Analyses for GMP Products or Release Analyses:

Within a GMP inspection of “Regierungspraesidium Tuebingen” we got in 2006 a recommendation to inform our customers about analyses for a GMP product or if a method is substance specific validated. This issue was also clarified during our last FDA inspection in 2008 that were finalized successfully without an 483.

Validations:

Our methods of analyses are all generically validated and offer high reproducibility. In respect of documentation and status of instruments we perform analyses in compliance with GMP regulations „Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients“. Additional requirements on standard injections and change control could be necessary for final drug substances and drug products in particular for data relevant for submission to authorities. It is to prove if substance specific validation is required that can be offered.

Analyses in duplicate

For GMP-products the analyses are run in duplicate. Homogeneity of the sample is examined, weighing errors and problems during sample preparation or chromatography will be indicated. OOS can be defined by a unusual standard deviation of the results of both analyses. If the customer would like to run a single analysis only it should be noted on the order.
Due to the analyses in duplicate a mean value of results can be calculated. We give a 10% discount on both analyses.
Analyses in duplicate may be advisable also for non GMP products for quantitation

- of the main product (eg AAA if peptide content is required) to calculate the mean value of the results and to be able to exclude a weighing error. The result could be also verified by eg. mass balance (eg. content of peptide + water + counter ion + residues of solvents ≈ 100%).
- water and acetate/TFA and other counter ions to exclude weighing error and inhomogeneity (standard procedure in CAT)
- residues of solvents to prove the homogeneity of the sample
- determination of enantiomeric purity via GC-FID to prove that the amino acid racemize during sample preparation in the range of the standard deviation of the method. Unexpected racemization will usually be indicated by higher standard deviation. In addition the homogeneity of the sample is proved. (standard procedure in CAT)

Minimum weight:

For determination of the content the minimum weight for the balances in accordance to USP are to observe. This means that we need 1-3mg for each analysis. Additional amount needed for sample handling depends on the physical properties. For freeze dried product additional amount is not necessary whereas an oily or an electrostatic loaded product needs some 10mg's. If this amount is not available the error of sample weight is higher and in consequence the error of the content. The error of the weighing above minimum weigh is <0.1%.

OOS:

For GMP analyses the customer will be informed about necessary investigations in an early stage if the results are out of specification. The in house documentation is more extensive.

Change Control:

If parameters of the methods need to be changed in a way that is not covered by the SOP's the customer will be involved in the decision. Substance specific validated methods leave very limited flexibility only.

Expanded Reports:

Expanded reports can be offered if additional information is needed which are not provided with the standard report. The following items will be provided with this report:

- ✓ more specific method description
- ✓ the chromatograms of the blind values
- ✓ the chromatograms of the standards
- ✓ standard concentrations and samples weights
- ✓ used equations for the calculations.

In consequence this report also shows the SST which is for most GC-analyses the standard chromatogram.
For some analyses regular performance qualifications (PQ) are run beside SST (e.g. for GC-MS). In this case the results of the PQ can be listed in the expanded report too.

Tübingen August 11, 2014