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Handling Sampling Recovery Results

This "Cleaning Memo" addresses how to handle sampling recovery data in a cleaning validation protocol. This includes both swab sampling recovery percentages and rinse sampling recovery percentages. Sampling recovery is a quantitative measure (usually expressed as a percentage) of the portion of target residue on a surface that can be removed by the sampling procedure and analyzed by the analytical technique. Most sampling procedures should be expected to give results in the range of 50-100% recovery, with higher recoveries being preferred.

There are two options for how this recovery percentage is handled. One is to include it in the residue limit calculation to transform the residue acceptance limit. For example, if the acceptance limit of an active (based on data such as lowest dose of the active, the maximum dose of the subsequent product, the minimum batch size, and the equipment surface area) is calculated to be 1.45 $\mu g/cm^2$, and the sampling recovery is determined to be 78%, then the recovery number is used to transform the acceptance limit. In this example, the acceptance limit would be determined by multiplying the calculated acceptance limit by the recovery value (expressed as a decimal) to give a transformed acceptance limit of 1.13 $\mu g/cm^2$. When analytical data on the samples is generated, the values as determined by the method are reported out, and compared to the transformed acceptance limit. The same principle is used if the acceptance limit is expressed as the limit in the actual analytical sample (although in that case, one would also need the area sampled and the sampling solution volume to calculate the acceptance limit). This is the method given in many early papers and presentations for cleaning validation.

A second method is to use the recovery percentage to transform not the acceptance limit, but rather the analytical result. Using the same information above, the acceptance limit would be established as 1.45 $\mu g/cm^2$. However, if analytical data showed a level of 0.43 $\mu g/cm^2$ present on the surface, this number would be transformed by dividing it by the recovery percentage (again expressed as a decimal). In this example, 0.43 $\mu g/cm^2$ measured actually represents 0.55 $\mu g/cm^2$ (0.43 divided by 0.78) being present.

Both approaches as to how the recovery factor is used will give the same result in terms of whether or not the analytical result was at or below the acceptance criterion. Therefore, for validation purposes either method can be used. However, the second method is preferred. Why? One reason is that it may simplify documentation. If one changes one's sampling method resulting in a different recovery percentage, it is not necessary to change the documentation on the established acceptance criteria. A second reason is that the first method creates the wrong impression of what might actually be present on surfaces. If for purposes other than comparison to the analytical number one were to use the 1.3 $\mu g/cm^2$ criteria, then that number would inaccurately represent the "quality" of the surface.

It should be emphasized again that either is acceptable. However, one should avoid the situation where the recovery percentage is used to transform both the acceptance limit and the analytical result. Such a use will make it much more difficult to meet one's acceptance criterion (it will result in numerous false failures). Therefore, one or the other use should be adopted uniformly throughout one facility or throughout one company.