

Comprehensive third-party research results Eastman Tritan™ copolyesters are free of estrogen and androgen activity.

Estrogen and testosterone are essential hormones to many important biological processes in animals and humans, including sexual differentiation and development. Studies have shown that certain synthetic and naturally occurring chemicals can interfere with these processes and lead to adverse effects.

To support the safety of Tritan copolyesters, Eastman asked various reputable, independent third-party laboratories to use well-recognized scientific methods to test Eastman Tritan™ copolyester for potential estrogenic or androgenic activity. This battery of tests included:

- **Quantitative structure activity relationships (QSAR)¹**
Computer modeling of monomers to assess each substance's molecular structure and its ability to bind to human estrogen and androgen (testosterone) receptors in a manner that could lead to their activation.
- **Receptor transactivation assays^{2,3}**
The estrogenic and androgenic activity of both the monomers and concentrated extracts of Tritan were also evaluated in vitro using both yeast and mammalian cell assays performed by two separate labs. These tests evaluate a substance's ability to bind to a hormone receptor and induce gene expression. Extracts were generated using FDA and European Union recommendations for food contact migration testing. Additional extracts were derived following a dishwasher simulation environment (10 days, 70°C, in Cascade™ solution).
- **Competitive binding assays²**
Despite the fact that neither the QSAR nor transactivation studies showed any evidence of binding or gene expression by estrogenic or androgenic pathways, a second tier of tests based on competitive binding assays was conducted. These tests confirm a substance's ability to specifically bind to a specific hormone receptor and can be used to calculate the Relative Binding Affinity (RBA).

- **Uterotrophic assay/Hershberger assay⁴**

These studies are considered the most definitive tests for assessing a chemical's potential to elicit estrogenic or androgenic responses in living biological systems. These two in vivo tests are part of the Tier I Endocrine Disruption Screening Program of the U.S. Environmental Protection Agency (EPA).

In addition, the monomers were tested in 13-week repeated exposure studies assessing their systemic toxicity potential as well as studies assessing their developmental toxicity potential. The results revealed no evidence of androgen- or estrogen-related effects at any dose level. The results of the monomer studies assessing endocrine activity and an explanation of the scientific approach to testing compounds for estrogenic and androgenic activity have been recently published in Food and Chemical Toxicology, Vol. 50, Issue 2, pages 2196–2205 (2012).

The uniformly negative responses seen in these complementary third-party studies overwhelmingly demonstrate that Eastman Tritan monomers and copolyesters are free of estrogenic and androgenic activity. These studies assessed a wide variety of receptor mediated mechanisms and biological end points. It is important to note that Tritan was evaluated by testing multiple end points using a battery of tests, including more definitive in vivo studies, which is the recommended approach by the Endocrine Disruption Screening Program, Office of Economic and Cooperative Development (OECD) and other international organizations. These studies were also submitted and reviewed by the USFDA which expressed no concerns for estrogenic or androgenic activity by Tritan for its intended end uses.

Furthermore, Eastman Tritan™ copolyesters have been reviewed independently and approved by regulatory agencies, including:

- Health Canada, which issued a Letter of No Objection allowing the use of Eastman Tritan™ copolyester in food contact applications.
- U.S. Food and Drug Administration, which cleared Tritan for use in food contact applications.
- European Food Safety Authority and the European Commission, which cleared Tritan and a key Tritan monomer for repeat-use food contact applications under the new Plastics Regulation.
- Japan Hygienic Olefin and Styrene Plastics Association (JHOSPA), which amended its list of certified polymers to include the composition of Tritan.

¹Conducted by Dr. William Welsh, Department of Pharmacology, UMDNJ-Robert Wood Johnson Medical School, Piscataway, New Jersey

²Conducted by CeeTox, Inc., Kalamazoo, Michigan

³Conducted by the Center for Environmental Biotechnology, University of Tennessee, Knoxville, Tennessee

⁴Conducted by WIL Research Laboratories, LLC, Ashland, Ohio



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It is the responsibility of the medical device manufacturer ("Manufacturer") to determine the suitability of all component parts and raw materials, including any Eastman product, used in its final product to ensure safety and compliance with requirements of the United States Food and Drug Administration (FDA) or other international regulatory agencies.

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