Glyphosate-resistant (GR) giant ragweed (Ambrosia trifida L.) has become an increasingly problematic weed of soybean production systems in Missouri and many areas of the Midwest. Currently, giant ragweed has been confirmed with resistance to glyphosate in 11 states and one Canadian province. The objectives of this research were to determine the effects of herbicide application timing and glyphosate tank-mix combinations on the survival of GR giant ragweed, and the influence of pre-plant (PREPLT) followed by (fb) 2-pass post-emergence (POST) herbicide programs in GR and glufosinate-resistant soybean on GR giant ragweed density, soybean yield, and net economic return. Results from this research indicate that POST applications to smaller plants can reduce the survival of giant ragweed compared to applications to larger plants. For a POST only management strategy, fomesafen plus glyphosate applied to 10-cm plants fb glyphosate late post-emergence (LPOST) resulted in 37% survival which was the lowest survival observed. Overall, giant ragweed was nearly eliminated with PREPLT fb 2-pass POST programs. For example, no more than 6 plants/plot were observed if PREPLT applications contained an effective tank-mix combination in either soybean system. However, 244 plants/plot were observed following a program that consisted of glyphosate PREPLT fb glyphosate plus fomesafen early post-emergence (EPOST) fb glyphosate LPOST. Few differences in yield or net return were observed in the PREPLT experiments. However, herbicide programs that contained an effective PREPLT treatment generally resulted in higher yield and net economic return. Results from this research suggest that POST-only programs are ineffective at controlling GR giant ragweed.