It is not mandatory to examine the microbial quality of drug product raw materials, non-sterile excipients, APIs, and finished solid oral drug products unless required by the compendia or a regulatory filing. However, a microbial assessment should be performed on all raw materials, non-sterile excipients, APIs, and finished drug products that are *not* required to be tested by compendia or regulatory filing.[1] This assessment will determine if microbial attributes testing is warranted.

Microbial attribute testing estimates the number of and/or types of microorganisms present in a sample of material or product by utilizing the total aerobic bacterial count test, the total yeast and mold count test, or the presence of specified microorganisms test. Because of the wide diversity of materials and finished solid oral drug products, not all products are equally susceptible to microbial contamination, and therefore, microbial attributes testing may not be the same for all products. This guidance has been developed to help determine the need for microbiological testing.

***Materials**:*
The raw materials, non-sterile excipients, and APIs of a solid oral dosage form are considered a potential major source of microbiological contamination in pharmaceutical products. Consequently, a risk assessment of each material is recommended to determine if microbial testing is appropriate. In order to assess each material used in the manufacture of non-sterile solid oral dosage forms, a decision tree has been appended to this guidance (see figure 1).

This decision tree is based upon such factors as regulatory requirements, material source, water activity[5], inherent inhibitory or antimicrobial properties, nutrients available for growth, historical bioburden data, and the manufacturing process of the material. A rationale for the decision to test or not to test can be generated based upon this decision tree. If it has been determined that testing of a raw material is needed, microbial attributes testing performed by the supplier can be accepted in lieu of on-site testing, provided that shipping and storage conditions are properly controlled and that the supplier has been audited and approved by a qualified site audit.

Finished Products:
Finished product testing of non-compendial solid oral dosage forms provides limited value for assessing the microbial quality of the product. This is because the lack of available water within solid dry products precludes microbial growth. In order to determine if microbial testing is needed for a solid oral dosage final product, a second decision tree has been appended to this guidance (see figure 2).

Microbial Limits Acceptance Criteria:
If the need for testing has been determined, the USP/EP recommends limits for solid oral dosage forms to be applied as follows: NMT10 Bacteria (CFU/g or ml), NMT 10 Fungi (CFU/g or ml), and the Absence of *E. coli* (in 1 g or ml). The USP/EP recommends limits for substances for Pharmaceutical use (APIs, excipients, raw materials) to be NMT10 Bacteria (CFU/g or ml) and NMT 10 Fungi (CFU/g or ml). Mandatory limits provided by individual monographs or other local regulatory agencies will supersede these recommended compendial limits.

