Annex III

Conditions for lifting the suspension of the marketing authorisation(s)

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For the suspension of ranitidine containing medicinal products to be lifted, the competent authorities shall ensure that the below conditions have been completed by the marketing authorisation holder(s).

Conditions to lift the suspension of the marketing authorisation for parenteral ranitidine preparations **for single use only** are as follows:

	Condition for lifting suspension
1.	In order to support a positive benefit-risk balance of these products the MAH should discuss the relevance of endogenous NDMA formation based on e.g. data on endogenous formation of NDMA in humans from ranitidine, additional experimental data (in vitro/in vivo) or literature information.
2.	A limit for NDMA should be set in the release specification of the medicinal product. This limit should take into account any increase in NDMA levels observed during stability studies. The limit at the end of shelf life should be based on the maximum daily dose of Ranitidine free base taking into account the route of administration in accordance with ICH M7(R1), with a maximum daily intake of NDMA of 96 ng/day.
3.	Compliance with the limit for NDMA up to the end of shelf-life of the medicinal product should be demonstrated through appropriate data from batches of the medicinal product.
4.	The MAH should implement a control strategy regarding N-nitrosamines for ranitidine containing medicinal products.

For all other ranitidine containing products for the suspension to be lifted, the Marketing Authorisation Holder(s) shall provide the following:

	Condition for lifting suspension
1.	The MAH should submit quantitative data on the endogenous formation of NDMA in humans from ranitidine and demonstrate whether the results support a positive benefit-risk balance of the product.
2.	A limit for NDMA should be set in the release specification of the medicinal product. This limit should take into account any increase in NDMA levels observed during stability studies. The limit at the end of shelf life should be based on the maximum daily dose of Ranitidine free base taking into account the route of administration in accordance with ICH M7(R1), with a maximum daily intake of NDMA of 96 ng/day.
3.	Compliance with the limit for NDMA up to the end of shelf-life of the medicinal product should be demonstrated through appropriate data from batches of the medicinal product.
4.	The MAH should implement a control strategy regarding N-nitrosamines for ranitidine containing medicinal products.