EUROTALC

Dr G.B.van der Voet
DECOS subcommittee 246
Health Council
PO Box 16052
2500 BB The Hague
The Netherlands

Brussels, 10 May 2012

Dear Dr. van der Voet,

On behalf of the Scientific Association of the European Talc Industry, EUROTALC AISBL, and its sister organisation the Talc/Wollastonite Section of the Industrial Minerals Association-North America (IMA-NA), we wish to submit the enclosed comments on the Evaluation of the carcinogenicity and genotoxicity of Talc drafted by the Subcommittee on the Classification of Carcinogenic Substances of the Dutch Expert Committee on Occupational Safety (DECOS), which was released on 15 February 2012.

We thank you in advance for your consideration of these comments and we are at your disposal for any question or comment in this relation.

Sincerely,

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EUROTALC and IMA-NA Comments on OCR –Talc 2012

The Scientific Association of the European Talc Industry, EUROTALC AISBL, a member of the Industrial Minerals Association-Europe (IMA-Europe), and their sister organisation the Talc/Wollastonite Section of the Industrial Minerals Association-North America (IMA-NA) are grateful to the Dutch Expert Committee on Occupational Safety (DECOS) for inviting comments on their Draft Evaluation of the carcinogenicity and genotoxicity of talc. Together, both organisations represent more than 95% of the European and North American talc industry.

We acknowledge the work performed by the DECOS in its Talc Evaluation of the carcinogenicity and genotoxicity and respectfully we would like to submit the following comments.

1. Talc identity and physico-chemical properties

The description of talc (chapter 2, p.6) reads as follows:

"Mineral talc is usually platy but may also occur as long, thin, asbestiform fibres in parallel bundles, which are easily separated from each other by hand pressure".

This wording is taken from the IARC Monograph **93** (2010). Out of context, it does not reflect the actual reality of the exceptional mineralogical occurrence of "asbestiform talc" as reported in the IARC Monograph. In the Monograph indeed as quoted in the Report Annex D (p.33), it is further mentioned that:

"Together with platy talc, asbestiform talc is found in the Gouverneur District of New York State, USA, and occasionally elsewhere; it may be associated with other minerals as observed by transmission electron microscopy."

Therefore, in order to more accurately define talc, we suggest to report in the chapter 2 (p.6) that:

"Mineral talc is usually platy but may also occur **occasionally and in exceptional cases** as long, thin, asbestiform fibres in parallel bundles, which are easily separated from each other by hand pressure".

2. Inhalation of talc (not containing asbestos or asbestiform fibres)

The Evaluation of data on talc carcinogenicity and genotoxicity is based on talc not containing asbestos or asbestiform fibres.

After a thorough analysis of the available scientific evidence, it concludes that:

> "(...) studies with populations of talc millers exposed to high levels of relatively pure talc in which no other occupational carcinogen was mentioned, no excess lung cancer mortality was reported (overall SMR of 0.92; 95% CI, 0.67–1.25, 42 cases). **These studies are in support of the view that talc is not carcinogenic to man.** On the other hand, in some population studies of talc miners and talc workers in

other industrial settings the cancer mortality risks were in excess. However, **in these studies exposure information was not always adequate and the talc exposure was confounded by other carcinogens such as quartz. Therefore, the results of these studies are not sufficient to exclude talc as a carcinogen."**

The primary conclusion to be drawn from studies biased by confounding factors is that they are not relevant for evaluating talc carcinogenicity and genotoxicity. These poor quality studies should not be taken into account in the evaluation. They should be disregarded for the reason of confounding elements. According to the DECOS report itself: "The carcinogenicity of talc (not containing asbestos or asbestiform fibres, although sometimes contaminated with other dusts) **involving extensive health studies on workers of talc mines, mills or factories chronically exposed to talc dusts**". These state-of-art studies have the highest potential for assessing the carcinogenicity of talc per se under unbiased conditions. In these circumstances, poor quality studies are not inducing doubts on talc non-carcinogenicity.

Under these circumstances, it is difficult to understand through which syllogism, or by virtue of which precautionary principle, the Committee comes to the below conclusion:

> "However, the Committee is also aware of the occupational studies on talc miners and other industrial populations which do not justify excluding talc as a lung carcinogen due to confounding exposure factors."

The confounding exposure factors, observed by the Committee, in the talc miners (exposed to radon) and other industrial populations (exposed to various contaminants) are irrelevant and the Committee should exclude these studies from the evaluation and certainly not be used "to not exclude" that talc is a carcinogen. These studies are not designed to provide any evidence of a synergetic effect, they are biased by the effects of a known carcinogen (e.g. Radon).

The DECOS Recommendation for classification (Executive Summary p.4, second paragraph and chapter 5.2, p24), reads as: "(...) the Committee is of the opinion that the data are as yet insufficient to evaluate the carcinogenic properties of talc (category 3)".

Incidentally, the wording "as yet" induces the idea that the Committee is of the opinion that it is only a matter of time before talc (with or without asbestos/asbestiform fibres) will be categorised as a carcinogen. In addition, it is not consistent with the category 3 definition and does not bring any relevant information to the opinion. For these reasons, we ask the Committee, when rephrasing the recommendation, to delete "as yet".

More fundamentally, from the body of evidence discussed above, it is sound to conclude that there is sufficient data from both epidemiological studies and experimental animal studies to suggest that carcinogenicity in man is unlikely. Therefore the Category 4 seems to be more appropriate than the Category 3 for talc.

3. Perineal Exposure and ovarian cancer

The Evaluation of data related to perineal exposure and ovarian cancer is based on talc-based body powder (not on talc powder) and is properly assessed. Altogether it concludes

that they are not very convincing with no demonstration of a clear exposure-response relationship, and no adequate mechanistic evidence.

> A clear exposure-response relationship (either frequency based or length in years based) was lacking in most of the studies or not even investigated. Several factors have to be kept in mind, such as the possibility of recall bias, selection bias and uncontrolled confounding. In addition, adequate mechanistic data are still absent, and the fact that several studies, including a cohort study are negative do raise questions regarding the exact association of perineal talc use and risk of ovarian cancer.

Given all the shortcomings of these studies acknowledged by the Committee, one would expect these to be disregarded from any consideration.

In addition, the Committee noted that:

> (...) body powders, baby powders, talcum powders and deodorizing powders, most of which contain cosmetic talc in varying amounts (...)

It is indeed very true that the use of talc in perineal applications is identified through patient's interviews, generally before surgery for ovarian cancer. In these circumstances, the powder brand and the nature of the powder is never identified.

The Committee discussed the possible biases coming from:
- the patients' knowledge of the suspicion of an association between talc and ovarian cancer,
- the potential contamination of body powder with minerals demonstrating a potential health effect,
- the fact that the use dates back to before the 1970s,

The Committee, however, did not question whether the body powder was really talc-based and whether or not it contained other potential organic contaminants such as perfume and the other functional additives.

In reality, the use of a dusting powder referred by patients as "talc" is not necessarily a talc powder. The public generally uses the name "talc" generically for body, baby and deodorizing powders without really knowing the powder's composition. Starch has replaced talc in loose powders for cosmetic and hygiene uses since a long time and even today nobody speaks about "starch" when naming these powders. Talc is used as a generic name for cosmetic and hygiene dusting powders in which talc may not be present at all or present in minuscule quantities.

In addition, in body powder used in perineal dusting, the composition of the body powders is complex and they may indeed contain many additives (e.g. biocides or preservatives and perfumes).

Finally, contrary to the recent IARC Monograph on talc, the Committee assimilates the evidence of perineal use of body powder to a talc effect, while the IARC evaluation acknowledges that the health effects are related to "talc-based body powders".

In no case this non-convincing evidence based on a complex manufactured product's supposed effects may be used to conclude on talc carcinogenicity.

Therefore, the Committee's below conclusion should be revised:

> The Committee considers the association between perineal exposure and ovarian cancer not very convincing but taken together the data are not sufficient to exclude talc as a carcinogen.

Should the Committee wish to address the perineal use of body powders, the recommendation should focus on body powder, not on talc.

4. Conclusion

In order to accurately define the term talc in the chapter 2 (p.6) as quoted from the IARC Monograph (**93,** 2010), we suggest to revise the wording of the last paragraph as follows:

"Mineral talc is usually platy but may also occur **occasionally** and in exceptional cases as long, thin, asbestiform fibres in parallel bundles, which are easily separated from each other by hand pressure".

The DECOS classification descriptions for categories 3 and 4 are copied here below:

Category 3: The available data are insufficient to evaluate the carcinogenic properties of the compound. The compound is classified into this category if there is insufficient, good quality human or experimental animal data on a compound's carcinogenicity.

Category 4: The compound is probably not carcinogenic to man.
A compound is placed in this category when there is sufficient data from both epidemiological studies and experimental animal studies to suggest that carcinogenicity in man is unlikely. A number of good epidemiological studies and experimental animal studies have been published. These studies either found no exposure-induced tumours, or the tumours (including the mechanism of action) that did develop in some animal species were not relevant to man.

From the body of evidence analysed and the conclusions drawn by the Committee on the quality of this evidence, it appears that there is sufficient data from both epidemiological studies and experimental animal studies to suggest that carcinogenicity in man is unlikely. Therefore, the Category 4 seems to be more appropriate than the Category 3 for talc (not containing asbestos or asbestiform fibres).

Should the Committee pronounce itself on the perineal use of body powder, the Evaluation should address body powder, not talc.

Brussels, 10 May 2012

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May 16, 2012

Sent via FedEx and email (b.v.d.voet@gr.nl)

DECOS subcommittee 246
Health Council
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2500 BB The Hague
The Netherlands

Attn: Dr. G. B. van der Voet

Dear DECOS subcommittee members,
Imerys Talc appreciates the opportunity to offer comments to the Dutch Expert Committee on Occupational Safety (DECOS) on their draft Evaluation of the carcinogenicity and genotoxicity of "Talc" (February 15, 2012).

Imerys Talc is the world's largest talc company, producing one million metric tonnes of talc annually, which represents15 percent of the global talc demand. It operates 9 talc mines and 13 processing plants globally, including 5 mines and 6 processing plants in Europe. Imerys Talc employs over 1,000 employees on 5 continents and serves over 3,000 customers directly and through distributors. The talc we mine and process is used as a functional mineral in myriads of applications including plastics, rubber, paint, paper, pharmaceuticals, cosmetics, agricultural products, ceramics, and many specialty applications. We pride ourselves on over 100 years of unparalleled expertise in talc processing, product innovation, and quality control. We only deliver the highest quality products to our customers after they have passed a series of intensive quality control tests.

We take the health of our employees seriously and control the dust level in our facilities. A number of health studies have been conducted on our mine and mill (processing plants) workers by independent experts. These studies have been peer-reviewed and published in international journals. Some of these studies (*e.g.* Léophonte and Didier 1990; Leophonte *et al.* 1983; Wild 2000; Wild *et al.* 2002; Wild 2006; Rubino *et al.* 1976; Rubino *et al.* 1976, 1979; Coggiola *et al.* 2003) were examined by IARC and taken into account by the DECOS sub-committee. All these studies concluded no adverse health effects on talc miners and millers. Imerys is committed to sustainable development and operating in an environmentally friendly manner to ensure the safety and health of its employees, customers, and the communities in which it operates.

Although we fully appreciate the DECOS evaluation of talc, we disagree with a Category 3 classification. We offer the following arguments in support of a Category 4 classification for talc:

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1. **When the full definition of Category 4 is considered, it is apparent that occupational exposures to talc should be classified in Category 4 rather than Category 3.**

The draft evaluation never quotes the Guidelines explanation for category 4, but it should. It seems apparent from the full definition of category 4 provided in the Guidelines that a category 4 classification is more appropriate for talc. Appendix E only gives the summary descriptor for the category, which is that "[t]he compound is probably not carcinogenic to man." (P. 42.) The draft evaluation states twice that the data reviewed are "mainly indicating [sic] the absence of carcinogenicity." (P. 4 lines 14-15, p. 24 lines 3-4.) Such statements appear to be consistent with a category 4 classification. However, the draft appears to explain its category 3 recommendation as justified by finding that not all studies indicate an absence of carcinogenicity, and that "[t]aken together" the overall body of studies are not sufficient to "prove" that talc is not a carcinogen. (P. 23, lines 8-9.) This conclusion is not consistent with the full definition of category 4. Not only does the summary descriptor speak in terms of "probably" not carcinogenic; but also, the full definition of category 4 does not require absolute "proof" of lack of carcinogenicity, or reliance on all studies regardless of their quality or relevance. The Guidelines explanation of category 4 is as follows:

> Category 4: The compound is **probably** not carcinogenic to man
>
> A compound is placed in this category when there is sufficient data from both epidemiological studies and experimental animal studies to **suggest** that carcinogenicity in man is **unlikely**. A number of **good** epidemiological studies and experimental animal studies have been published. These studies either found no exposure-induced tumours, or the tumours (including the mechanism of action) that did develop in some animal species were not relevant to man.

We have highlighted the qualifying terms "probably," "suggest," "unlikely," and "good" to emphasize that category 4 does not require unequivocal "proof" of non-carcinogenicity; nor does it require use of all studies. The emphasis is on probabilities and the use of "good" studies. Requiring "proof" of non-carcinogenicity, based on consideration of all studies, whether of good or poor quality or relevance, is not consistent with the Guidelines. As discussed below, we believe that the higher quality (or "good") scientific evidence requires that talc occupational exposures be given a category 4 classification.

The studies of exposure to millers, which are the most relevant and of good quality, have found no carcinogenicity. In contrast, the studies of talc miners and workers in other industries are of poor quality and relevance for purposes of this evaluation.

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Talc miners are almost invariably exposed to a variety of inhalation exposures such as radon and respirable crystalline silica that confound any epidemiologic study. Millers, on the other hand, are exposed only to talc. Thus, the epidemiologic studies of millers are more relevant and of higher quality in addressing the potential carcinogenicity of talc. As the draft evaluation acknowledges, "if only the results of the occupational studies in talc millers were to be evaluated, talc should be classified as not carcinogenic to humans." (P. 22 lines 12-16, p. 23 lines 1-3.) In view of the full definition of category 4 quoted above, with its emphasis on "good" studies, the studies of talc millers should take precedence over the poorer quality studies of miners and workers in other industries, and occupational exposures to "talc" should be classified in category 4.

2. **The epidemiologic studies involving "perineal use of talc-based body powder," and the IARC evaluation of those studies, are not relevant to the occupational situation and address "talc-based" substances of unknown composition rather than "talc."**

The DECOS evaluation should maintain a distinct focus on occupational exposures to "talc," and should not incorporate data from studies that have addressed personal direct application of talc-based body powders and other substances by females to the perineal area. As the draft states, its evaluation is directed to "substances to which workers are occupationally exposed." (P. 4.) The draft also acknowledges that the perineal use studies "may not be relevant to the occupational situation." (P. 23 line 7.) The perineal use studies are in fact not relevant to the occupational situation for a variety of compelling reasons, as the IARC working group recognized when it separated its evaluation of such studies from evaluation of occupational exposures.

The perineal use epidemiologic studies are not studies of "talc," as IARC recognized, but, rather, are at most studies of "talc-based" body powder. Body powders sold at retail and used personally are proprietary products of unspecified composition and may contain many substances such as preservatives, biocides, and fragrances that are not present in the occupational environment. They are also applied directly by dusting or spraying.

Although most of the perineal use studies use the term "talc" to describe the exposures, a review of the studies, including those considered most informative by IARC, will show that in fact many were based on questioning of subjects as to whether they had used not just talc or talcum powder, but talcum, baby, or deodorizing powders, or just "powders."[1] Many baby, body, or deodorizing

[1] For example, in Cramer DW *et al.*1999, the subjects were asked whether they had "regularly used talc, baby, or deodorizing powders dusted or sprayed." And in Harlow BL *et al.* 1992, most of the subjects reported simply their use of "baby powder." See also, Cook LS *et al.* 1997, Cramer DW *et al.* 2005, Gates MA *et al.*

powders are cornstarch-based, rather than talc-based, and deodorizing sprays might not have any talc or particulate content at all, and therefore it is not accurate to portray such studies as "talc" studies. Furthermore, it is not at all clear that the general female public understands that talcum powder refers to a powder containing the specific mineral talc; instead, many members of the public might well consider talcum powder to be any kind of white, soft powder, regardless of its exact composition.

In addition, as discussed in the IARC monograph, there were many reports (some disputed) concerning potential contamination of talcum powders with asbestos during the 1970s. A review of the epidemiologic studies relied on by IARC regarding perineal use will show that, although most of the studies did not give information on when subjects first started using talcum or other body powders, the ages of the subjects at the time of diagnosis, as given in the studies, will show that if many of the subjects started using body powders in their 20s, they would have been using such powders well prior to the mid-1970s. Since asbestos is a known human carcinogen, this means that most, if not all, of the perineal use epidemiologic studies are not relevant or are suspect because they might well have involved exposures to powders containing asbestos, and talc containing asbestos is specifically excluded from the DECOS draft evaluation. Moreover, the IARC monograph expressed concern that even as of 2006 asbestos contamination of body powders might not have been eliminated outside the United States. (P. 33 lines 32-34.)

DECOS should note the action taken by U.S. government health agencies when it encountered this problem of the composition of cosmetic body powders, and should take similar action. In 2000, an external peer review committee convened by the U.S. National Toxicology Program[2] ("NTP") voted decisively against listing talc in the U.S. Report on Carcinogens. The NTP further reviewed the issue during the next five years and in 2005, it formally withdrew the nominations for listing commercial and cosmetic talc in the Report on Carcinogens. The NTP concluded that "[i]t has become evident that the literature on both forms of talc, with few exceptions, provides an inadequate characterization of the actual materials under study to enable one to reach

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2008, Gertig DM *et al.* 2000, Hankinson SE *et al.* 1993, Harlow & Weiss 1989, Karageorgi S *et al.* 2010, Merritt MA *et al.* 2008, Mills PK *et al.* 2004, Ness RB *et al.* 2000, Rosenblatt KA *et al.* 2011, Vitonis AF *et al.* 2011, and Cramer DW *et al.* 2011. (The exact question asked is not always provided in the study report, but can be obtained by reference to related studies and their questions, such as the 1982 questionnaire used in the U.S. Nurses Health Study.)

[2] The National Toxicology Program is comprised of all the major U.S. Government health agencies and is administered by the National Institute of Environmental Health Sciences.

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definitive conclusions concerning the specific substances responsible for the range of adverse health outcomes reported."[3] Shortly thereafter IARC proceeded with a similar review, but tried – unsuccessfully in our view -- to avoid the exposure characterization problem by referring to its evaluation as one for "talc-based body powder" rather than "talc." In view of the many studies that incorporated probable use of non-talc-based powders, such a title was inappropriate.

3. **Pure talc is widely accepted by the medical community as a superior agent for intrathoracic treatment of malignant and non-malignant pleural effusions and pneumothorax. The thoracic surgery community would probably be surprised to learn that DECOS does not consider talc to be non-carcinogenic.**

   The literature on this point is very extensive. An online literature search for "talc pleurodesis" will quickly demonstrate the above point.

RECOMMENDATIONS

1. Confine the evaluation to occupational exposures. Do not discuss the literature on perineal use as relevant.

2. Rely on the highest quality evidence and classify occupational exposure to "talc" in category 4 as "probably not carcinogenic to man."

In addition to providing these comments we would like to request a follow-up meeting to discuss our comments in more detail.

If you have any questions regarding these comments, please feel free to contact me at shripal.sharma@imerys.com

Respectfully submitted,

Shripal Sharma
Global Director, Product Stewardship

[3] 70 Federal Register 60548, 60553 (Oct. 18, 2005).