Prior to initiating the testing of a substance, an NIEHS/NTP staff scientist develops a research concept document. This research concept outlines the general elements for a program of study of the substance to address specific research needs raised in its nomination to the testing program. Additional information about the nomination, review, and selection of substances for study by the NTP is provided from ***Nominations to the NTP Testing Program*** (**http://ntp.niehs.nih.gov/go/nom**).

NTP Concept Document: Di-n-Butyl Phthalate (DBP)

There were four outcomes from the discussions concerning the toxicity and particularly the developmental induction of Leydig cell adenomas by DBP.

1. A specific study investigating the long term effects of DBP with continuous exposure from *in utero* through 2 years was approved. This would be specifically aimed at the Leydig cell tumor issue with the use of Sprague Dawley rats (i.e. evaluate male offspring only in one species), a greater than normal number of dose levels (5 was suggested), the use of intermediate times for necropsy of animals (at different developmental ages) that would be coupled with genomic approaches in target tissues to evaluate mechanisms and potential biomarkers of exposure or effect.

2. Based on the developmental data already available for DBP, a series of other short-term studies (*in utero* to adulthood – 3 months of age) would be conducted with other phthalate esters to investigate the ability of developmental exposure to induce testicular tumors and reproductive tract abnormalities. This should aid in the demonstration of a common mechanism for the chemical class and provide further data on dose –response and SAR relationships (with DBP being the index chemical with a long term study).

3. The study team should consider approaches to the study of mixtures of phthalate esters based on the short-term model and dose response data developed in (2). This should provide critical data sets on cumulative and aggregate hazard and risk from exposure to multiple phthalates. At least two approaches would be available – (a) using the known mixtures of phthalates to which humans are exposed, based on NHANES data (and multiples thereof) and (b) deriving equivalency values for induction of different adverse effects from the dose response data in (2) and specifically addressing the hypothesis that the effects noted would be dose additive.

4. Standard bioassays for DBP in the F-344 rat and B6C3F$_1$ mouse with dosing commencing at weaning. These basic hazard characterization data are not available for DBP. However, these studies would be considered a low priority versus 1 to 3 above.

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