N° d'enregistrement :
Ares(2013)3356441

To whom it may concern,

please find below my proposals with explanation and my comments on Annex 16.

Proposals:

2. General principles

2.2. However, the responsibility ... lies with the QP **(with the support of the top management)** certifying that batch as being suitable for release.

Explanation: without the support and responsibility of the top management the continuous compliance with the MA is not sufficient assured.

5. Handling of unplanned deviations

5.2. Where a deviation has occured **before or** during manufacture or testing of a batch ....

5.2.1. The deviation is unexpected, unplanned **or if any unexpected fact is revealed/explored before manufacturing or testin**g and relates to the manufacturing process and/or the analytical control methods as described in the MA.

Explanation: the cause of some deviation is known before manufacturing and testing, but can not be avoided. The deviation will not e.g. endanger the MA, only the routine processes or SOP. Or the exploration of cause is at "last minute" or at a time where it can not be managed before the activity. Or an irrelevant deviation which will not have a negative affect on the quality or the affect can be controlled is know before production/testing. Nevertheless with "planned" deviation handling the product quality, safety, efficacy, and final product compliance with MA can be assured.

6. The release of a batch

6.1. ... Until a batch is released it should remain at the site of manufacturer or be shipped under quarantine to another authorised site **or subsidiary, which is under control of the parent company.**

Explanation: Companies could have local subsidiaries at several countries under their control. To ship batches under quarantine to this subsidiaries is safe and controlled. Unreleased batches can not enter the market, but with the quarantine shipment there is considerable time to win, shortages can be avoided.

Comments on points:

2.4.3. Any local relevant legal requirements should be incorporated and taken into account during the registration process of a particular product/country. This local professional requirements should

be part of the MA and should be specified. The QP needs the support of the registration authorities. Sometimes even GMP requirements are not taken into account in registration processes. I mean especially when a local legal requirement (or GMP requirement) has an affect on a particular manufacturing or testing step, than if those are not taken into consideration during registration process and are not incorporated into the registartion file, the QP will not have sufficient support to reach compliance.

Best regards,