

5 Anthraquinone to NIH

CHEMICAL PRODUCTS CORPORATION

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November 15, 2002

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

Subject: Submission of Information Quality Request For Correction - NTP Summary of Draft TR-494 at <http://ntp-server.niehs.nih.gov/htdocs/LT-studies/tr494.html>

Dear Madam or Sir;

This letter is an Information Quality Request For Correction submitted by Chemical Products Corporation (CPC), a Georgia corporation located in Cartersville, Georgia. CPC produces Anthraquinone aqueous suspensions for use by the North American paper industry as a catalyst in the Kraft pulping process. CPC's affiliate, Chemical Products Technologies, LLC markets these Anthraquinone aqueous suspensions to the North American paper industry.

CPC requests that the Abstract of Draft Technical Report TR-494, Toxicology and Carcinogenesis Studies of Anthraquinone (CAS No. 84-65-1) in F344/N Rats and B6C3F1 Mice (Feed Studies) be withdrawn from the NTP web site and all other locations where it is available to the public. We request that it be replaced with a statement explaining that a contaminant in the Anthraquinone sample tested by NTP confounded the results of the testing and that Draft TR-494 will be withdrawn, rewritten, and resubmitted for peer review.

Copies of three letters from Dr. Kenneth Olden to CPC are enclosed herewith. In response to information submitted to him by CPC, Dr. Olden initiated laboratory testing to determine the identity of an unidentified contaminant in the NTP Anthraquinone sample employed in the TR-494 studies, committed to conducting mutagenicity tests on pure Anthraquinone samples, and stated that the results of this further work would be incorporated into a rewritten TR-494.

CPC applauds Dr. Olden's obvious commitment to sound science at NTP. We are grateful that he was willing to objectively consider the information we supplied to him and that he took decisive action when he determined that action was warranted. In this regard, we believe that he is uniquely laudable. However, it has been more than 2 years since CPC received Dr. Olden's letters. During this time the Abstract of TR-494 on the NTP web site has not been modified to give the public any indication that there are highly significant unresolved issues concerning the conclusions of Draft TR-494.

We submit that the Abstract of Draft TR-494 is known to NTP to contain information which does not conform to the Guidelines for Ensuring the Quality of Information Disseminated to the Public.

The Anthraquinone sample tested in the long term NTP studies reported in Draft TR-494 contains a mutagenic contaminant which has rendered the Draft TR-494 report and the peer review of that Draft report invalid. The Draft TR-494 stated, "Anthraquinone was mutagenic in *Salmonella typhimurium* strains TA98 and TA100 with and without S9 metabolic activation enzymes." This statement was acknowledged by Dr. Kenneth Olden to be incorrect in his letter dated September 26, 2000 wherein he states, "We agree that there is still considerable uncertainty about the mutagenicity of anthraquinone". The peer review of Draft TR-494 was conducted based upon the incorrect assumption that Anthraquinone was conclusively known to be mutagenic. In fact, a preponderance of published data demonstrate that Anthraquinone is not a mutagen.

The following information about this Request For Correction is provided following the specific format outlined in the "Responsibility of the Complainant" section of the HHS Guidelines for Ensuring the Quality of Information Disseminated to the Public.

- A detailed description of the specific material that is proposed for correction, including where the material is located, i.e., the publication title, date, and publication number, if any, or the web site and web page address (URL), or the presentation, presenter, date and mode of delivery; - The material proposed for correction is the Abstract of Draft Technical Report TR-494 Toxicology and Carcinogenesis Studies of Anthraquinone (CAS No. 84-65-1) in F344/N Rats and B6C3F1 Mice (Feed Studies), Report date May 1999, NIH Publication Number 99-3953, found on the NTP web site under "long term studies" at <http://ntp-server.niehs.nih.gov/htdocs/LT-studies/tr494.html>, and possibly elsewhere within NTP.

- the specific reasons for believing that the information does not comply with OMB, HHS, or NIH guidelines and is in error, and supporting documentation, if any: - In reviewing all of the information available concerning Anthraquinone, including the Draft TR-494, CPC discovered important discrepancies between the statements in TR-494 and other published information. Specifically, many Anthraquinone samples had been tested for mutagenicity in *Salmonella typhimurium* and had been determined not to be mutagenic; this fact was not fully considered in TR-494.

CPC learned that NTP had not actually tested the Anthraquinone sample employed in TR-494 for mutagenicity. CPC obtained a portion of the Anthraquinone retained sample from NTP and submitted it to a respected independent laboratory for mutagenicity testing along with three other samples of Anthraquinone.

Of four samples of Anthraquinone submitted for testing, only the NTP TR-494 sample was mutagenic in *Salmonella typhimurium* strains TA98 and TA100. CPC submitted this information to Dr. Kenneth Olden along with information about the

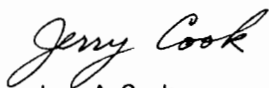
contents of EPA's TSCA file for Anthraquinone which describes a sample of Anthraquinone found to be mutagenic; this sample was purified to remove trace nitroanthracene contamination and was found not to be mutagenic on retesting. In response to these submissions by CPC, Dr. Kenneth Olden acknowledged that the mutagenicity of pure Anthraquinone was in question.

- Suggested recommendations for what corrective action(s) should be taken: - CPC requests that the Abstract of Draft TR-494 be immediately withdrawn from the NTP web site and replaced with a statement that a mutagenic contaminant in the Anthraquinone sample tested by NTP was subsequently identified thus confounding the conclusions of the draft report and invalidating the peer review of Draft TR-494 conducted in May, 1999 before the presence of the contaminant became known.

- A description of how the person requesting the correction is affected by the information error: - CPC and Chemical Products Technologies, LLC are adversely affected by reduced sales of their Anthraquinone suspension product to the North American paper industry. We believe that the North American paper industry has been reluctant to realize the increased pulp recovery benefits of Anthraquinone use because of the conclusions of NTP Draft Report TR-494 and concern about possible adverse consequences of employing a catalyst in the Kraft pulping process which has been alleged to have carcinogenic activity in rats and mice.

- Complete contact information for the requester, including name, mailing address, telephone number, e-mail address, and organizational affiliation, if any, - This letter is submitted by Jerry A. Cook, Technical Director, Chemical Products Corporation, P.O. Box 2470, Cartersville, GA 30120-1692, telephone number 770-382-2144 extension 272, email JACook@CPC-Ga.com who is affiliated with Chemical Products Corporation and Chemical Products Technologies, LLC.

Sincerely,



Jerry A. Cook
Technical Director

Enclosures: Dr. Olden letter dated August 21, 2000
Dr. Olden letter dated September 26, 2000
Dr. Olden letter dated October 26, 2000



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of
Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, N.C. 27709

August 21, 2000

Mr. Jerry A. Cook
Technical Director
Chemical Products Corporation
Cartersville, Georgia 30120

Dear Mr. Cook:

Thank you for your letter of July 25 concerning Technical Report Number 494 on the Toxicology and Carcinogenesis Studies of Anthraquinone.

We are unaware of any factual errors in the draft of Technical Report Number 494; presumably you are referring to the 0.1% contaminant in the sample of anthraquinone used for this study, which was not identified at the time the study was conducted. However, to ensure that the report accurately reflects the test material that was evaluated, we are currently in the process of determining that the sample used in our studies did indeed contain one or more nitroanthracene isomers. The identity of the isomers is also being determined.

Since anthraquinone prepared by the oxidation of anthracene might contain nitroanthracene isomers as contaminants, the method used to manufacture the test sample is also being determined. Please be assured that the final version of Technical Report Number 494 will contain this information, and will discuss its potential impact on the interpretation of the results of the anthraquinone study.

Sincerely yours,

Kenneth Olden, Ph.D.
Director

cc:
Dr. Richard Irwin



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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P.O. Box 12233
Research Triangle Park, N.C. 27709

September 26, 2000

Mr. Jerry A. Cook
Technical Director
Chemical Products Corporation
Post Office Box 2470
Cartersville, Georgia 30120

Dear Mr. Cook:

Thank you for your letter of August 24 and for the information contained therein. We agree that there is still considerable uncertainty about the mutagenicity of anthraquinone, its metabolites and 9-nitroanthracene. We, therefore, are initiating a series of mutagenicity tests with these compounds using material which has been verified to be 100% pure.

Once again, let me assure you that the results of this testing will be included in the final version of Technical Report 494 along with a complete discussion of their impact on the interpretation of the results.

Sincerely yours,

Kenneth Olden, Ph.D.
Director

cc:
Dr. Richard Irwin



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of
Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, N.C. 27709

October 26, 2000

Mr. Jerry A. Cook
Technical Director
Chemical Products Corporation
Post Office Box 2470
Cartersville, Georgia 30120

Dear Mr. Cook:

Thank you for the copy of the report from BioReliance on your most recent mutagenicity studies. As I stated in my previous letter, we have initiated a series of mutagenicity tests on anthraquinone and its metabolites. The results of these studies and other pertinent information on the purity of the anthraquinone sample used in our two-year study will be included in the final version of Technical Report 494 along with a discussion of the impact of this information on the interpretation of the two-year study.

Sincerely yours,

A handwritten signature in cursive script that reads "Ken Olden".

Kenneth Olden, Ph.D.
Director

cc:
Dr. Richard Irwin