Regulatory Basis:
FDA Quality Systems Regulations

Reference: FDA CFR - Code of Federal Regulations Title 21

General Discussion
This document discusses the basic principles of water activity and the importance it has in the manufacture of pharmaceuticals. It also provides direction on when and where testing for water activity can be most beneficial.

Water activity (a_w) is defined as the ratio of product vapour pressure to pure water vapour pressure. It is a measure of the water available for chemical or microbiological activity within a product. It is not a measure of the total water content of an item, as water can be chemically bound and not be available for use. Its values are typically expressed as a decimal value and can range from 0.0 (completely dry) up to 1.0 (pure water).

Though the principles of water activity have been used for centuries (e.g. salting, drying, mummification), its use by the FDA occurred in the 1980's when water activity testing was added to existing strategies for microbiological control in food products. Water activity is significant to the pharmaceutical industry in that it affects the quality of ingredients and finished product through their chemical stability, a reduced need for chemical preservatives, and a potential reduction in the need for microbial limits testing.

Microbial growth requires water. Water dissolves solutes within a viable cell and is required for metabolic function. When an (a_w) value is associated with a micro-organism it serves as an indication of potential metabolic activity. While organism proliferation ceases below certain water activity levels, some species have the ability to adapt slightly and continue to grow at levels below their optimum range.

Organisms grown in an environment outside of their optimal a_w range will most likely be more resistant to thermal means of destruction.

There is a comprehensive understanding of microorganisms and their associated a_w values. The optimal a_w range for microorganism growth lies between 0.995 and 0.980. Most bacteria cannot grow below levels of 0.90. Yeasts typically survive down to levels of 0.87. Molds can tolerate a_w levels down to about 0.80. Microbiological growth at any level ceases at a_w values of about 0.60. Thus, by controlling the water activity of products, the growth of microorganisms, when present, can be controlled as well.

The a_w also has an effect on the chemical processes within a product or formulation. Lowering the a_w may increase chemical stability. The activity of proteins and enzymes, which may lead to chemical changes, requires maintenance of specific a_w levels that can be controlled or minimized. Browning, or Maillard reactions, can be controlled by altering a_w as well.

In addition to the benefits of increased microbiological and chemical stability, reduced need for chemical preservatives may be another important benefit. Pressure

