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: Butyl Paraben (BP)

Outcomes:

Development by a study team of detailed proposals was recommended to incorporate the following toxicological issues in priority order:

1. To undertake *in vitro* / high throughput studies aimed at a number of potential toxicities of BP, but especially (i) interaction with steroid receptors (eg Androgen Receptor) (ii) evaluation of effects on steroidogenesis (eg in H295R cells) (iii) mitochondrial function. It was recommended that such studies should not only include BP and its likely major metabolites (eg p-hydroxybenzoic acid), but other members of the parabens class (and their presumed metabolites).

2. To undertake a series of directed TK studies in the SD rat to compare oral with dermal exposure. This would involve blood levels of parent compound and metabolites, especially those found "active" from the *in vitro* studies in 1. Studies should also incorporate exposure during pregnancy to evaluate fetal levels of BP and metabolites. Dual labeling of the ring and side chain was suggested as a possibility to evaluate the stability of the ester side chain.

3. To conduct a modified RACB study in the SD rat to evaluate functional effects on reproduction and post-natal development. The design of this study should incorporate sufficient additional components so as to provide an appropriate sub-chronic evaluation of the parental generation (including hematology, detailed pathology etc) to substitute for a stand-alone 90-day rat study. The use of the SD rat should be fully justified based on its preference for use in the RACB, over the standard, F/344 rat (i.e. historical control data available). The F344 has a smaller litter size, poor maternal behavior and is specifically not recommend for reproduction studies in standard regulatory reproductive toxicity guidelines. If possible, the study team should evaluate whether some F_1 animals may be held for at least 90 days after birth to evaluate potential testicular neoplasia (similar to that previously noted with phthalates).

4. The *in utero* carcinogenicity study was given a low priority.

A mouse 90-day study was not recommended. There were no additions or changes to the proposed study team.

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