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Guidelines for Categorization of Type of Application as New Product or Variation for Parenteral Biological Preparations

Scope:

This guideline addresses the application submission of parenteral biological formulations whether to submit the application as a new product or as variation.

Definitions:

Pharmaceutical form: The pharmaceutical form is the form in which a pharmaceutical product is presented in the medicinal product package as supplied by the marketing authorization holder/manufacturer/distributor.

Dosage form: The dosage form is the physical manifestation of a product that contains the active ingredient(s) and/or excipient(s) that are intended to be delivered to the patient; it may refer to the form of presentation or the form of administration. Different parental dosage forms are described in annex 1.

Strength: The strength represents the amount of active substance in the pharmaceutical form, which can be defined per unit dose or as a concentration. The concentration can be stated per unit of mass (250mg/g) or per unit of volume (2mg/ml) or in percentage (5%). For the purpose of this guideline:
- for single-dose preparations, total use, the strength is defined as the amount of active substance per unit dose;
- for single-dose preparations, partial use, the strength is defined as the concentration expressed as the amount of active substance per ml, per puff, per drop, per kg, per m2, in percentage as appropriate;
- for multi-dose preparations, the strength is defined as the concentration expressed as the amount of active substance per ml, per puff, per drop, per kg, per m2 as appropriate;

Types of submission:

1- A change from multi-dose to single-dose or vice-versa always results in submission of a new application (for both addition and replacement).

2- A different strength (as defined above) results in submission of a new application (table 1)

3- Any change in container, pack-size, fill-volume or fill-weight, which does not involve a change in strength and/or composition, is submitted as variation.

4- A change or addition of a dosage form results in submission of a new application.

5- For changes in route of administration see examples in table 2.

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Examples

Table 1 : Examples of changes of strengths and containers

Liquid ready-to-use – Single-dose, total use	Strength	Type of submission
Solution for injection (pre-filled syringe) *From* 100 mg/1 ml To 200 mg/1 ml *From* 100 mg/1 ml To 200 mg/2 ml *From* 100 mg/1 ml To 100 mg/0.5 ml ***i.e. If the Strength is changed, it is considered as a new file***	 100mg 200 mg 100 mg 200 mg 100 mg 100 mg	 New New Variation
Powder for reconstitution – Single-dose, total use		
Powder for solution for injection *From* 100 mg (to 2 ml) To 200 mg (to 2 ml) *From* 250 IU (to 5 ml) To 500 IU (to 5 ml) *From* 100 mg (to 2 ml) To 200 mg (to 4 ml) *From* 3 g (to 5 ml) To 3g (to 10 ml) ***i.e. If the Strength is changed, it is considered as a new file***	 100 mg 200 mg 250 IU 500 IU 100 mg 200 mg 3 g 3 g	 New New New Variation
Liquid ready-to-use – Multi-dose or Single-dose, partial use		
Solution for injection (vial) *From* 500 mg/50 ml To 1000 mg/50 ml *From* 500 mg/10 ml To 1000 mg/20 ml ***i.e. If the concentration is changed, it is considered as a new file***	 10 mg/ml 20 mg/ml 50 mg/ml 50 mg/ml	 New Variation
Powder for reconstitution – Multi-dose or Single-dose, partial use		

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Powder for concentrate for infusion *From* 500 mg (to 50 ml) To 1000 mg (to 50 ml) *From* 200 IU (to 100 ml) To 600 IU (to 200 ml) *From* 500 mg (to 50 ml) To 1000 mg(to 100ml ***i.e. If the concentration after reconstitution is changed, it is considered as new file***	 10 mg/ml 20 mg/ml 20 IU/ml 30 IU/ml 10 mg/ml 10 mg/ml	 New New Variation
Concentrate for solution		
Concentrate for solution for infusion *From* 1 g/10 ml To 2 g/10 ml From 1 g/10 ml To 2 g/20 ml ***i.e. If the concentration before dilution is changed, it is considered as a new file***	**BEFORE DILUTION** 100 mg/ml 200 mg/ml 100 mg/ml 100 mg/ml	 New Variation
Parenterals – different containers		
Solution for injection *From* vial To pre-filled syringe *(same concentration)* Solution for injection *From* vial To ampoule *(same concentration)*		Variation Variation
5. Solution for injection(insulins) *From* *Vial* *To* *cartridge* *(same concentration)* *From* *cartridge* *To* *cartridge in disposable pen* *(same conc. &cartridge)*		Variation Variation
Powder + Solvent ***solvent*** *From* vial to pre-filled syringe *(same concentration)*		Variation

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Table 2 : Examples of *change in route of administration of parenterals*

Replacement	Presentation	Type of submission
e.g. From SC *To* IM		
a) **No** change in the composition and/or specifications of the finished product	IM (one product)	Variation
b) change in the composition and/or specifications of the finished product	IM (one product)	New
Addition of a different presentation		
e.g. From SC *To* SC and IM	IM and SC (two products)	New
Addition to the same presentation		
e.g. From SC *To* SC/IM		
c) **No** change in the composition and/or specifications of the finished product	SC/IM (one product)	Variation
d) change in the composition and/or specifications of the finished product	SC/IM (one product)	New

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Annex I

Parenteral Dosage Forms

Name
Solution for infusion in administration system
Solution for injection
Suspension for injection
Emulsion for injection
Gel for injection
Powder for solution for injection
Powder for suspension for injection
Powder and solvent for solution for injection
Powder and solvent for suspension for injection
Concentrate for solution for injection
Solution for infusion
Emulsion for infusion
Powder for solution for infusion
Concentrate for solution for infusion
Powder and solvent for solution for infusion
Lyophilisate for solution for infusion
Solvent for parenteral use
Lyophilisate for solution for injection
Lyophilisate for suspension for injection

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