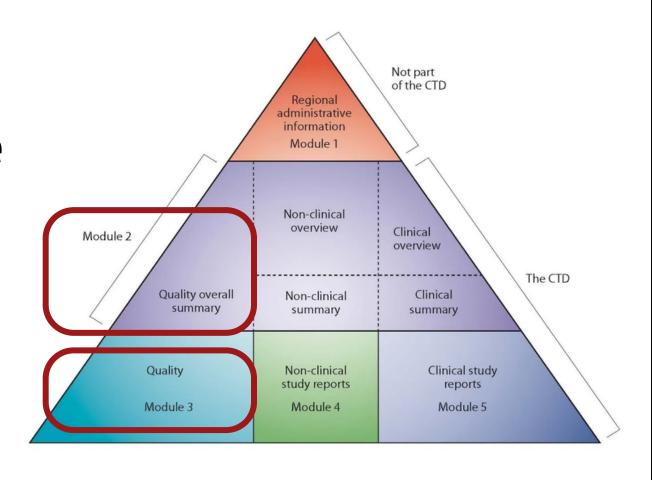
CONSISTENCY

Information presented in QOS (Module 2) and Module 3 should be consistent and in a concise PDF document (not scanned)



EXPECTATIONS



(a) Process outline:

Give a brief narrative step-by-step description of the manufacturing process from the starting materials to the final substance.

The chemical reactions and at least critical purifications procedures should be mentioned, the inprocess controls as well as identification of steps, intermediates, reagents and solvents used should be indicated. Do not include the detailed description from dossier in Module 3, hence amounts of materials or details of process operative parameters do not need to be reported here. Indicate the maximum batch size (or range) for the final substance.

(b) Synthesis scheme / or diagram for non-synthetic process

Provide the synthetic process scheme, from the starting materials to the final substance including the structural formula for the starting materials and all intermediates (indicate when intermediates are not isolated). Mention all solvents, reagents, catalysts and process-aids used in the process. Include names or numbering of all steps. In case a convergent synthesis is followed the scheme should reflect all the synthetic branches. For starting materials and intermediates include chemical name and in-house code names if any (in particular in case different code names linked to different manufacturers or sites are used in the dossier, Module 3). Mass / MW values do not have to be reported here.

Quick understanding of the process applied e.g. synthetic route, materials used, purification strategies and controls... understanding of potential & existing impurities

PRESENTATION OF DATA

Tabulated format is helping assessors during review



2.3.S.2.4 Controls of Critical Steps and Intermediates

(a) Indicate critical steps if any, and in-process controls which are performed

Step:		
Test	Acceptance criteria	Analytical method

(b) Control of intermediates:

List the controls performed

Name of the intermediate (step x):				
Test Acceptance criteria Analytical method *				

^{*} indicate when the method used for related substances is same as in the final substance.

CONTROL STRATEGY

2.3.S.3.2 Impurities

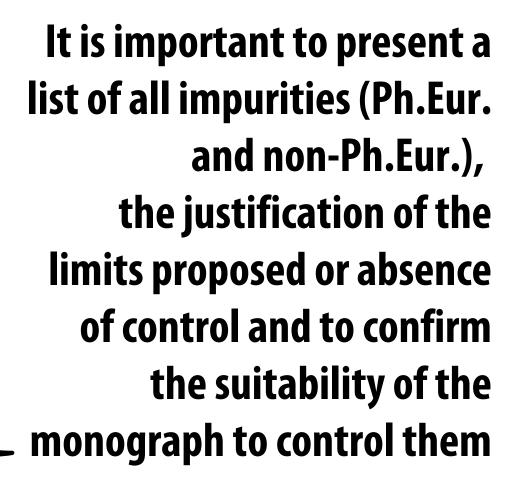
This section should make clear which control strategy is applied.

(I) Related substances

Identify all the potential and actual impurities, their origin and fate in the process, and briefly justify the specification applied or the absence of control.

Impurity*	Origin	Company	Ph. Eur.	Test re	sults **	Analytical
		acceptance criteria	acceptance criteria	at release	in stability studies, as available***	method****
Impurity X						
Unspecified impurities						
Total	-					

^{*} Refer to the Ph. Eur. name when one exists, otherwise chemical /in-house name



^{**} typical levels in the final substance or any other appropriate intermediate stage

^{***} in case a re-test period is requested

^{****} indicate whether the Ph. Eur. method is used or an in-house method

CONTROL STRATEGY

Specifically discuss mutagenic impurities, using ICH M7 as reference (!) Risk for N-nitrosamine impurities should also be addressed

Mutagenic impurities:

(a) Summarise the specific discussion on potential mutagenic impurities arising from the synthesis of the final substance, its starting materials and degradation products, with reference to ICH M7 guideline or the applicable guideline in veterinary products. Briefly justify each impurity classification as per ICH M7 guideline section 6 i.e. class 1 to 5 and, as applicable, the applied control strategy i.e. identify and justify the control approach option according to ICH M7 section 8.1. Justification should be supported by carryover data as needed.

Impurity *	Origin	Class	Control option justification, acceptance criteria

^{*} presenting relevant structural alert or known mutagen

RE-TEST PERIOD

2.3.S.7.1 Stability Summary and Conclusions

Indicate the stability testing studies performed:

naidate the stability	testing studies periorified.		
Study conditions	Accelerated conditions	Long-term conditions	Intermediate conditions
			(if any)
	e.g. 40°C±2°C / 75%±	e.g. 25°C± 2°C/60%±	
	5% RH	5% RH	
Data available	x months, number of	x months, number of	x months, number of
	batches	batches	batches
Batch size			
Manufacturing			
date			
Packaging	Indicate if it is the same		
	as for commercial		
	purpose		

Additional summary tables may be needed to cover different container closure systems or climatic zones.

- Briefly report on control parameters excluded from stability studies compared to those at release.
- Any significant change has been observed in the parameters tested (Yes/ No), briefly comment on the available study results in support of the requested re-test period.

Express clearly the length of the proposed period and storage conditions applied

