Comments on the Drafts of Japanese Pharmacopoeia

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf	22-26	Uniformity of delivered dose of nasal preparations	Introduction
Corresponding part and/or Amendment	An example of a combined intra- and inter-container sampling scheme is to take 10 containers and collect the first dose from 3 containers, the middle does from 4 containers and the last dose from 3 containers and then determine the delivered dose.		
Reason and/or Comment	The example described doesn't provide entire contents intra-container sampling.		
Attachment (Yes ・ No)			

2

File name	Line number	Monograph/Test name	Section
001-2403eng.pdf	37-43	Uniformity of delivered dose of nasal preparations	1.Intra-container testing. 1.1 Metered-dose nasal sprays. 1.1.1 Apparatus
Corresponding part and/or Amendment	Description of test apparatus		
Reason and/or Comment	Description of apparatus is vague potentially resulting in significant variation in test results between different labs. Furthermore, given the variability associated with nasal sprays, this represents a good opportunity to encourage mechanical or automated actuation.		
Attachment (Yes ・ No)			

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf	38-43	Uniformity of delivered dose of nasal preparations	1.Intra-container testing. 1.1 Metered-dose nasal sprays. 1.1.1 Apparatus
Corresponding part and/or Amendment	"*At the very minimum, the following aspects should be taken into consideration when selecting an apparatus: actuation direction (vertical or tilted), connection between container and apparatus, sampling efficacy, need for an airflow system, venting of collection apparatus and mode of actuation.*"		
Reason and/or Comment	Please define what the authors mean by "mode of actuation".		
Attachment (Yes ・ Non)			

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf	45-48 92-95	Uniformity of delivered dose of nasal preparations	1.1.2. Procedure 1.2.2. Procedure
Corresponding part and/or Amendment	"*Unless otherwise prescribed or justified and authorized, perform 10 determinations of the delivered dose by collecting the first 3 doses, the middle 4 doses and the last 3 doses from a single container using the procedure described below*"		
Reason and/or Comment	This sentence has been repeated on lines 45-48 for the metered dose liquid nasal sprays and lines 92-95 for the metered dose nasal powders. Yet, it was also introduced as a general example in lines 22-26. We suggest removing 'an example' in line 22 and introducing this as a standard procedure unless otherwise prescribed. This way, the authors can refer to the standard procedure unless prescribed otherwise without repeating the exact same sentence three times on a single page.		
Attachment (Yes ・ Non)			

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf	49-50	Uniformity of delivered dose of nasal preparations	1.Intra-container testing 1.1 Metered-dose nasal sprays 1.1.2. Procedure
Corresponding part and/or Amendment	"*Unless otherwise prescribed in the instructions to the patient discharge the first delivery to waste.*"		
Reason and/or Comment	Add a comma between 'patient' and 'discharge'		
Attachment (Yes ・ Non)			

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf	56-57	Uniformity of delivered dose of nasal preparations	1.Intra-container testing 1.1 Metered-dose nasal sprays 1.1.2. Procedure
Corresponding part and/or Amendment	"*Repeat the procedure for an additional 2 doses using the same container.*"		
Reason and/or Comment	Does this mean sample collection in triplicates? If so, move the sentence to the rest of the above paragraph without starting a new paragraph, as it's continuous with the previous sentence.		
Attachment (Yes ・ Non)			

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf	77-81	Uniformity of delivered dose of nasal preparations	1.Intra-container testing 1.1 Metered-dose nasal sprays 1.1.2. Evaluation
Corresponding part and/or Amendment	"*Since tolerance of the uniformity of delivered dose required for a nasal preparation is different depending on the kind of active ingredients, its content, delivered dose and dosage form, the appropriate tolerance range should be set for each product.*"		
Reason and/or Comment	1. Does "nasal preparation" mean "nasal device preparation"? Please revise or clarify. 2. What's the difference between "the kind of active ingredients" and "its content"? The authors perhaps mean the active and other components of the formulation. Please revise for better clarity. 3. "Dosage form" in this paragraph is too broad since we are in the metered dose nasal sprays section. The reviewer suggests revising to "liquid dosage form, solution, and 'suspension."		
Attachment (Yes ・ Non)			

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf	84-90	Uniformity of delivered dose of nasal preparations	1.Intra-container testing 1.2 Metered-dose nasal powders 1.2.1 Apparatus
Corresponding part and/or Amendment	Description of test apparatus		
Reason and/or Comment	Description of apparatus is vague potentially resulting in significant variation in test results between different labs. Furthermore, given the variability associated with nasal sprays, this represents a good opportunity to encourage mechanical or automated actuation.		
Attachment (Yes ・ No)			

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf	85-90	Uniformity of delivered dose of nasal preparations	1.Intra-container testing 1.2 Metered-dose nasal powders 1.2.1 Apparatus
Corresponding part and/or Amendment	"*At the very minimum, the following aspects should be taken into consideration when selecting an apparatus: actuation direction (vertical or tilted), connection between container and apparatus, sampling efficacy, need for an airflow system, venting of collection apparatus and mode of actuation.*"		
Reason and/or Comment	Please define what the authors mean by "mode of actuation".		
Attachment (Yes ・ Non)			

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf	120-130	Uniformity of delivered dose of nasal preparations	2.Inter-cointainer testing
Corresponding part and/or Amendment	Inter-container testing		
Reason and/or Comment	The example given assumes that a batch of containers behave the same through life. More comprehensive testing of the 10 containers should be recommended.		
Attachment (Yes ・ No)			

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf		Uniformity of delivered dose of nasal preparations	
Corresponding part and/or Amendment	Consider adding a suggestion that testing be done using automation.		
Reason and/or Comment	These products are notoriously variable if actuated manually. Automation would improve reproducibility.		
Attachment (Yes ・ Non)			

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File name	Line number	Monograph/Test name	Section
001-2403eng.pdf		Uniformity of delivered dose of nasal preparations	
Corresponding part and/or Amendment	Consider recommending a final 'filter' / stage to capture all the finer particles, i.e. <10µm		
Reason and/or Comment	To limit unintended delivery to the lung.		
Attachment (Yes ・ Non)			