# Factsheet: Reference Standards in Europe

The EDQM is responsible for establishing, monitoring and distributing the official reference standards (RS) of the European Pharmacopoeia (Ph. Eur.), which provide the legal and scientific basis for the control of the quality of medicines in Europe and worldwide.

These physical standards are substances used for the tests and assays to be carried out in accordance with the Ph. Eur. monographs. This means that every batch of medicine marketed in Europe requires RSs for quality control; therefore any shortages of RSs may have an adverse impact on patients' access to medicines.

In addition, the EDQM currently prepares, stores and distributes World Health Organization (WHO) Reference Standards (see below), demonstrating that the EDQM's expertise in the manufacturing, storage and distribution of primary standards is widely recognised.

**Purpose of Reference Standards**

The Ph. Eur. official RSs are essential for the application of the quality control tests described in the Ph. Eur. monographs. They are needed to identify the pharmaceutical substance or product tested, determine its content or potency and control the impurities that may originate from its manufacturing process.

Reference standards can be of different types and they include chemical reference substances, herbal reference standards and biological reference preparations. They are established by the EDQM Laboratory with the participation of external laboratories.

To date more than 3000 RSs are available from the EDQM, including the WHO International Chemical Reference Substances (ICRS) and International Standards for Antibiotics (ISA).

**RSs at the EDQM**

These standards are produced in a 1000 square meter dedicated facility, the Manufacturing Section, at the EDQM premises in Strasbourg. They are manufactured and filled into containers by the Reference Standards and Samples Division, or DRS for short. They are then distributed to

manufacturers of medicines or pharmaceutical ingredients worldwide, as well as to public institutions involved in the quality control of medicines.

Within the Strasbourg's premises, samples covering all kinds of reference standards are stored at temperatures ranging from plus 5 to minus 80 degrees Celsius, depending on the properties of the respective material. With its new secondary site in Metz area, the storage capacity of the EDQM will increase even further to well more than double the present capacity.

**Safe storage procedures**

The Manufacturing Section has all the specialised equipment that may be needed for dealing with the types of substances to be processed: from harmless excipients to toxic substances. For example, substances prone to oxidation or sensitive to humidity are handled using equipment housed in a glove box (or isolator) with argon gas. This ensures that the substance is manufactured in a highly-pure and inert atmosphere.

In the case of highly potent substances, special equipment is used to protect both staff and the environment. The external sides of the vials are washed after manufacturing in order to protect the end user.

**Strict controls for the safety of staff and the environment**

This strict environmental control system covers the whole Manufacturing Section in Strasbourg and is an essential part of the prevention of contamination risks.

Protecting staff in the working areas is very important, and a range of protective measures is in place for this purpose: each of these measures is adapted to the specific manufacturing process.

Technicians and operators wear protective clothing depending on the risk-level of the substance they handle, and they follow strict hygiene protocols when entering and leaving the facilities.

**Distribution across the entire world**

Each vial or ampoule of reference standard has a barcode and a label bearing an article code, a batch number and a unique identifier. This barcode allows each reference standard unit to be tracked individually throughout the whole distribution chain, from when it is labelled at the EDQM until it is delivered to the end-user.

The EDQM applies all the relevant transport regulations prescribing how the various types of reference standards should be packed and labelled for dispatch.

The scientific expertise and the technical equipment of the EDQM ensure that the reference standards can be used by all manufacturers and independent control laboratories as a reliable means of controlling the quality of medicines and their ingredients.


This is how the official reference standards of the European Pharmacopoeia ensure that patients in Europe and beyond have access to safe and good quality medicines.