CHEMICAL PRODUCTS CORPORATION

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July 13, 2006

Associate Director for Communications
Office of the Director
National Institutes of Health
Building 1, Room 344
9000 Rockville Pike
Bethesda, MD 20892

Subject: May 31, 2006 **Request For Correction** of National Toxicology Program Technical Report 494, NIH Publication Number 05-3953 – Request that TR494 be withdrawn because of factual errors – Additional information

Dear Madam or Sir;

A Request For Correction was submitted by Chemical Products Corporation (CPC), a Georgia corporation located in Cartersville, Georgia on May 31, 2006 under the auspices of NIH's Information Quality Guidelines. CPC requested at that time that National Toxicology Program Technical Report 494 (TR494), NIH Publication No. 05-3953, be withdrawn because the conclusions presented in this technical report were accepted by NTP's Board of Scientific Counselors' Technical Reports Review Subcommittee on December 9, 2004 based upon undocumented genetic toxicology data presented for the first time on December 9, 2004, and subsequently incorporated into TR494.

As a result of a Freedom of Information Act request an additional page of information was provided to CPC on July 11, 2006 in addition to that provided as an attachment to our May 31, 2006 Request for Correction; this single page of additional information is attached hereto along with the NIH letter which accompanied it. This additional information does not provide any indication that Sample A07496 in Appendix E, Table E3 of TR494 is an aliquot of the TR494 test article, Lot No. 5893, as stated in TR494. The origin of Sample A07496

cannot be verified through National Toxicology Program documents and records, thus CPC reiterates its request that TR494 be withdrawn.

The copy of a single page Bulk Chemical Shipment Report attached to this letter demonstrates that 4 samples of Anthraquinone, designated as Chemical Lot No.'s GSTU 2517770, 64005, 2Y011, and 5893, were shipped from Battelle, NTP's contractor, to BioReliance Corporation on June 22, 2004. The TR494 test article, Lot 5893, is included in this shipment; the reported last analyzed purity (BCR, 11/19 – 11/20/98) of this sample as 99.4% relative purity conflicts with the reported 99.8% purity of the test article in TR494.

If one presumes that these four samples are the four samples in Tables 3,4, 5, and 6 of TR494 Appendix E - Genetic Toxicology, then one of these four samples was found to be mutagenic to Salmonella typhimurium strains TA98 and TA100 with and without S9 metabolic activation. When CPC submitted an aliquot of the TR494 test article, labeled Lot 5893 when received by CPC, to BioReliance Corporation for preincubation genetic toxicology testing 41/2 years prior to Battelle's submission, Lot 5893 was found to be mutagenic to Salmonella typhimurium strains TA98 and TA 100 without S9 metabolic activation and mutagenic to strain TA98 with S9 metabolic activation.

NTP has been unable to produce any records relating the genetic toxicology testing results for the four samples identified on the attached Shipment Report as Lot No.'s GSTU 2517770, 64005, 2Y011, and 5893, to the samples reported for the first time on December 9, 2004 in TR494 Appendix E as A07496, A65343, A54984, and A40147.

This additional information has raised two additional concerns regarding the veracity of TR494. First, the Lot 5893 test article is shown on the attached shipment report as being "99.4% relative purity" as opposed to the 99.8% purity of the TR494 test article stated in TR494. Secondly, the attached shipment

report states, "Recommended Storage Conditions: Room Temperature (~25°C)". The recommended storage conditions stated by Battelle conflict with information provided to the December 9, 2004 peer review panel to answer their concerns about decomposition of impurities in the AQ during many years of storage. TR494 at page 20, second column, describes discussion of this issue during the third peer review on December 9, 2004 as follows, "Dr. Klaunig asked if the samples assayed were the original test material and if any degradation might have occurred during the interval. Dr. Smith replied that this was the same material used in the animal studies, and it was stored frozen under argon, so degradation was unlikely."

Mutagenicity assay data, first introduced by NTP in the third peer review of TR494 on December 9, 2004, purports to demonstrate that the TR494 test article is not contaminated by mutagenic impurities, even though NTP had been notified 4 and 3 years earlier of positive mutagenicity assay results on 2 independently obtained and tested aliquots of the TR494 test article, Lot 5893. The TR494 test compound, Anthraquinone, CAS # 84-65-1, is not a mutagen, so the presence of a direct acting mutagenic impurity in the TR494 test article confounds the conclusions presented in TR494.

On February 18, 2004, concern over the confounding effects of contamination of the TR494 test article with at least one direct-acting mutagen prompted NTP's Board of Scientific Counselors' Technical Reports Review Subcommittee to restrict the scope of the conclusions in TR494 by adding language stating that these conclusions applied only to "Anthracene-derived Anthraquinone". Contamination of the TR494 test article with mutagens was believed to be the result of its method of manufacture - oxidation of Anthracene. An explanation of the two more common alternative manufacturing processes, the Friedel-Crafts process and the Diels-Alder process was also presented in TR494. Anthracene-derived Anthraquinone is very rarely, if ever, encountered in commerce in the United States.

The final TR494, issued in September, 2005, was substantially altered from the document accepted by the NTP's Board of Scientific Counselors' Technical Reports Review Subcommittee on February 18, 2004. Acceptance of the altered TR494 on December 9, 2004 was based upon new genetic toxicology test data offered by NTP's principal investigator to demonstrate that the TR494 test article was not mutagenic to Solmonella typhimurium strains TA98, TA100, and TA1537, with and without rat S9. NIEHS's response to a Freedom of Information Act request submitted by CPC has revealed that mutagenicity assay data purporting to demonstrate the absence of mutagenicity in the TR494 test article cannot be associated with an aliquot of the TR494 test article submitted by NTP's contractor, Battelle, to BioReliance Toxicology Test Article Repository. CPC requests that TR494 be withdrawn until NTP can provide documentation that the TR494 test article is not mutagenic to Salmonella typhimurium strains TA98, TA100, and TA1537 without or with S9 metabolic activation, as is asserted in TR494.

If I can answer any questions concerning the contents of this letter, or provide any further information, please telephone me at 770-382-2144 extension 272 or email me at jcook@cpc-us.com.

Sincerely,

Jerry A. Cook

Jerry A. Cook
Technical Director

Cc: Ms. Holli Beckerman Jaffe

Attachments – 2 pages

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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July 11, 2006

Mr. Jerry A. Cook
Technical Director
Chemical Products Corporation
P.O. Box 2470
Cartersville, Georgia 30120-1692

RE: FOI Case No. 32439

Dear Mr. Cook:

I write in further reference to my letter to you dated May 19, 2006. One page was inadvertently omitted from the responsive records sent to you.

Please accept our apologies for this error. If you have questions about this release, please contact me.

Sincerely,

Kim Minneman

Kim L. Minneman
Freedom of Information Coordinator

Enclosure

Chemistry Support Services for the NTP
NIH Contract No.: N01-ES-05456
Battelle Project No.: G004110-CCR
NTP ChemTask No.: CHEM08048
CAS No.: 84-65-1

BULK CHEMICAL SHIPMENT REPORT

ANTHRAQUINONE

9-064-SHIP-379

June 22, 2004

CAS No.: 84-65-1	Amount Shipped: ~2 g of each lot into one 15-mL amber glass bottle each, shipped at ambient temperature
Battelle Task No.: 9-064-SHIP-379	Shipping Date: 6/1/04
NTP ChemTask No.: CHEM08048	Chemical Lot No's.: GSTU 2517770, 64005, 2Y011, & 5893
Program Supported: GTX	Last Analyzed Purity: Lot No. GSTU 2517770 (BCLA, 2/25-5/22/03): ~99.9% Lot No. 64005 (BCLA, 2/25-5/22/03): ~99.8% Lot No. 2Y011 (BCLA, 2/24-5/22/03): ~99.4% Lot No. 5893 (BCR, 11/19-11/20/98): 99.4% relative purity
Shipped To: [Non-key contact emp] BioReliance Coordinator, Chemical Repository 9630 Medical Center Drive Rockville, MD 20850	Recommended Storage Conditions: Room temperature (~25°C)

This report was prepared by Darren Brown and reviewed for accuracy by Melissa Cloud.

Approved By:

For Brian Burbank
Donna B. Browning, B.S.
Task Leader

Approved By:

Melissa A. Cloud
Melissa A. Cloud, B.S.
Discipline Leader, Data Management

Submitted to:

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National Institute of Environmental Health Sciences
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