NAIMA
NORTH AMERICAN INSULATION
MANUFACTURERS ASSOCIATION

VIA OVERNIGHT MAIL AND E-MAIL

July 15, 2004

JUL 16 2004

Dr. C.W. Jameson
National Toxicology Program
Report on Carcinogens
Building 4401, Room 3118
79 Alexander Drive
Research Triangle Park, NC 27709

RE: Comments on the NTP'S 21 Substances, Mixtures and Exposure Circumstances Proposed for Listing in the Report on Carcinogens, Twelfth Edition – 69 Fed. Reg. 28,940 (May 19, 2004)

Dear Dr. Jameson:

The North American Insulation Manufacturers Association ("NAIMA") respectfully submits the enclosed comments on the National Toxicology Program's 21 Substances, Mixtures and Exposure Circumstances Proposed for Listing in the Report on Carcinogens, Twelfth Edition – 69 Fed. Reg. 28,940 (May 19, 2004).

If you have any questions, please do not hesitate to contact the undersigned.

Sincerely,

Angus E. Crane

Angus E. Crane
Vice President
(acrane@naima.org)

Enclosures

BEFORE THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

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COMMENTS ON THE NATIONAL TOXICOLOGY PROGRAM'S 21 SUBSTANCES, MIXTURES AND EXPOSURE CIRCUMSTANCES PROPOSED FOR LISTING IN THE REPORT ON CARCINOGENS, TWELFTH EDITION – 69 FED. REG. 28,940 (MAY 19, 2004)

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SUBMITTED BY THE
NORTH AMERICAN INSULATION MANUFACTURERS ASSOCIATION (NAIMA)

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July 16, 2004

COMMENTS OF THE
NORTH AMERICAN INSULATION
MANUFACTURERERS ASSOCIATION ("NAIMA")

The North American Insulation Manufacturers Association ("NAIMA"), a trade association representing the manufacturers of glass wool in the United States and throughout North America, is pleased to present the following comments in response to the National Toxicology Program's ("NTP") proposed delisting of glass wool (respirable size).

These comments build upon NAIMA's Petition for Delisting Glass Wool (Respirable Size) from the Report on Carcinogens submitted to NTP on January 28, 2002 (TAB 1). In support of its Petition, NAIMA provided NTP with copies of the International Agency for Research on Cancer ("IARC") Monograph, Volume 81, Man-Made Vitreous Fibres (2002); access to the articles relied upon by IARC in its finding that insulation glass wool was not classifiable as to its carcinogenicity to humans; and copies of relevant articles on synthetic vitreous fibers ("SVFs") published since the IARC decision.

BASIS FOR DELISTING

The delisting of glass wool (respirable size) is supported by the recent (October 16, 2001) IARC decision to downgrade the classification of "glass wool insulation" from Group 2B to Group 3 and the substantial body of science supporting that decision.[1]

IARC's reclassification concluded that the human data remained "inadequate," but that the animal data were no longer "sufficient;" instead, IARC reclassified the animal data as "limited."[2] IARC also determined that mechanistic considerations regarding fiber durability provided additional scientific data supporting the downgrading.

Human Data

In the IARC re-evaluation, the human data were determined to be "inadequate." A very large database is now available on the epidemiology of glass wool manufacturing workers, and as the IARC press release stated:

> These [synthetic vitreous fiber or SVF] products, including glass wool . . . have been in use for decades and have been extensively studied to establish whether fibres that are released during manufacture, use, or removal of these products present a risk of cancer when inhaled. Epidemiologic studies published during the 15 years since the previous IARC Monograph[']s review of these fibres in 1988 provide no evidence of increased risks of lung cancer or of mesothelioma (cancer of the lining of the body cavities) from

[1] IARC (2002) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 81, *Man-made Vitreous Fibres*, Lyon, IARC*Press*.

[2] IARC retained the Group 2B classification ("possibly carcinogenic to humans") for refractory ceramic fibers and "certain special-purpose glass wools not used as insulating materials." (See IARC Press Release at TAB 2). NAIMA's delisting nomination applies only to glass wool insulation categorized by IARC as Group 3.

> occupational exposures during manufacture of these materials, and inadequate evidence overall of any cancer risk.[3]

A significant part of the data in IARC's glass wool designation was the "Historical Cohort Study of US Man-Made Vitreous Fiber Production Workers" by Dr. Gary M. Marsh, *et al.*[4] One of the largest epidemiology studies ever conducted, the Marsh study covers over 40,000 U.S. production workers and over one million person-years of observation.

One additional note on the findings of the epidemiology studies is significant. In the Monograph, IARC stated:

> Of some concern are risks for workers in industries that use or remove these products (e.g., construction), who may have experienced higher, but perhaps more intermittent, exposure to man-made vitreous fibres. The data available to evaluate cancer risks from exposure to man-made vitreous fibres in these populations are very limited.[5]

Subsequent to the publication of the Monograph, a paper specifically addressing this question entitled "Fiber glass and rock/slag wool exposure of professional and do-it-yourself installers"[6] was published in *Regulatory Toxicology and Pharmacology*. The abstract reads as follows:

> The fiber glass (FG) and rock/slag wool (RSW) manufacturers have developed a Health and Safety Partnership Program (HSPP) with the participation and oversight of the Occupational Safety and Health Administration (OSHA). Among its many provisions the HSPP includes the continuing study of FG and RSW workplace concentrations in manufacturing facilities operated by the FG/RSW producers and among their customers and end users. This analysis estimates the probable cumulative lifetime exposures (fiber-months/cubic centimeter [f-months/cc]) to those who install FG and RSW insulation in residential, commercial, and industrial buildings in Canada and the United States. Both professional and do-it-yourself (DIY) cohorts are studied and the estimated working lifetime exposures are compared with benchmark values derived from an analysis of the epidemiological studies of FG and RSW manufacturing cohorts. The key finding of this analysis is that both of these end-user cohorts are likely to have substantially lower cumulative lifetime exposures than the manufacturing cohorts. As the most recent updates of the epidemiological studies have concluded that there was no significant increase in respiratory system cancer among the manufacturing cohorts, there is likely to be even less risk for the installer cohorts. This analysis also underscores the wisdom of stewardship activities in the HSPP, particularly those directed at measuring and controlling exposure.

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[3] See TAB 2. See also: www.iarc.fr/pageroot/PRELEASES/pr137a.html.
[4] *Journal of Occupational and Environmental Medicine*, September 2001.
[5] IARC 81, p. 331.
[6] L. Daniel Maxim, W. Eastes, J.G. Hadley, C.M. Carter, J.W. Reynolds, and R. Niebo, "Fiber glass and rock/slag wool exposure of professional and do-it-yourself installers," *Regulatory Toxicology and Pharmacology* 37 (2003) 28-44.

The findings of significantly lower exposures in the user industries should provide additional reassurance of the safety of the workers who use and install these products.

Additionally, NAIMA has published a large database of airborne fiber concentrations measured during manufacturing and installation operations.[7] The database was created as a key component of an ongoing voluntary health and safety program, the Health and Safety Partnership Program ("HSPP") developed by NAIMA and the U.S. Occupational Safety and Health Administration ("OSHA").[8] This database demonstrates that concentration of airborne fibers during production and installation of glass wool are generally below 1 f/cc.[9] The HSPP establishes 1 f/cc as a voluntary permissible 8-hour time weighted average ("TWA") exposure limit.[10]

Animal Data

The animal evidence was downgraded by IARC from "sufficient" to "limited." This was due to: (1) the availability of well-conducted chronic inhalation studies in two species conducted at or above the maximum tolerated dose ("MTD"), which showed no evidence of either fibrosis or significant tumor induction with the glass wool insulations; and, (2) the growing consensus regarding the relevance of route of administration in assessing the hazard of fibers.

It is important to note that an early report on the multidose rat inhalation study[11] was evaluated by NTP prior to the listing of glass fibers in the 7th RoC. At that time, NTP raised two questions regarding the study. The first related to the adequacy of the doses used and the second was the relatively high background tumor rate in the concurrent control group. Since the original listing, new research findings have been published that directly address these two questions.

Regarding doses used, T.W. Hesterberg, *et al*, in "Use of Lung Toxicity and Lung Particle Clearance to Estimate the Maximum Tolerated Dose (MTD) for a Fiber Glass Chronic Inhalation Study in the Rat,"[12] reported on subchronic studies assessing lung toxicity and lung particle clearance to estimate the MTD for a fiber glass chronic inhalation study in rats. The authors concluded that ". . . the chronic and subchronic data support a conclusion that the 30 mg/m3 (approximately 230-300 fibers/cc) aerosol concentration was the appropriate highest dose for the FG chronic inhalation study in the rat." Additionally, C.L. Tran, *et al.*, in "Evidence of overload,

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[7] G.E. Marchant, M.A. Amen, C.H. Bullock, C.M. Carter, K.A. Johnson, J.W. Reynolds, F.R. Connelly, and A.E. Crane, "A Synthetic Vitreous Fiber (SVF) Occupational Exposure Database: Implementing the SVF Health and Safety Partnership Program," *Applied Occupational and Environmental Hygiene*, Volume 17(4): 276-285, 2002.

[8] NAIMA (North American Insulation Manufacturers Association). 1999. Letter to Adam Finkel, Director of Health Standards, Occupational Safety and Health Administration on voluntary health and safety partnership program for fiber glass, rock and slag wool fiber products from Kenneth D. Mentzer, Executive Vice President of the North American Insulation Manufacturers Association (NAIMA), May 18, 1999. http://208.186.168.18/~admin42/pages/benefits/hspp/NAIMA_ltr_to_OSHA.html

[9] Marchant, pp. 276-285.

[10] NAIMA. http://208.186.168.18/~admin42/pages/benefits/hspp/NAIMA_ltr_to_OSHA.html

[11] T.W. Hesterberg, W.C. Miiller, E.E. McConnell, J. Chevalier, J.G. Hadley, D.M. Bernstein, P. Thevenaz, and R. Anderson, "Chronic Inhalation Toxicity of Size-Separated Glass Fibers in Fischer 344 Rats," *Fundamental and Applied Toxicology* 20, 464-476 (1993).

[12] T.W. Hesterberg, E.E. McConnell, W.C. Miiller, J. Chevalier, J. Everitt, P. Thevenaz, H. Fleissner, and G. Oberdorster, "Use of Lung Toxicity and Lung Particle Clearance to Estimate the Maximum Tolerated Dose (MTD) for a Fiber Glass Chronic Inhalation Study in the Rat," *Fundamental and Applied Toxicology* 32, 31-44 (1996).

dissolution and breakage of MMVF10 fibres in the RCC chronic inhalation study,"[13] found "[e]vidence of overload, dissolution and breakage of MMVF 10 fibres in the RCC chronic inhalation study," suggesting the highest dose may have exceeded the MTD.

On the issue of background tumor rates, subsequent to the original NTP listing, C.E. Rossiter and J.R. Chase published "Statistical Analysis of Results of Carcinogenicity Studies of Synthetic Vitreous Fibres at Research and Consulting Company, Geneva."[14] That report concludes:

> No insulation wool (glass, stone, or slag) exposure group had a lung tumour rate that differed statistically significantly from the tumour rate for the respective concurrent control groups, sham-exposed to filtered air. There were no significant difference in the total tumour rates between the four insulation wool groups and the control animals, and no significant dose-response relation above the respective sham-exposed control tumour rates.[15]

The IARC in 2002 acknowledged the significance of these inhalation studies. Specifically referring to these studies IARC stated:

> More recent inhalation studies in rodents have addressed the technological limitations of the earlier studies using test fibres prepared by new size separation methods. Such fibres are respirable by rats and long enough to be biologically active, with nominal diameters of 1 x 20 μm. An aerosolization system has been designed to create uniform, high concentrations of airborne fibres without destroying the biologically important long-thin fibre geometry.
>
> In the chronic inhalation studies of MMVFs reviewed in section 3, the Working Group has clearly noted those studies that they considered to be 'well-conducted long-term inhalation studies' which meet the criteria summarized above.[16]

In addition to these studies on glass wools, "well conducted long term inhalation studies" were reported for rock and slag wools, again showing no lung or pleural tumors.[17]

The fundamental importance of these findings is that for each of the three major types of insulation wools – glass, rock and slag – the IARC Working Group found the overall evidence of carcinogenicity in animals to be "limited" only because there were reports of tumor formation

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[13] C.L. Tran, A.D. Jones and K. Donaldson, "Evidence of overload, dissolution and breakage of MMVF10 fibres in the RCC chronic inhalation study," *Exp. Toxic Pathol* 48: 500-504 (1996).
[14] C.E. Rossiter and J.R. Chase, "Statistical Analysis of Results of Carcinogenicity Studies of Synthetic Vitreous Fibres at Research and Consulting Company, Geneva," *Ann. Occup. Hyg.*, Vol. 39, No. 5, pp. 759-769, 1995.
[15] Ibid., p. 759.
[16] IARC 81, p. 37.
[17] McConnell, E.E., Kamstrup, O., Musselman, R., Hesterberg, T.W., Chevalier, J., Miiller, W.C., and Thevanez, P., "Chronic Inhalation Study of Size-Separated Rock and Slag Wool Insulation Fibers in Fischer 344/N Rats," *Inhal. Toxicol.*, 6, 571-614 (Nov.-Dec. 1994).

with each of the insulation wools only following intraperitoneal injection. The IARC Working Group summarized the data as follows:

Insulation glass wool [animal evidence "limited"]

Insulation glass wools were tested in well-designed, long-term inhalation studies in rats and hamsters. No significant increase in lung tumours and no mesotheliomas were observed in rats and no lung tumours or mesotheliomas were observed in hamsters exposed to insulation glass wool. Two different asbestos types used as positive controls produced increases in lung tumours and mesotheliomas.

Two insulation glass wools that produced no increase in tumours when administered by inhalation did induce mesotheliomas when injected at high doses (approximately 10^9 fibres) into the peritoneal cavity of rats.[18]

Rock (stone) wool [animal evidence "limited"]

In a well-designed, long-term inhalation study in which rats were exposed to rock (stone) wool, no significant increase in lung tumour incidence and no mesotheliomas were observed. Crocidolite asbestos was used as the positive control and led to high lung tumour and one mesothelioma.

After intratracheal instillation of rock (stone) wool in two studies, no significant increase in the incidence of lung tumours or mesotheliomas was found. Tremolite asbestos was used as a positive control and induced lung tumours.

In several studies of intraperitoneal injection of high doses (approximately 10^9 fibres), rock (stone) wool induced a significant increase in mesothelioma incidence. The more biopersistent rock (stone) wool fibres produced a higher incidence of tumours than fibres with lower biopersistence.[19]

Slag wool [animal evidence "limited"]

In a well designed, long-term inhalation study of slag wool in rats, no statistically significant increase in the incidence of lung tumours and no mesotheliomas were observed. Crocidolite asbestos was used as a positive control and led to high lung tumour incidence. In two intraperitoneal studies, a high dose (approximately 10^9 fibers) of slag wool induced a statistically significant increase in the incidence of mesotheliomas.[20]

The second major factor significant to IARC's downgrading of the animal evidence to "limited" was the growing consensus as to relevance of various routes of exposure for hazard assessment.

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[18] IARC 81, p. 332.
[19] Ibid.
[20] Ibid., p. 333.

See, e.g., the report from a 1996 workshop sponsored by the U.S. EPA Office of Pollution Prevention and Toxics in collaboration with NIEHS, NIOSH and OSHA[21] that concluded:

> After extensive discussion and debate of the workshop issues, the general consensus of the expert panel is that chronic inhalation studies of fibers in the rat are the most appropriate tests for predicting inhalation hazard and risk of fibers to man.

This position is also supported by the National Research Council's ("NRC") Subcommittee on Manufactured Vitreous Fibers, Committee on Toxicology, Board of Environmental Studies, Commission on Life Sciences, in its 2000 "Review of the U.S. Navy's Exposure Standard for Manufactured Vitreous Fibers." In Chapter 5, the Subcommittee states:

> It appears reasonable to conclude that extrapolations from animal toxicity data to humans for MVF can best be made when experimental animals are exposed to fibers via inhalation.[22]

Additionally, regarding the issue of intracavitary injection studies, the same NRC report states:

> The subcommittee agrees with a WHO scientific panel's conclusion that the intraperitoneal model should not be used for quantitative risk assessment or for comparing relative hazards posed by different fibers (WHO 1992).[23]

Finally, the now well-established role of fiber biopersistence in the potential biological activity of fibers also played an important role in the downgrading of the animal data. This finding by IARC is also consistent with the above-cited NRC report, which states that "The potential hazards posed by a given MVF is directly related to its ability to persist in the lung long enough to cause chronic disease."[24]

Based on the extensive published research and conclusions reached by both IARC and the NRC's recent review, glass wool (respirable size) does not meet either the criteria for human or animal evidence that are required for listing in the RoC. Additionally, mechanistic considerations on the role of biopersistence support the conclusion that the animal data derived from intracavitary injection studies are no longer considered adequate to provide "sufficient evidence of animal carcinogenicity."

THE USE OF GLASS WOOL (RESPIRABLE SIZE) AS AN INSULATION PRODUCT

Glass wool (respirable size) products are used primarily as thermal and acoustical building insulation. One of the principal benefits from insulation is energy savings. Reduced energy use also reduces the amount of the pollution released into the atmosphere. Two recent Harvard

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[21] V. Vu, J.C. Barrett, J. Roycroft, L. Schuman, D. Dankovic, P. Baron, T. Martonen, W. Pepelko, and D. Lai, "Workshop Report, Chronic Inhalation Toxicity and Carcinogenicity Testing of Respirable Fibrous Particles," *Regulatory Toxicology and Pharmacology* 24 (1996) 202-212.

[22] National Research Council, *Review of the U.S. Navy's Exposure Standard for Manufactured Vitreous Fibers* (2000), p. 39.

[23] Ibid.

[24] Ibid., p. 33.

School of Public Health studies[25] showed that energy saving would significantly reduce pollution that is directly responsible for health problems. The studies concluded that properly insulated homes would significantly reduce atmospheric emissions of sulfur oxide, nitrous oxide, and fine particulate matter. The benefits found in the Harvard School of Public Health studies show the importance of insulation.

For a more complete listing of uses for glass wool, see Figure 8 in the IARC Monograph.[26]

SPECIAL PURPOSE FIBERS

NAIMA's January 2002 nomination to delete fiber glass from the RoC makes clear that the nomination was limited to glass wool (respirable size). In the recent Federal Register notice (69 Fed. Reg. 28,940 (May 19, 2004)), the NIEHS has through its own nomination recommended that Special Purpose Fibers (SPFs) be listed on the RoC. NAIMA offers the following information as clarification to distinguish glass wool (respirable size) from the SPFs.

As a small subset of all SVFs, SPFs are used primarily for special purposes, such as battery separator media, filtration media, and aerospace insulation. In its discussion of SPFs, IARC refers to E-glass and 475 fibers; however, E-glass and 475 fiber formulations do not differ from other SPFs but are instead only examples of SPFs that have been tested extensively in animal inhalation studies. Although other SPFs have not been as extensively tested as these two, all SPFs share certain chemical and physical similarities that are described in more detail below. Importantly, IARC considers the human evidence for the carcinogenicity of all SPFs to be inadequate.

Special Purpose Glass Fibers Are Used Only in Specialized Applications Requiring Unique Performance Properties Not Found in Glass Wool Insulation

In contrast to the insulation wools, SPFs are more highly engineered and hence, significantly more expensive than glass wool insulation. Unlike typical insulation wools, SPFs make up a very small percentage of the man-made vitreous fiber market, accounting for about one percent of the total annual production of SVFs. SPFs are sold in final products by the fiber manufacturer to commercial users or alternatively to other manufacturers where they are made into final products. SPFs are not typically available for direct purchase by consumers.

A significant market for SPFs is in battery separator media. This SPF is composed of an acid-resistant borosilicate glass fiber with specified fiber diameters. The purpose of the media is to physically separate the positive and negative plates within the battery while allowing the sulfuric acid electrolyte to pass through the media creating an electrical charge and filtering impurities.

[25] Y. Nishioka, J.I. Levy, G.A. Norris, A. Wilson, P. Hofstetter, and J.D. Spengler, "Integrating Risk Assessment and Life Cycle Assessment: A Case Study of Insulation," *Risk Analysis*, Vol. 22, No. 5, 2002 and J.I. Levy, Y. Nishioka, and J.D. Spengler, "The public health benefits of insulation retrofits in existing housing in the United States," *Environmental Health: A Global Access Science Source* 2003, 2:4.
[26] IARC 81, p. 77.

SPFs are also used for both air and liquid filtration. The key to creating successful filtration media is the ability to consistently produce fibers to specific fiber diameters. Both the method of manufacture and the specific chemical formulations are designed to meet these performance requirements.

Fine filtration or high efficiency filtration media include those designed for removal of particulates less than 1 μm in diameter. These filtration media are normally comprised of SPFs with average diameters from 1 to 0.1 μm. A special category of high efficiency filter media includes HEPA glass filters that are used as filter materials in high performance settings, primarily in the form of pleated "papers". HEPA glass filters are capable of removing 0.025 μm particles. These papers are comprised of some of the smallest SPFs known – some with mean diameters of 0.2 μm and below.

SPF media have also been used in the separation of particulates from liquids, typically as part of cylindrical filter "cartridges" where they are employed as separate concentric layers in a composite that also includes a structural core and various reinforcing or protective organic fabric layers.

The properties of SPFs allow manufacturers to use them to produce a thin blanket of insulation for use in high temperature appliances, where space restrictions are important and high thermal efficiency and fine fiber diameters are essential. The IARC press release stated that MMVFs remaining in Group 2B included "certain special purpose glass wools not used as insulating materials." This statement may have left an impression that the small amounts of SPFs used as specialized insulation were somehow characteristically different from the typical SPFs described herein. When SPFs are used for insulation purposes, these fibers exhibit the same unique characteristics as found in other applications of SPFs. Therefore, insulation wools used in industrial, commercial, and residential settings do not share the same performance and physical/chemical properties as the SPFs used for special insulation in aircraft and spacecraft.

SPFs are used as insulation materials on both aircraft and spacecraft where they have been specially designed for high efficiency at low weight. In commercial aircraft, SPFs are employed principally as a quilted or non-quilted blanket applied to the outer frame, where it serves as the primary thermal insulation for the fuselage, and also as an acoustical barrier for engine and other external noise. These blankets are typically made of fibers with mean diameters from 1 to 1.5 μm.

Distinctions Between SPFs and Insulation Glass Wool

There are very specific distinctions between SPFs and insulation glass wool. As explained more fully below, these distinctions include chemical composition, durability, applications, health effects data, and classification by other expert entities.

Differences in the Chemical Composition of Special Purpose Fibers and Glass Wool Insulations

The chemistry of most SPFs include the addition of oxides such as $Zr0_2$, ZnO, and BaO that improve both the ability to fiberize the glass at submicron diameters as well as the durability of the finished fiber at those diameters.

Special Purpose Fibers Are More Biopersistent Than Glass Wool Insulation

SPFs are also typically more durable than insulation wools – in some instances, by an order of magnitude both as measured *in vitro* by k_{dis} and by $T_{1/2}$ and $WT_{1/2}$ in well-designed animal inhalation studies. The biopersistence of SPFs is due in part to their chemistry but may also be due, in part, to the method of manufacture.

The Available Animal Data Supports Different Conclusions on the Possible Carcinogenicity of SPFs and Glass Wool Insulation

The animal studies database for the insulation glass wools is composed of data from well-designed, chronic inhalation studies that found no increase in either lung or pleural tumors. In contrast, the SPF database contains certain positive data from inhalation and intratracheal instillation studies, which led the Working Group to find the animal evidence "sufficient."

Importantly, there is no difference in the human database for glass wools and SPFs. Extensive studies of manufacturing workers covering over one million person years have not identified any association between all SVFs (including SPFs) and human disease. The Marsh study included workers from plants making SPFs.[27] Given the limited production of SPFs, the number of workers involved in SPF manufacture is, of course, smaller than the number involved in insulation wool manufacturing.

Expert Entities That Have Assessed the Carcinogenicity of Glass Fibers Have Separated SPFs From Glass Wool Insulation

In 2001, IARC made a formal distinction in its classification scheme between glass wool insulations from SPFs, thereby adopting the same separation scheme previously reported by the WHO/IPCS in their 1990 document on "Safety in the use of Mineral and Synthetic Fibres," the Canadian Government's assessment of fiber safety in their 1993 document titled "Priority Substances List Assessment Report: Mineral Fibres (Man-Made vitreous fibres)," and the ACGIH Documentation of TLV's (1994). In each of these cases, SPFs were separated from the glass wool insulation.

Attachments

[27] See footnote 4 above.

NAIMA
NORTH AMERICAN INSULATION
MANUFACTURERS ASSOCIATION

VIA OVERNIGHT MAIL

January 28, 2002

C.W. Jameson, Ph.D.
National Toxicology Program
National Institute of Environmental
Health Sciences
Building 4401, EC/3118
79 Alexander Drive
Research Triangle Park, NC 27709

Re: Delisting Glass Wool (Respirable Size) from Report on Carcinogens

Dear Dr. Jameson:

This letter nominating Glass Wool (Respirable Size) for delisting from the Report on Carcinogens (RoC) is presented by the North American Insulation Manufacturers Association ("NAIMA"), a trade association representing the manufacturers of glass wool in the United States and throughout North America. NAIMA promotes energy efficiency and environmental preservation through the safe manufacture and use of fiber glass insulation products. NAIMA encourages and conducts scientific investigations into the health aspects of these products and disseminates the results to government agencies, industry, customers, employers and the general public.

BASIS FOR DELISTING

This nomination for delisting is based on the recent (October 16, 2001) International Agency for Research on Cancer ("IARC") decision to downgrade the classification of "glass wool insulation" from 2B to 3 and the science supporting that decision. IARC's reclassification concluded that the human data remained "inadequate," but that the animal data was no longer "sufficient," reclassifying it as "limited."[1]

IARC also determined that mechanistic considerations regarding fiber durability provided additional information supporting the downgrading.

Human Data

In the IARC re-evaluation the human data were determined to be "inadequate." A very large database is now available on the epidemiology of glass wool manufacturing workers, and as the IARC press release stated:

[1] IARC retained the Group 2B classification ("possibly carcinogenic to humans") for refractory ceramic fibers and "certain special-purpose glass wools not used as insulating materials." (See IARC Press Release at Tab 1). This delisting nomination only applies to glass wool insulation categorized by IARC as Group 3.

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> "These [SVF] products, including glass wool . . . have been in use for decades and have been extensively studied to establish whether fibres that are released during manufacture, use, or removal of these products present a risk of cancer when inhaled. Epidemiologic studies published during the 15 years since the previous IARC Monographs review of these fibres in 1988 provide no evidence of increased risks of lung cancer or of mesothelioma (cancer of the lining of the body cavities) from occupational exposures during manufacture of these materials, and inadequate evidence overall of any cancer risk."[2]

A significant part of the data in IARC's glass wool designation was the "Historical Cohort Study of U.S. Man-Made Vitreous Fiber Production Workers" by Dr. Gary Marsh, *et al.*[3] One of the largest epidemiology studies ever produced, this study covers over 40,000 U.S. production workers and over one million person years of occupational exposure. (See Tab 2.)

Animal Data

The animal evidence was downgraded by IARC from "Sufficient" to "Limited." This was due to (1) the availability of well conducted chronic inhalation studies in two species conducted at or above the MTD, which showed no evidence of either fibrosis or significant tumor induction with the glass wool insulations; and (2) the growing consensus regarding the relevance of route of administration in assessing the hazard of fibers.

It is important to note that an early report on the multidose rat inhalation study (Hesterberg, *et al.*, 1993)[4] (see Tab 3) was evaluated by NTP prior to the listing of glass fibers in the 7th RoC. At that time, NTP raised two questions regarding the study. The first related to the adequacy of the doses used and the second was the relatively high background tumor rate in the concurrent control group. Since the original listing, significant new research has been published which directly addresses these two questions.

Regarding doses used, Hesterberg, *et al.* (1996)[5] (see Tab 4) reported on subchronic studies assessing lung toxicity and lung particle clearance to estimate the MTD for a fiber glass chronic inhalation study in rats. The authors reported that the dose used in the chronic study was the

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[2] A copy of the IARC October 24, 2001 press release is attached. (See Tab 1.) See also: www.iarc.fr - Press Releases (October 24, 2001).

[3] *Journal of Occupational and Environmental Medicine*, September 2001. Copies of this and all other journal articles referred to herein are enclosed for your information and convenience.

[4] T.W. Hesterberg, W.C. Miller, E.E. McConnell, J. Chevalier, J.G. Hadley, D.M. Bernstein, P. Thevenaz, and R. Anderson, "Chronic Inhalation Toxicity of Size-Separated Glass Fibers in Fischer 344 Rats," *Fundamental and Applied Toxicology* 20, 464-476 (1993).

[5] T.W. Hesterberg, E.E. McConnell, W.C. Miller, J. Chevalier, J. Everitt, P. Thevenaz, H. Fleissner, and G. Oberdorster, "Use of Lung Toxicity and Lung Particle Clearance to Estimate the Maximum Tolerated Dose (MTD) for a Fiber Glass Chronic Inhalation Study in the Rat," *Fundamental and Applied Toxicology* 32, 31-44 (1996).

highest dose appropriate for the rat inhalation study. Additionally, Tran, *et al.* (1996)[6] found "[e]vidence of overload, dissolution and breakage of MMVF 10 fibres in the RCC chronic inhalation study," further supporting the adequacy of the dosing in the chronic study. (See Tab 5.)

On the issue of background tumor rates, subsequent to the original NTP listing, Rossiter and Chase published "Statistical Analysis of Results of Carcinogenicity Studies of Synthetic Vitreous Fibres at Research and Consulting Company, Geneva" (Rossiter and Chase, 1995)[7] (see Tab 6). That report concludes:

> "No insulation wool, (glass, stone, or slag) exposure group had a lung tumour rate that differed statistically significantly from the tumour rate for the respective concurrent control groups, sham-exposed to filtered air. There were no significant difference in the total tumour rates between the four insulation wool groups and the control animals, and no significant dose-response relation above the respective sham-exposed control tumour rates."[8]

The second major factor significant to IARC's downgrading of the animal evidence to "limited" was the growing consensus as to relevance of various routes of exposure for hazard assessment. See, for example, the report from a 1996 workshop sponsored by the U.S. EPA Office of Pollution Prevention and Toxics in collaboration with NIEHS, NIOSH and OSHA (Vu, *et al.*, 1996)[9] (see Tab 7) that concluded "After extensive discussion and debate of the workshop issues, the general consensus of the expert panel is that chronic inhalation studies of fibers in the rat are the most appropriate tests for predicting inhalation hazard and risk of fibers to man." Also see chapter 5 of the recent National Research Council Report (Tab 8):

> "It appears reasonable to conclude that extrapolations from animal toxicity data to humans for MVF can best be made when experimental animals are exposed to fibers via inhalation."[10]

Additionally, regarding the issue of intracavitary injection studies, the same National Research Council Report states:

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[6] C.L. Tran, A.D. Jones and K. Donaldson, "Evidence of overload, dissolution and breakage of MMVF10 fibres in the RCC chronic inhalation study," *Exp. Toxic Pathol* 1996: 48: 500-504.
[7] C.E. Rossiter and J.R .Chase, "Statistical Analysis of Results of Carcinogenicity Studies of Synthetic Vitreous Fibres at Research and Consulting Company, Geneva," *Ann. Occup. Hyg.*, Vol. 39, No. 5, pp. 759-769, 1995.
[8] Ibid. at 759.
[9] V. Vu, J.C. Barrett, J. Roycroft, L. Schuman, D. Dankovic, P. Baron, T. Martonen, W. Pepelko, and D. Lai, "Workshop Report, Chronic Inhalation Toxicity and Carcinogenicity Testing of Respirable Fibrous Particles," *Regulatory Toxicology and Pharmacology* 24, 202-212 (1996).
[10] National Research Council, *Review of the U.S. Navy's Exposure Standard for Manufactured Vitreous Fibers* (2000), p. 39.

> "The subcommittee agrees with a WHO scientific panel's conclusion that the intraperitoneal model should not be used for quantitative risk assessment or for comparing relative hazards posed by different fibers (WHO 1992)."[11]

The now well-established role of fiber biopersistence in the potential biological activity of fibers also played an important role in the downgrading of the animal data. This finding by IARC is also consistent with the NRC report which states that "The potential hazards posed by a given MVF is directly related to its ability to persist in the lung long enough to cause chronic disease."[12]

Based on the extensive published research and conclusions reached by both IARC and the NRC's recent review, Glass Wool (Respirable Size) does not meet either the criteria for human or animal evidence that are required for listing in the RoC. Accordingly, Glass Wool (Respirable Size) is an appropriate candidate for nomination for delisting from the NTP's RoC. Additionally, mechanistic considerations on the role of biopersistence support the conclusion that the animal data derived from intracavitary injection studies are no longer considered adequate to provide "sufficient evidence of animal carcinogenicity."

NAIMA will augment this correspondence with additional information once the IARC monograph has been published. In addition, NAIMA will provide NTP with supplemental data that will assist in the review of glass wool. Specifically, NAIMA will furnish to NTP searchable CDs containing published articles from peer-reviewed sources. These CDs, which are in .pdf format, have been updated to include articles published in the peer-reviewed literature that were not yet available at the time that the CDs were prepared for IARC and which proved very useful during its recent re-evaluation of man-made vitreous fibers. We anticipate shipping the CDs no later than early March 2002.

NAIMA also offers as a resource for NTP the NAIMA exposure database, historic research documents and knowledge acquired from a long affiliation with the glass wool industry. NAIMA and its members look forward to assisting NTP in whatever manner is appropriate and useful. Please contact Angus Crane at (703) 684-0084 or acrane@naima.org if NAIMA can provide further assistance or information.

Sincerely,

Kenneth D. Mentzer
President and CEO

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[11] *Ibid.* at 39.
[12] *Ibid.* at 33.

John G. Hadley, Ph.D.
Chairman, NAIMA Health and Safety Advisory Subcommittee

Thomas W. Hesterberg, Ph.D.
NAIMA Health and Safety Advisory Subcommittee

Enclosures

IARC MONOGRAPHS PROGRAMME RE-EVALUATES CARCINOGENIC RISKS FROM AIRBORNE MAN-MADE VITREOUS FIBRES

A scientific working group of 19 experts from 11 countries convened by the Monographs Programme of the International Agency for Research on Cancer (IARC) has concluded its re-evaluation of the carcinogenic risk of airborne man-made vitreous fibres.

Man-made vitreous fibres in the form of wools are widely used in thermal and acoustical insulation and in other manufactured products in Europe and North America. These products, including glass wool, rock (stone) wool, and slag wool, have been in use for decades and have been extensively studied to establish whether fibres that are released during manufacture, use, or removal of these products present a risk of cancer when inhaled. Epidemiologic studies published during the 15 years since the previous IARC Monographs review of these fibres in 1988 provide no evidence of increased risks of lung cancer or of mesothelioma (cancer of the lining of the body cavities) from occupational exposures during manufacture of these materials, and inadequate evidence overall of any cancer risk.

Beside this, much industrial effort has gone into development of newer materials that have similar insulation properties to the older products, but which disappear from body tissues much more rapidly. The reason for this effort is that asbestos, a known human carcinogen which causes both mesothelioma and lung cancer and had been used as insulating material for several decades, is extremely slow to decompose and disappear from body tissues in which it has been deposited. This characteristic, known as high biopersistence, is correlated with the high carcinogenic potency of asbestos fibres. Some of these newer materials have now been tested for carcinogenicity and most are found to be non-carcinogenic, or to cause tumours in experimentals animals only under very restricted conditions of exposure.

The Monographs working group concluded that only the more biopersistent materials remain classified by IARC as possible human carcinogens (Group 2B). These include refractory ceramic fibres, which are used industrially as insulation in high-temperature environments such as blast furnaces, and certain special-purpose glass wools not used as insulating materials. In contrast, the more commonly used vitreous fibre wools including insulation glass wool, rock (stone) wool and slag wool are now considered not classifiable as to carcinogenicity to humans (Group 3). Continuous glass filaments, which are used principally to reinforce plastics, are also considered not classifiable as to carcinogenicity to humans.

For further details of the Monographs evaluation, consult http://monographs.iarc.fr, under "Agents most recently evaluated," or inquire by e-mail to grosse@iarc.fr.

For further details of current research at IARC on man-made vitreous fibres, inquire by e-mail to boffetta@iarc.fr.

For more general information, contact Dr Nicolas Gaudin, Chief, Communications (gaudin@iarc.fr).