

## Identifying Reference Chemicals for Androgen Receptor Activity

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Mandated testing of thousands of chemicals to identify those that may act as androgen receptor agonists or antagonists will cost millions of dollars and take decades to complete using current validated methods. Alternative methods using high-throughput screening and computational toxicology technologies, such as those developed in the ToxCast and Tox21 screening programs, can provide rapid and cost-effective identification of potential androgen-active chemicals. Development and evaluation of alternative test methods and testing strategies will require high-quality reference data from *in vivo* and *in vitro* assays for anti/androgenic activity. To focus the search for quality *in vitro* data, a list of 121 putative androgen-active or inactive chemicals for which ToxCast data were available was compiled from previous ICCVAM, ECVAM, and OECD validations of *in vitro* androgen receptor binding and transactivation assays. We conducted semi-automated literature searches for *in vitro* androgen activity data on these chemicals using PubMatrix and Scopus. High-quality *in vitro* binding and transactivation data were extracted from identified references and compiled into a single database, which will be publicly available on the NTP website (<http://ntp.niehs.nih.gov/go/40658>). Detailed assay information and results were recorded in the database using a standardized ontology. These data were analyzed for reproducibility, consistency, and specificity of results across assay systems and receptor types. Antagonist data were only considered in the analysis if cytotoxicity was evaluated concurrently. Based on quantitative data such as relative binding affinity and transactivation activity concentrations, chemicals with reproducible results were assigned potency ranges. Reference chemical lists and supporting documentation resulting from this effort will be made available to the public and submitted to OECD via the Validation Management Group-Non Animal to facilitate the international harmonization of test method evaluations. *This work does not reflect EPA policy. This project was funded in whole or in part with Federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.*