Hello, this is Kevin O'Donovan, and I'd like to welcome you to the National Institute of Environmental Health Sciences Superfund Research Program monthly Research Brief podcast.

This month, we're discussing how commercial paper and rubber products contain activators of the aryl hydrocarbon receptor.

The Research Brief, Number 225, was released on September 4, 2013, and was written by SRP contractor Sara Mishamandani in conjunction with SRP-supported researchers Michael Denison and Richard Di Giulio.

Common commercial and consumer products, including newspapers and rubber bands, contain chemicals that are recognized by the body as toxins, according to a collaborative study by researchers at the Duke University and University of California, Davis Superfund Research Program Centers. Solvents extracted from everyday rubber and paper products were shown to activate the aryl hydrocarbon receptor (or AhR), which can potentially produce a wide variety of harmful effects in the body.

Dioxins, particularly 2, 3, 7, 8- Tetrachlorodibenzo-p-dioxin (or TCDD), and related dioxin-like chemicals are widespread environmental contaminants that produce an assortment of toxic and biological effects, including reproductive and developmental problems, damage to the immune system, cancer, and endocrine disruption. Most biological effects related to dioxin-like chemicals are mediated by the AhR, a protein involved in the regulation of various biological responses and a regulator of enzymes that metabolize chemicals in the body. Although most dioxin-like chemicals are structurally related, recent studies have shown that the AhR will bind to a wide variety of structures, many of which can produce similar health effects.

During an analysis of food products for AhR activators, the accidental use of a rubber cap liner instead of a Teflon cap on vials containing the organic solvent dimethylsulfoxide (or DMSO) revealed that chemicals extracted from the rubber cap liner could stimulate AhR DNA binding, while the Teflon-capped vials showed no activation. Based on this finding, the researchers wanted to examine how widespread AhR activators were in commercial and consumer products.

Researchers extracted chemicals from paper, rubber, and plastic products and measured whether they could stimulate AhR DNA binding and/or AhR-dependent gene expression in cultured cell lines, zebrafish embryos, and samples of human skin. They demonstrated that chemicals from the rubber and paper product extracts can bind to the AhR, stimulate AhR DNA binding, and induce AhR-dependent gene expression in cell lines. Solvent extracts of rubber products also caused AhR-dependent developmental toxicity in zebrafish, with zebrafish embryos exposed to rubber extracts exhibiting substantial developmental malformations, including severe deformities in the lower jaw, accumulation of fluid in the brain and near the heart, and cell death in tissues.

According to the authors, since these commercial products and consumer products contain chemicals with significant AhR binding activity, they may also produce endocrine disrupting

effects in exposed animals. They demonstrated that rubber product extracts could stimulate estrogen receptor (or ER)-dependent gene expression. While endocrine disrupting chemicals have been identified from a number of environmental sources, most studies focus on identification of known endocrine disruptors, rather than assessing the overall activity of an extract then identifying the responsible chemicals.

The study tested for ER and AhR activity in the chemical extracts and did not look for specific known ER or AhR active chemicals. Although they know now that there are ER- and AhR-active chemicals in the extracts, they do not know yet exactly what the chemicals are, just that they are widely found in these everyday products. Ongoing studies are currently attempting to identify the responsible chemicals.

The study also suggests that AhR- and ER-active chemicals present in rubber and paper products can complicate experimental study by contributing dioxin- and estrogen-like chemicals/activity to sample or sample extracts that come in contact with these materials. Accordingly, the authors suggest that background levels of extractable AhR and ER active chemicals must be determined in sample collection and processing materials in experiments using appropriate method blanks.

If you'd like to learn more about this research, visit the Superfund Research Program website at www.niehs.nih.gov/srp. From there, click on "Who We Fund" and follow the links to the Duke University and University of California, Davis research summaries. If you have any questions or comments about this month's podcast or if you have ideas for future podcasts, contact Maureen Avakian at avakian@niehs.nih.gov.

Join us next month as we discuss more exciting research and technology developments from the Superfund Research Program.