

Risk Assessment and Prioritization

To ascertain which raw material, in-process control (IPC) and intermediate test methods require validation, it is suggested that a documented Risk Assessment be carried out on test methods currently utilized at an API site. This risk assessment approach can be used to evaluate legacy or new test methods.

This risk assessment evaluation may be based upon the following suggested principles:

Regulatory expectations at the time of product filing or re-registration
Methods may generally be grouped from low risk to high risk. This risk grouping helps to prioritize those areas that need validation based on a science based evaluation of impact to final API product quality. The following table (Table 1) gives an example grouping strategy for the analytical methods within the scope of this procedure:

Table 1: Methods, types and their recommended risk levels

Evaluation Process:

Conduct a cross functional and documented analytical test method evaluation based upon an understanding of the test data utilization by the Site Quality Authority and other site functions.

This cross functional review might be conducted by colleagues drawn from the Site Quality Authority, Site Production Operations, development support and other site based or center technical functions as necessary.

Methods may be grouped for this evaluation, such as in the above table to set prioritization for the team.

During this evaluation phase, a number of contributing factors tend to determine impact to quality. Downstream effects may also need to be considered. For example, once the material is isolated, tested, and discharged from the equipment, one may have to reprocess/ rework material because of potentially inaccurate data from the earlier IPC test method.

The use of what-if scenarios can assist in the risk analysis. For example, consider the following:

- *Stage in the API Process: Where does this test method's result lie within the overall quality 'control' or 'assurance' strategy in producing a quality API?*
- *Critical Quality Attribute: Can analytical data gleaned from this early stage of the step highlight where an impurity or its precursor is forming?*
- *Critical Quality Parameter: Could the process step be adjusted within allowable parameters to marginalize or purge unwanted impurities before isolation?*