



C T Talc. ovarian Cancer A

THE COSMETIC, TOILETRY, AND FRAGRANCE ASSOCIATION

Memorandum

TO: Talc Interested Party Task Force

CJE

E. EDWARD KAVANAUGH
PRESIDENT

FROM: Carol J. Eisenmann, Ph.D., Research Associate

DATE: August 10, 1998

SUBJECT: Dr. Wehner's response to: Daly M, Oubram GI. 1998. Epidemiology and risk assessment for ovarian cancer. *Seminars in Oncology* 25(3):255-264.

Attached is a copy of a letter Dr. Wehner wrote to Dr. Yarbo, an editor of *Seminars in Oncology*. In my conversation with Dr. Wehner, he indicated that *Seminars in Oncology* publishes only invited papers, and that they do not publish comments.

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August 3, 1998

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Dear Dr. Yarbrow:

With reference to our discussion over the telephone earlier today, I would greatly appreciate if my comments could be conveyed to the readers of Seminars in Oncology.

The informative paper "Epidemiology and Risk Assessment for Ovarian Cancer" by Daly and Obrams (Seminars in Oncology, 25: 255-264, 1998) contains a reference (#36, p. 258) to my review paper on biological effects of talc.¹ In referencing my paper the authors state, "some data indicate that talc (deposited on the perineum or in the vagina; APW) may be transported retrograde through the fallopian tubes to the ovaries." This statement is misleading and requires clarification. I made the following points in my review:

- (1) Under normal physiological conditions, the laws of physics make it improbable for inanimate particles with no locomotion of their own, and unable to respond to chemotactic stimuli, to translocate from the perineum or the vagina to the ovaries. These particles would have to breach the formidable barrier presented by the cervix; traverse the uterus; and swim upstream through the fallopian tubes to reach the ovaries. However, translocation can and does occur under certain other than normal physiological conditions, including cases of lacerated cervix; patients in the Trendelenberg position; intended or unintentional manipulation.
- (2) The most frequently cited references in support of particle translocation either are based on flawed experimental protocols in which cases the findings can be plausibly explained by other phenomena, or the results do not really support the position of those who cited them. For details I refer to my review and the original papers referenced therein.
- (3) Our work with neutron-activated talc in cynomolgus monkeys (the animal model most closely resembling the human female in parameters relevant to our investigation) under conditions favoring translocation, and employing state-of-the-art technology, showed that no translocation occurred.²

- (4) What remains to be explained are the observations of Henderson et al and several other authors who found talc particles in or on ovarian tissue. Were these particles deposited by translocation or by contamination during sample collecting and processing? Particles such as talc, carbon black and asbestos fibers are ubiquitous air contaminants. Sample contamination appears to be a possibility, particularly in the light of findings by Lee et al³ and our own work⁴ trying to replicate the observations of Egli and Newton⁵.
- (5) In summary, evidence on particle translocation from the perineum or vagina to the ovaries is contradictory, ambiguous and therefore inconclusive.

Regarding the reported weak statistical link between hygienic use of talc and ovarian cancer, the following observations are relevant.

- . Several epidemiological case-control studies have generated, but not tested, the hypothesis that hygienic talc use presents a risk factor for ovarian cancer. Given the fragility of data from such studies, many epidemiologists consider odds ratios (OR) of 2, or even higher, of no biological significance for human risk assessment. The OR of the studies in question generally were about 1.5 or lower.
- . None of the authors having reported the above-mentioned statistical link has claimed to have established causality.
- . No animal study (including the Lovelace inhalation study conducted for the National Toxicology Program) and no in-vitro experiments have demonstrated that cosmetic talc is carcinogenic or genotoxic.
- . No scientific or regulatory agency anywhere has declared cosmetic talc a carcinogen.
- . The etiology of ovarian cancer is poorly understood. Many agents and factors have been linked with this disease but causality has been established for none of them.
- . In 1994, the International Society of Regulatory Toxicology and Pharmacology in collaboration with the Food and Drug Administration sponsored a public workshop "Talc: Consumer Uses and Health Perspectives" at which all available evidence was examined. At the end of the workshop a panel of experts concluded that hygienic use of talc does not present a risk to the consumer. A couple of epidemiological studies published after the workshop have provided no new information that would require a re-examination of the panel's conclusion.

Finally, an intriguing question begs to be answered. Talc is a recognized fibrogenic agent. If talc particles were able to translocate from the perineum/vagina to the ovaries in sufficient numbers and remain there sufficiently long to cause cancer, would one not expect fibrosis to develop long before cancer? Yet ovarian fibrosis has never been reported in the studies linking hygienic talc use with this disease.

For more on this subject I refer to the special issue of COMMENTS ON TOXICOLOGY on talc (in press).

REFERENCES

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2. Wehner,AP,Weller, RE, Lepel EA: On talc translocation from the vagina to the oviducts and beyond. Food Chem Toxicol 24:329-338,1986
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5. Egli,GE, Newton,M: The transport of carbon particles in the human reproductive tract. Fert Steril 12:151-155,1961

Sincerely



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cc:M.Daly,M.D.