Cancer Prevention Coalition

Fighting for a safer environment at home, in the community and at work

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September 26, 1995

Commissioner David Kessler (By fax and mail)
Food and Drug Administration
5600 Fischer Lane
Rockville, MD 20857

Dear Commissioner Kessler,

In a September 21 press conference in Washington D.C., the Cancer Prevention Coalition (CPC) along with Ralph Nader, released a "Dirty Dozen" list of consumer products: cosmetics and toiletries; foods and beverages; and also household products.

The list detailed information on a wide range of undisclosed toxic and carcinogenic ingredients and contaminants in foods and summarized undisclosed information on their hazards, and also on the hazards of cosmetics.

Responding to the "Dirty Dozen" list, FDA spokeswoman Betsy Adams is quoted in a 9/21 Reuters news story as saying, "The Food and Drug Administration believes that all these products are generally safe under conditions for normal use."

In further clarification of FDA's position, I would appreciate your confirmation that there is no FDA requirement for any pre-market safety testing of cosmetics. Could you also confirm that there is no requirement for labelling cosmetics and food for any known risks relating to their content of toxic and carcinogenic ingredients and contaminants (with the exception of saccharin in diet foods).

Would you also comment on the fact that FDA has still taken no action to require disclosure of the contamination of cosmetics with carcinogenic nitrosamines, nor of any warning of their cancer risks in spite of the following considerations:

- In 1979 (FR April 10, 1979), FDA published a notice calling for the cosmetic industry to remove triethanolamine (TEA) and diethanolamine (DEA), which interact with nitrite preservatives or contaminants to form carcinogenic nitrosamines.

- Following pressure by the German Federal Health Office in 1987, the German cosmetic industry phased out their use of DEA and TEA, and thereby reduced cancer risks of these products.

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- In 1988, FDA issued a "Progress Report" warning of the presence of nitrosamines in 37 percent of cosmetics tested.

I enclose the following Citizen Petitions: with regard to risks of ovarian cancer following the use of talcum powder (filed 11/17/94); and with regard to risks of childhood cancer following the consumption of nitrite-hot dogs (filed 4/27/95). In these petitions, CPC details the scientific basis of these concerns. Apart from formal acknowledgement, we have not yet received any response to these petitions. Would you also kindly explain what are the "conditions of normal use" which would ensure the safety of cosmetic talc and nitrite-hot dogs.

I await a reply at your early convenience.

Sincerely,

Samuel S. Epstein, MD
Chairman, Cancer Prevention Coalition

cc. Ralph Nader

Citizen Petition Seeking Labeling of Nitrite-Preserved Hot Dogs For Childhood Cancer Risk

April 25, 1995

David A. Kessler, M.D.
Commissioner
Food and Drug Administration, Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

The undersigned submits on behalf of the Cancer Prevention Coalition, Inc. (CPC), Samuel S. Epstein, M.D., Chair, and on behalf of the Center for Constitutional Rights, Michael Deutsch, Esq., Legal Director. This citizen petition is based on accumulating scientific information on excess risks of childhood brain tumors and leukemia from the consumption of hot dogs containing nitrite preservatives.

The undersigned submits this petition under 21 U.S.C. 321 (n), 361, 362, and 371 (a); and 21 CFR 740.1, 740.2 of 21 CFR 10.30 of the Federal Food, Drug, and Cosmetic Act to request the Commissioner of the Food and Drug Administration (FDA) to label hot dogs that contain nitrites with a cancer risk warning.

A. Agency Action Requested

This petition requests that FDA take the following action:

(1) Immediately require nitrite-containing hot dogs to be labelled with warnings such as "hot dogs containing nitrites have been shown to pose risks of childhood cancer."

(2) Pursuant to 21 CFR 10.30 (h) (2), a hearing at which time we can present our scientific evidence.

B. Statement of Grounds

Nitrites are widely used as preservatives in hot dogs, besides other meat products. Nitrites combine with amines naturally present in meat to form carcinogenic N-nitroso compounds. [1,2,3,4] N-nitrosodimethylamine has been identified in nitrite-preserved meat products.[5,6] There is overwhelming evidence on the carcinogenicity of N-nitrosodimethylamine in animal experiments.[7] Furthermore, epidemiologic evidence has associated N-nitroso carcinogens with cancer of the oral cavity, urinary bladder, esophagus, stomach and brain.[8,9,10]

There is substantial evidence on the risks of childhood cancer from the consumption of meats

containing nitrites.[11,12,13] In 1982, Preston-Martin, *et al.* found that "consumption during pregnancy of meats cured with sodium nitrite has been associated with development of brain tumors in the offspring."[14]

Recent case-control studies have confirmed the risks of cancer from consumption of hot dogs. Eating many hot dogs by children, as well as maternal hot dog consumption during pregnancy, has been shown to be associated with brain cancer and leukemia in children. [15,16,17]

Bunin, *et al.* studied children who were diagnosed with brain cancer before age six, between 1986 and 1989. Of 53 foods and beverages and three alcoholic beverages consumed by mothers during pregnancy, only hot dogs were associated with an excess risk of childhood brain tumors.[18]

Sarusua and Savitz studied 234 childhood cancer cases in Denver and found a strong association between the consumption of hot dogs and brain cancer. Children born to mothers who consumed hot dogs one or more times per week during pregnancy had approximately double the risk of developing brain tumors. Children who ate hot dogs one or more times per week were also at higher risk of brain cancer. In addition, children who ate hot dogs and took no vitamins, which retard the formation of N-nitroso carcinogens, were more strongly associated with both acute lymphocytic leukemia (ALL) and brain cancer.[19] Sarusua and Savitz concluded:

> "The results linking hot dogs and brain tumors (replicating an earlier study) and the apparent synergism between no vitamins and meat consumption suggest a possible adverse effect of dietary nitrites and nitrosamines."[20]

Peters, *et al.* studied the relationship between the intake of certain foods and the risk of leukemia in children from birth to age 10 in Los Angeles County between 1980 and 1987. The researchers found that children who ate 12 or more hot dogs per month had approximately nine times the normal risk for developing childhood leukemia. A strong risk for childhood leukemia also existed for those children whose fathers' intake of hot dogs was 12 or more per month.[21] Peters, *et al.* concluded:

> "Our results provide evidence for an association between consumption of hot dogs and risk of childhood leukemia. Adjustments for all factors thought to be potential confounders did not affect these associations. Independent risks were associated with both children's and fathers' consumption. . .The findings, if correct, suggest that reduced consumption of hot dogs could reduce leukemia risks, especially in those consuming the most. "[22]

These findings are of particular significance considering a 38 percent increase in the incidence of brain and nervous system cancers in children from 1973-1991.[23] Brain tumors account for about one in five childhood cancers.[24]

C. Claim for Categorical Exclusion

A claim for categorical exclusion is asserted pursuant to 21 CFR 25.24 (a) (11).

D. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

This petition is submitted by:

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Signature of petitioner Date

Signature of petitioner Date

Council to the Cancer Prevention Coalition:

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Endnotes

1. Lijinsky W, Epstein, S. "Nitrosamines as environmental carcinogens," *Nature* 225 (5227):21-12, 1970.

2. Anonymous. "Nitrates and nitrites in food," *Medical Letter on Drugs & Therapeutics*. 16(18): 75-6, 1974

3. Issenberg P. "Nitrite, nitrosamines, and cancer," Federation Proceedings 35(6): 1322-1326, 1976.

4. IARC, "Monograph on the evaluation of the carcinogenic risk of chemicals to humans: some N-nitroso compounds," 17:36-38, 136-144, 1978.

5. Ibid.

6. Issenberg P, "Nitrite, nitrosamines, and cancer," Federation Proceedings 35 (6): 1322-1326, 1976.

7. IARC, "Monograph on the evaluation of the carcinogenic risk of chemicals to humans: some N-nitroso compounds."

8. Fraser P et al "Nitrate and human cancer: A review of the evidence." *Int. J. Epidemiol*, 9: 3-11, 1980.

9. Reed PI. "The role of nitrosamines in cancer formation." *Biblthca. Ntur. Dieta* 37: 130-8, 1986.

10. Craddock VM, "Nitrosamines, food and cancer: assessment in Lyon," *Fd Chem. Toxic.* 28(1):63-65, 1990.

11. Preston-Martin S *et al.* "N-nitroso compounds and childhood brain tumors: A case-control study." *Cancer Res.* 1982; 42: 5240-5

12. Bunin GR, *et al.* "Relation between maternal diet and subsequent primitive neuroectodermal brain tumors in young children." *N Engl J Med* 329:536-41, 1993.

13. Bunin GR, *et al.* "Maternal diet and risk of astrocytic glioma in children: a report from the children's cancer group (United States and Canada)," *Cancer Causes & Control* 5: 177-87, 1994.

14. Preston-Martin S. *et al* "N-nitroso compounds and childhood brain tumors: A case control study."

15. Bunin GR, *et al*, "Maternal diet and risk of astrocytic glioma in children."

16. Sarasua S, Savitz D. "Cured and broiled meat consumption in relation to childhood cancer: Denver, Colorado (United States)," *Cancer Causes & Control* 5:141-8, 1994.

17. Peters J, *et al* "Processed meats and risk of childhood leukemia (California, USA)" *Cancer Causes & Control* 5: 195-202, 1994.

18. Bunin GR, *et al*, "Maternal diet and risk of astrocytic glioma in children."

19. Sarasua S, Savitz D. "Cured and broiled meat consumption in relation to childhood cancer."

20. Ibid

21. Peters J, Preston-Martin S, London S, *et al.* "Processed meats and risk of childhood leukemia (California, USA)"

22. Ibid.

23. Reis L et al. (eds), *SEER Cancer Statistics Review, 1973-1991: Tables and Graphs*, National Cancer Institute. NIH Pub. No. 94-2789, Bethesda, MD, 1994, p. 428.

24. Bunin, GR, *et al*, "Maternal diet and risk of astrocytic glioma in children," 177-87.

Citizen Petition Seeking Carcinogenic Labeling on all Cosmetic Talc Products.

17 November 1994

David A. Kessler, M.D.
Commissioner
Food and Drug Administration, Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

The undersigned submits on behalf of the Cancer Prevention Coalition, Inc. (CPC), Samuel S. Epstein, M.D., Chair and National Advisor of the Ovarian Cancer Early Detection and Prevention Foundation (OCEDPF), Nancy Nehls Nelson, member of the Ovarian Cancer Early Detection and Prevention Foundation, Peter Orris, M.D. and Quentin Young, M.D. This citizen petition is based on scientific papers dating back to the 1960s which warn of increased cancer rates resulting from frequent exposure to cosmetic grade talc.

The undersigned submits this petition under 21 U.S.C. 321 (n), 361, 362, and 371 (a); and 21 CFR 740.1, 740.2 of 21 CFR 10.30 of the Federal Food, Drug, and Cosmetic Act to request the Commissioner of Food and Drugs to require that all cosmetic talc products bear labels with a warning such as "Talcum powder causes cancer in laboratory animals. Frequent talc application in the female genital area increases the risk of ovarian cancer."

A. AGENCY ACTION REQUESTED

This petition requests that FDA take the following action:

(1) Immediately require cosmetic talcum powder products to bear labels with a warning such as "Talcum powder causes cancer in laboratory animals. Frequent talc application in the female genital area increases the risk of ovarian cancer."

(2) Pursuant to 21 CFR 10.30 (h)(2), a hearing at which time we can present our scientific evidence.

B. Statement of Grounds

Ovarian cancer is the fourth deadliest women's cancer in the U.S., striking approximately 23,000 and killing approximately 14,000 women this year. Ovarian cancer is very difficult to detect at the early stages of the disease, making the survival rate very low. Only three percent of ovarian cancer cases can be attributed to family history.[1] One of the avoidable risk factors for ovarian cancer is the daily use of talcum powder in the genital area.[2]

Research done as early as 1961 has shown that particles, similar to talc and asbestos particles, can translocate from the exterior genital area to the ovaries in women.[3,4,5] These findings provide support to the unexpected high rate of mortality from ovarian cancer in female asbestos workers.[6,7,8] Minute particles such as talc are able to translocate through the female reproductive tract and cause foreign body reactions in the ovary.

There is a large body of scientific evidence, dating back thirty years, on the toxicity and mineralogy of cosmetic talc products. As early as 1968, Cralley *et al.* concluded:

> All of the 22 talcum products analyzed have a...fiber content...averaging 19%. The fibrous material was predominantly talc but probably contained minor amourts of tremolite, anthophyllite, and chrysotile [asbestos-like fibers] as these are often present in fibrous talc mineral deposits...Unknown significant amounts of such materials in products that may be used without precautions may create an

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[1] SEER Cancer Statistics, 1973-1990.

[2] Harlow BL, Cramer DW, Bell DA, Welch WR. "Perineal exposure to talc and ovarian cancer risk." Obstet Gynecol. 80: 19-26, 1992.

[3] Egli GE, Newton M.. "The transport of carbon particles in the human female reproductive tract." Fertility Sterility. 12: 151-155, 1961.

[4] Venter PF, Iturralde M. "Migration of particulate radioactive tracer from the vagina to the peritoneal cavity and ovaries." S African Med J. 55: 917-919, 1979.

[5] Henderson WJ, Hamilton TC, Baylis MS, Pierrepoint CG, Griffiths K. "The demonstration of migration of talc from the vagina and posterior uterus to the ovary in the rat." Environ Research. 40: 247-250, 1986.

[6] Newhouse ML, Berry G, Wagner JC, Turok ME. "A study of the mortality of female asbestos workers." Brit J Indust Med. 29: 134-141, 1972.

[7] Wignall BK, Fox AJ. "Mortality of female gas mask assemblers." Brit J Industrial Med. 39: 34-38, 1982.

[8] Acheson ED, Gardner MJ, Pippard E, Grime LP. "Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: a 40-year follow-up." Brit J Ind Med. 39: 344-348, 1982.

unsuspected problem.[9]

As a follow-up to previous findings, Rohl, *et al.*, examined 21 samples of consumer talcums and powders, including baby powders, body powders, facial powders and pharmaceutical powders between 1971-1975. (See Appendix I) The study concluded:

> "...cosmetic grade talc was not used exclusively. The presence in these products of asbestiform anthophyllite and tremolite, chrysotile, and quartz indicates the need for a regulatory standard for cosmetic talc...We also recommend that evaluation be made to determine the possible health hazards associated with the use of these products."[10]

Talc is a carcinogen, with or without the presence of asbestos-like fibers. In 1993, the National Toxicology Program published a study on the toxicity of non-asbestiform talc and found *clear evidence of carcinogenic activity.*[11]

Recent cancer research in the United States has found conclusively that frequent talcum powder application in the genital area increases a woman's risk of developing ovarian cancer.[12,13,14,15] Cramer, *et al.*, suggested that talc application directly to the genital area around the time of ovulation might lead to talc particles becoming deeply imbedded in the substance of the ovary and perhaps causing foreign body reaction (granulomas) capable of causing growth of epithelial ovarian tissue.[1617]

Harlow, *et al.*, found that frequent talc use directly on the

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[9] Cralley LJ, Key MM, Groth DH, Lainhart WS, Ligo RM. "Fibrous and mineral content of cosmetic talcum products." Am Industrial Hygiene Assoc J. 29: 350-354, 1968.

[10] Rohl AN, Langer AM, Selikoff IJ, Tordini A, Klimentidis R, Bowes DR, Skinner DL. "Consumer talcums and powders: mineral and chemical characterization." J Toxicol Environ Health. 2: 255-284, 1976.

[11] National Toxicology Program. "Toxicology an dcarcinogenesis studies of talc (CAS Nº 14807-96-6) in F344/N rats and B6C3F1 mice (Inhalation studies)." Technical Report Series Nº 421. September 1993.

[12] Hartge P, Hoover R, Lesher LP, McGowan L. "Talc and ovarian cancer." letter. JAMA. 250: 1844, 1983.

[13] Rosenblatt KA, Szklo M, Rosenshein NB. "Mineral fiber exposure and the development of ovarian cancer." Gynecol Oncol. 45: 20-25, 1992.

[14] Whittemore AS, Wu ML, Paffenbarger RS, Sarles DL, Kampert JB, Grosser S, Jung DL, Ballon S, Hendrickson M. "Personal and environmental characteristics related to epithelial ovarian cancer. II. Exposures to talcum powder, tobacco, alcohol, and coffee." Am J Epidemiol. 1128: 1228-1240, 1988.

[15] Harlow, 1992.

[16] Ibid.

[17] Cramer DW, Welch WR, Scully RE, Wojciechowski CA. "Ovarian cancer and talc: a case control study." Cancer. 50: 372-376, 1982.

genital area during ovulation increased a woman's risk threefold. That study also found:

> "The most frequent method of talc exposure was use as a dusting powder directly to the perineum [genitals]...Brand or generic "baby powder" was used most frequently and was the category associated with a statistically significant risk for ovarian cancer."

In Harlow's report, arguably the most comprehensive study of talc use and ovarian cancer to date, 235 ovarian cancer cases were identified and compared to 239 controls, women with no sign of ovarian cancer or related health problems. Through personal interviews, Harlow, *et al.*, found that 16.7% of the control group reported frequent talc application to the perineum.[18] This percentage is useful in estimating the number of women in the general population exposed to cosmetic talc in the genital area on a regular basis. Harlow, *et al.*, concludes:

> "...given the poor prognosis for ovarian cancer, any potentially harmful exposures should be avoided, particularly those with limited benefits. For this reason, we discourage the use of talc in genital hygiene, particularly as a daily habit."

Clearly, large numbers of women - an estimated 17% - are using cosmetic talc in the genital area and may not be adequately warned of the risk of ovarian cancer from daily use.

C. Claim for Categorical Exclusion

A claim for categorical exclusion is asserted pursuant to 21 CFR 25.24 (a)(11).

D. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition

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[18] Harlow, 1992.

This petition is submitted by:

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Jill A Cashen — 11/17/94
Signature of petitioner — Date

[signature] — 11-17-94
Signature of petitioner — Date

Council to the Cancer Prevention Coalition:
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ROUTING SLIP
GENERATED BY: HF-40
DATE: OCT 02, 1995

FDA CONTROL NUMBER: 95 8994 **TRACER #:** **OS #:**

DATE OF CORRESPONDENCE: 09/26/95 **DATE INTO FDA:** 09/29/95

TO: DAVID A KESSLER HF-1

FROM: SAMUEL S EPSTEIN, CPC, CANCER PREVENTION COALITION

SYNOPSIS: REQUESTS CLARIFICATION OF REGULATION OF COSMETICS AND FOLLOWUP ON TWO CITIZEN PETITIONS

LEAD OFFICE: HFS-1 **HOME OFFICE:** HF-40

CONTACT/PHONE#: NANCY L TILLER 301-443-3428

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COORDINATION:

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REFERRALS FROM HF-40

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HFS-1	PREPARE DIRECT REPLY	10/30/95

REMARKS: PLEASE SEND COPY OF RESPONSE TO NANCY TILLER WITH FDA CONTROL NUMBER INDICATED