

AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT		1. CONTRACT ID CODE	PAGE 1	OF 2
2. AMENDMENT/MODIFICATION NO. 1	3. EFFECTIVE DATE See Block 16C	4. REQUISITION/PURCHASE REQ. NO.	5. PROJECT NO. (if applicable)	
6. ISSUED BY CODE National Institute of Environmental Health Sciences RCB, DERT, NIH, PHS, DHHS P.O. Box 12874 Research Triangle Park, NC 27709		7. ADMINISTERED BY (If other than Item 5) CODE Attn: Marilyn B. Whaley OMB No. 0990-0115		
8. NAME AND ADDRESS OF CONTRACTOR (No., street, city, county, State and ZIP Code) All Recipients of RFP No. NIH-ES-04-12 entitled "STUDIES TO EVALUATE THE TOXIC AND CARCINOGENIC POTENTIAL OF TEST ARTICLES IN LABORATORY ANIMALS FOR THE NATIONAL TOXICOLOGY PROGRAM (NTP)"		( <input checked="" type="checkbox"/> ) ) X	9A. AMENDMENT OF SOLICITATION NO. NIH-ES-04-12	
			9B. DATED (SEE ITEM 11) August 18, 2004	
			10A. MODIFICATION CONTRACT/ORDER NO.	
CODE	FACILITY CODE		10B. DATED (SEE ITEM 13)	

**11. THIS ITEM ONLY APPLIES TO AMENDMENTS OF SOLICITATIONS**

The above numbered solicitation is amended as set forth in item 14. The hour and date specified for receipt of Offers,  is extended,  is not extended. Offers must acknowledge receipt of this amendment prior to the hour and date specified in the solicitation or as amended, by one of the following methods: (a) By completing Items 8 and 15, and returning 1 copies of the amendment; (b) By acknowledging receipt of this amendment on each copy of the offer submitted; or (c) By separate letter or telegram which includes a reference to the solicitation and amendment numbers. FAILURE OF YOUR ACKNOWLEDGMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF OFFERS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER. If by virtue of this amendment you desire to change an offer already submitted, such change may be made by telegram or letter, provided each telegram or letter makes reference to the solicitation and this amendment, and is received prior to the opening hour and date specified.

**12. ACCOUNTING AND APPROPRIATION DATA (if required)**

**13. THIS ITEM APPLIES ONLY TO MODIFICATIONS OF CONTRACTS/ORDERS, IT MODIFIES THE CONTRACT/ORDER NO. AS DESCRIBED IN ITEM 14.**

( <input checked="" type="checkbox"/> )	A.	THIS CHANGE ORDER IS ISSUED PURSUANT TO: (Specify authority) THE CHANGES SET FORTH IN ITEM 14 ARE CONTRACT ORDER NO. IN ITEM 10A.
	B.	THE ABOVE NUMBERED CONTRACT/ORDER IS MODIFIED TO REFLECT THE ADMINISTRATIVE CHANGES (such as paying office, appropriation date, etc.) SET FORTH IN ITEM 14, PURSUANT TO THE AUTHORITY OF FAR 43.103(f)
	C.	THIS SUPPLEMENTAL AGREEMENT IS ENTERED INTO PURSUANT TO AUTHORITY OF:
	D.	OTHER (Specify type of modification and authority)

**E. IMPORTANT:** Contractor  is not,  is required to sign this document and return \_\_\_\_\_ copies to the issuer.

**14. DESCRIPTION OF AMENDMENT/MODIFICATION (Organized by UCF section headings, including solicitation/contract subject matter where feasible.)**

The purpose of this amendment is to delete and replace page 8 of Sample Work Assignment C of Attachment 1, the Statement of Work (copy attached).

Effective with the date of this amendment, the RFP is hereby revised to delete and replace page 8 of Sample Work Assignment C of Attachment 1, the Statement of Work, with the attached page 8 which corrects the rat specie in Paragraph IV. A, the number and basis for concentrations for dams in Paragraph IV.B.1., and the number of test groups for treatment and totals for treatment and control groups for pups in Paragraph IV.B.2 in the Optional Phase 4: 2-year study. The RFP otherwise remains unchanged.

The due date and time for receipt of proposals of 3:00 pm on October 14, 2004 remains unchanged. Please note the acknowledgment requirements in Block 11 above.

As provided herein, all terms and conditions of the document referenced item 9A or 10A, as heretofore changed, remains unchanged and in full force and effect.

15A. NAME AND TITLE OF SIGNER (Type or print)		16A. NAME AND TITLE OF CONTRACTING OFFICER Marilyn B. Whaley Contracting Officer	
15B. CONTRACTOR/OFFEROR	15C. DATE SIGNED	16B. UNITED STATES OF AMERICA	16C. DATE SIGNED
BY _____ (Signature of person authorized to sign)		BY <u>Marilyn B. Whaley</u> (Signature of Contracting Officer)	9/9/04

## IV. OPTION - PHASE 4: 2-YEAR STUDY

## A. PURPOSE

To evaluate the toxic and carcinogenic potential of sodium tungstate dihydrate in ~~Fischer-344~~ *Harlan Sprague-Dawley*<sup>1</sup> rats exposed perinatally and up to 2 years.

## B. TREATMENT AND OBSERVATIONS

## 1. DAMS

Male and female Harlan Sprague-Dawley rats and C3H/HeN male and C57Black/6N female mice shall be approximately 7-8 weeks of age upon receipt. These F<sub>0</sub> rats/mice will be housed separately, 5 per cage, for a 10-14 day quarantine period. Then, one breeder male will be housed with 2 breeder females. During cohabitation, vaginal smears are to be taken daily to determine the presence of sperm. Adequate females are to be bred to produce the required number of pregnant dams within a 1-week period so that F1 rats and are approximately the same age when weaned and started on treatment (20-27 days for rats and 18-25 days for mice). Breeder males will be discarded after breeding. The pregnant dams shall be randomly assigned to treatment and control groups and housed individually. At each of ~~five~~ *three*<sup>1</sup> concentrations (to be determined based on the ~~7-week~~ *18-week*<sup>1</sup> study) plus a control group, pregnant dams shall receive the subject test article mixed in drinking water, starting on gestational day 6 for rats and day 5 for mice and continuing until the end of the nursing period. The breeder rats/mice will receive NIH-07 diet from time of receipt, through cohabitation, gestation, and until pups are weaned. [Note: All pups will be weaned on the same day, the day the last litter born reaches PND20 for rats or PND 18 for mice.] Water consumption will be measured weekly for dams from the time they are assigned to a treatment group through weaning of pups. Dams shall be weighed at the time they are determined to be pregnant and assigned to a treatment group, and then weekly until the pups are weaned, at which time dams will be killed and a complete necropsy will be performed and all tissues saved. Dams that do not deliver within 3-4 days of anticipated delivery date shall be euthanized, examined for uterine implantations/resorptions, and these findings recorded.

	<u>Pregnant Dams</u>		<u>Test Groups</u>		<u>Species</u>		<u>Total</u>
Treatment	25	x	3	x	2	=	150
Controls	25	x	1	x	2	=	<u>50</u>
							200

## 2. PUPS

## a. BIRTH TO WEANING

The number, sex, and body weight of the pups shall be recorded the day after delivery (PND 1). On PND 4 pups will be culled to a maximum of eight per litter (i.e., 4 males and 4 females) and shall be tattooed (on a limb) for unique identification. All pups shall be weighed on PND 4, 7, and weekly thereafter, until weaned. All pups will be weaned on the same day, the day the last litter born reached PND20 for rats or PND 18 for mice. This will result in pups being between 20-27 days of age at weaning for rats or 18-25 for mice.

Pups (PND 4 to Weaning)

	<u>Litters</u>		<u>Pups</u>		<u>Sexes</u>		<u>Test Groups</u>		<u>Species</u>		<u>Total</u>
Treatment	25	x	4	x	2	x	<del>5</del> <i>3</i>	x	2	=	<del>800</del> <i>1200</i> <sup>1</sup>
Controls	25	x	4	x	2	x	1	x	2	=	<del>160</del> <i>400</i> <sup>1</sup>
											<del>960</del> <i>1600</i> <sup>1</sup>

## b. WEANING TO SACRIFICE – 104-WEEK STUDY

At weaning, pups shall be culled to 2 males and 2 females per litter. Pups will then be tail tattooed using unique consecutive numbers. The day of weaning and start of exposure using NTP-

<sup>1</sup> Revised by Amendment 1 after RFP issued.