

Guidelines for Pharmaceutical Equivalence Requirements

Version 1.0 (August 2009)

DRAFT

This draft is for comments;
Please send your comments or suggestions to SFDA
E-Mail: Drug.comments@sfd.gov.sa, Fax No. 0096612057637
3292 North Highway Al Nafal Unit (1) - Riyadh 13312 – 6288, Saudi Arabia

Table of Contents

I.	FOREWORD	3
II.	BACKGROUND.....	3
III.	PHARMACEUTICAL EQUIVALENCE.....	3
IV.	IDENTICAL MEDICINAL INGREDIENTS	4
V.	DETERMINATION OF PHARMACEUTICAL EQUIVALENCE.....	4
VI.	GENERIC PARENTERAL DRUGS.....	5
VII.	PHARMACEUTICAL QUALITY OF AQUEOUS SOLUTIONS.....	6

I. FOREWORD

The Guideline for Pharmaceutical Equivalence Requirements will provide assistance to generic drugs manufacturers with respect to the determination of pharmaceutical equivalence of their products with reference to the innovator products.

It is the responsibility of Saudi Food and Drug Authority (SFDA) to ensure that the generic products available in the Kingdom of Saudi Arabia adequately meet the requirements of pharmaceutical equivalence when compared with the reference products.

Guidance documents are administrative instruments do not establish legally enforceable responsibilities and, as such, allow flexibility in approach. Alternate approaches to SFDA are acceptable, provided they are supported by adequate scientific justification.

SFDA reserves the right to request information or material and to define conditions not specifically described in these guidelines so as to access the safety, efficacy and quality of the generic products. These guidelines should be used in conjunction with other relevant guidelines such as the chemistry and manufacturing and bioavailability guidelines.

II. BACKGROUND

The purpose of this guideline is to outline the requirements of pharmaceutical equivalence of Generic Drugs that are manufactured in different dosage forms. The safety, efficacy and quality of generic products are established on the basis of comparative Pharmaceutical Equivalence as well as therapeutic equivalence.

Almost all Generic Drug applications for oral solid dosage form(s) are required to demonstrate their Bio-Equivalency by comparing with the reference innovator product. Furthermore, these products are also required to fulfill the regulatory requirements of Pharmaceutical Equivalency. This is usually accomplished by performing a comparative assessment of quality attributes with the designated reference innovator product. The guideline also discusses other dosage forms (see Appendix 1)

III. PHARMACEUTICAL EQUIVALENCE

Pharmaceutical Equivalence is the condition in which drug products, containing the identical quantity of active substance (but not necessarily containing the same excipients), in an identical comparable dosage form, meets all applicable standards of identical strength, quality, purity and potency.

The following criteria should be considered in the determination of Pharmaceutical Equivalence.

- Identical amount of active substance(s) (e.g. Salt or Ester)
- Same dosage form or comparable dosage form (e.g. Tablets vs. Capsules)
- Same route of administration

It should be noted that pharmaceutical equivalence does not necessarily apply to therapeutic equivalence. Therapeutic equivalence requires a product to be pharmaceutically equivalent and to have the same safety and efficacy profile after administration of the same dosage.

IV. IDENTICAL MEDICINAL INGREDIENTS

The term Identical Medicinal Ingredients can literally be interpreted to imply medicinal ingredients that are both physically and chemically identical. It is important that the “chemical identical” of medicinals must be taken into account while determining pharmaceutical equivalency. In other words, pharmaceutical equivalent products should contain chemical identical ingredients, but not necessarily physical identical ingredients.

It is recognized that differences in physical attribute (e.g. Particle size, polymorphism) of the medicinal ingredient could potentially cause differences in the safety and efficacy profiles of drug products. In order to address these differences in physical properties of the identical medicinal ingredients, appropriate *in vivo* or *in vitro* studies should be performed

Medicinal ingredients containing the same active moiety can be classified into identical or non-identical medicinal ingredients. The following guidelines are suggested to establish such differences:

- If active moiety is anhydrous or hydrated, the drug substance would be considered identical.
- If active moiety is un-solvated or in various solvated forms, it would also be considered identical with the acceptable solvate content.
- If active moiety is in the form of complexes, ester or salt, it would be considered non-identical.
- If active moiety is in different forms of isomer or mixture, it would be considered non-identical.

V. DETERMINATION OF PHARMACEUTICAL EQUIVALENCE

Depending on the particular dosage form, the comparison on the relevant pharmaceutical characteristic will include the following:

- Formulation
- Physiochemical properties
- Device Attributes (devices used along with the drug)

FORMULATION:

In order for a subsequent- entry product to be pharmaceutical equivalent to the reference innovator product, it must contain identical amounts of identical medicinal ingredients.

PHYSIOCHEMICAL PROPERTY

Studies comparing the physicochemical property (generic product) against the reference product (innovator product) should be conducted and the results should be submitted. If the results are not identical/similar, the test product may be considered not equivalent.

DEVICE ATTRIBUTES

In the case of a device, a qualitative and quantitative analysis for the physical and operating characteristics of the device for the test product (generic product) against the reference (innovator product) should be conducted and the result should be submitted.

NOTE: For the purpose of this policy of establishing pharmaceutical equivalence of a generic product against the reference product, at least one batch of the reference product should be compared with two batches or lots of the test product (generic product).

VI. GENERIC PARENTERAL DRUGS

For the purpose of this document on the requirements of generic drugs applications, the following groups have been established:

GROUP I PRODUCTS:

- Water soluble powders for reconstitution where there are no excipients
- Aqueous solutions where there are no excipients other than the vehicle(s)
- Non-aqueous single solvent solutions, other than an oil preparation, where there are no excipients, other than the vehicle

The requirement for the above products is proof of pharmaceutical equivalence.

If no pharmaceutical equivalence is established, then clinical studies must be performed.

GROUP II PRODUCTS:

- I. Lyophilized powder
- II. Powder containing buffer or other excipients
- III. Aqueous solutions with other excipients
- IV. Non-aqueous solutions, other than an oil preparation, with other excipients

The requirements for the above products are:

- Proof of pharmaceutical equivalence
- Pharmaceutical equivalence will not be accepted if
 - Excipients are not accepted for such preparations
 - The quantity of excipients falls outside the acceptable range ($\pm 5\%$)

GROUP III PRODUCTS:

- Oil preparations having a single oil

The product will not be considered pharmaceutically equivalent if:

- Excipients are not considered to be safe
- The quantity of excipients is outside the limits ($\pm 5\%$)
- The oil used in the product is different than the reference product

GROUP IV PRODUCTS:

- Specialized preparations (Suspension, Emulsion or other complex formulation)

Pharmaceutical equivalence studies alone are not acceptable but require full clinical studies on a case-by-case basis.

VII. PHARMACEUTICAL QUALITY OF AQUEOUS SOLUTIONS

This preparation includes oral, dermatology, ophthalmic, otic, nasal, inhalation and injectable preparations. It is important that the medicinal ingredients in these preparations be identical. The excipients in the test product should be qualitatively the same and quantitatively essentially the same (essentially the same means $\pm 5\%$). When performing the pharmaceutical Equivalence of this preparation, a side-by-side comparative results should be submitted.

Appendix 1

The following table indicates the test parameters required for various types of dosage forms subject to pharmaceutical equivalence:

Dosage forms	Route of Administration						
	Oral	Derm.	Ophth.	OTIC	Nasal	Inhal.	Inject.
Description	A	A	A	A	A	A	A
Identification	A	A	A	A	A	A	A
Assay	A	A	A	A	A	A	A
Impurities	A	A	A	A	A	A	A
pH	A	A	A	A	A	A	A
Microbiological limit	A	A	N/R	A	A	A	N/R
Uniformity of dosage limit	A	A	A	A	A	A	A
Anti Microbial Preservative	A	A	A	A	A	A	A
Anti-Oxidant	A	A	A	A	A	A	A
Viscosity	A	A	N/R	A	A	N/R	N/R
Osmolality/osmolarity	N/R	N/R	A	A	A	A	A
Particulate matter	N/R	N/R	A	N/R	N/R	N/R	A
Sterility	N/R	N/R	A	N/R	N/R	N/R	A
Bacterial Endotoxin	N/R	N/R	A	N/R	N/R	N/R	A

A: Generally performed on finished product

N/R: Not Required

Note: Certain preparations may require some other tests.