IPRP
International Pharmaceutical Regulators Programme

Criteria for when a Separate ASMF/DMF should be Submitted

Quality Working Group for Generics (QWGG)

Version	Description of Change	Author	Effective Date
v 1.0	Original publication	Quality WG	7 June 2017
V 1.1	Change to QWGG	QWGG	20 Sep 2018

Foreword

In order to achieve the QWGG's objective to promote collaboration and convergence in the area of generic drug regulation, the QWGG has developed a series of reference documents covering a number of technical and procedural aspects of assessment.

These documents were developed among participating QWGG members and observers as model documents. These QWGG documents have been made available for use by any interested party.

The implementation of these documents by a given QWGG member or observer, either as a whole or in part, is not mandatory. Each QWGG member or observer works within their own specific regulatory setting and some or all aspects of a document may, for a variety of reasons, not be applicable. Equally, a given IGDRP member or observer may for practical reasons choose to revise the format or written language of a model document.

IPRP Quality Working Group for Generics (QWGG) Criteria for when a Separate ASMF/DMF should be Submitted

A common question often arises as to what differences in API-details may be included in a single ASMF/DMF and under what circumstances should a separate ASMF/DMF be submitted.

The IPRP (formerly IGDRP) performed a Gap Analysis of the ASMF systems in the various IPRP jurisdictions and a questionnaire was also circulated among members to ascertain the criteria for issuing a new ASMF.

The following common criteria have been identified for when a separate ASMF/DMF should be submitted. The list is indicative only and not exhaustive. Ultimately, the legislation or regulation in force in each country takes precedence. Nonetheless, this information is deemed useful to ASMF/DMF holders and other regulators.

Each of the following examples is considered to be a situation where a separate ASMF/DMF should be submitted.

a) A different active substance

b) A different salt of an active substance

c) A different complex of an active substance

d) A different co-crystal of an active substance

e) A different solvate or hydrate form of an active substance

f) A different isomer or mixture of isomers of an active substance

g) A racemate of an optically pure active substance

h) An optically pure enantiomer of an active ingredient racemate

i) The enantiomer of an optically pure active substance

j) The introduction of a new substantially different route of synthesis (i.e. resulting in a different specification for the active substance)

k) A different polymorphic form of an active substance (resulting in substantially different physicochemical and/or pharmacokinetic properties)

l) Any other change to the active substance that results in substantially different physicochemical and/or pharmacokinetic properties)

m) A sterile grade of an active substance previously prepared in a non-sterile manner.

n) A non-sterile grade of an active substance previously prepared in a sterile manner.

o) Change/addition of raw materials of different animal origin (only where there is a substantial change in the safety of the active substance)

The following examples would not necessarily result in the need to submit a separate ASMF/DMF and in most cases could be incorporated in a single ASMF/DMF.

a) Slightly different routes of synthesis that do not result in substantially different physicochemical and/or pharmacokinetic properties.

b) Different manufacturing sites using the same or similar routes of synthesis (i.e. same specification for the active substance).

c) Different particle size grades (this should be controlled in the drug product manufacturer's active substance specification).

d) Different container closure systems resulting in a different re-test and storage conditions

e) Other changes that do not result in substantially different physicochemical and/or pharmacokinetic properties).

f) Transfer of ownership of an existing ASMF/DMF from one ASMF/DMF holder to another

g) Change in the name and/or address of the existing ASMF/DMF holder