Epidemiological and State of Art Evidence Presented in Cosmetic Talc and Ovarian Cancer Litigation

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INTRODUCTION
In 2016, there will be an estimated 22,280 new cases of ovarian cancer and 14,240 ovarian cancer deaths in the United States alone. Since the 1960’s, there has been speculation that the genital, or perineal, application of talc powder products is associated with ovarian cancer. In 2006, the International Agency for Research on Cancer (IARC) reviewed studies examining perineal powder use and ovarian cancer and classified talc as a possible carcinogen. The proportion of US women ever using talc powder on the perineum was estimated in 2001 to be approximately 40%, and 52% of women reported ever applying cosmetic talc powder to their perineal area.

It is no secret that one of the more recent trends of toxic tort/products liability related litigation involves claims based on this perineal exposure to cosmetic talc products. Courts across the country have seen an upswing of cosmetic talc related filings. Like any litigation, the volume and intensity of this litigation varies among the jurisdictions. St. Louis has seen over a thousand new filings based on ovarian cancer claims based on perineal application of cosmetic talc products. The 2016 plaintiffs' verdicts against Johnson & Johnson in Fox ($72 million including $62 million in punitive damages) and Ristesund ($55 million, $50 million in punitive) have garnered national attention and have provided templates for the litigation in other jurisdictions. On October 27, 2016, a St. Louis jury awarded a $70.1 million verdict against Johnson & Johnson to Deborah Giannecchini of Modesto, California, for ovarian cancer caused by Johnson & Johnson’s Baby Powder product. By noon the next day, Johnson & Johnson shares had dipped 65 cents to $115.27.

Cases filed in six counties in California have resulted in the institution of a coordinated talc/ovarian cancer coordinated docket, where all cases are litigated before a centralized judge.

One of the primary defenses asserted in traditional toxic substance exposure cases involves the presentation of epidemiological scientific studies to show the lack of increased risk of the development of disease associated with certain products, occupations or work practices. A further defense asserted involves the presentation of the existing knowledge at the time of manufacture of the product or exposure of the plaintiff as evidence of the “state of the art,” relevant to the standard of care or the imposition of punitive damages.

With the onset of this new wave of civil filings related to cosmetic talc and ovarian cancer, new areas of epidemiological and “state of the art” evidence are being investigated, compiled and presented to juries in these cases.

EARLY CLAIMS OF ASSOCIATION BETWEEN TALC AND OVARIAN CANCER
The primary proposed mechanism linking perineal powder use to ovarian cancer is an inflammatory response. In ovarian cancer trials, plaintiffs claim that talc particulates from perineal application have been shown to migrate to the ovaries, disrupting the surface ovarian epithelial tissue leading to entrapment of the talc particles within inclusion cysts.

According to plaintiffs’ attorneys, research done as early as 1961 has shown that particles, similar to talc, can translocate from the exterior genital area to the ovaries in women.
In 1967, a study by the Grahams highlighted the similarity of ovarian cancer and mesothelioma. This study claimed that the intraperitoneal injection of asbestos produced epithelial changes in the ovaries of guinea pigs and rabbits, which were “similar to those seen in patients with early ovarian cancer.” Graham claimed that “these observations are compatible with the thesis that asbestos is an etiologic factor in ovarian cancer.”

The first report that suggested an association between talc and ovarian cancer was published by W.J. Henderson in Cardiff, Wales in 1971. That summary of case reports described talc particles “deeply embedded” in 10 of 13 ovarian tumors, 12 of 21 cervical tumors, one primary carcinoma of the endometrium and 5 of 12 “normal” ovaries from women with breast cancer. While admittedly not a epidemiological study using controls, In the Berg case, Dr. Cramer opined that this is the “The first study to suggest a possible link between ovarian cancer and talc.”

In 1977, Lancet published an editorial stating that skepticism about the 1971 Henderson report was “well-founded” since there had been no confirmatory evidence in the six subsequent years. Lancet described standards promulgated by the “major” talc manufacturers that ensure that cosmetic grade talc would not be contaminated by fibrous minerals and concluded that “there is no reason to believe that normal consumer exposure to cosmetic talc has in the past led either to cancer at any site or to measurable loss of lung function. It seems unlikely that future exposure to cosmetic talc of the specifications now agreed to by major manufacturers will present a health hazards.”

Following this editorial, a letter to Lancet was published in 1979 from Henderson’s group in which they cited additional studies which they claim had been performed subsequent to the 1971 article and which they said supported their contention that the particles found were talc.

Also in 1979, after the Henderson letter, a commentary on talc and ovarian cancer appeared in Lancet entitled “Cosmetic Talc and Ovarian Cancer.” This article was authored by Daniel L. Longo who went on to become Director of the National Institute of Aging and Robert C. Young who became President of Fox Chase Cancer Center. Longo presented no new data but reviewed current evidence and concluded that “[e]pidemiological, experimental, and clinical data seem to link asbestos and talc with ovarian cancer. Direct passage of talc or asbestos-contaminated talc to the ovarian surface may play an etiologic role. Further systematic evaluation of talc and asbestos as ovarian carcinogens is needed.”

Despite the debate and discussion about talc and ovarian cancer from 1970 to 1980, no formal epidemiologic study addressing the association was performed during that period.

**FORMAL EPIDEMIOLOGICAL STUDIES**

In 1982, Dr. Daniel Cramer performed the first epidemiological study on talc powder use in the female genital area and its possible association with ovarian cancer. This National Institutes of Health (NIH) funded case-control study found a statistically significant 92% increased risk in ovarian cancer with women who reported genital talc use. Additionally, it found 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 capable of causing growth of epithelial ovarian tissue. Dr. Cramer was retained and testified for the plaintiffs in the Berg, Fox and Ristesund trials against Johnson & Johnson, and is currently active as an expert witness for plaintiffs in talc litigation.

In 1983, Patricia Hartge and Robert Hoover of the National Cancer Institute and Linda Lester and Larry McGowan of the George Washington University Medical Center performed a case-control interview study regarding ovarian cancer. Although no association was proven due to the small sample size, the study found an “excess relative risk” of 2.5 (of ovarian cancer for women who use talcum powder in the genital area.

In 1988, a case-control study by Whittemore of 188 women in the Bay Area diagnosed with epithelial ovarian cancer and 539 control women found that 52% of the cancer patients habitually used talcum powder on the perineum before their cancer diagnosis. The study showed that women using talc daily on their perineum had 1.4 times the risk of ovarian cancer then women that did not use talc daily, showing a positive dose-response relationship.

A case-control study published in 1989 by Dr. Booth of the Department of Epidemiology of the London School of Hygiene found similar results. This hospital-based case-control study examined ovarian cancer patients in London and Oxford between October 1978 and February 1983. The study looked at 235 women diagnosed with epithelial ovarian cancer and 451 controls and found an increased risk in ovarian cancer with women who reported genital talcum powder use more than once per week.

Another case-control study conducted in 1989 by Bernard Harlow of Harvard Medical School at Brigham and Women’s Hospital, found an increased risk of ovarian cancer generally from genital talc use after bathing and found a statistically significant increased risk of ovarian cancer from women that used talc-containing powders in combination with deodorizing powders on their perineum. This study also found
positive dose-response relationship.\textsuperscript{21}

A 1992 case-control study, also by Drs. Harlow and Cramer, found that frequent and long term talc use on the genital area during ovulation resulted in a threefold increase of a woman's risk of ovarian cancer. The study stated: “t[c]he most frequent method of talc exposure was use as a dusting powder directly to the perineum (genitals) . . . was the category associated with a statistically significant risk for ovarian cancer.” This study looked at 235 ovarian cancer cases and 239 controls, and concluded that “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.”\textsuperscript{22}

Also in 1992, a case-control study was conducted by Karin Rosenblatt from the Department of Epidemiology of John's Hopkins School of Hygiene and Public Health. This study showed that the development of ovarian cancer may be associated with genital fiber exposure (especially talc on sanitary napkins) finding a relative risk of 4.8 for talc use on sanitary napking.\textsuperscript{23}

Additionally, another 1992 case-control study of Chinese women conducted by Yong Chen of 112 diagnosed epithelial ovarian cancer cases and 224 age-matched community controls, found an elevated risk for ovarian cancer for women who applied talc-containing dusting powder to the lower abdomen and perineum for longer than 3 months.\textsuperscript{24}

In 1993, the United States National Toxicology Program, which is comprised of a number of governmental agencies including the CDC, the NIH, the NCI and NIOSH, published a study on the toxicity of non-asbestiform, cosmetic grade talc and found clear evidence of carcinogenic activity in rats. The study found “some evidence of carcinogenic activity in male rats” and “clear evidence of carcinogenic activity in female rats.” Talc was found to be a carcinogen, with or without the presence of asbestos-like fibers.\textsuperscript{25}

In 1993, Tzonou published a study describing a hospital-based case-control study of ovarian cancer patients conducted in Athens. Tzonou concluded, “t[h]ere was no evidence that perineal application of talc was associated with increased risk, but the frequency of reporting talc use was low in the study population.”\textsuperscript{26}

In 1995, the largest case-control study to date was conducted in Australia by David Purdie, involving over 1600 women. This study reported a 27% increased risk in ovarian cancer for women who regularly use talc in the region of the abdomen or perineum.\textsuperscript{27}

In 1997, a case-control study of the Cancer Surveillance System of Western Washington identified 313 women with ovarian cancer and 422 without this disease, and found that the women with cancer were more likely to have applied talcum powder to their external genitals area. Women using these products had a 50% to 90% higher risk of developing ovarian cancer.\textsuperscript{28}

In 1997, a case-control study was conducted by Stella Chang and Harvey Risch from the Department of Epidemiology and Public Health, Yale University School of Medicine which included over 1,000 women. The study found a statistically significant increased risk for ovarian cancer for women who applied talc via sanitary napkins to their perineum. The study indicated that “[c]ommercial talc substitutes often replace talc with cornstarch. Furthermore, women may choose to powder or dust with cornstarch instead of talc. When cornstarch was assessed in relation to risk of ovarian carcinoma, no associations were found.” The study concluded, “The results of this study appear to support the contention that talc exposure increases risk of ovarian carcinoma. Dusting with talcum powder is not an unusual practice for women, and, given the heterogeneity of the etiology and course of ovarian carcinoma, any possible harmful practices, particularly those with little benefit, should be deliberated.”\textsuperscript{29}

In a 1998 case-control study of 170 women conducted in Canada by Beatrice Godard, an increased risk of ovarian cancer was found in women based on factors such as age and family history. A statistically insignificant number admitted use of talc-based powders on their perineum.\textsuperscript{30}

In 1999, Dr. Cramer conducted a case-control study of 563 women newly diagnosed with epithelial ovarian cancer and 523 control women. The study found a statistically significant 1.60 odds ratio of ovarian cancer in women that used talc-based body powders on their perineum. “We conclude that there is a significant association between the use of talc in genital hygiene and risk of epithelial ovarian cancer that, when viewed in perspective of published data on this association, warrants more formal public health warnings.” The study was funded by a grant from the National Cancer Institute.\textsuperscript{31}

In 2000, Roberta Ness, from the University of Pennsylvania, produced a case-control study of over 2,000 women. This study found a statistically significant 50% increased risk of ovarian cancer from genital talc use in women. The study also found that talc causes inflammation and that inflammation contributes to cancer cell development.\textsuperscript{32}

In 2000, Gertig did the first of two known cohort studies related to perineal use of talc. Studying a cohort of over 78,000 women who admitted talc use, the study concluded “[o]ur results provide little support for any substantial association between perineal talc use and ovarian cancer risk overall; however, perineal talc use may modestly increase the risk of invasive serous ovarian cancer.”\textsuperscript{33}
In 2003, a meta-analysis by Huncharek was conducted which re-analyzed data from 16 studies published prior to 2003 found a 33% increase in ovarian cancer risk among talc users. Despite this finding, Huncharek stated: “Despite this finding, the data showed a lack of a clear dose-response relationship making the RRs of questionable validity. Further sensitivity analyses showed that hospital-based studies showed no relationship between talc use and ovarian cancer risk, i.e. RRs 1.19 (0.99-1.41) versus population-based studies (RRs = 1.38, CI = 1.25-1.52). This suggests that selection bias and/or uncontrolled confounding may result in a spurious positive association between talc use and ovarian cancer risk in population-based studies.”

In 2004, a case-control study of 256 women from 22 counties was performed in Central California. This study found a statistically significant 37% increased risk of epithelial ovarian cancer from women’s genital talc use. The study also found a 77% increased risk of serous invasive ovarian cancer from women’s genital talc use. The study looked at women’s use of cornstarch powders and found no increased risk in ovarian cancer in women who used these types of powders on the perineum as “cornstarch is also not thought to exert the same toxicological reaction in human tissue as does talc.”

Interestingly, this study also found a 54% increased risk in ovarian cancer from talc use in women who had not undergone a tubal ligation, whereas the study found no impact on women who had their tubes tied. Because it had been found in previous studies that talc particles migrate up the fallopian tubes in women, plaintiffs argue that this finding provides strong evidence to support the idea that talc particles transmigrate and are a carcinogen.

In 2007, Dr. Cramer published a case report indicating the finding of talc particles in the pelvic lymph nodes of a woman reporting ovarian cancer and long-term genital exposure to cosmetic talc. In this report, Cramer claimed that talc did not need to reach the ovaries to affect ovarian cancer risk, but added that the inflammatory reaction increased the “harmful effect.”

In 2008, Margaret Gates performed a combined study of over 3,000 women from a New England-based case-control study and a prospective Nurses’ Health Study with additional cases and years of follow up from these studies. This study was funded by the National Cancer Institute (NCI), was conducted to analyze the interactions between talc use and genes in detoxification pathways (GSTM1, GSTT1 and NAT2) to assess whether the talc/ovarian cancer association is modified by variants of genes potentially involved in the response to talc. This study concluded that there was a suggestion that women with certain genetic variants may have a higher risk of ovarian cancer.

In October of 2008, Michael Thun, Vice-President of Epidemiology and Surveillance Research at the American Cancer Society commented on the Gates Study. He stated the dose-response relationship between talc and ovarian cancer had finally been satisfied by this study. Dr. Thun said, “There are very few modifiable risk factors for ovarian cancer. The main one is the use of oral contraceptives, which has been clearly established to lower the risk for ovarian cancer. Others include tubal ligation, hysterectomy, and parity. Then there are factors that ‘probably’ increase the risk for ovarian cancer, and this is where talc fits in, alongside asbestos, postmenopausal hormone therapy, and radiation.”

In 2008, Melissa Merritt, from the Australian Cancer Study (Ovarian Cancer) and Australian Ovarian Cancer Study Group, conducted a case-control study of over 3,000 women where a statistically significant increased risk of ovarian cancer for women who used talc on their perineum was confirmed. This study also confirmed a statistically significant increased risk of ovarian cancer of a serous subtype in women who used talc on their perineum.

In 2009, a case-control study by Wu of over 1,200 women in Los Angeles County found the risk of ovarian cancer increased significantly with increasing frequency and duration of talc use. The study found an overall statistically significant 53% increased risk of ovarian cancer from genital talc use. The study also found a 108% statistically significant increased risk of ovarian cancer in women with the longest duration and most frequent talc use (20 yrs./30 times per month). The study concluded by stating, “that risk of ovarian cancer is significantly associated with talc use and with a history of endometriosis, as has been found in recent studies.”

In 2013, Muscat published a meta-analysis of some 16 case-control studies and the Gertig cohort study wherein he reported a summary relative risk is about 1.3, but indicated an opinion summarizing the difficulties in ascertaining data accuracy and disputing a causal link. Muscat further implied that there has been no indication of carcinogenesis related to the use of cosmetic grade talc in pleurodesis procedures. Muscat stated:

“The heterogeneity in the perineal dusting studies has raised important concerns over the validity of the exposure measurements, and the lack of a consistent dose-response effect limits making causal inferences. Perhaps more importantly, whereas it is unknown whether external talc dust enters the female reproductive tract, measures of internal talc exposure such as talc-dusted diaphragms and latex condoms show no relationship with ovarian cancer risk. In addition, the therapeutic use of high dose cosmetic grade talc for pleurodesis has not been shown to cause cancer in patients receiving these treatment modalities. Talc is not genotoxic. Mechanistic, pathology and animal model studies have not found evidence for a carcinogenic effect. In summary, these data collectively do not
indicate that cosmetic talc causes ovarian cancer.\(^{42}\)

In 2014, the second known epidemiological prospective cohort study disputed the association between perineal talc exposure and ovarian cancer reported in case-control studies. Serena Houghton, of the Division of Biostatistics and Epidemiology, University of Massachusetts Amherst, found that over 52% of 61,576 postmenopausal women in the Women’s Health Initiative Observational Study cohort reported perineal use of talc products. The data showed no increased risk of ovarian cancer when compared with those women reporting never use, and Houghton reported perineal powder use does not appear to influence ovarian cancer risk.\(^{43}\)

SUMMARY OF STATE OF ART EVIDENCE CITED IN COSMETIC TALC CASES

In 1971, a case report on the use of an extraction-replication technique used to examine ovarian tumor tissues found talc particles deeply embedded in the tissue.\(^{44}\)

Shortly after Dr. Cramer’s 1982 study was published, Dr. Bruce Semple of Johnson & Johnson contacted and visited Dr. Cramer about his study. Dr. Cramer advised Dr. Semple that Johnson & Johnson should place a warning on its talcum powders about the ovarian cancer risks so that women can make an informed decision about their health.\(^{45}\)

On August 12, 1982, in a New York Times article entitled “Talcum Company Calls Study on Cancer Link Inconclusive,” Johnson & Johnson admitted being aware of the 1982 Cramer article, and that Cramer concluded women were three times more likely to contract ovarian cancer after daily use of their talcum powder in the genital area.\(^{46}\)

In 1992, after these various studies, the Personal Care Products Council (formerly known as the CTFA) created the Talc Interested Party Task Force to defend the talc industry and help with publication relations and talking points for press releases regarding the connection between talc and ovarian cancer. Johnson & Johnson, Luzenac and Sanofi were members of this organization. According to plaintiffs in talc litigation, this organization lobbied various organizations including the National Toxicology Program to prevent talc from being labeled as a carcinogen.\(^{47}\)

On November 10, 1994, the Cancer Prevention Coalition mailed a letter to then Johnson & Johnson’s CEO, Ralph Larson, informing Johnson & Johnson that studies as far back as 1960’s “show ...conclusively that the frequent use of talcum powders in the genital area poses a serious risk of ovarian cancer.” The letter cited a study by Dr. Bernard Harlow from Harvard Medical School confirming this fact and quoted a portion of the study where Dr. Harlow and his colleagues discouraged the use of talc in the female genital area. The letter further stated that 14,000 women per year die from ovarian cancer and that this type of cancer is very difficult to detect and has a low survival rate. The letter concluded by requesting that Johnson & Johnson withdraw talc products from the market because of the alternative of cornstarch powders, or at a minimum, place warning information on its talc-based body powders about the ovarian cancer risk they pose.\(^{48}\)

On November 17, 1994, the Cancer Prevention Coalition joined by Chair and National Advisor of the Ovarian Cancer Early Detection and Prevention Foundation filed a “Citizen Petition Seeking Carcinogenic Labeling on All Cosmetic Talc Products” stating that research dating back to 1961 had shown that cosmetic grade talc could translocate to the ovaries in women and increase the risk of developing ovarian cancer. This petition was submitted to the Commissioner of the Food and Drug Administration under the Federal Food, Drug, and Cosmetic Act. The agency action requested was that the FDA “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.”\(^{49}\)

In 1996, the condom industry stopped dusting condoms with talc due to the health concerns of ovarian cancer. According to a newspaper report, “[c]oncern about talc as an ovarian carcinogen goes back 50 years in the medical literature. By the 1970s, evidence was mounting that talc particles might migrate into a woman's fallopian tubes where they could cause scarring and irritation in the ovaries. Scientists believed in some cases that the scarring led to infertility or cancer.”\(^{50}\)

On September 17, 1997, Alfred Wehner, a toxicology consultant retained by Johnson & Johnson, wrote a letter to Michael Chudkowski, manager of Pre-Clinical Toxicology at Johnson & Johnson Consumer Products, Inc., stating that on three separate occasions the Talc Interested Party Task Force (TIPTF) of the Cosmetic, Toiletry, and Fragrance Association (CTFA) which included Johnson & Johnson, Luzenac and Sanofi, had released false information to the public about the safety of talc. Specifically addressing a November 17, 1994, statement released by the CTFA, Dr. Wehner said the following:

“The response statement dated November 17, 1994, is just as bad. The second sentence in the third paragraph reads: 'The workshop concluded that, although some of these studies suggested a weak association might exist, when taken together the results of the studies are insufficient to demonstrate any real association.' This statement is also inaccurate, to phrase it euphemistically. At that time there had been about 9 studies (more by now) published in the open literature that did show a statistically significant association...
between hygienic talc use and ovarian cancer. Anybody who denies this risks that the talc industry will be perceived by the public like it perceives the cigarette industry: denying the obvious in the face of all evidence to the contrary.

The workshop did not conclude that 'the results of the studies are insufficient to demonstrate any real association.' As pointed out above, a "real" statistically significant association has been undeniably established independently by several investigators...

In 2002, E. Edward Kavanaugh, President of CTFA, wrote a letter to Dr. Kenneth Olden, Director of the National Toxicology Program (NTP) and National Institute of Environmental Health Sciences, U.S. Department of Health and Human Services, in an attempt to stop the NTP from listing cosmetic talc as a carcinogen in an upcoming report. The NTP had already nominated cosmetic talc for this classification. In this letter, according to plaintiffs, the CTFA admitted that talc was "toxic", that "some talc particles... can reach the human ovaries", and acknowledge and agreed that prior epidemiologic studies have concluded that talc increases the risk of ovarian cancer in women.

In February of 2006, IARC published a paper whereby they classified perineal use of talc-based body powder as a possible "Group 2B" human carcinogen. IARC concluded that studies from around the world consistently found an increase risk in ovarian cancer in women from perineal use of talc. IARC found that between 16-52% of women in the world were using talc to dust their perineum and found an increase risk of ovarian cancer in women talc users ranging from 30-60%. IARC concluded with this "[o]verall evaluation": "Perineal use of talc-based body powder is possibly carcinogenic to humans (Group 2B)."

In 2006, the Canadian government under The Hazardous Products Act and associated Controlled Products Regulations classified talc as a "D2A," "very toxic," "cancer causing" substance under its Workplace Hazardous Materials Information System (WHMIS). Asbestos is also classified as "D2A."

In 2006, Imerys began placing an ovarian cancer warning on its Material Safety Data Sheets (MSDS) it provides to its talc customers, including Johnson & Johnson. These MSDSs not only provided the warning information about the IARC classification but also included warning information regarding "States Rights to Know" and warning information about the Canadian Government’s "D2A" classification of talc as well. Plaintiffs claim that Johnson & Johnson would have received these MSDSs and did not pass this warning information on to the consumers. On September 26, 2012, the corporate representative of Imerys testified in open court that his company exclusively supplied Johnson & Johnson with talc used for its Baby Powder product and that ovarian cancer is a potential hazard associated with a women's perineal use of talc-based body powders, like Johnson & Johnson’s Baby Powder.

In May 2008, the Cancer Prevention Coalition submitted a citizen’s petition “seeking a cancer warning on cosmetic talc products.” The petition sought to require all cosmetic talc products to bear labels with warnings such as, “Frequent application of talcum powder in the female genital area substantially increases the risk of ovarian cancer” or “Frequent talc application in the female genital area is responsible for major risks of ovarian cancer.” (Emphasis added). The petition cited numerous studies and publications and sought a hearing to present scientific evidence.

On October 19, 2012, Johnson & Johnson’s former in-house toxicologist and current consulting toxicologist, Dr. John Hopkins, testified on Johnson & Johnson’s behalf that Johnson & Johnson "[a]re and were aware of . . . all publications related to talc use and ovarian cancer."

SUMMARY
From an epidemiological standpoint, Plaintiffs will claim that there is abundant literature indicating an association between perineal application of talc products and ovarian cancer.

The peer-reviewed literature, however, begins in 1982 and consists entirely of case reports. There have been only a pair of cohort studies, by Gertig in 2000, and Houghton in 2014, and both conclude that there is no evidence of increased risk of association. Furthermore, a 2013 meta-analysis by Muscat points out insufficiencies and inaccuracies in the data collection process and casts doubt on the findings of twenty-five years of case-control studies.

Similarly, the Cramer study in 1982 seems to be the beginning of the applicable state of the art evidence. While there is evidence that Johnson & Johnson knew and reacted to the Cramer study at that time, there seems to be no industry wide response until 1992, and no governmental response until after 2002. IARC did not classify cosmetic talc as a “possible” carcinogen until 2006.

1 National Cancer Institute, Surveillance, Epidemiology and End Results Program (SEER). SEER Cancer Fact Sheets, Ovarian Cancer, 2016.


6 Judicial Council Of California, Civil Case Coordination Proceeding (JCCP) Log. (http://www.courts.ca.gov/documents/CivilCaseCoord_2005toPresent_JCCPLog.pdf.)


36 Id.


49 Id.


51 Estrada Complaint, supra, at ¶ 65.

52 Chakalos Complaint, supra at ¶ 791


54 Id., at ¶ 42.

55 Estrada Class Action Complaint, supra, at ¶ 66.

57 Estrada Class Action Complaint, supra, at ¶ 67.