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

Co-funded by the European Union

EUROPEAN UNION

COUNCIL OF EUROPE

CONSEIL DE L'EUROPE

Co-funded and implemented by the Council of Europe

General European OMCL Network (GEON)
GENERAL DOCUMENT

PA/PH/OMCL (06) 81 R12

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 R12
Document type	Position Paper
Legislative basis	Council Directive 2001/83/EC and Regulation (EU) 2019/6, 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 2025
Previous titles/other references / last valid version	An "aide-mémoire" for the testing of suspected illegal and counterfeit medicines, PA/PH/OMCL (06) 81 R10
Custodian Organisation	The present document was elaborated by the OMCL Network / EDQM of the Council of Europe
Concerned Network	GEON

Explanatory Notes on the Document

The original version of this document was produced in response to many presentations given at a number of Annual General Meetings of the General European OMCL Network (GEON).

The paper provided some practical and theoretical advice to OMCLs on the development of protocols for the confirmation or determination of falsified medicinal products or active ingredients and was adopted by the Network in 2007.

Subsequently, the testing of potentially illegally traded and falsified medicines (medicinal products or active ingredients) throughout the Network has expanded and many laboratories have now established processes and expertise.

At the GEON annual meeting in June 2015, it was agreed that the “aide-mémoire” document should be revised and updated to provide an overview of the overall approaches that should be taken for OMCLs analysing suspected illegally traded/falsified medicines

This document has been prepared to include examples of high-level process flows/decision trees to assist OMCLs and promote a harmonised approach across the Network. It is recognised that OMCLs will have existing processes in place and this document does not supersede existing systems. This document is intended as an “aide-mémoire” only and OMCLs are not expected to be audited for compliance with the document.

The techniques listed in this document are examples only and should not be seen as exclusive or even preferred techniques. OMCLs should choose and use appropriate equipment to meet their testing needs.

The individual OMCL’s choice of specific analytical techniques and detailed testing SOPs are outside the scope of this document and should be decided locally in accordance with local legislation or policies (for example, some OMCLs may routinely quantify APIs found but others may not – either approach is acceptable), equipment availability and staff expertise/preferences.

The final decision on what techniques to use and equipment to purchase and exactly what testing to apply is left to individual OMCLs.

The document was updated again in 2018 to harmonise terminology with the Falsified Medicines Directive definitions. The terms “counterfeit” and “illegal medicine(s)” have been replaced by “falsified” and “illegally traded medicine(s)” throughout.

In addition, following the introduction of authenticity checks on parallel distributed (PD) products to the CAP testing programme, the Falsified Medicines WG decided to update the aide-mémoire to include guidance on what checks could be applied to PD products as part of this revision (Section 4). It was also noted that the PD checks could be applied to parallel imported products, as they are similar with respect to re-packaging for supply and distribution to other member states.

In the 2019 revision, a test protocol to identify falsified/illegally traded APIs was included.

In the 2025 revision, a protocol to identify falsified medical devices was introduced. In addition, some terms used in the test protocol to identify falsified/illegally traded APIs were aligned with the latest edition of the document “API surveillance - Position paper for OMCLs” (PA/PH/OMCL (12) 51).

An “aide-mémoire” for the testing of suspected illegally traded and falsified medicines

1. 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 (medicinal products or active ingredients) must therefore be carried out on several levels to be successful.

The role of the laboratories in the European OMCL Network is vital, as 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 action 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” and “counterfeit” medicines mean.

A definition of “falsified medicinal product” was introduced in Directive 2011/62/EC, amending 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 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,
- in falsified packaging.

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

In line with the work-sharing principle established within the GEON, OMCLs are encouraged to contact another OMCL for laboratory assistance, in case they do not have the expertise or necessary equipment in place to carry out the required analysis.

3. Product receipt

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, the analyst might gather 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 provide background information as to the possible status of the sample. *Example 1* shows a decision tree to determine what testing may be applied; a “Screening Protocol” is presented in *Example 2*; a “Medicine Protocol” is shown in *Example 3* and a “Falsified Protocol” in *Example 4*.

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.

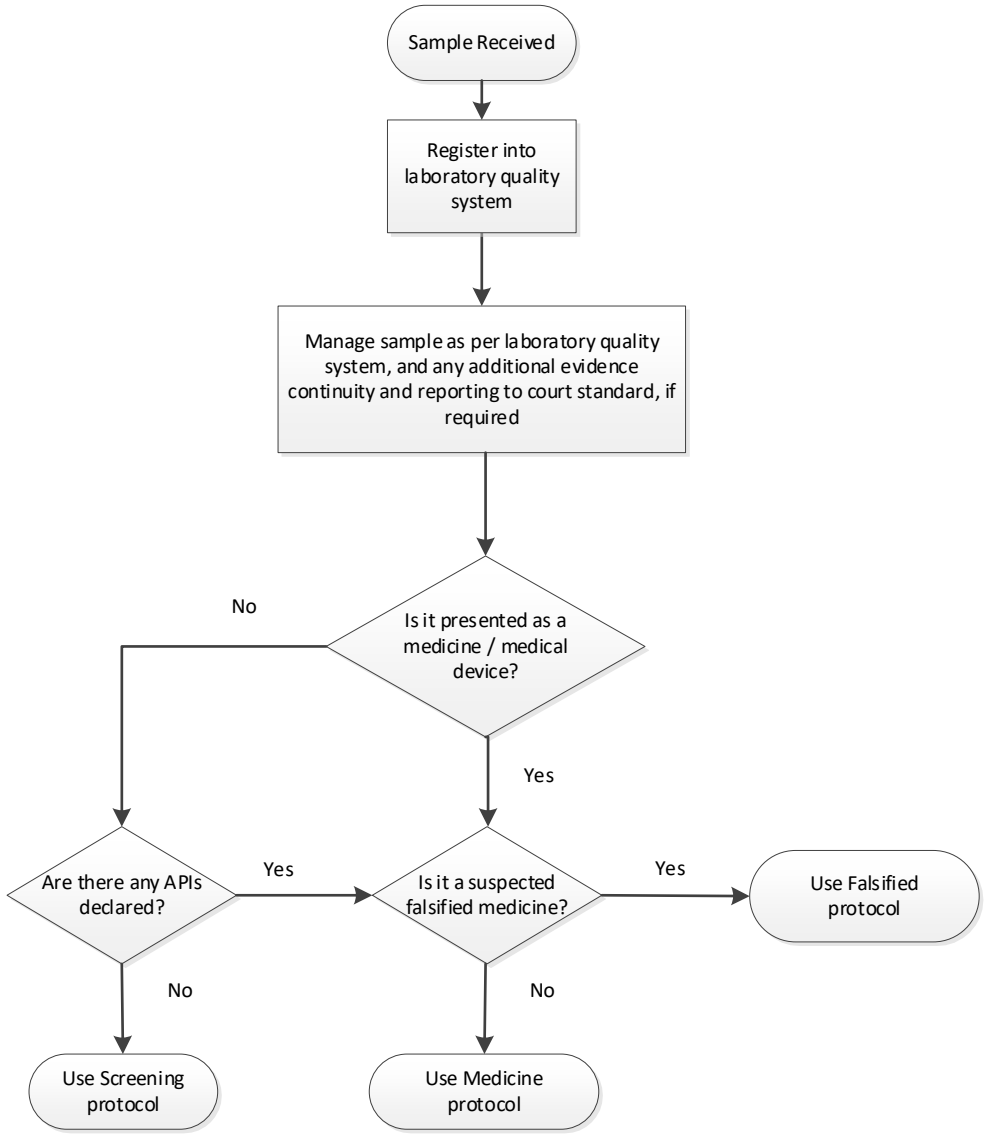
5. Detection of falsified/illegally traded APIs

When an OMCL receives an API sample suspected of being falsified, it is imperative to contact the MAH of the finished product in which this API should be present. In the first instance, the product should be identified and the compliance to the monograph (if available) or to the MAH specification should be verified. In the event of compliance, authenticity should be checked. In order to confirm the authenticity of an API with respect to its source, the use of fingerprint techniques applying chemometric methods may be helpful. The applicable protocol is provided in *Example 6*.

6. Medical devices

Medical devices cover a broad range of products and from an analytical point of view, distinction should be made between products with chemical compounds (e.g. rinsing fluids for contact lenses, dermal patches, band aids, dermal fillers), pure physical or electronic devices (e.g. hospital beds, implants, pacemakers) and *in vitro* diagnostics. The applicable protocol is provided in *Example 7*.

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



Note:

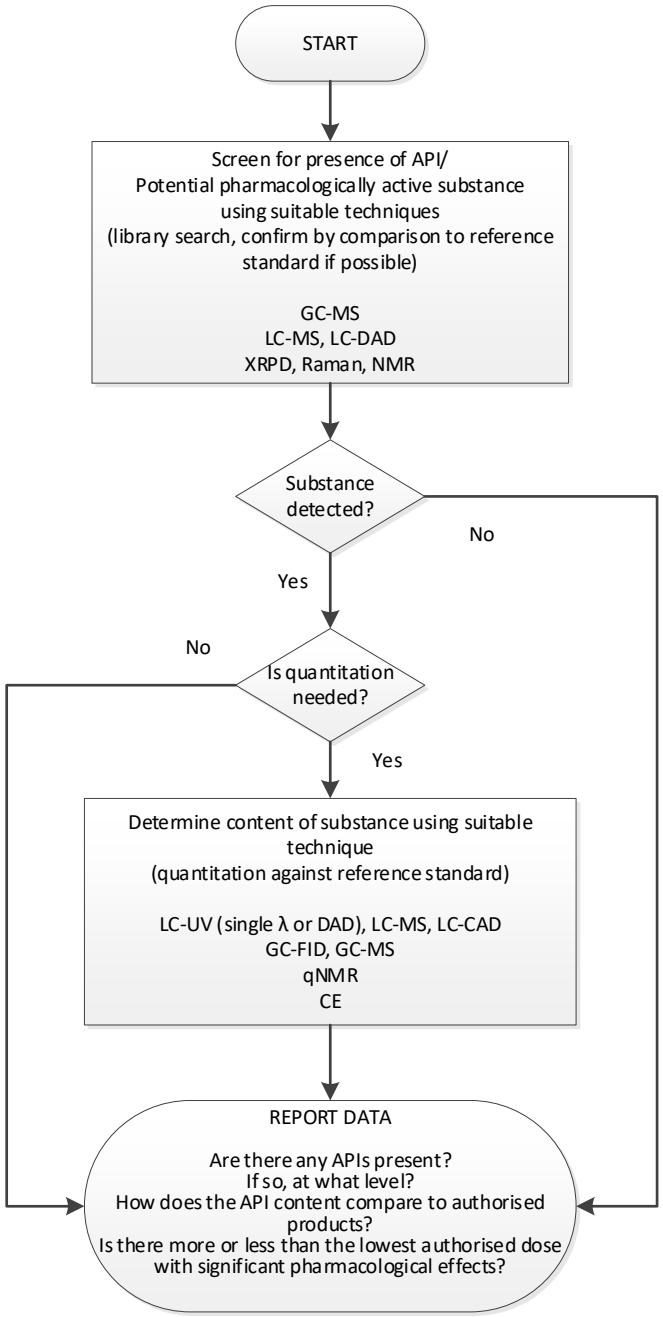
Where no APIs are declared, often the name or marketing of the item can indicate what APIs may be present (for example, products may be marketed as weight loss or sexual potency enhancers or have evocative pictures/branding that implies the product’s intended effect). In addition, internet searches using 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/potentially pharmacologically active substances present and, if there are, 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.

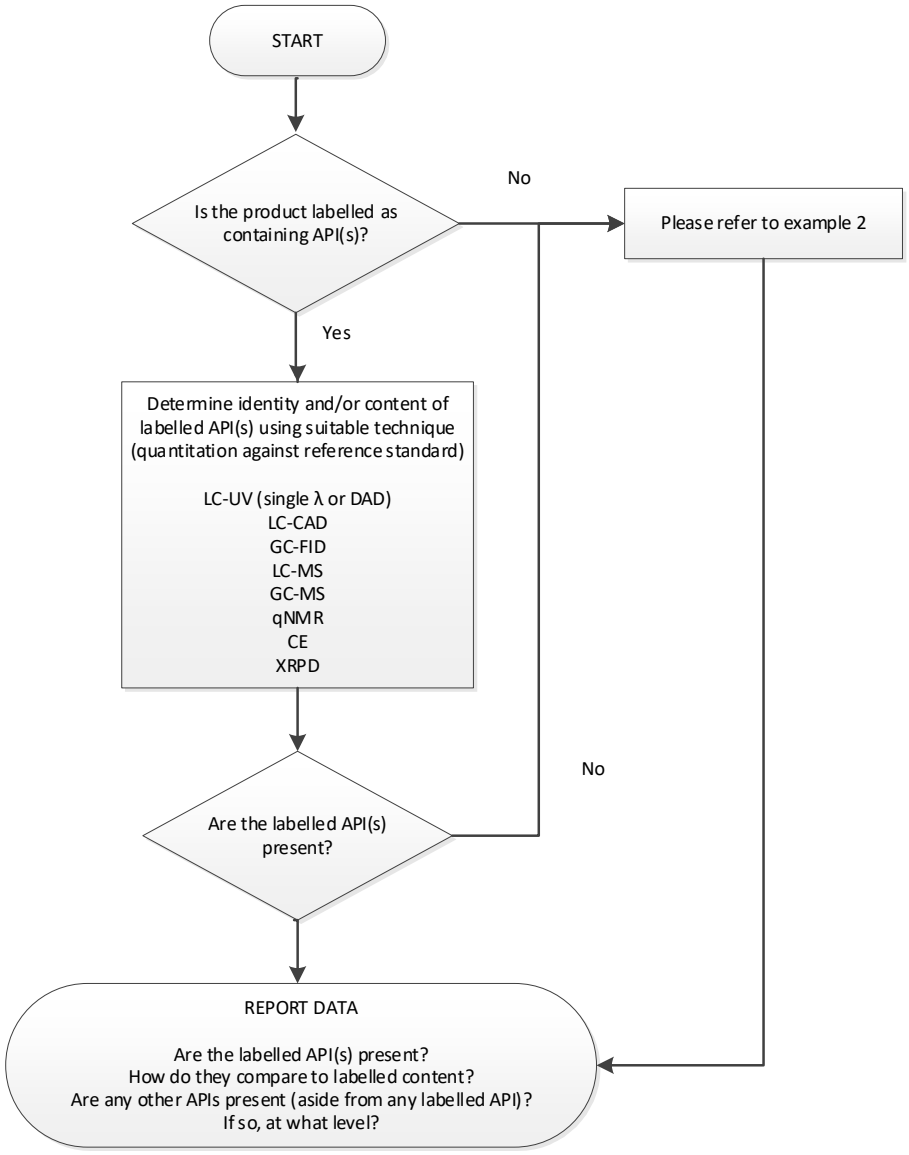
For unknown or new molecules, advanced techniques may be needed to provide structure elucidation.

Bear in mind the importance of sample preparation especially if LOQ are very low.

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 may 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.

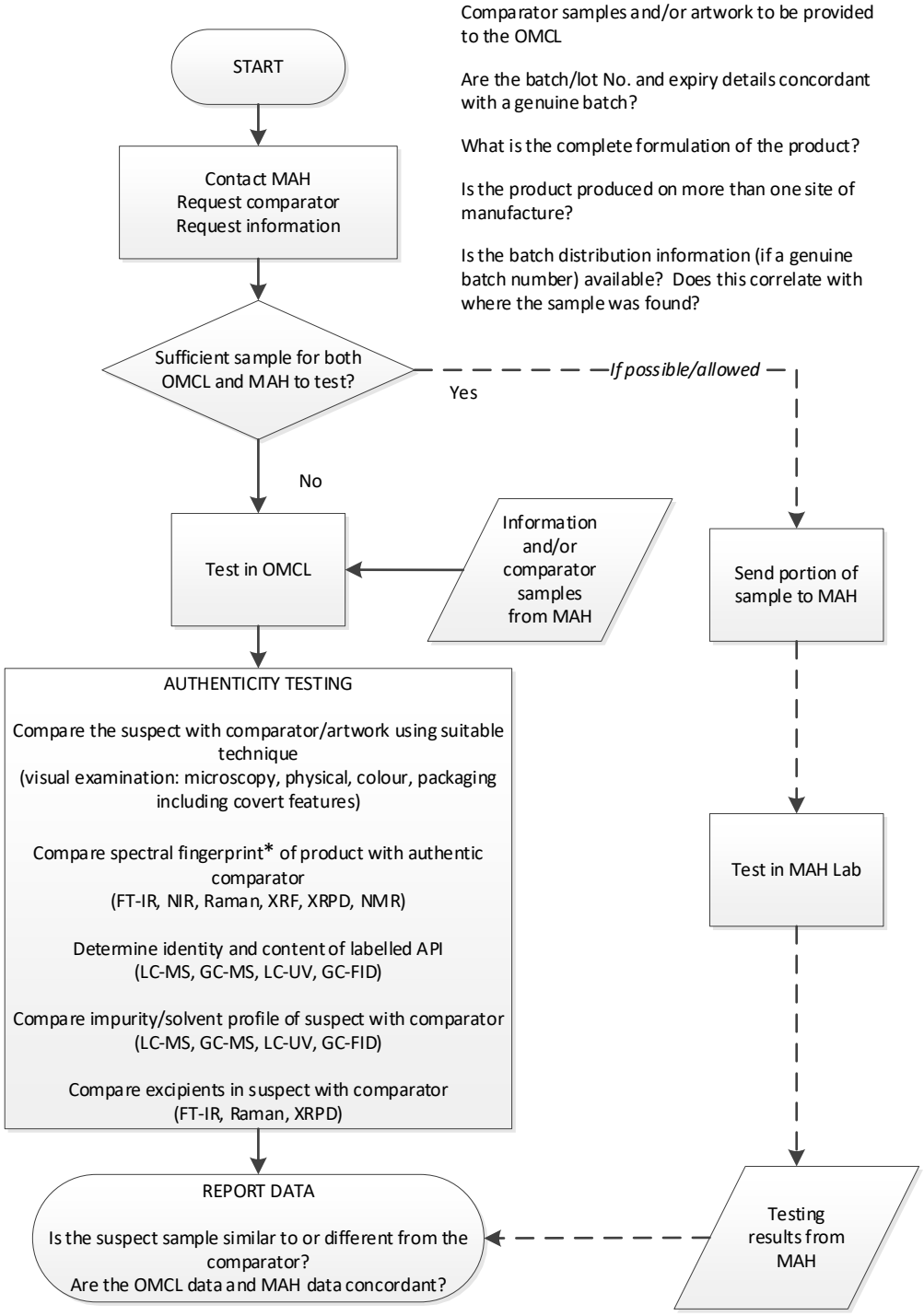
The priority of the testing is to establish that the labelled API is present, and (if required) at what level.



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 usually not 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.



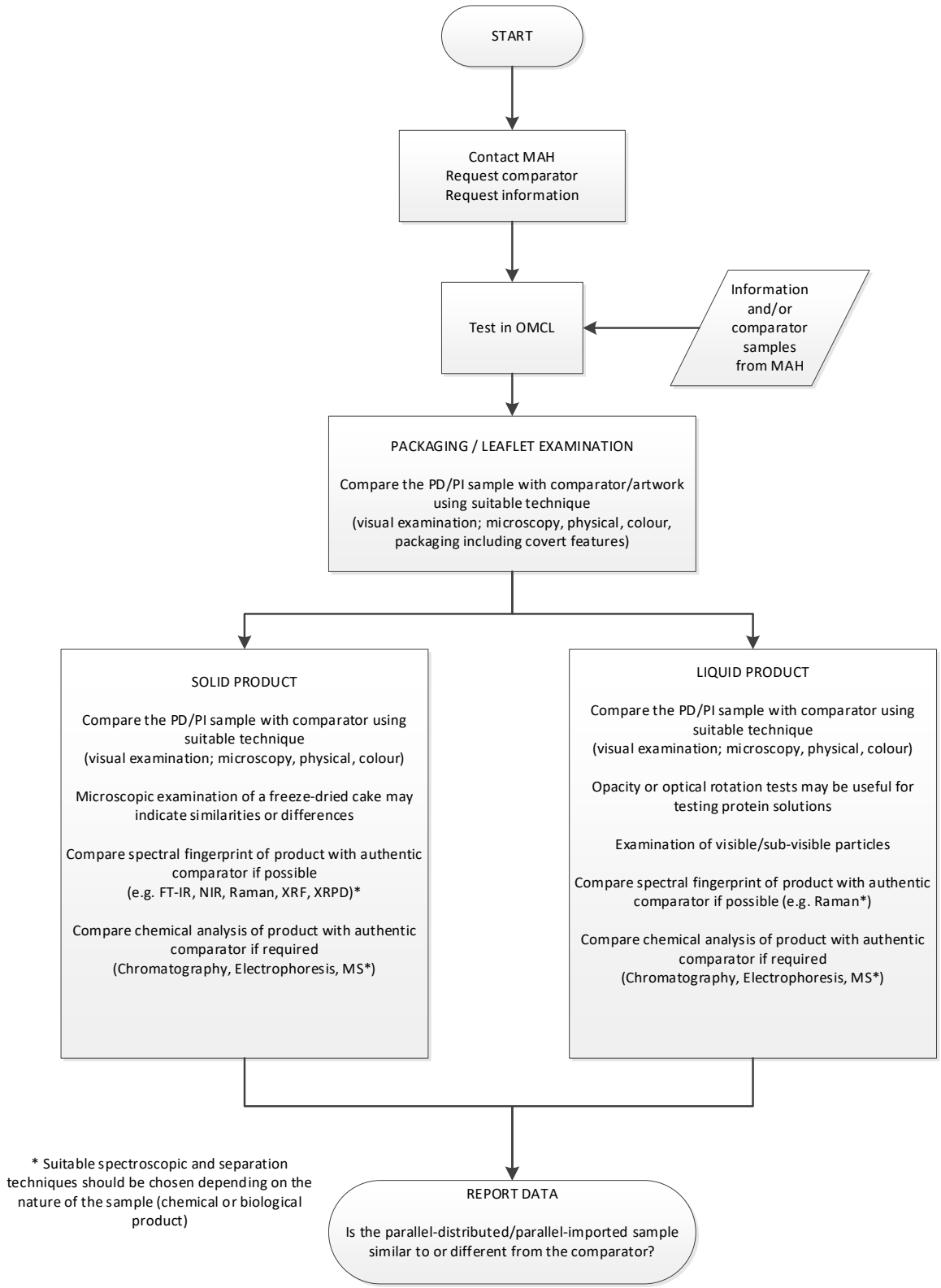
Note: when a suspect sample is found not to contain labelled API, the OMCL may wish to apply the screening protocol to determine what, if anything is present.

* Alternatively, testing of the suspected samples and the comparator can be done using the MAH methods and specifications for impurities/related substances and assay, if the OMCL is not used to fingerprinting methods or lacks equipment for fingerprinting techniques.

Example 5. Parallel distribution/importation protocol

The EMA maintains a public PD Register which can be searched to check that the parallel distribution of the particular sample is authorised (https://iris.ema.europa.eu/registerpd/). For parallel imported products, registers are kept by the national competent authorities.

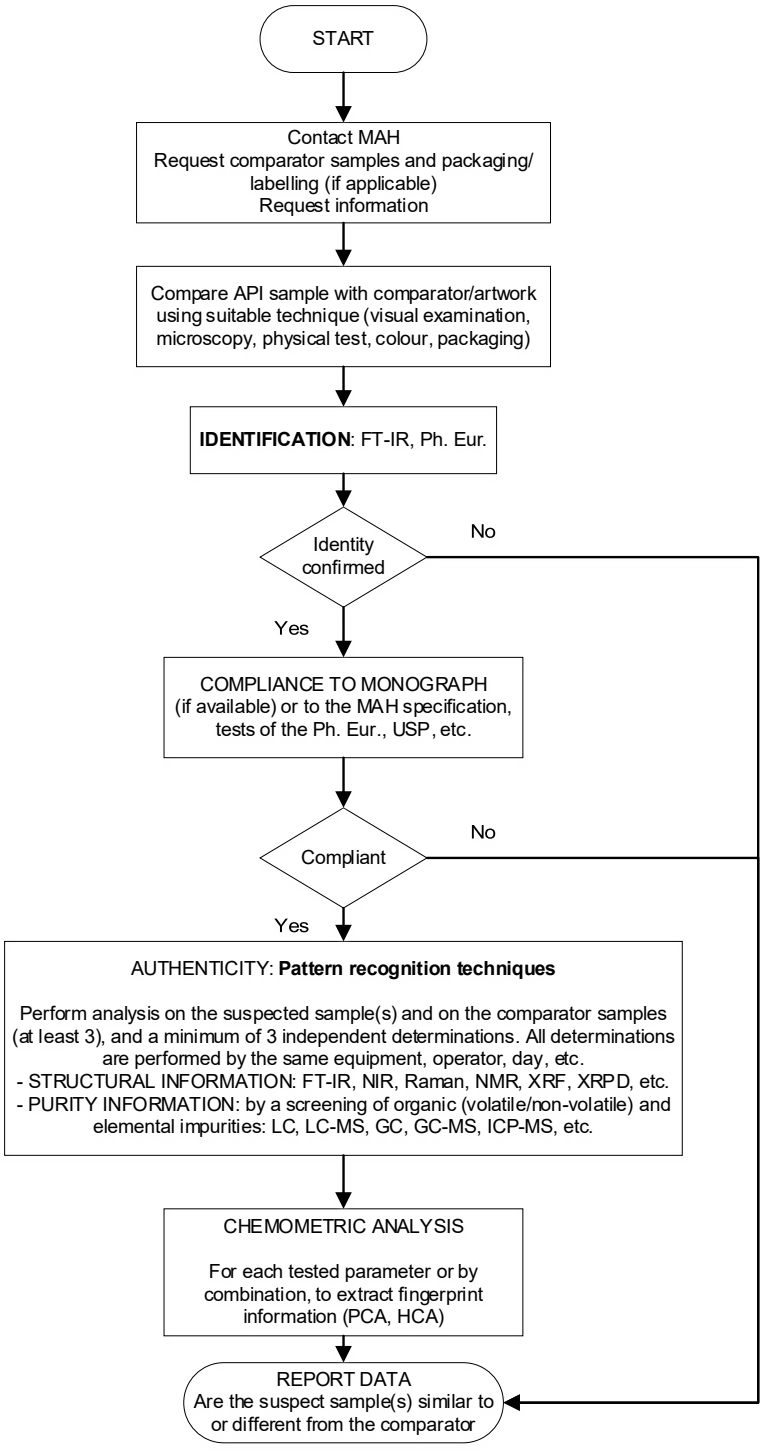
It should be noted that for PD or parallel imported samples that have been over-labelled, it may be difficult or impossible to see the original batch numbers. In these cases, “MAH” in the flowchart below can refer to the original MAH or the Parallel Distributor or Parallel Importer.



Example 6. Falsified/Illegally traded APIs

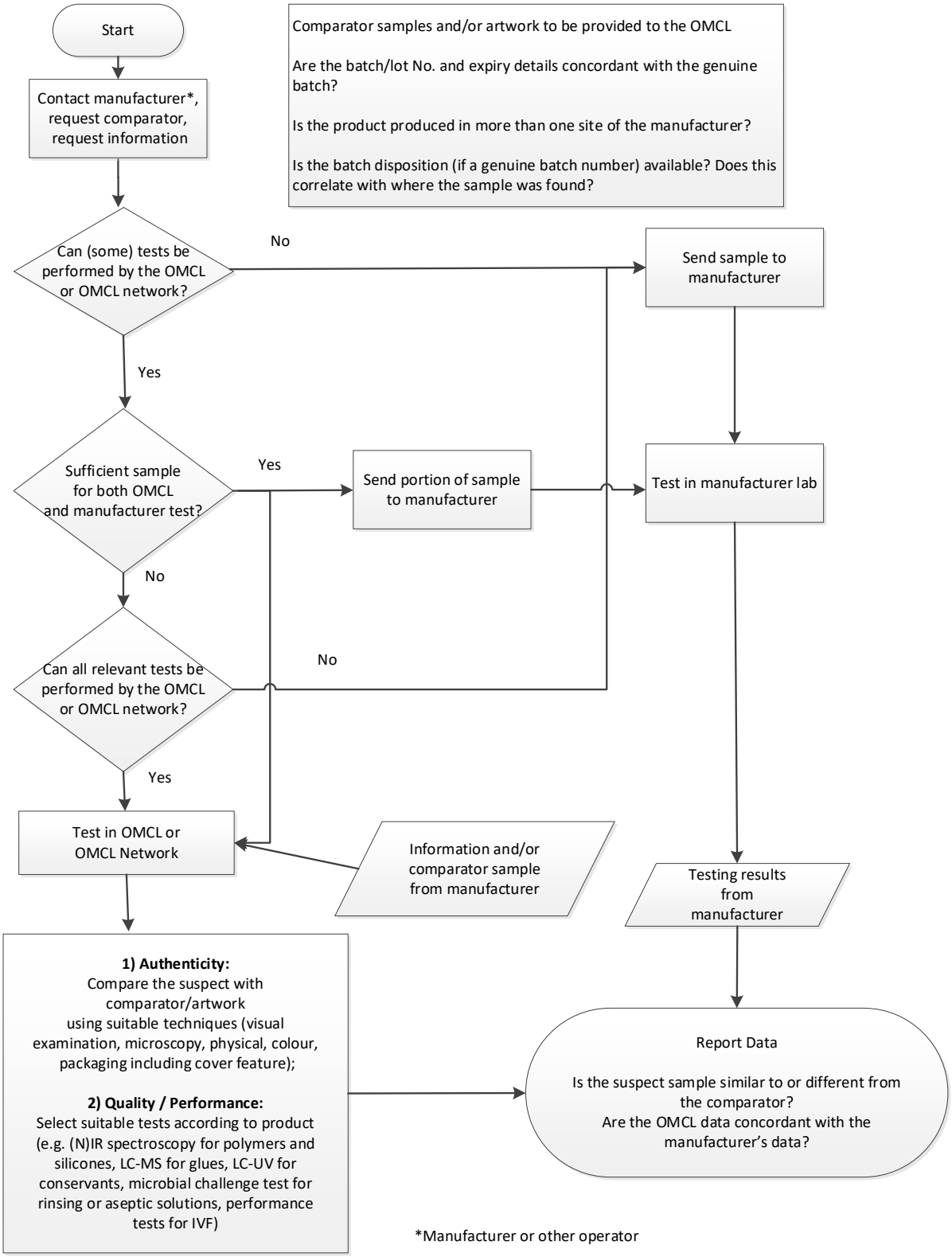
For API samples that are suspected of being falsified, it is essential that the OMCL is able to make contact with the MAH(s) of genuine products in which this API is declared. This may either be directly or through the competent authority, inspectorate or enforcement group.

Comparison of the suspect samples(s) is performed with at least 3 different comparator samples (batches) that should be obtained from the MAH. The fingerprint analysis, employing pattern recognition techniques individually or by combination, would be able to differentiate the suspect samples from the comparator samples if they are falsified or illegally manufactured. A position paper dedicated to the possibilities offered by chemometrics is available on the EDQM website: Benefits of Chemometrics for OMCLs.



Example 7: Medical Devices

In case of suspicion of falsification, authenticity is the first aspect that should be investigated and, for all types of medical devices, it is imperative to contact and to collaborate with the manufacturer or other operator (e.g. importer, distributor) to obtain information and, if required, a comparator sample. For devices which are purely physical or electronic, the OMCLs can rely on tests performed by the manufacturer.



For products where no falsification suspicion exists, but concerns may arise about their safety, quality, accuracy, efficiency, etc, testing should be performed in order to verify their compliance to the European regulations (2017/745 and 746 and, more specifically, Annex I) or to European standards. This verification should preferably be done within the OMCL and/or the OMCL Network (centres of expertise), or in collaboration with university or even private laboratories.