CHEMICAL PRODUCTS CORPORATION

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July 17, 2006

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

Subject: Addendum to May 31, 2006 **Request For Correction** of National Toxicology Program Technical Report 494, NIH Publication Number 05-3953
A Critical Factual Error in TR494 has now been documented

Dear Madam or Sir;

Chemical Products Corporation (CPC) submitted a Request for Correction of NTP Technical Report 494 (TR494) dated May 31, 2006 and submitted a further information letter dated July 13, 2006. This letter is an addendum to our May 31, 2006 Request for Correction asking that TR494 be withdrawn. In addition to the information provided earlier, CPC can now document a critical factual error in the information presented to the December 9, 2004 Peer Review Panel which approved the conclusions contained in TR494.

The third draft of TR494 was presented to a third Peer Review Panel on December 9, 2004. This third draft TR494 based its conclusions on the surprising assertion that, contrary to the information contained in the second draft TR494 presented on February 18, 2004 for peer review, NTP had since that time determined that the TR494 test article had not been contaminated with one or more mutagenic impurities when it was administered during TR494 testing in the mid-1990's. This was an extraordinarily surprising assertion because an aliquot of the TR494 test article had been found to be mutagenic to Salmonella typhimurium strains TA98 and TA100 in a genetic toxicology assay in 1999 and a second aliquot of the TR494 test article had been found to be mutagenic in a

second genetic toxicology assay in 2000. Anthraquinone is not mutagenic, so positive genetic toxicology assay results on these two aliquots demonstrated that the TR494 test article was contaminated with one or more direct-acting mutagens which confounded the findings presented in TR494.

NTP made two critical assertions to the December 9, 2004 Peer Review Panel: first, that the negative genetic toxicology assay conducted in the second half of 2004 by BioReliance Corporation on Sample A07496, presented as an aliquot of the TR494 test article, was definitive evidence that mutagenic contaminants had not been present in the TR494 test article and that this result negated the positive assay results on aliquots of the TR494 test article in 1999 and again in 2000; and second, that the aliquot of TR494 test article that was submitted to BioReliance Corporation on June 1, 2004 by Battelle, NTP's contractor, had been maintained "frozen under argon" during the 7-plus year period between the end of TR494 animal dosing and the 2004 genetic toxicology assay to make the possibility of deterioration of any mutagenic impurities contained in the aliquot "unlikely".

CPC's May 31, 2006 Request for Correction reported that, based upon information obtained under a Freedom of Information Act request, there were no records within NTP to demonstrate that Sample A07496, for which genetic toxicology assays results were presented in December 2004 as proof that the TR494 test article was not mutagenic, was an aliquot of the TR494 test article archived by Battelle as Lot 5893 Anthraquinone.

As a result of a second Freedom of Information Act request, CPC has obtained records demonstrating that a critical factual error was presented by NTP to the December 9, 2004 Peer Review Panel. The conditions under which the aliquot of TR494 test article submitted to BioReliance Corporation for genetic toxicology assay on June 1, 2004 had been stored by Battelle for the previous 7-plus years at room temperature (~25°C) under air rather than being "frozen under argon".

Thus, the likelihood of decomposition of any mutagenic impurities contained in the TR494 test article between the time it was administered to animals in the mid-1990's and the time of its submission to BioReliance by Battelle on June 1, 2004 was misrepresented to the December 9, 2004 Peer Review Panel.

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."

Three chemical storage reports and the NIH cover letter received with them are enclosed with this letter and labeled Attachment 1. These demonstrate that three separate aliquots of the TR494 test article, Anthraquinone Lot 5893, were received by Battelle for storage. One of these three can be unequivocally distinguished from the others in that the entry for "Last Analyzed Purity" on the chemical storage report is "(BCR, 11/19-11/20/98): 99.4% relative purity" whereas the other two chemical storage reports show different "last analyzed" dates and a different purity. This single "80-ounce amber glass bottle nominally containing a total of 1395.3 g of anthraquinone" Lot No. 5893, was received at room temperature and subsequently stored at room temperature. That chemical storage report states, "Storage Conditions: Room Temperature (~25°C)" with no recommendation for an inert atmosphere.

Attachment 2 is the Bulk Chemical Shipment Report dated June 22, 2004 for the anthraquinones sent by Battelle to BioReliance Corporation on June 1, 2004; this shipment included an Anthraquinone Lot No. 5893 aliquot (the TR494 test article). The Anthraquinone Lot No. 5893 aliquot is described on the Bulk Chemical Shipment Report as "(BCR, 11/19-11/20/98): 99.4% relative purity". The chemical analysis date and stated purity demonstrate conclusively that the

aliquot of Anthraquinone Lot 5893 sent to BioReliance Corporation for genetic toxicology assay on June 1, 2004 was from the 80-ounce amber glass bottle that had been stored under air at room temperature for the 7-plus year interval between TR494 test animal dosing and the late 2004 genetic toxicology assay. This shipment report also records recommended storage conditions for these anthraquinone samples as "Room Temperature (~25°C)". Thus, there is no possibility that the genetic toxicology assay data presented by NTP for the first time to the December 9, 2004 Peer Review Panel can demonstrate that the conclusions presented in TR494 were not confounded by mutagenic impurities present in the test article.

CPC respectfully submits the above described factual error was a critical determinant in the December 9, 2004 Peer Review Panel's acceptance of NTP's assertion in the third TR494 draft that the TR494 test article had been demonstrated to be non-mutagenic and that the conclusions presented in the third draft TR494 should be accepted as written. Thus, we submit that documentation of this factual error, in and of itself, is sufficient to render the conclusions in TR494 scientifically untenable. CPC again requests that TR494 be immediately withdrawn.

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 – Attachment 1: 4 pages
Attachment 2: 1 page

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

ATTACHMENT 1 a

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National Institutes of Health
National Institute of
Environmental Health Sciences
P. O. Box 12233, MD NH-10
Research Triangle Park, NC 27709-2233

July 12, 2006

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

RE: FOI Case No. 32776

Dear Mr. Cook:

This is a final response to your June 16, 2006, Freedom of Information Act (FOIA) request addressed to me. You requested a copy of documents with specific storage conditions under which the Anthraquinone (CAS #84-65-1) test article employed for the studies in NTP Technical Report 494 (NIH Publication Number 05-3953) has been archived including temperature, inert atmosphere (if any) in contact with the test article, and degree of protection from light (if any).

We located three pages responsive to your request. Enclosed are three Chemical Storage Reports on Anthraquinone.

Provisions of the FOIA and Department of Health and Human Services FOIA Regulations allow us to recover part of the cost of responding to your request. Because the cost is below the $25 minimum, there is no charge for the enclosed materials.

Sincerely,

Kim L. Minneman

Kim L. Minneman
Freedom of Information Coordinator

Enclosure:
3 pages

ATTACHMENT 1 6

Battelle
. . . Putting Technology To Work

BATTELLE-CS
Chemistry Support Services for the NTP
NIH Contract No. N01-ES-55395
Battelle Project: G002840-GN
NTP ChemTask Number: CHEM02425

CHEMICAL STORAGE REPORT

ANTHRAQUINONE

2-064-CS-7

February 24, 1997

CAS No.: 84-65-1	Amount Received: 80.128 kg
Battelle Log No.: 2-064-CS-7	Battelle Receipt Date: 1/16/97
NTP ChemTask No.: CHEM02425	Received From: Battelle-Columbus
Program Supported: CAR	Lot No.: 5893
Appearance: Yellow powder	Last Analyzed Purity (11/27/96): 100.0%
	Storage Conditions: Room temperature

Anthraquinone (80.128 kg) was received from Battelle-Columbus on January 16, 1997. It was received in 38 amber glass bottles at room temperature. The lot number was 5893. The chemical was stored at room temperature.

Prepared By:

Donna Browning
Task Leader

Approved By:

Steven Graves
Principal Investigator

Submitted to:

Dr. Cynthia S. Smith
National Institute of Environmental Health Sciences
P.O. Box 12233
111 T.W. Alexander Dr.
Research Triangle Park, NC 27709-2233

ATTACHMENT 1c

Battelle
. . . Putting Technology To Work

BATTELLE-CS
Chemistry Support Services for the NTP
NIH Contract No. N01-ES-55395
Battelle Project: G002840-GN
NTP ChemTask Number: CHEM02424

CHEMICAL STORAGE REPORT

ANTHRAQUINONE

2-064-CS-6

February 24, 1997

CAS No.: 84-65-1	Amount Received: 100 g
Battelle Log No.: 2-064-CS-6	Battelle Receipt Date: 1/16/97
NTP ChemTask No.: CHEM02424	Received From: Battelle Columbus Toxicology
Program Supported: CAR	Lot No.: 5893
Appearance: Yellow powder	Last Analyzed Purity (11/27/96): 100.0%
	Storage Conditions: Frozen (≤-20°C)

Anthraquinone (100 g) was received from Battelle Columbus Toxicology on January 16, 1997. It was received frozen in an amber glass bottle. The lot number was 5893. The chemical was stored at ≤-20°C.

Prepared By:

Donna Browning
Task Leader

Approved By:

Steven Graves
Principal Investigator

Submitted to:

Dr. Cynthia S. Smith
National Institute of Environmental Health Sciences
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84-65-1

ATTACHMENT 1d

Battelle
. . . Putting Technology To Work

BATTELLE-CS

Chemistry Support Services for the NTP
NIH Contract No. N01-ES-55395
Battelle Project: G002840-GN
NTP ChemTask Number: CHEM04174
CAS No.: 84-65-1

CHEMICAL STORAGE REPORT

ANTHRAQUINONE

4-064-CS-41

February 2, 1999

CAS No.: 84-65-1	Amount Received: ~1395.3 g
Battelle Log No.: 4-064-CS-41	Battelle Receipt Date: 1/5/99
NTP ChemTask No.: CHEM04174	Received From: Battelle Columbus
Program Supported: CAR	Lot No.: 5893
Appearance: Yellow powder	Last Analyzed Purity (BCR, 11/19-11/20/98): 99.4 % relative purity
	Storage Conditions: Room temperature (~25°C)

One 80-ounce amber glass bottle nominally containing a total of 1,395.3 g of anthraquinone was received from Battelle Columbus on January 5, 1999. It was received and subsequently stored at room temperature. The Lot Number was 5893.

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Steven Graves
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ATTACHMENT 2

Battelle
The Business of Innovation

BATTELLE-SHIP

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 Burdak

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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