AN OVERVIEW OF GLYPHOSATE MODE OF ACTION: WHY IS IT SUCH A GREAT HERBICIDE? Dale Shaner, Plant Physiologist, USDA-ARS, Fort Collins, CO 80526.

Glyphosate dominates world herbicide usage due to its broad spectrum, ease of use and environmental attributes. The introduction of glyphosate resistant crops has increased the amount of the herbicide applied to soybeans, corn and canola over 10-fold since 1995. Why is glyphosate such a good herbicide? The three primary reasons are 1) the target site, 2) the ability of the herbicide to translocate in plants and 3) the inability of plants to rapidly detoxify the herbicide.

Glyphosate kills plants by inhibiting 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS). EPSPS is a key enzyme in the shikimate biosynthetic pathway which is necessary for the production of the aromatic amino acids, auxin, phytoalexins, folic acid, lignin, plastoquinones and many other secondary products. Over 30% of the carbon fixed by plants passes through this pathway. Inhibition of EPSPS by glyphosate deregulates the pathway, leading to even more carbon flowing through the pathway with accumulation of shikimate and shikimate-3-phosphate. Up to 16% of the plant's dry matter can accumulate as shikimate. Glyphosate occupies the binding site on EPSPS for phosphoenol pyruvate, a substrate of EPSPS, by mimicking an intermediate state of the enzyme-substrates complex. There are two forms of EPSPS in nature, EPSPS I, which is found in plants, fungi, and most bacteria, and is sensitive to glyphosate, and EPSP II, which is found in glyphosate resistant bacteria and is not inhibited by glyphosate. It is the gene for an EPSPS II that has been used to genetically engineer resistance in crops.

The shikimate pathway is most active in meristematic tissue. Hence, glyphosate has to translocate to the meristematic tissue to be effective. Glyphosate translocates in the plant from a source to sink direction. Up to 70% of absorbed glyphosate can translocate out of the treated leaves to the root and shoot apices. However, glyphosate translocation is self-limiting and only occurs for the first 48-72 h after application. The reason for this self-limiting phenomenon is not clear, but is related to the site of action of the herbicide, since there is greater translocation in glyphosate resistant crops compared to susceptible plants. Glyphosate's ability to translocate readily in plants results in it controlling not only annual, but also perennial weeds.

The extremely broad spectrum of activity of glyphosate is primarily due to the inability of most plant species to rapidly metabolize the herbicide to non-toxic forms. While certain species, such as soybeans, can cleave glyphosate into glyoxylate and aminomethylphophonate, the rate of degradation is not rapid enough for tolerance. The two metabolism genes that have been used to generate glyphosate resistant plants, glyphosate oxidase and glyphosate acetyltransferase, were derived from bacteria.

Given the mechanism of action of glyphosate and the difficulty in genetically engineering glyphosate resistant crops, it was speculated that selection of resistance in weeds would be a very rare event. However, there are now 11 species in which resistant biotypes have been selected. The two mechanisms of resistance are 1) alterations of the target site, EPSPS, and 2) decreased uptake/translocation of glyphosate to the meristematic tissues. The levels of resistance that have been selected to date is between 2 and 10 fold. Both mechanisms of resistance appear to be overcome by increasing the rate of glyphosate. However, as more resistant biotypes are selected, the levels of resistance

may increase. While there are only two mutations characterized in glyphosate resistant weeds (Pro106-Ser, Pro106-Thr), there are other sites where mutations have been shown in model plants that can result in resistance. These and other as yet undiscovered mutations could be found in the future. The mechanism of reduced uptake/translocation is still being studied.

A question that has been asked is "Why aren't there more resistant biotypes?" There may be several reasons. The first is that genes encoding for glyphosate resistance appear to be a very rare. Second, the time for selecting resistance is still relatively short. Until the introduction of glyphosate-resistant crops 10 years ago, glyphosate was rarely used as a stand-alone product on millions of acres. The continued intensive and widespread use of glyphosate will select for more resistant biotypes in the future. The ultimate effect will most likely be that glyphosate will continue to be the foundation of many weed management programs and additional herbicides or other methods will be used to manage resistant biotypes.