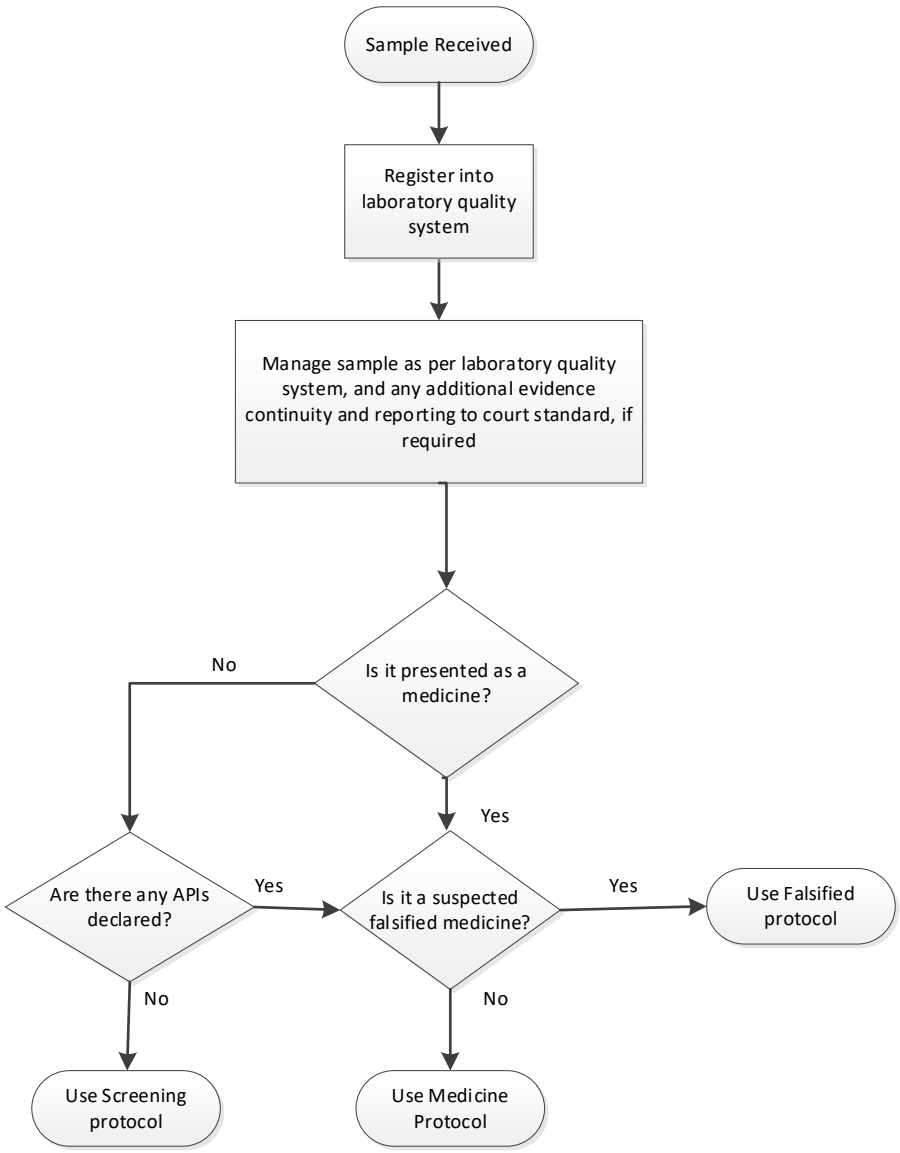
These questions will all provide background information as to the possible status of the sample and should be answered as fully as possible. Example 1 shows a decision tree to determine what testing may be applied.

## 4. Authenticity checks as part of the annual CAP Testing programme

As part of the annual CAP sampling programme, samples may be obtained from parallel distribution sites. In these cases, the samples will be examined by OMCLs to assess whether they are consistent with the originator product (see example 5). It is likely that a limited amount of sample will be available to OMCLs, so non-destructive tests should be applied first, if possible. If this is not possible, then appropriate destructive tests can be performed.

Issues which are applicable to parallel distribution products are also valid for parallel imported products and therefore, the parallel distribution protocol can be used for parallel imported products, if deemed suitable.

**Example 1. Decision tree to determine testing requirements (samples under investigation)**




*Note*:

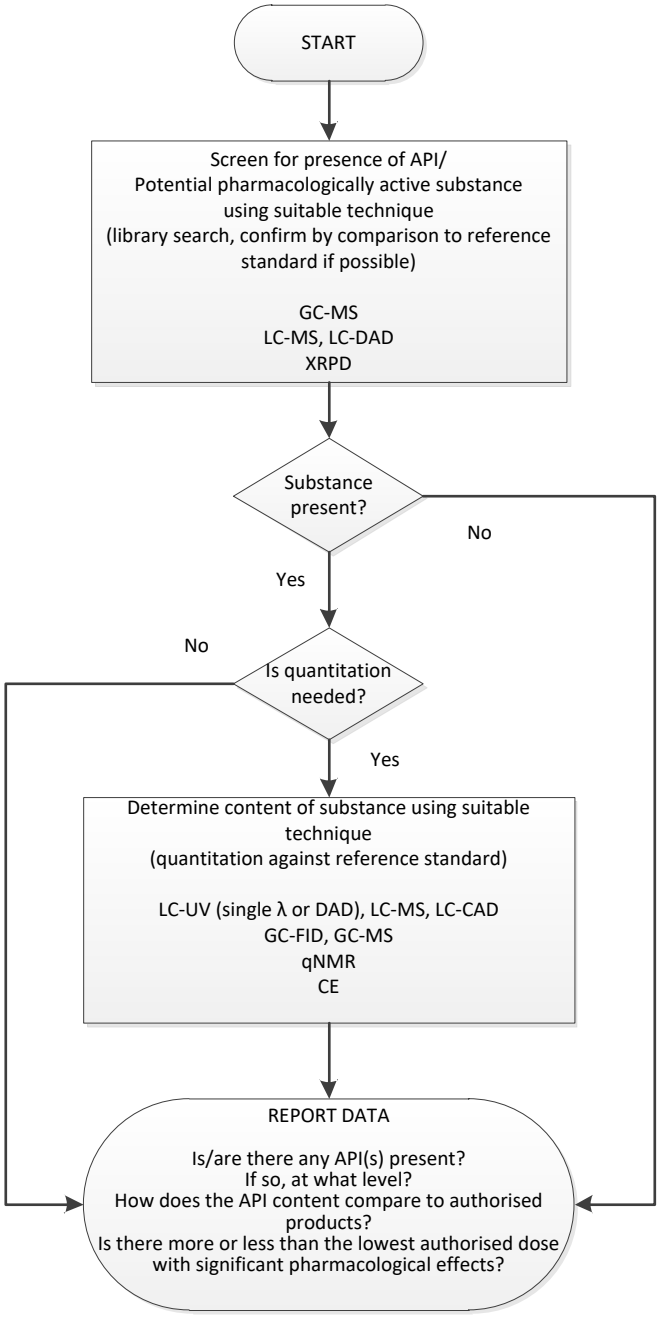
Where no APIs are declared, often the name or marketing of the item can indicate what APIs may be present (for example, products may be marketed as weight loss or sexual potency enhancers or have suggestive pictures/branding that implies the product's intended effect). Also, internet searches using the product or producer name of the item can often provide information on APIs, use and/or indication.

Further details of the protocols that may be applied are given in the following sections.

**Example 2. Screening protocol (testing for "medicines in disguise")**

Samples may be presented as a food supplement, health tonic, "nutraceutical" or naturally-derived or herbal product. Usually there will be either no mention of API(s) in the product or even a more positive statement such as "100 % natural extracts" or similar. Alternatively, samples may be presented in foreign language variants, or even unlabelled.

In these circumstances the priority of the testing is to establish whether there are any APIs/potential pharmacologically active substances present and, if there is, at what level (if required).




Note: screening methods may not detect every possible substance and OMCLs may operate more than one method (e.g. for different drug classes).

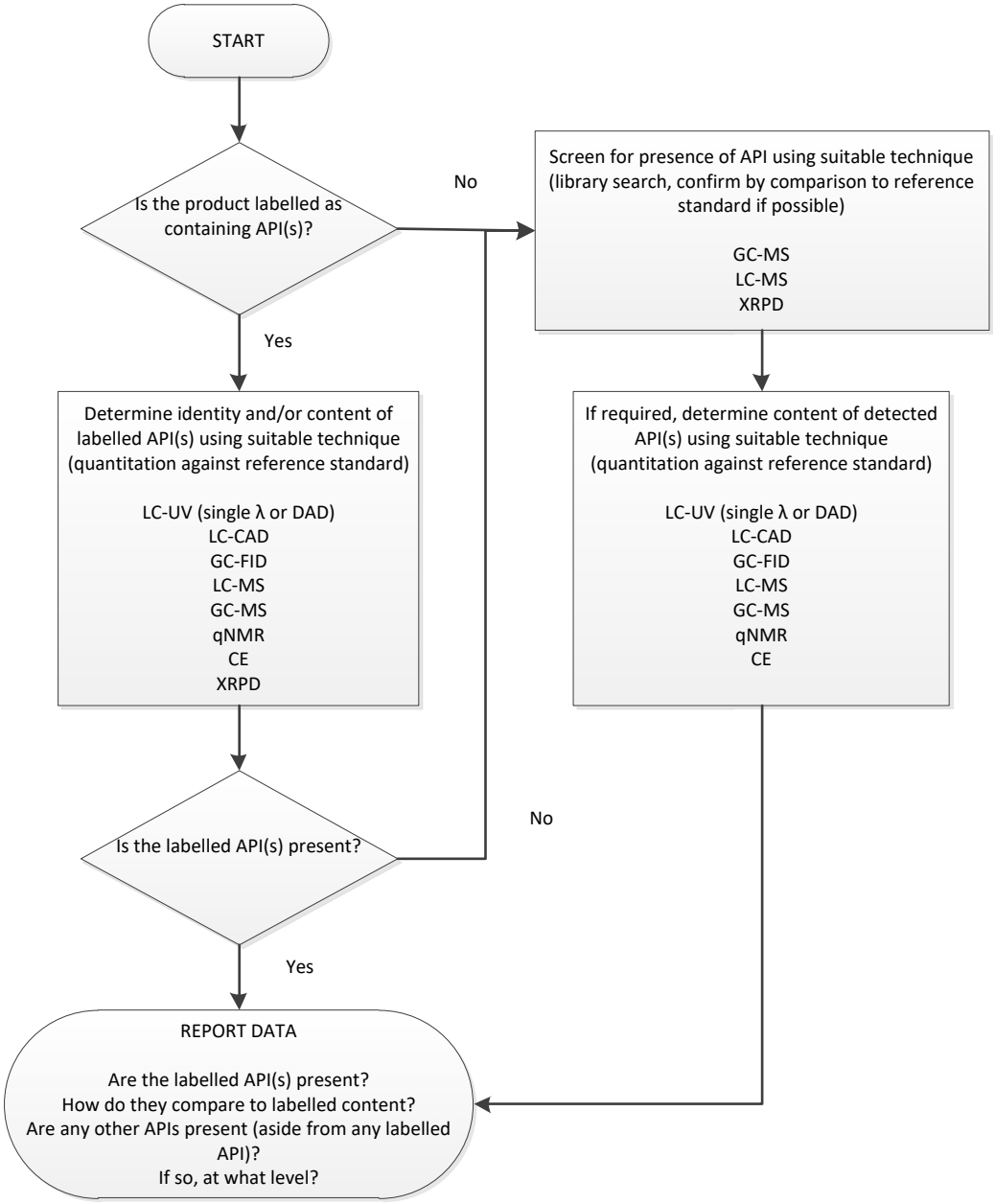
Methods will need to be updated to include new molecules as they are discovered.

For unknown or new molecules, advanced techniques may be needed to provide structure elucidation.

**Example 3. Medicine protocol (testing of illegally traded medicines/"unapproved products")**

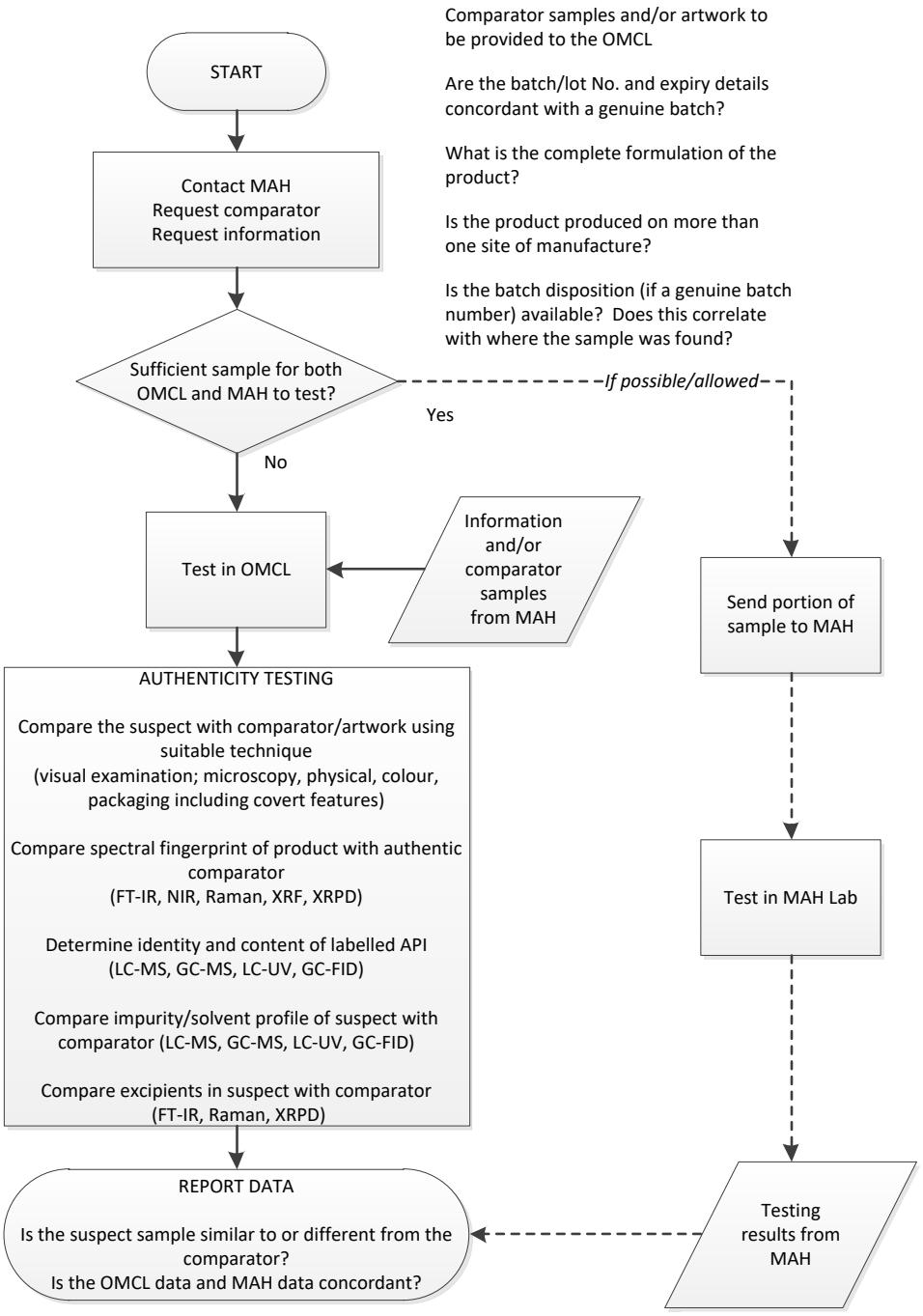
Samples may be legal, licensed medicines in other countries, but not necessarily in the country where they have been found, or they may be legal medicines sold outside of the correct, legal supply chain. They might also contain drug substances that are not licensed or legally authorised for sale or treatment. Usually the API(s) in the product will be listed on the label and the product will be packaged and presented as a medicine. In some cases, the samples may be presented in foreign language variants, so the API(s) present may be unclear.

The priority of the testing is to establish that the labelled API is present, and (if required) at what level.



### Example 4. Falsified protocol

For samples that are presented as licensed medicines but are suspected of being falsified, it is essential that the OMCL is able to make contact with the MAH of the genuine product. This may either be directly or through the Competent Authority, Inspectorate or Enforcement Group. Genuine comparator batches (ideally 3 batches including the suspicious lot) should be obtained. If the product is manufactured at a variety of production sites samples should be obtained from each. It is not usually possible for a laboratory to determine conclusively that a sample of product is falsified based on testing alone. The priority of the testing can only be to say whether the suspect sample is consistent with the genuine product or not.




Note: when a suspect sample is found not to contain labelled API, the OMCL may wish to apply the screening protocol to determine what, if anything is present

## Example 5. Parallel distribution / importation protocol

EMA maintains a public PD Register which can be searched to check that the parallel distribution of the particular sample is authorised (https://fmapps.emea.europa.eu/paradist/search.php). For parallel imported products respective registers are kept by the national competent authorities.

It should be noted that for PD or parallel imported samples that have been over-labelled, it may be difficult or impossible to see the original batch numbers. In these cases, "MAH" in the flowchart below can refer to the original MAH or the Parallel Distributor or Parallel Importer.