

## Water Activity Leves Required to Support Microbial Growth

| Microorganism                                      | Type   | Water Activity (aw) (Typical Values) |
|--|--|--------------------------------------|
| <i>Pseudomonas aeruginosa</i>                      | Bacteria (Gram-negative rod)                     | 0.97                                 |
| <i>Bacillus cereus</i>                             | Bacteria (Gram-positive, spore forming)          | 0.95                                 |
| <i>Clostridium botulinum</i>                       | Bacteria (Gram-positive, spore forming anaerobe) | 0.95                                 |
| <i>Escherichia coli</i>                            | Bacteria (Gram-negative rod)                     | 0.95                                 |
| <i>Salmonella spp.</i>                             | Bacteria (Gram-negative rod)                     | 0.95                                 |
| <i>Bacillus subtilis</i>                           | Bacteria (Gram-positive, spore forming)          | 0.90                                 |
| <i>Saccharomyces cerevisiae</i>                    | Yeast  | 0.90                                 |
| <i>Staphylococcus aerus</i>                        | Bacteria (Gram-positive coccus)                  | 0.86                                 |
| <i>Aspergillus niger</i>                           | Filamentous fungus                               | 0.77                                 |
| <i>Zygosaccharomyces rouxii</i>                    | Osmophilic yeast                                 | 0.62                                 |
| <i>Xeromyces bisporus</i>                          | Xerophilic filamentous fungus                    | 0.61                                 |
| <i>No microbial proliferation below this level</i> |  | 0.50                                 |

## USP-Proposed Microbial Limit Testing Strategies

| Product Type                | Typical $a_w$ | Potential Contaminants           | Testing Recommended in USP <1111>  | Testing Recommended in USP <1112> Based on a                     |
|-----------------------------|---------------|----------------------------------|--|--|
| Nasal liquid inhalant       | 0.99          | Gram-negative rods               | TAM and TYMC; absence of <i>S.aureus</i> and <i>P.aeruginosa</i>                     | TAM and TYMC; absence of <i>S.aureus</i> and <i>P.aeruginosa</i> |
| Topical cream               | 0.97          | Gram-positive bacteria           | TAM and TYMC; absence of <i>S.aureus</i> and <i>P.aeruginosa</i>                     | TAM and TYMC; absence of <i>S.aureus</i> and <i>P.aeruginosa</i> |
| Oral liquid                 | 0.90          | Gram-positive bacteria and fungi | TAM and TYMC; absence of <i>S.aureus</i> and <i>P.aeruginosa</i>                     | TAM and TYMC   |
| Oral suspension             | 0.87          | Fungi                            | TAM and TYMC, absence of <i>E.coli</i>   | Reduced testing  |
| Topical ointment            | 0.55          | None                             | TAM and TYMC; absence of <i>S.aureus</i> and <i>P.aeruginosa</i>                     | Reduced testing  |
| Compressed tablets          | 0.36          | None                             | TAM and TYMC, absence of <i>E.coli</i>   | Reduced testing  |
| Vaginal suppositories       | 0.30          | None                             | TAM and TYMC; absence of <i>S.aureus</i> , <i>P.aeruginosa</i> and <i>C.albicans</i> | Reduced testing  |
| Liquid-Filled oral Capsules | 0.30          | None                             | TAM and TYMC, absence of <i>E.coli</i>   | Reduced testing  |