THE
BLUE BOOK

2nd EDITION

# Marketing Authorization

## of Pharmaceutical Products with Special Reference to Multisource (Generic) Products

*A manual for National Medicines Regulatory Authorities (NMRAs)*

World Health Organization

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# PREFACE

In 1999, WHO published a manual entitled Marketing Authorization of Pharmaceutical Products with Special Reference to Multisource (Generic) products - a Manual for a Drug Regulatory Authority. After an initial distribution of two thousand copies to the Regulatory Authorities of WHO member countries, more than three thousand additional copies were printed and distributed in response to requests. Feedback was received from many who have used the manual in their assessment work or in training courses. The manual became known as the Blue Book and has been used as reference document when the WHO Prequalification of Medicines Programme started in 2001.

This is the second edition of the Blue Book. In developing this new edition, many practical suggestions made by regulatory officials were taken into account and incorporated as far as possible. Now included are a series of documents that will be of practical assistance to regulatory authorities, including checklists, flow charts, model evaluation reports and model correspondence. Relevant WHO guidelines (such as those concerning stability and bio-equivalence testing) are referenced in the text but are no longer attached for these reasons:

- With the additional material to be incorporated in this edition, the Blue Book could have become long and cumbersome;
- Updated versions of guidelines may become available before a new version of the Blue Book is produced;
- All of the relevant guidelines are available via the WHO website[1].

Conference on Harmonization (ICH), to date ICH has focussed on new chemical and biological substances, and new dosage forms that contain new substances. However regulatory requirements for multisource (generic) medicines are somewhat different, and these are the main focus of the Blue Book.

Like the first edition, the new Blue Book offers regulatory authorities a number of options for the administration of medicines regulation. In the case of pre-marketing evaluation, the options can be grouped into three broad categories:

- No pre-marketing evaluation;
- Verification of regulatory status in other countries;
- Full assessment of application data.

The first option puts patients and public health at risk and is obviously not acceptable. For most countries the most realistic approach is a combination of the other two options. This requires setting up a system that will permit:

- Identification of reference countries or authorities whose regulatory decisions are considered acceptable or recognizable; and
- Conducting assessments of applications on the basis of a number of criteria established within the limits imposed, on one side, by a reasonable certainty of filtering out substandard, unsafe products and, on the other side, by the available human and material resources.

This manual is based on the above considerations and aims at providing technical advice to countries