

BATCH TESTING AND PRODUCT RELEASE OF MEDICINES IMPORTED INTO THE EUROPEAN UNION

AUTHOR: BIRGIT SCHUMACHER, PH.D., BUSINESS DEVELOPMENT MANAGER, SGS LIFE SCIENCE SERVICES, GERMANY

The sale of medicines in the European Union (EU; formerly, European Community [EC])/European Economic Area (EEA) is regulated according to specific guidelines put in place to ensure the efficacy and safety of these medicines. The EEA is composed of the 27 member states of the EU, as well as Iceland, Liechtenstein and Norway. For the sale of medicines manufactured outside of the EU/EEA, each medicinal product batch must obtain certification by appropriate officials in the importing country.

TABLE 1: TERMINOLOGY ASSOCIATED WITH BATCH RE-TESTING

TERM	DEFINITION	EXPANDED DEFINITION
EEA	European Economic Area	Includes the 27 member states of the European Union, plus Iceland, Liechtenstein and Norway ¹ .
EMA	European Medicines Agency; (Formerly, European Agency for Evaluation of Medicinal Products)	Decentralized body of the EU; scientifically evaluates human and veterinary medicines for use in the EU ⁷ .
EU	European Union (Formerly, European Community [EC])	A political and economic union between 27 member states.
MA	Marketing Authorization	Defines the specific arrangements between exporting country and importing the importing EU country for batch release ² .
MRA	Mutual Recognition Agreement	An agreement between an EU country and a non-EEA country specifying conformity in reports, certificates, authorizations for the approval of sale of medicinal products in EU countries. Currently exist between the EU and Australia, Canada, New Zealand and Switzerland ² .
THIRD COUNTRY	Any country outside EU/EEA that does not hold an operational MRA	Medicinal product batches from third countries must be re-tested ² .
QP	Qualified Person	Person who certifies a medicinal product batch for release after being satisfied that the GMP have been met ² .

MUTUAL RECOGNITION AGREEMENTS (MRA)

An MRA is an agreement between an EU country and a country outside the EU/EEA². This agreement provides specific details about the standardized accepted procedures for medicine manufacturing, shipping, storage and quality control. Countries that currently have MRAs with the EU are Australia, Canada, New Zealand and Switzerland. All other countries outside the EU/EEA that do not have an MRA are called “third countries.” Manufacturers in third countries, including the United States, interested in entering EU country markets must undergo batch re-testing (see FIGURE 1).

An established MRA between non-EEA countries and the EU offers multiple advantages both to the manufacturer and the importing country. Importantly, MRAs provide assurance to the importing country that the manufacturer operates under the Good Manufacturing

Practices (GMP) of the EU, ensuring the safety and efficacy of imported medicines.

Manufactures from countries with an MRA in place may bypass batch re-testing for certification. This streamlining of the certification process significantly reduces costs to the manufacturer, including costs associated with re-testing as well as those due to delayed entry into the market of the importing country.

THE ROLE OF THE QUALIFIED PERSON (QP)

The QP is responsible for ensuring the quality of each medicinal product batch being sold in the EC/EEA². After the QP is satisfied that the batch meets appropriate standards, he or she certifies the whole or partial batch. When no MRA exists between the EU and the exporting country, the QP certifies the batch when he or she approves of the batch re-testing results (FIGURE 1).

Medicine batches from manufacturers located in countries that do have an operational MRA in place must still undergo certification by a QP, unless otherwise noted in the MRA². However, the QP may trust the manufacturer’s confirmation of adherence to all GMP procedures, and re-testing may be bypassed. Importantly, manufacturers, regardless of whether an operational MRA is in place, need to provide evidence that each part of a batch is manufactured, shipped and stored consistently and safely (FIGURE 2).

DIRECTIVES FROM THE EUROPEAN PARLIAMENT

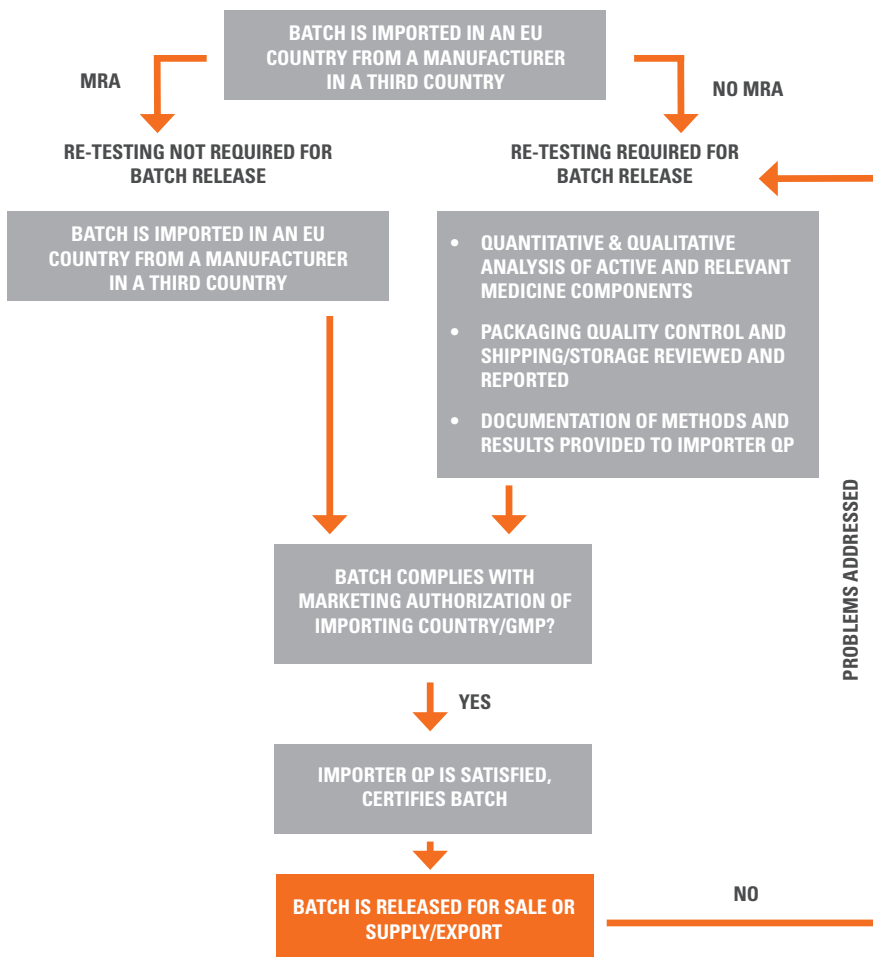
In 2001, the European Parliament passed two principle directives that provided the legal basis requiring a medicinal product batch to undergo full qualitative and quantitative analysis in an EU member state. Directive 2001/83/EC specifically established this testing for batches of medicines for human use³, while Directive 2001/82/EC did so for medicines for veterinary use⁴. These directives require the certification of each medicinal product batch by a QP. Additionally, the EU member states must ensure that the QP is performing his or her job adequately by ensuring proper administrative oversight. Additional laws under Directive 2003/94/EC were approved in 2003 and established that contract laboratories operating in accordance with Directive 2001/83/EC may perform this batch re-testing⁵.

MORE DETAILS ESTABLISHED BY ANNEX 16

While the directives establish the need for qualitative and quantitative testing and QP certification, they do not provide specific details about these regulations. Annex 16 to the “EU Guide to Good Manufacturing Practice” legally requires a QP of the importer to certify the finished medicinal product before the batch may be released for sale in EU/EEA countries⁷. This annex also allows for the QP of one country in the EU/EEA to accept certification of a QP from another EU/EEA country, which may further streamline the process.

Annex 16 legally requires medicines from non-EC/EEA countries to undergo batch testing, with the exception of countries

FIGURE 1: BATCH RE-TESTING PROCESS



that have an MRA with the EU⁶. If a medicinal product batch is imported in separate parts, either conditions of consistency between the parts need to be proven, or each part of the batch must be re-tested individually (FIGURE 2). These conditions include demonstrating that individual parts belong to the same batch; the sample tested is representative of the entire batch; and that each part has been manufactured, shipped and stored in a manner equivalent to that of the sample tested.

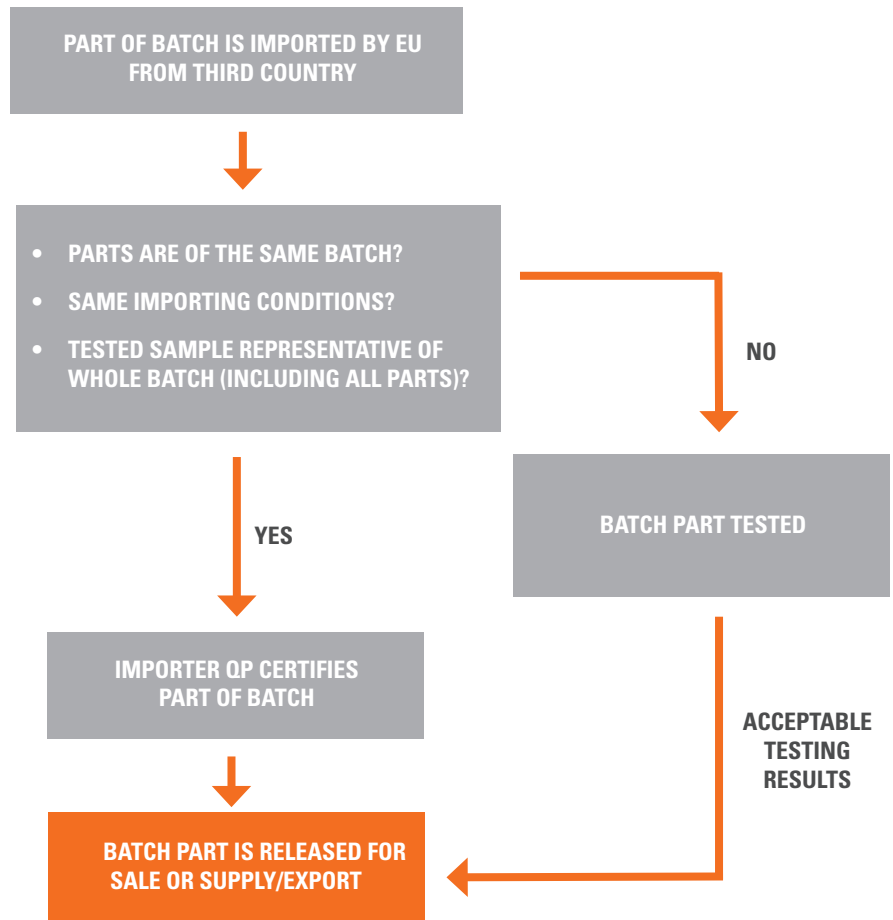
EU LAWS GUIDE LOCAL LEGISLATION

For importation of medicine batches into EC/EEA member countries, the regulations of Annex 16 and the two directives require each country to establish local legislation stipulating that these procedures be put into practice.

CONCLUSION

When batch re-testing is required, a skilled contract laboratory can handle all of the quality control testing and validation necessary to release a medicinal batch for sale in the European Union. SGS Life Science Services facilities located in Frankfurt (Taunusstein) and Berlin, Germany; Brussels (Wavre), Belgium; and Paris (Clichy), France are each qualified to conduct the re-testing required for batch release. Each facility conducts a diverse array of pharmaceutical testing, including analytical chemistry, microbiology, method development and validation. Due to their exclusive role in pharmaceutical testing and not medicine manufacturing, SGS Life Science Services functions as a trusted and independent partner.

FIGURE 2: RE-TESTING OF SUBSEQUENT PARTIAL BATCHES



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3. "Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Medicinal Products for Human Use." Official Journal L – 311, 28/11/2004, p. 67 – 128. Specifically, Article 51 (1b) and Article 51 (2).
4. "Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Veterinary Medicinal Products." Official Journal L -311, 28/11/2004, p. 1 – 66. Specifically, Article 55 (1) and (2).
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CONTACT INFORMATION

EUROPE

BELGIUM

+32 10 42 11 11
be.pharmaqc@sgs.com

FRANCE (PARIS)

+33 1 41 06 95 93
fr.pharmaqc@sgs.com

FRANCE (POITIERS)

+33 (0) 5 49 57 04 04
clinicalresearch@sgs.com

GERMANY (BERLIN)

+49 30 3460 7500
de.pharmaqc@sgs.com

GERMANY (FREIBURG)

+49 761 6116 7760
de.pharmaqc@sgs.com

GERMANY (TAUNUSSTEIN)

+49 6128 744 245
de.pharmaqc@sgs.com

SWITZERLAND (GENEVA)

+41 22 794 8374
pharmaqc@sgs.com

UK (WOKINGHAM)

+44 (0) 1189 896940
pharmaqc@sgs.com

ASIA

INDIA

+91 44 2254 2601
in.pharmaqc@sgs.com

SINGAPORE

+65 677 53 034
sg.pharmaqc@sgs.com

CHINA

+86 21 6115 2197
cn.pharmaqc@sgs.com

TAIWAN

+886 2 2299 3279 ext 2500
tw.pharmaqc@sgs.com

NORTH AMERICA

CANADA

+ 1 905 364 3757
ca.pharmaqc@sgs.com

USA (FAIRFIELD, NJ)

+ 1 888 747 8782
us.pharmaqc@sgs.com

USA (LINCOLNSHIRE, IL)

+1 847 821 8900
us.pharmaqc@sgs.com

USA (WEST CHESTER, PA)

+ 1 610 696 8210
us.pharmaqc@sgs.com

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