March 4, 2025 **BOME Pharma LLC** tel 856.759.1299
www.BOMEpharma.com *World's first safe & effective allergy treatment for Poison Oak & Ivy*. fax 856.759.1288
C:\L1\AA\Rscho\4 tech 2302\bome\What is ADBP 2503.wpd email BOMEpharma@gmail.com
1122 N. High Street, Millville NJ 08332-2529

(updated 3/4/25) What is ADBP? (formerly VDBP)

What's in a name? : After years of inconsistent nomenclature the World Allergy Organization agreed to classify all antigenic substances administered to modify the immune response to the same antigens as "vaccines" irrespective of whether they were designed and administered to induce tolerance in allergic diseases or protective sensitization in infectious diseases and cancer. However, the term "vaccine" has now become politically divisive. To avoid alienating potential users because of negative associations with the name we will generalize our name for this process from "Vaccine Delivery by Precipitation" (VDBP) to "Antigen Delivery by Precipitation" (ADBP), antigens being a general category of which vaccines are a subset. It may also have applications to the delivery by precipitation of other therapeutic substances.

Until we discovered and patented ADBP, medications were approved for injected into solid body tissues in only two ways. Meds that are soluble in water, including most US-licensed therapeutic allergenic products, could be injected as aqueous solutions (solutions in which they are dissolved in water). Meds injected as aqueous solutions spread very quickly from the injection site as individual molecules. Or, they can be formulated as complexes that are not soluble in water. These are injected as blobs, typically under the skin, that mostly remain where they are injected. They dissolve and release their medication slowly, but also one molecule at a time. Meds that are not soluble in water can sometimes be formulated into water-soluble complexes that behave much like water-soluble drugs.

For ADBP, a therapeutic substance-of-interest must be insoluble in water but a therapeutic dose must be soluble in a medically safe small volume of a solvent that mixes freely with water. The three water-miscible solvents that are medically safe for delivery to many body tissues if given in small enough amounts are ethanol, acetonitrile and dimethylsulfoxide. To achieve ADBP the volume of solvent in which the dose is dissolved must be small enough to be rapidly diluted by the water content of the target tissue. Speed of dilution is important because as the solvent is diluted the water-insoluble substance-of-interest becomes insoluble and precipitates. The more rapid the dilution, the larger the number and smaller the size of the particles into which it precipitates. Depending on the substance, the resulting particles may be either small particles of solid or small globules of liquid. Particles in the size range from 0.5 to 5 microns in diameter happen to be bite-sized snacks for the wandering antigen-presenting cells (APCs) that perform continuous immunological surveillance of all body tissues except the eyes, spine and brain, and bring samples of what they find to the structures within lymph nodes where immune response switching takes place.

Looking at numbers, If an injection of 0.15ml of an ethanol solution containing 100 mg of urushiol per ml is diluted at a rate to deliver a median particle size in the middle of this range, 2.6 microns in diameter, it will populate the volume around the injection site with 200 million such particles. We have not yet been able to make measurements of actual particle spatial and size distribution, hoping to find a collaborator and the funding to do this study in an animal model some time in the future. On the basis of what else is known about the functioning of the immune system, we can conclude with a high degree of certainty that ADBP works by suddenly sprinkling hundreds of thousands to tens of millions of particles sized for efficient uptake by APCs into a volume of tissue around the injection site where it causes a feeding frenzy of APCs. By discovering and employing

ADBP we achieved history's first delivery of a large enough load of this antigen to the switching machinery of the immune system to flip its response from sensitization to tolerance.

When a new technology solves one problem in medicine, it's usually worth looking at for others. For ADBP the challenge for other therapeutic antigens is to prepare formulations with the solubility properties needed for ADBP without compromising the antigenicity we want feeding frenzies of APCs taking up those formulations to bring to the immune switching mechanism. Other applications for immunomodulation from sensitization to tolerance include the sensitizing allergens of foods and stinging insect venoms, other substances causing allergic contact dermatitis, latex, the metals and cements used in and with structural surgical implants, and possibly to prevent rejection in tissue and organ transplantation.

The mechanism by which the immune response switches between different forms of sensitization and tolerance is the same in both directions. With different choices of target tissue and other measures to bias the system toward one direction or the other, we believe ADBP can be used to achieve immunomodulation from tolerance to protective sensitization in cancer, and from naivete to protective sensitization in infectious diseases for which other modalities of vaccine delivery have been ineffective or suboptimal, including malaria, tuberculosis, Zika, Ebola and Sars CoV-2.