ANNEX I

PETITION FORM FOR SUBSTANTIAL MODIFICATION TO THE PRODUCT UNDER INVESTIGATION

National Health Surveillance Agency
Clinical Trial Substantial Modification
Investigational Product Petition Form

Document Identification
(For use by the receiving agency)

1	DDCM Process Number	2	Office Hours
Company Data			
3	Applicant	4	Authorization / Registration Number
5	Manufacturer	6	Authorization / Registration Number
DDCM data			
7	**Modification Type** : a) Modification resulting from recommendations or alerts issued by health authorities?		a) ( ) Yes ( ) No
8	**Reasons for Substantial Modification** : **a) Changes related to the Active Pharmaceutical Ingredient – API/Active Substance (biological products)?** i. Replacement/Inclusion of new manufacturing site or manufacturing stages?		**a) ( ) Yes ( ) No** i. ( ) Yes ( ) No

	ii . Change in the synthesis route (synthetic/semisynthetic)?	ii . ( ) Yes ( ) No
	iii . Change in the manufacturing process of the active substance of biological products?	iii . ( ) Yes ( ) No
	iii.1 Changes in cell banks, involving:	
	iii.1.1 Generation of a new Master Cell Bank (MCB) from the same expression construct with the same or highly similar cell line?	iii.1.1 ( ) Yes ( ) No
	iii . 1.2 Generation of new BCM from a different expression construct with the same coding sequence and the same cell line?	iii.1.2 ( ) Yes ( ) No
	iii . 1.3 Adaptation of a new BCM in a new culture medium?	
	iii.1.4 Generation of new BCM for a recombinant product or viral vaccine?	
	iii.2 Changes in seed banks, involving:	iii.1.3 ( ) Yes ( ) No
	iii . 2.1 Establishment of a new Master Seed Bank (MSB)?	
	iii . 2.2 Extension of the number of Working Seed Bank (WSB) passes beyond the approved level?	iii.1.4 ( ) Yes ( ) No
	iii.3 Change of manufacturing location of the cell bank or seed bank ?	
	iii.4 Alteration of fermentation process or viral or cellular propagation,	iii.2.1 ( ) Yes ( ) No
	fractionation or extraction:	iii.2.2 ( ) Yes ( ) No
	iii.4.1 Critical change (change with high potential impact on the quality of the active substance or finished product, e.g. incorporation of disposable bioreactor technology)?	iii.3 ( ) Yes ( ) No
	iii.4.2 Change with moderate potential to impact the quality of the active substance or finished product (e.g. extension of in vitro cell age beyond validated parameters)?	iii.4.1 ( ) Yes ( ) No
	iii.5 Changing the purification process :	
	iii.5.1 Critical change (change with high potential impact on the quality of the active substance and the finished product, e.g. a change that may potentially impact the viral removal/inactivation capacity or impurity profile of the active substance)?	iii.4.2 ( ) Yes ( ) No
	iii.5.2 Change with moderate potential to impact the quality of the active substance and the finished product (e.g. change in the chemical separation method, such as replacement of ion-exchange HPLC with reversed-phase HPLC)?	iii.5.1 ( ) Yes ( ) No
	iii.6 Change in the scale of the manufacturing process:	
	iii.6.1 In the fermentation or viral or cellular propagation stage ?	iii.5.2 ( ) Yes ( ) No
	iii.6.2 In the purification stage?	
	iv . Change, inclusion or exclusion of API/active substance production equipment with a different design and operating principle?	

	v. Changes in the physicochemical properties of the API/Active substance with an influence on the quality of the investigational medicinal product (e.g. particle size distribution, polymorphism, etc.)?	iii.6.1 ( ) Yes ( ) No iii.6.2 ( ) Yes ( ) No
	vi. Changes related to quality control, such as expanding specification limits, deleting tests and changing the non -compendial analytical method for critical quality parameters such as content and impurity quantification, provided that the method is not equivalent or superior to the original method?	iv . ( ) Yes ( ) No v. ( ) Yes ( ) No
	b) Modifications related to the Experimental Drug? i. Replacement/Inclusion of new manufacturing site or manufacturing steps, except for immediate/conventional release synthetic and semi-synthetic drugs? ii . Modifications with an impact on the release of the API or active substance of the investigational medicinal product or critical quality parameters, including stability and impurities, and: ii.1 Qualitative changes in composition? ii.2 Change in the manufacturing process and inclusion or exclusion of equipment with a different design and operating principle? ii.3 Increase in lot size above 10 (ten) times the initially approved lot size? ii.4 Change of primary packaging? iii . Changes related to quality control such as expanding specification limits, deleting tests and changing the non- compendial analytical method for critical quality parameters, provided that the method is not equivalent or superior to the original method? iv . Extension of the validity period and/or change in conservation care, provided that there has been a change in the previously established stability assessment criteria, that the values are not within the permitted ranges or that the validity period is defined based on reduced stability study plan models (grouping and matrixing)? v. Inclusion of a new presentation that will require new stability studies? vi. Inclusion of new concentration? vii . Inclusion of new pharmaceutical form? viii . Inclusion of a new route of administration with a change in the pharmaceutical form?	vi. ( ) Yes ( ) No **b) ( ) Yes ( ) No** i. ( ) Yes ( ) No ii.1 ( ) Yes ( ) No ii.2. ( ) Yes ( ) No ii.3. ( ) Yes ( ) No ii42. ( ) Yes ( ) No iii . ( ) Yes ( ) No iv . ( ) Yes ( ) No
	c) Modifications related to Placebo or Modified Active Comparator? i. Inclusion of placebo and/or modified active comparator not previously provided for in the DDCM?	

		v. ( ) Yes ( ) No vi. ( ) Yes ( ) No vii . ( ) Yes ( ) No viii . ( ) Yes ( ) No **c) ( ) Yes ( ) No** i. ( ) Yes ( ) No
	d) Others, at the sponsor's discretion (including justifications)	**d) ( ) Yes ( ) No**

ANNEX

TEMPLATE FOR SUBMITTING UPDATED STABILITY INFORMATION

LONG TERM STABILITY STUDY (30°C ± 2°C / 75 RH ± 5% RH)

Product:
Active ingredient:
Name and Address of IFA Manufacturer:
Name and Address of Finished Product Manufacturer:
Primary packaging:
Pharmaceutical form:
Date of Manufacture:
Number of samples analyzed per period:

Study Start Date:
Study End Date:
Batch:
IFA Batch:
Batch sizes (IFA and Finished Product):
Dosage:
Lot destination:
Packaging Position:

Test	Specification	Method	Initial (t0)	3 months	6 months	9 months	12 months	18 months	24 months	36 months
		*	**	**	**	**	**	**	**	

* Also inform whether it is pharmacopoeial or not

** Justifications must be provided for any methods that will not be or were not performed at all analysis times.