GENERAL BACKGROUND ON THE
LIST OF INTERNATIONAL COMPARATOR
PHARMACEUTICAL PRODUCTS
(June 2016)

REVISED DRAFT FOR COMMENT

Should you have any comments on the attached text, please send these to:
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Ms Marie Gaspard (gaspardm@who.int), by 30 June 2016. In line with the recommendations of the Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP), the list is planned to be published as a living document. Comments received after the indicated date will be considered.

Working documents are sent out electronically and they will also be placed on the Medicines website for comment. If you do not already receive directly our draft guidelines please let us have your email address (to bonnyw@who.int) and we will add it to our electronic mailing list.

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SCHEDULE FOR THE PROPOSED ADOPTION PROCESS OF DOCUMENT QAS/14.586:
GENERAL BACKGROUND ON THE INTERNATIONAL LIST OF COMPARATOR PHARMACEUTICAL PRODUCTS

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
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<tbody>
<tr>
<td>Revisions of the list of comparator products based on input from users, the WHO Collaborating Centre for Research on Bioequivalence Testing of Medicines, Frankfurt/Main, Germany, manufacturers, the WHO Prequalification Team (PQT) and based on updates of the Essential Medicines List (EML)</td>
<td>2008–2013</td>
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<tr>
<td>Preliminary feedback for revision of the selection of comparator products during informal consultation with experts and the PQT</td>
<td>July 2013</td>
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<tr>
<td>Presentation of the outcome of the above consultation to forty-eighth meeting of the WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP)</td>
<td>October 2013</td>
</tr>
<tr>
<td>Discussion in context with revision of <em>multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability</em> guidelines developed by Dr J. Gordon with input from the PQT and Professor J.D. Dressman, WHO Collaborating Centre for Research on Bioequivalence Testing of Medicines, Frankfurt/Main, Germany</td>
<td>April 2014</td>
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<tr>
<td>Editing of the list of comparator products and revisions by Thomas Human, WHO Intern, based on publicly available information</td>
<td>April–June 2014</td>
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<tr>
<td>Discussion during an informal consultation held together with regulatory experts from national regulatory authorities, the PQT and the WHO Collaborating Centre for Research on Bioequivalence Testing of Medicines, Frankfurt/Main, Germany. Proposal: two separate documents, one on the selection of a comparator product, one with the list of comparator products</td>
<td>5–6 July 2014</td>
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<tr>
<td>Event Description</td>
<td>Date</td>
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<tr>
<td>Presentation of above proposals to forty-ninth meeting of the WHO ECSPP and adoption of general guidance on selection of comparator products</td>
<td>October 2014</td>
</tr>
<tr>
<td>Discussion of the entries to the list of international comparator products and possible collaboration at the steering committee of the International Generic Drug Regulators Programme (IGDRP)</td>
<td>November 2014</td>
</tr>
<tr>
<td>Revision of list of international comparator products with support of the regulatory experts Dr. A. Garcia, Dr. J. Gordon and Mr. J. Welink</td>
<td>March–September 2015</td>
</tr>
<tr>
<td>Presentation to fiftieth meeting of the WHO ECSPP</td>
<td>October 2015</td>
</tr>
<tr>
<td>Revision of the list of international comparator products as recommended by the WHO ECSPP in collaboration with regulatory experts from NRAs and the PQT</td>
<td>November 2015–January 2016</td>
</tr>
<tr>
<td>Circulation of the list of international comparator products and <em>General Background on the list of comparator pharmaceutical products</em> for consultation to interested parties as recommended by the WHO ECSPP</td>
<td>February 2016</td>
</tr>
<tr>
<td>Compilation of feedback and preparation of an updated list of international comparator products</td>
<td>Mai 2016</td>
</tr>
<tr>
<td>Posting of the working documents list of international comparator products and <em>General Background on the list of comparator pharmaceutical products</em> on the WHO website as recommended by the WHO ECSPP</td>
<td>June 2016</td>
</tr>
<tr>
<td>Presentation to fifty first meeting of the WHO ECSPP and discussion of the maintenance process</td>
<td>October 2016</td>
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**Note from the Secretariat:** This working document is intended as stand-alone guidance to explain the actual list of international comparator products which will be published as a living document on the website as recommended by the WHO ECSPP.
1. INTRODUCTION

The need for revision of the comparator products guidance has been recommended by the WHO Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) on the basis of the changes due to globalization, mergers and changes to the Essential Medicines List (EML) (1), the recommended comparator products used within the WHO Prequalification Team (PQT)–Medicines as well as the evolved experience and scientific understanding in the multisource product area (2).

During the informal consultation held on 5–6 July 2014, it was proposed to prepare two new, separate working documents, one on the selection of comparator products, including the general guidance on how to select comparator products (guidance on the selection of comparator pharmaceutical products for equivalence assessment of interchangeable multisource (generic) products (3)), and a second one comprising the list of international comparator products (presented here). The aim was to facilitate the updating and maintenance process.

In connection with the revision of these guidelines the following related guidance texts are under regular review and update:

- **Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability;**
- **Proposal to waive in vivo bioequivalence requirements for WHO Model List of Essential Medicines immediate-release, solid oral dosage forms;**
- **Guidance for organizations performing in vivo bioequivalence studies.**

Please consult the WHO website for the most current version of these guidance texts (4).

2. LIST OF INTERNATIONAL COMPARATOR PRODUCTS

The list of international comparator products provides information about pharmaceutical products from the EML (1), and includes specific finished pharmaceutical products which can be selected as comparators (column headed “International comparator product”) and markets where the product’s quality, safety and efficacy is considered as best documented (column headed “Market”).
The list of international comparator products will be revised and regularly adapted to the newest version of the EML. WHO relies on the support of drug regulatory authorities and information provided by manufacturers.¹

Comparator products recommended by PQT are included in the list of international comparator products (column headed “PQ comparator product”). Please refer to the guidance documents of PQT for further information regarding PQ comparator products (2).

Please refer to the Guidance on the selection of comparator pharmaceutical products for equivalence assessment of interchangeable multisource (generic) products (4) for full instructions on how to select the comparator pharmaceutical product and to the Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability (3) for full details on what kind of equivalence testing is required.

General principles for selection of a comparator pharmaceutical product listed in order of preference (extracted from the above referenced guidances):

1. the innovator product for which quality, safety and efficacy has been established if this product has been granted a national marketing authorization (nationally authorized innovator);
2. national market leader product for which a national marketing authorization has been granted;
3. the WHO-recommended comparator product included in the International list of comparator products or, if different and if it exists for the active pharmaceutical ingredient in question, the one suggested within the context of PQT;
4. an innovator product approved by a stringent regulatory authority (SRA), i.e. a country associated to The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH);
5. a product that has been granted approval in an ICH-associate country;

¹ In case a comparator product is no longer available or is being replaced, please contact QAS@who.int.
6. in the case that no innovator or comparator product can be identified according to the above, the choice of the comparator should be made carefully and should be comprehensively justified by the applicant. In this case, the most important selection criteria in order of preference are:

— prequalification (PQ) by WHO,
— extensive documented use in clinical trials reported in peer reviewed scientific journals,
— a long and unproblematic period of post-market surveillance.

3. EXPLANATION OF ENTRIES

PQ comparator/PQ comparator product
PQT prequalifies medicinal products used for HIV/AIDS, malaria, tuberculosis and for reproductive health, i.e. PQT recommends comparator products for these therapeutic areas only.

N/I
Not included in the invitation for expression of interest (EOI) by PQT.

N/A
Classes of products (e.g. vaccines, immunoglobulins) where the concept of interchangeability according to the Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability does not apply.

SRA
Markets with stringent regulatory authority (according to the WHO definition).

An entry in **bold** in the column headed “International comparator product” signifies that a product of the dosage form or dose strength is available on the market instead of, or in addition to, those in the EML.
REFERENCES

1. WHO Model List of Essential Medicines:

2. Guidance documents PQ comparator products:
   http://apps.who.int/prequal/info_applicants/info_for_applicants_BE_comparator.htm

3. Guidance on the selection of comparator pharmaceutical products for
   equivalence assessment of interchangeable multisource
   (generic) products. In: WHO Expert Committee on Specifications for

4. WHO – Related regulatory standards – Interchangeability:
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/regulatory_stan
   dards/en/

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