Practical Applications

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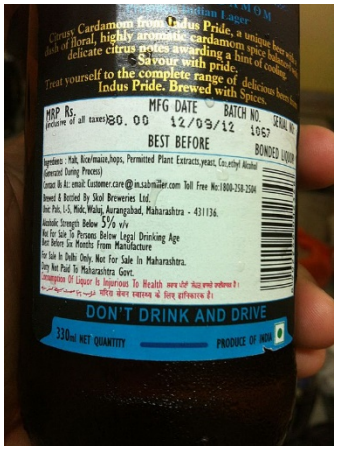
Question 1

Lab analyst noted that there is no indication that the reference standard was characterized under GLP.



Question 1 – What to Do?

- Yahoo! I noticed.
- Ignore it. I need to get these samples done.
- I'll let the SD know when I have a chance. The SD will approve its use.
- Other options?

Answer

- HQ SOPs indicate that Testing Facility Management (TFM) will determine whether adequate data exists to move forward.
- Operational handbook is being updated.

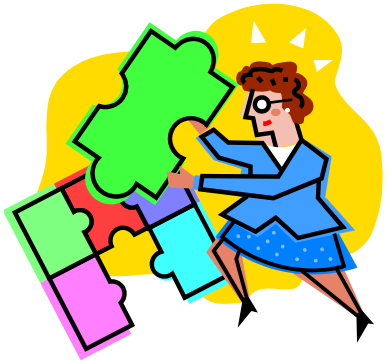
(So what does this mean?)

Background

- Any available characterization data will be requested, and provided to management.
- TFM will make the final decision on whether the data is sufficient to establish identity and purity.
- Protocol deviation and GLP compliance statement are still needed if the reference substance is used prior to confirmation of the GLP status.

Why is it important?

- The residue results depend on the reference substance. If the identity and purity cannot be supported, the results cannot be defended. The study may not be acceptable.



Question 2

The study is completed, and during ASR prep, it was noted that for one run, the residue results are not on the standard curve, but are above by 5%. Is this a concern?

- It is only 5%. Don’t worry about it.
- Hope QA doesn’t notice
- Write a deviation and move on.
- Other thoughts?
- Table groups to discuss.

More Questions

- What is the procedure for the analyst to approve the run?
  - What results are checked as data is being generated?
    - (peak area on the curve, concurrent fortifications acceptable, r-squared value, data initialed and dated immediately after data generation?).
  - What is an acceptable r-squared value, and why is it in your SOPs?
    - Is one standard “driving” the r-squared value?

Answer

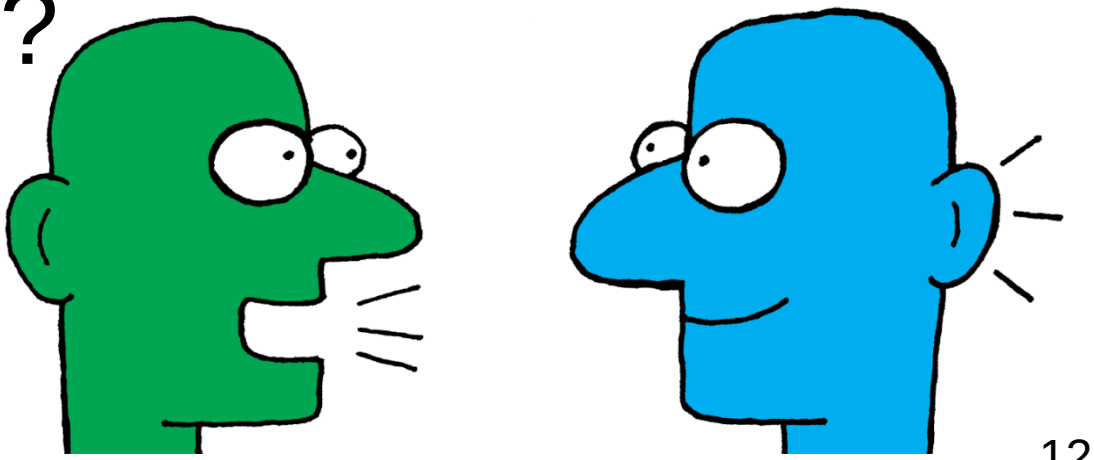
- Dilution of samples and re-injection is simple, when addressed immediately.
- Takes much more time to re-extract the sample at the end of the study.
- Preference is that a process is in place so it doesn't come up. However, if it does…. is it important?

Why is it important?

- We must be able to defend our data. Look at all the residue values, is this the highest value, what are the r-squared values in this run and other runs.
- Even if SD accepts, keep in mind that registrants and regulatory agencies review our data. It appears sloppy and can lead to questions about whether there are appropriate controls in study.

Question 3

Lab sends request for approval for a change in the method. How much information needs to be included in the request?



Answer

- The study director will need enough information to assess the impact on the study.
- The analyst will have the technical expertise to assess, but the information needs to be transferred.
  - We added a clean-up step for dried matrix to help achieve the recoveries, and will demonstrate suitability during method validation (or by adding concurrent recoveries.)

Why is it important?

- The technical information must be transferred for the SD to make an informed decision. Lab personnel and study directors may have different technical backgrounds. Effective communication is needed for the process to run smoothly.
- Ask questions.

Question 4

Concurrent recoveries at 0.01 ppm are 65% and 69%. The lab asks the SD to approve the results. What should the SD do?

More Questions

- What were the results in the validation run?
- Additional info
  - Validation completed at 0.01 ppm with a range of 68-75% (6 samples at LLMV) and that is after much effort to get to that level. SD accepted the validation results
    - LLMV by definition is lower limit.
    - Low results are acceptable to EPA if they are tightly clustered.

Answer

- SD accepts the results
  - The method is difficult
  - The results mirror the validation results

More Questions

- Additional info
  - Validation completed at 0.01 ppm with a range of 85-97% on the same or a similar matrix.

Answer

- If it is the same matrix, rerun the samples – something has happened.
- If validation was on a “similar” matrix, run additional concurrent recoveries at the LLMV, to show that perhaps the “similar” matrix isn’t similar.

Why is it important?

- IR-4 must be able to defend the analytical results to the registrant and the regulatory agencies.
  - It is difficult to confirm that the analytical results are valid if the concurrent fortifications are below the protocol specifications (which are based on EPA guidance) and well below the validation results.

Question 5

The lab has tried and tried to get to the LLMV of 0.01 ppm for a commodity but nothing seems to work. Should the LLMV be raised?

More Questions?

- Reference method has demonstrated a 0.01 ppm level in other crops. What is the matrix?
  - Some matrices are more difficult than others.
  - Difficult matrices include: Asparagus, hops, sugar beets, oily crops – avocado, sunflower seed, dried crops, others?

Answer

- When can the LLMV be raised?
  - If the residue is expected to be 10x or more than the LLMV, the SD can approve raising the LLMV. A screening run may be needed to determine the approximate residue values.
  - If the risk cup is getting full, and no residues or low residues are expected, must discuss with the registrant. For some chemistries, registrant will not submit if there are residues above the LLMV or above existing tolerance.

Why is it important?

- Try to meet the reference method LLMV. However, don't waste months to attain a 0.01 ppm LLMV, if the residues are 10x higher than that.
- If low residues are expected, don't jeopardize potential submission of a study. SD to check with the registrant before raising the LLMV.

Question 6

Who documents a change to the protocol? Same person for amendments and deviations?

Answer

- As a general rule:
- For an amendment, such as raising the LLMV, the study director will initiate.
- For a deviation, where the lab knows best what occurred, the lab director will initiate.
- Discussion between lab director and study director will occur in both cases, and will be documented by both.

Why is it important?

- Documentation of study changes must occur in a timely manner.
- Everyone is busy and being as efficient as possible. We are a team and we help each other to successfully move a study forward to completion.


Buckeyes
Buurma
FARMS
GREENS
RADISHES
Buurma
FARMS
GREEN ONIONS

Questions?

THANKS FOR ALL YOUR EFFORTS!!

Thank You!