James Bruckner, a toxicology professor in the University of Georgia College of Pharmacy, recently was awarded a $898,179 contract for two years by the Consumer Specialty Production Association to assess potential neurotoxic risks posed by pyrethroid insecticides to infants and children. The association, said Bruckner, is a consortium of 18 chemical companies that manufacture and/or sell these insecticides. The findings of this research will be forwarded to the U.S. Environmental Protection Agency (EPA), so it can develop scientifically based exposure guidelines to assure safe levels of pyrethroids in agriculture and in the home, he added.

“When the EPA banned the use of neurotoxic DDT and organophosphates as insecticides, it forced chemical companies to switch to pyrethroids without having established scientific guidelines for their safe use,” said Bruckner, adding that relatively little is known about how the body handles or responds to most pyrethroids, particularly infants and children.

Numerous physiological and biochemical processes, which affect absorption, distribution, metabolism and elimination of foreign chemicals, change substantially during maturation. Age-dependent changes in these processes can result in significant differences between adults and children in the amount of toxic chemicals that reach and affect target organs, such as the brain, liver and kidneys, he said.

“Generally infants and young children are incapable of de-toxifying high doses of chemicals, but the high-dose experiments performed in the past often may not be relevant to lower real-life doses,” he added.

“We think that these pyrethoids may be non-toxic in children in environmentally relevant doses, due to efficient detoxification and the absence of other age-related factors that significantly affect the body’s handling of the chemicals,” he said. “If we’re correct, pyrethroids in low doses may still be safely used as effective insecticides.”

Experiments are planned that will test the hypothesis that young rodents and humans have adequate amounts of plasma and liver enzymes to inactivate all of the very low environmentally relevant doses of pyrethroids. This should result in comparable, non-toxic brain levels in all age groups, he noted.

Bruckner’s interdisciplinary research team from the Department of Pharmaceutical and Biomedical Sciences -- Michael Bartlett, Brian Cummings, Cathy White and Jason Zastre – will focus on understanding gastrointestinal (GI) absorption; plasma protein and lipoprotein binding; and blood-brain-barrier (BBB) permeability of selected pyrethroids. Experiments will be conducted in mature rats, cultured human cells and blood from children and adults, to learn whether the chemicals are actively carried across GI and BBB membranes by transport proteins.

The results, Bruckner said, will be utilized to develop and assess the ability of physiologically based pharmacokinetic (PBPK) computer models to accurately forecast blood and brain pyrethroid concentrations in people of different ages. Validated PBPK models provide a scientifically based alternative, and an indirect means of predicting target organ levels and resulting adverse effects of toxic chemicals in infants, children and adults for realistic insecticide exposure scenarios.

This study is a continuation of the work Bruckner developed and validated for EPA on the pyrethroid deltamethrin during the past decade. With more than $860,000 in EPA funding, he conducted pharmacokinetic studies to describe how the body handled the insecticide, from absorption and distribution to metabolism and excretion. Using rats at different stages of development, he measured the systemic disposition and health-related consequences of pyrethroid insecticide exposure and found infants more susceptible than adults to neurotoxicity, due to infants’ inability to metabolically inactivate high doses of pyrethroids.

Bruckner’s goal with the EPA study was to develop physiological models based on the results of the animal studies that can accurately predict how much of an oral dose of deltamethrin insecticide reached the brain and caused neurotoxic effects in animals of different ages, not just adults. With this new funding, the models can be developed and validated to forecast health risks for additional pyrethroid compounds, with the results extrapolated from rats to humans of all ages.