



Mary
NATIONAL TOXICOLOGY PROGRAM
Department of Health and Human Services

NATIONAL INSTITUTE OF
ENVIRONMENTAL HEALTH SCIENCES
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P.O. BOX 12233
RESEARCH TRIANGLE PARK, NC 27709-2233

August 14, 2003

John O. Snyder
Executive Director
Styrene Information and Research Center
1300 Wilson Boulevard, Suite 1200
Arlington, Virginia 22209

Dear Mr. Snyder:

I am writing in response to your letter dated June 10 to Dr. C. W. Jameson, Head of the Report of Carcinogens, sent on behalf of the Styrene Information and Research Center, Inc. (SIRC). SIRC requests the technical correction of information about styrene-7,8-oxide found in the press release and factsheet announcing publication of the Tenth Edition of the Report on Carcinogens. This request was submitted pursuant to a concern that information in these documents about the use of styrene-7,8-oxide is incorrect and does not comply with the National Institutes of Health *Guidelines for Ensuring the Quality of Information Disseminated to the Public*. We appreciate you bringing this issue to our attention, and I would like to inform you about what action we are taking to address your concern.

We agree that information about the use of styrene-7,8-oxide in the press release and factsheet for the Tenth Edition of the Report on Carcinogens is incorrect and have edited the entry in both documents to read as follows:

Styrene-7,8-oxide, is used primarily in the production of styrene glycol and its derivatives, as a reactive diluent in epoxy resins, as a treatment for textiles and fibers, and as a chemical intermediate in the manufacture of such materials as perfumes and surface coatings. It is listed in the report based on sufficient evidence of cancer formation from studies of this chemical in experimental animals.

The revised press release and factsheet will replace the ones previously posted on the National Toxicology Program's Report on Carcinogen web site (<http://ntp-server.niehs.nih.gov/NewHomeRoc/AboutRoC.html>). We anticipate completing this task within 30 days. A copy of each revised document is enclosed for your information.

Page 2 – Mr. John O. Snyder

I would like to let you know that you may appeal our agency's decision in writing or electronically within 30 days of receiving this response. Your request should state the reasons for your appeal. It does not need to reference a tracking number. The request may be sent electronically to InfoQuality@od.nih.gov or in hardcopy to the Associate Director for Communications, Office of the Director, National Institutes of Health, Building 1, Room 344, 9000 Rockville Pike, Bethesda, Maryland 20892. If the appeal is sent in hardcopy, please clearly mark the appeal and outside envelope with the phrase "Information Quality Appeal."

Thank you again for bringing this issue to our attention.

Sincerely,

/s/

Christopher J. Portier, Ph.D.
Associate Director

Enclosure

cc:

Dr. C.W. Jameson



FOR RELEASE:
Dec. 11, 2002
NIEHS PR # 02-11

NIEHS/NTP Contact: Bill Grigg
(301) 402-3378
grigg@niehs.nih.gov

New Federal Report on Carcinogens Lists Estrogen Therapy, Ultraviolet, Wood Dust

The federal government today published its biennial *Report on Carcinogens*, adding steroidal estrogens used in estrogen replacement therapy and oral contraceptives to its official list of "known" human carcinogens. This and 15 other new listings bring the total of substances in the report, "known" or "reasonably anticipated" to pose a cancer risk, to 228.

This, the tenth edition of the report, was forwarded to Congress and released to the public today by the Department of Health and Human Services. It was prepared by the National Toxicology Program, an arm of the HHS located at the National Institute of Environmental Health Sciences, one of the National Institutes of Health. The reports are published every two years after lengthy study and scientific reviews by three successive expert panels of government and non-government scientists.

In a statement releasing the report, HHS Secretary Tommy Thompson today thanked "the hundreds of scientists who have contributed to this report through their original research or their careful reviews of these important studies. The public is well served by this dispassionate report that helps all of us ensure that the American public is made aware of potential cancer hazards."

The tenth report newly lists the group of hormones known as steroidal estrogens as "known human carcinogens." A number of the individual steroidal estrogens were already listed as "reasonably anticipated carcinogens" in past editions, but this is the first report to so list all these hormones, as a group. As with all the other medications listed, the *Report on Carcinogens* does not address or attempt to balance potential benefits of use of these products.

Also newly listed as "known" causes of cancer in humans are broad spectrum ultraviolet radiation, whether generated by the sun or by artificial sources; wood dust created in cutting and shaping wood; nickel compounds and beryllium and its compounds commonly used in industry. Beryllium and beryllium compounds are not new to the list but was previously listed as "reasonably anticipated to be a human carcinogen."

The report is mandated by Congress as a way for the government to help keep the public informed about substances or exposure circumstances that are "known" or are "reasonably anticipated" to cause human cancers. The report also identifies current regulations concerning these listings in an attempt to address how exposures have been reduced.

The report makes a distinction between "known" human carcinogens, where there is sufficient evidence from human studies and "reasonably anticipated" human carcinogens, where there is either limited evidence of carcinogenicity from human studies and/or sufficient evidence of carcinogenicity from experimental animal studies.

The report does not assess the magnitude of the carcinogenic risk, nor does it address any potential benefits of listed substances such as certain pharmaceuticals. Listing in the report does not establish that such substance presents a risk to persons in their daily lives. Such formal risk assessments are the responsibility of Federal, State, and local health regulatory agencies.

Newly listed as known human carcinogens are:

- **Steroidal estrogens**
These are a group of related hormones that control sex and growth characteristics and are commonly used in estrogen replacement therapy to treat symptoms of menopause and in oral contraceptives. The report cites data from human epidemiology studies that show an association between estrogen replacement therapy and a consistent increase in the risk of endometrial cancer (cancer of the endometrial lining of the uterus) and a less consistent increase in the risk of breast cancer.
As for the other common use for steroidal estrogens, the report says the evidence suggests estrogen-containing oral contraceptives may be associated with an increased risk of breast cancer but may protect against ovarian and endometrial cancers.
- **Broad Spectrum Ultraviolet Radiation (UVR)**
UVR is produced by the sun as part of solar radiation and by artificial sources such as sun lamps and tanning beds, in medical diagnosis and treatment procedures, and in industry for promoting polymerization reactions. The report cites data indicating a cause-and-effect relationship between this radiation and skin cancer, cancer of the lip and melanoma of the eye. The report goes on to say that skin cancers are observed with increasing duration of exposure and for those who experience sunburn. The individual components of UVR, which includes ultraviolet A, ultraviolet B and ultraviolet C radiation, are listed in the report, not as “known”, but as “reasonably anticipated” human carcinogens – See below.
- **Wood dust**
Listed as a “known human carcinogen” in this report, wood dust is created when machines and tools cut, shape and finish wood. Wood dust is particularly prevalent in sawmills, furniture manufacture and cabinet making. According to the report, unprotected workers have a higher risk of cancers of the nasal cavities and sinuses.
- **Nickel compounds**
Used in many industrial applications as catalysts and in batteries, pigments and ceramics, the report newly lists nickel compounds as “known” human carcinogens based on studies of workers showing excess deaths from lung and nasal cancers and on their mechanisms of action.

One group of substances was upgraded from “reasonably anticipated” to “known” human carcinogen:

- **Beryllium and beryllium compounds**
About 800,000 workers are exposed via inhalation of beryllium dust or dermal contact with products containing beryllium. Workers with the highest potential for exposure include beryllium miners, beryllium alloy makers and fabricators, ceramics workers, missile technicians, nuclear reactor workers, electric and electronic equipment workers, and jewelers. According to data cited in the report, they have higher risks for lung cancer which increase with their exposures and which cannot be explained by tobacco smoking or other occupational exposures.

Twelve substances or groups of substances are newly listed as “reasonably anticipated to be human carcinogens”:

IQ, or 2-amino-3-methylimidazo[4,5-f]quinoline, which is formed during direct cooking with high heat of foods such as meats and eggs and also found in cigarette smoke, is listed as “reasonably anticipated to be a human carcinogen” based on long-term animal studies. The report also states there are several published human studies that suggest there is an increased risk for breast and colorectal cancers related to consumption of broiled or fried foods that may contain IQ and/or other similar compounds formed during cooking at high temperatures.

2,2-bis-(Bromomethyl)-1,3-propanediol (technical grade), a flame retardant chemical used to make some polyester resins and rigid polyurethane foam is listed as “reasonably anticipated” based on long-term animal feeding studies.

Ultraviolet A, Ultraviolet B and Ultraviolet C Radiation, listed as “reasonably anticipated to be human carcinogens” because, according to the report, animal studies show a cause-and-effect

relationship between exposure to each of these wavelength groups of broad spectrum ultraviolet radiation (UVR) and skin cancer. The report points out that the data on skin cancer in humans for these different wavelengths of UVR are limited, because it has been impossible to determine if the people in these studies were exposed to "pure" individual components of UVR or, as is more likely the case, to "mixtures" of the different components thus making it impossible to say that the observed skin cancers were due only to one of the "pure" individual components.

Chloramphenicol. An antibiotic with restricted use in the US because it can cause fatal blood disorders, is listed in the report as "reasonably anticipated to be a human carcinogen". The report says the listing is based on limited evidence from human studies that showed an increased cancer risk for the occurrence of leukemia after chloramphenicol therapy.

2,3-Dibromo-1-propanol a chemical used as an intermediate in the production of flame-retardants, insecticides, and pharmaceuticals, is listed in the report as "reasonably anticipated to be a human carcinogen" based on strong evidence of cancer formation from skin painting study in experimental animals.

Dyes metabolized to 3,3'-dimethoxybenzidine are dyes that have been used to color leather, paper, plastic, rubber and textiles and are listed in the report because they are metabolized to 3,3'-dimethoxybenzidine, which is "reasonably anticipated to be a human carcinogen".

Dyes metabolized to 3,3'-dimethylbenzidine are dyes that have been used in printing textiles, in color photography and as biological stains and are listed in the report because these dyes are metabolized to 3,3'-dimethylbenzidine, which is "reasonably anticipated to be a human carcinogen".

Methyleugenol, occurs naturally in oils, herbs and spices and is used in smaller amounts in its natural or synthetic form in flavors, insect attractants, anesthetics and sunscreens. It is listed in the report based on sufficient evidence of cancer formation from oral studies of this chemical in experimental animals.

Metallic nickel, this metal is used mainly in alloys with most exposures by inhalation or skin contact in the workplace. (It should be noted that metallic nickel is not contained in the nickel coin.) It is listed in the report based on sufficient evidence of cancer formation from studies of this chemical in experimental animals.

Styrene-7,8oxide, is used primarily in the production of styrene glycol and its derivatives, as a reactive diluent in epoxy resins, as a treatment for textiles and fibers, and as a chemical intermediate in the manufacture of such materials as perfumes and surface coatings. It is listed in the report based on sufficient evidence of cancer formation from studies of this chemical in experimental animals. (Text corrected July 22, 2003).

Vinyl bromide, which has been used in polymers in making fabrics for clothes and home furnishings, as well as in leather and metal products, drugs and fumigants. It is listed in the report based on sufficient evidence of cancer formation from studies of this chemical in experimental animals.

Vinyl fluoride, which is used in making polyvinyl fluoride and related weather-resistant fluoropolymers. Support for the listing came from inhalation studies in experimental animals. It is listed in the report based on sufficient evidence of cancer formation from studies of this chemical in experimental animals.

The report is immediately accessible at <http://ntp-server.niehs.nih.gov>

For available hard copies, email ehponline@niehs.nih.gov, visit <http://www.ehponline.org> or write Environmental Health Perspectives, Attn: Order Processing, 1001 Winstead Drive, Suite 355, Cary, NC 27513. Requests for hard copies may also be faxed to (919) 678-8696.

Fact sheets – “What is the Report On Carcinogens?” and “Q and A on the RoC” as well as background documents for the new listings – can be accessed at <http://ntp-server.niehs.nih.gov/>

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The URL for this press release is <http://www.niehs.nih.gov/oc/news/10thrc.htm>

Tenth Edition of the Report on Carcinogens



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Toxicology
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*The report is immediately accessible at <http://ntp-server.niehs.nih.gov>
(select Report on Carcinogens (RoC)).*

Technical inquiries should be directed to the NTP Liaison and Scientific Review Office at: telephone (919) 541-0530, fax (919) 541-0295, e-mail: liaison@starbase.niehs.nih.gov

Press inquiries should be directed to Mr. Bill Grigg at: telephone (301) 402-3378, fax (301) 496-0563, e-mail: grigg@niehs.nih.gov

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