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Late, but not too late? How to best define the final time point of a stability study?

Ask our Experts

"What is the best procedure for selecting samples from a stability chamber in the final test interval of ongoing stability tests? Could you please give me more detailed information on this? I know that it is the responsibility of companies to define a tolerance for taking samples from storage and that +/- 1 month in an interval of at least one year is acceptable. Is it advisable to make an exception to a +/- 1 month rule for the selection of samples from the stability chamber in the final test interval after (and strictly defined as) + 1 month (stability start + x months + 1 month)? Is it good practice to assume, as a general rule, that the test will not start at the last point before the expiry date?"

This question and further inquiries were answered by the **authors of the** GMP Compliance Adviser Chapter 14.E "Stability testing". Both are **pharmacists** and answered as follows:

"As a test point, you should stay at +/- 1 month to ensure that your data are representative for the times defined in the stability protocol. At the end of stability, the decision depends on the objective of the study. If the intention is to show that the data are within specification at the end of the shelf life, the study can be completed at the expiry date. If you want to use the results to demonstrate usability beyond, e.g. 36 or 48 months, you also need this test point. This can be important if the study is to be used for the submission of marketing authorization applications/stability commitments. The authorities then usually expect data for the entire storage period. The decision to test only at the end of the study and not additionally beyond the expiry date should be made on a product-based basis. If there is a risk that the expiry date will be met, but there is a probability of OOS results at 36 months, for example, you should use an additional test point to prove that the expiration was at least still within the specification and that you have no problems with the product on the market. This is important for the annual stability check during which batches are normally on the market. If no risk is expected, the test point after the expiry date can be omitted."

After this answer, the customer explains the situation in more detail and introduces further questions: **"All series included in the stability programme should also deliver results at the end of the shelf life that are well within the specification. We have the special rule not to test the sample at the last point in time in the period one month before the expiry date, because we want to cover the full shelf life of the stability sample and test it at the latest one month after the expiry date (for all types of samples)."**

The expert confirms that this is acceptable.

"If there is an OOS result at the expiry date (continuous stability, annual batch) obtained at the expiry date + 1 month - is it usual to present it as appropriate because it was obtained in the period immediately after the expiry date (at the latest one month after the expiry date)? Not in my opinion. "

The expert agrees: "You are right, this is difficult and can raise questions in discussions with authorities. In principle, it is acceptable to say that "not passed" does not apply because it goes beyond the expiry date. But you need reliable data from other studies that show that the product is usually within specification at the expiry date. If it is an annual stability study, it is representative for the whole year, so there must be a good justification why no action is needed and the quality is still achieved at the expiry date."

The customer's final question was: **"If there is a correspondence between the expiry date and the final test point of the stability interval - should it be avoided to test the sample in the period of the last date + 1 month? Is it acceptable to test the sample at the last point in time (i.e. coinciding with the expiry date) in the period one month before the expiry date, although these results would cover one month less than the full shelf life?"**

The expert explains: "This depends a little on how this +/- 1 month is justified in the procedure. There should be good reasons (and product knowledge) to argue on the one hand that +/- 1 month is representative of the test point and/or the expiry date, on the other hand an OOS after + 1 month is not a problem because it goes beyond the expiry date. Therefore this decision has to be well documented for each individual case."

Read more on stability testing, its requirements, storage conditions and stability studies in the GMP Compliance Adviser Chapter 14.E Stability tests.