

Cancer and mineral wool

Why Rockwool is wrong, when they claim that stonewool are acquitted for causing cancer.



Actiongroup of workers and academics. 2002.

Preface:

Stone, slag and glass wool *may* be carcinogenic

In 2001 the largest Danish producer of mineral wool products, Rockwool, distributed a lavish multicolour brochure to its customers, trade unions and other persons and firms working with these type of products. The message on the front page was unmistakable: A big bale of Rockwool mineral wool and the word: "acquitted".

If we were to believe the words of Rockwool, and if it was scientifically established that you do not increase your risk of getting a cancer illness by working with mineral wool (stone- slag- or glass wool), we and many others would breathe a sigh of relief. It would be a message that everybody who worries about occupational health, would receive with gratification. Unfortunately it is *not* a true and correct message that Rockwool have spent so much PR-money to disseminate.

This booklet deals with the still relevant suspicion about carcinogenic effects of man-made mineral fibers. There is no bullit-proof scientific documentation for increased risk of cancer from working with mineral wool, but the opposite is just as true: there is no documentation that man made mineral fibers do *not* increase risk of cancer. Workers, working with insulation in the building trade, are recognized as having far more lung-diseases than other workers. Whether working with mineral wool is a contributing factor to this fact, is still discussed by scientists. But this is more than a scientific debate. Just as much as it is a power struggle between on the one hand an extremely wealthy business and on the other hand the trade union movement and other people and organizations trying to protect workers and others that come into contact with this material. And it is a question of attitude and values: Do thousands of people have to keep on working with mineral wool and run the risk of getting cancer from it, or should our point of departure rather be the Precautionary Principle that would lead us to phase out man-made mineral fibres and give priority to the development and use of less dangerous materials of insulation.

The fibre working group from AAA

The fibre working group is one of the active groups in AAA. The group has earlier made a danish newsletter about asbestos.

The action group of workers and academics, "Aktionsgruppen Arbejdere Akademikere" (AAA), is an organisation of critical working environment people - from trade unions, the Danish Working Environment Service, the Occupational Health Service Centre, researchers and students.

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1. A Question of Power or a Struggle for Health - Stone wool, cancer risk and corporate lobbyism

By Palle Bisgaard and Michael Voss

Palle Bisgaard is chairman of the construction workers in the Copenhagen branch of the Union of Wood, Industrial, and Construction Workers. Michael Voss is a journalist and is employed by the parliamentary party secretariat of the Red Green Alliance (Unity List). They are both members of the working group on fibres established by the Action Group of Workers and Academics.

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Signed by 6 representatives of international union federations and 3 representatives of national union federations

5. No Effect or No Information? - Comments on a Nested Case-Control Study of Lung Cancer among European Rock and Slag Wool Production Workers

By Eva S. Hansen, PhD. Department of Occupational and Environmental Health, Institute of Public Health, University of Copenhagen

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1.

A Question of Power or a Struggle for Health - Stone wool, cancer risk and corporate lobbyism

By Palle Bisgaard and Michael Voss. Palle Bisgaard is chairman of the construction workers in the Copenhagen branch of the Union of Wood, Industrial, and Construction Workers. Michael Voss is a journalist and is employed by the parliamentary party secretariat of the Red Green Alliance (Unity List). They are both members of the working group on fibres established by the Action Group of Workers and Academics

Workers in the building trades are recognized as suffering from lung cancer as a result of working conditions to a far greater extent than workers in other branches. Asbestos is undoubtedly the main cause, but mineral fibre insulation is also under suspicion of causing cancer.

Whether or not this is the case is under discussion by researchers, but it is more than a mere question of science. It is as much a question of a power struggle between an extremely well capitalized industry on the one hand and trade unions and others who are attempting to protect industrial workers and others who use this material. In truth, it comes down to a question of interest and position.

Shall thousands of people continue to work with spun mineral insulation and run the risk of getting cancer, or shall the necessary point of reference be the Precautionary Principle, with a gradual reduction of the use of this material, and a high priority on the development and use of other less dangerous insulating material?

This conflict about science, point of interest, and economic power reached its most recent highpoint last October when WHO's cancer section, the International Agency on Research in Cancer (IARC) undertook to determine how well a scientific link between mineral fibres and cancer could be established. Shortly after IARC's session, Rockwool, Denmark's largest producer of mineral fibre insulating material issued an attractive, full colour information folder to its customers, to the trade unions, and others who work with their products. The message on the front cover couldn't be misunderstood; there was the picture of a big bale of Rockwool and the words "Not Guilty".

If one were to believe Rockwool, that it has been scientifically established there is no risk of lung cancer in working with mineral fibres, then many would breathe a sigh of relief. This was news everyone in the insulation and building trades sector should greet with joy.

Unfortunately, the glad tidings that Rockwool spent its marketing money on dispensing is not at all correct.

Firstly, the IARC did not decide to give spun mineral fibres a clean bill of health, but to reclassify them from the group of agents which are possibly cancer causing to the group of those whose cancer causing qualities cannot be determined.

Secondly, there are several good reasons to question IARC's conclusion. It is built on a strongly criticized research project, and IARC's decision was taken at a meeting where the mineral fibre industry was represented in remarkable strength.

We, like many others, are used to seeing the WHO as a neutral and factually based institution, one setting health above other concerns. When we allow ourselves to sow doubt about the IARC's and WHO's judgment, it is not only because of developments in the case of mineral fibre material. It has become a general problem that the industries that produce hazardous substances have an unwarranted influence on decisions of the IARC, and that they have tried to keep this influence hidden. Because of this, 32 medical experts wrote an open letter to WHO-director Gro Harlem Brundtland in which they accused the IARC and WHO of "capitulation to corporate influence". Among signatories were two former heads of the IARC.

The suspicion that mineral fibres could be a cause of cancer arose in the 1970's, at the same time as asbestos was determined to be a carcinogenic. More correctly stated, it was at that time it became public knowledge that for fifty years the asbestos industry had known asbestos to be fatal to health, and that the industry had managed to keep this knowledge secret during all that time.

Like asbestos spun mineral is a fine fibre substance, with characteristics some similar to, and some different from asbestos. That fact makes it reasonable to raise the question of an increased cancer risk in working with mineral fibres.

Study of statistics on industrial injuries and occupational diseases from the Danish National Board of Industrial Injuries shows clearly that building workers suffer from cancer more frequently than others in comparable employment. While workers in the building trades comprise 7% of the work force, they suffer from 28.4% of the recognized cases of cancer. Those in the building trades who especially work with insulation suffer with an extremely higher frequency. On the average cancer comprises 1.3% of all recognized occupational diseases and work-related injuries, but for carpenters and building joiners the rate is 6.6%, and for insulation workers the rate is 32.3%.

There is no doubt that many of these cases are caused by asbestos, but there is no guarantee that other materials building workers are in contact with do not share responsibility for these high cancer rates.

All of these facts occasioned the mineral fibre industry in the early 70's to begin a series of studies involving 22,000 workers in mineral fibre plants in different European countries, comparing the frequency of cancer in these workers with that of the general population. Results showed a frequency that was from 30% to 50% higher, while animal trials demonstrated a cancer risk in spun mineral fibre.

This caused the IARC to characterize the spun mineral material as "possibly cancer causing in humans". The classification system used by the IARC has 5 groups: (1), causing cancer in humans; (2A), probably causing cancer in humans; (2B), possibly causing cancer in humans; (3), not possible to determine as to its cancer causing properties in humans; (4), probably not cancer causing in humans. The IARC therefore decided to place spun mineral fibre material in group 2B.

Like other nations, and in a manner consistent with its classification of similar materials, Denmark placed mineral fibre material on its cancer list in 1988. This did not, however, result in the implementation of safety and protective measures for work with mineral fibres similar to those required with all other substances on the cancer list. Rockwool's lobby activity was, as on many other occasions, effective, and spun mineral fibre products received their own set of regulations with weaker safety precautions than other cancer suspected substances. That, however, is another story.

In any case, Rockwool and its cooperating partners in the European mineral fibre industry were not satisfied with the placement of their product in group 2B. A suspicion of risk hung over the product and could disturb sales. They therefore decided to conduct a new study in cooperation with the IARC as a follow-up to the first.

It attempted to eliminate those cancer cases where there had been exposure to asbestos. The results published in 1997, however, were the same, a clear overrepresentation of cancer cases. Similar studies conducted in the United States at the same time showed the same results.

The mineral fibre industry didn't give up, but began a new study. This differed from the first by comparing mineral fibre workers with cancer with mineral fibre workers without, instead of comparing with the general population. A similar study was conducted in the United States using this basis of comparison. While in Europe the study was about the use of stone wool fibres, in the United States it involved workers associated with glass wool fibres. Both these studies were released at the end of 2000 and concluded that there was no relation between exposure to mineral fibre and the occurrence of cancer.

Based on these results, the IARC decided that the status of mineral fibre should be reviewed. It is that review from October of last year, previously mentioned, that lowered the risk classification to group 3, with the causality of cancer "not possible to determine". In the course of a substance classification review, the IARC considers both animal studies and studies in humans - epidemiological studies.

At their session in October, the IARC working group found the results of the animal studies as damning as before, but concluded that the new epidemiological studies weakened the case against mineral fibres. The only new study related to stone wool fibres was the European study. Without this study, it is unlikely that the IARC would have reduced the risk classification of mineral fibre. Thus it is of crucial importance to know that this study suffers from a series of serious errors.

The researcher and physician Dr. Eva Støttrup Hansen in Sept. 2001 presented a critical review of this study and concluded, "The study's peculiar results principally reflect the study design chosen and the particular characteristics of the data used. However, concerning the carcinogenic properties, the study has *no informational value* (our emphasis - PB/MV) on the topic of MMVF exposure's possible contribution to lung cancer among production workers." (MMVF is the technical designation for mineral fibre material - PB/MV).

Eva Støttrup Hansen pointed out several curious "findings" in the study. It cannot show any relation between exposure to asbestos and lung cancer, even though a large percentage of the subject group had been exposed to asbestos, and even though the particular form of cancer, mesothelioma, which can *only* be caused by asbestos, occurred in the group. Moreover, if one were to accept the data of the study at face value, in Germany working with mineral fibre material appears to be having a *preventative* effect for cancer, but not so in three other European countries in the study.[!]

Dr. Støttrup Hansen pointed first and foremost to a series of methodological errors, all slanting results in the direction of an underestimation of the possible relationship between exposure to mineral fibre and cancer. In addition, she identified an unusually high number of errors in the calculation of data and unexplained contradictions in the numerical data used.

Immediately upon completion of her report, she sent all of the authors of the IARC report a resume of her conclusions in English. To this date, none have replied. The Danish Cancer Society, which conducted the Danish portion of the survey, has admitted some of the factual errors, but none the

less continues to support its worth. The IARC was also sent a copy of her report, but nevertheless its conclusion is based on the criticized study.

But aren't the IARC working group right? We're talking about some of the most distinguished scientists in the field. This is true, but that was not a completely neutral group meeting to conduct the revision.

Unfortunately the IARC and WHO rules do not demand that participants in such a study group reveal their possible relationships with the industry whose products they are to evaluate, to the public. This information must be given to the IARC and the WTO, but it is to be kept strictly secret. We know only what can be culled from the *official* presentations of a single of the delegates: Dr. Tom W. Hesterberg from the study group is employed by the John Manville Corporation, of the United States, one of the world's largest producers of mineral fibre material. Nothing in the rules hinders the participation of a man with Dr. Hesterberg's background. The only thing that the IARC's guidelines demand is that Dr. Hesterberg must not "represent" his employer. We must sincerely hope that Dr. Hesterberg kept this in mind.[!]

People with knowledge of this branch of the scientific world did note that several of the group participants are among those scientists who always defend industry and its products, and that there were many more participants who beforehand did not consider mineral fibre material cancer causing than those who beforehand thought it was a cancer risk.

At a session like this, an observation group is always accompanying such a scientific working group. The members of the observer group may participate in both formal and informal discussions, but are barred when the final decision making session is held.

In that observer group there were several representatives of the mineral fibre industry, including Dr. Ole Kamstrup from Rockwool. There were on the other hand no representatives from either the trade unions or from other organisations representing mineral fibre product users.

Some will think that we are overly suspicious when we call into question the scientific basis of the re-evaluation with a reference to the firms which will suffer if their products are labelled cancer causing. The suspicion is not ours alone.

As mentioned in the introduction, 32 medical experts raised the same point in an open letter to the general director of the WHO. This letter sent the 25th of Feb. 2002 has among its signatories James Huff, the former director of the IARC department which evaluates the causal relationships between various substances and cancer. In addition, the former director of the IARC, Lorenzo Tomasi is a signatory, along with Professor Philippe Grandjean, from the University of Southern Denmark in Odense, and Benedetto Terracini who was the leader of the IARC working group which evaluated the cancer risk in 1,3-butadiene, used in rubber production.

The workings of this group were cited as an example of how strong the influence of lobby interests is. After completing its work by a vote of 17 to 13 that butadiene was cancer causing, one of the group members favouring that decision left the session, whereupon observer delegates began to revise the opinions of those who had voted affirmative, with the result that on the following day a new vote resulted by 15 to 14 in a change from "causing cancer" to "probably causing cancer" in humans.

Dr. Terracini, though group chairman, was not even allowed to disclose how close the voting had been. The letter also cites other example of seeming conflicts of interest, and the signers feel able to identify a tendency for the IARC to evaluate chemicals "more mildly" than previously. As

mentioned above, they accuse the IARC and WHO for capitulation in the face of industry at the expense of health concerns.

As a first step towards the correction of this development, the signers call upon Gro Harlem Brundtland to see that information given to the WHO and IARC by the scientific experts about their present and previous relations to the industry concerned, becomes public knowledge. Secondly, they recommend that scientists directly dependent on their connection to industries affected by WTO and IARC studies be excluded from participation in the working groups.

WTO and IARC evaluations are of great importance in the formation of general public opinion on matters of risk and health, and as the basis of laws and regulations adopted by authorities around the world in protection of their citizens. It is our intention herewith to point out the advisability of maintaining a critical watch on the work of the WTO and the IARC. Additionally, to point out the likelihood that Rockwool will use the IARC's re-evaluation of mineral fibre to effect a change in standards on the part of the Danish Environmental Protection Agency and the Danish National Health and Safety Inspectorate.

We most strongly advise against a weakening of the rules governing the use of mineral fibre materials. On the contrary, we think there is every reason to suspect that both mineral fibre and glass fibre materials are causes of cancer.

Perhaps there are no risks in working with these materials, but why must hundreds of thousands of individuals be exposed to them "experimentally" as long as the question is in doubt, particularly as mineral fibre material is the known cause of bronchitis, skin and eye irritation, exema, and allergies. In matters of the environment and work safety the importance of the Precautionary Principle is increasingly recognized. This dictates avoiding the use of a substance or material if there exist grounds to think it dangerous. In the case of mineral fibre, this is an obvious choice, since there exist a number of alternative isolation materials whose properties are harmless or clearly less dangerous. Were Rockwool a firm as forward looking as one might think such a large business enterprise should be, one might expect them to give up their stubborn defence of such a problematical material and set to work developing alternatives.

To all great misfortune, this is not the case. It is therefore of utmost importance that:

Danish authorities set stronger rules guiding the use of mineral fibre materials and for the use of substitutes where possible,

The Danish government continues to support the development of non- hazardous alternatives,

The Danish trade unions continue to campaign vigorously for all developments furthering that process.

2.

An open letter to the General Director of WHO, Gro Harlem Brundtland, about the implementation of WHO Guidelines on Disclosure of Interest by Members of WHO Expert Panels

February 25, 2002

Dr. Gro Harlem Brundtland
Director-General
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SWITZERLAND

Re: Implementation of WHO Guidelines on Disclosure of Interest by Members of WHO Expert Panels

Dear Dr. Brundtland,

We are concerned about the problems of corporate influence and undisclosed conflicts of interest in the development of documents by WHO agencies, particularly regarding the cancer-causing properties of major industrial products and pollutants. There are two WHO agencies involved in this area about whom serious questions of scientific objectivity have been raised. The WHO's recent development of Disclosure of Interest Guidelines in the selection of outside experts was an important step in the right direction, but the implementation of these Guidelines will make all the difference in determining whether the problems will be properly handled.

Problems in evaluation of carcinogenicity of chemicals have been recently identified at a WHO organization, the International Agency for Research on Cancer (IARC) in Lyon. Dr. Lorenzo Tomatis, former Director of IARC, suggests that IARC has begun a new trend towards downgrading carcinogen classifications of chemicals on which there were positive results in experimental bioassays (1): "Evidence for carcinogenicity provided by the results of experimental bioassays has been disregarded on the basis of unproven mechanistic hypotheses." Dr. Tomatis warns that if those hypotheses are shown to be incorrect once they have been tested, very serious consequences for public health may follow. Newly released data on cancer in workers at a U.S. plant making one of the chemicals whose carcinogenic rating was downgraded by IARC, the herbicide atrazine, suggests that positive experimental cancer findings were indeed predictive of carcinogenicity in humans (2).

Experimental findings in cancer bioassays have an extremely high correlation with human carcinogenicity in the substances on which relatively complete information exists. All human carcinogens that have been tested in animals are likewise significantly carcinogenic experimentally. Equally important, nearly one-third of the known human carcinogens were first discovered in

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animals and only subsequently in humans. An improved understanding of mechanism(s) of action of carcinogens may indeed contribute to strengthen the evaluation of cancer risks. However, toxicological research openly or surreptitiously sponsored by industrial concerns should not lead to hastily reached conclusions, largely based on unproven hypotheses championed as being either correct or exclusive in explaining the complex critical effects of toxic substances on experimental animals, let alone on humans.

Another UN agency, the International Program on Chemical Safety (IPCS), is also now set to embark on a scientific analysis of mechanistic hypotheses of interpretation of the human relevance of positive experimental findings in cancer bioassays. If IPCS gets into this area, it should be done by an impeccable panel of independent experts whose qualifications and scientific objectivity are beyond question, given the recent pattern of these theories being used to undermine regulation of major industrial chemicals. It was a protest by 81 scientists over corporate influence at IPCS that led WHO to develop its Disclosure Guidelines (3).

The Natural Resources Defense Council (NRDC) and the California Environmental Protection Agency wrote earlier this year to IARC, protesting the presence of at least 3 scientists closely allied with the styrene industry on a Task Group who had been invited by IARC to serve on a Task Group that will this month be evaluating the carcinogenic potential of chemicals including styrene. NRDC is the leading environmental non-governmental organization (NGO) in the U.S. in the field of toxic substances control. IARC official J. Rice would not consider removing the styrene industry related scientists from the panel. He suggested that IARC *might* permit a scientist from NRDC or some other NGO to come as a nonvoting observer, at NRDC's expense, to a future IARC panel meeting.

We are also concerned about the role of "observers" at meetings of WHO agency scientific expert groups. At the IARC Task Group meeting where the carcinogenic evaluation of 1,3-butadiene was made in 1998, there was a highly unusual second vote conducted the day after the group had voted 17-13 to classify butadiene as a human carcinogen. One of the scientists who voted in the majority left the meeting that day and thus did not return the next day. Observers and panel members allied with the oil and rubber industries were that evening able to persuade two others to reverse their votes, and without any discussion of why such re-voting was justified, a second vote was allowed the next day, with the result that butadiene was downgraded to *probable* human carcinogen by a vote of 15-14. The panel chairman, Benedetto Terracini, requested IARC to disclose in the "monograph" that the vote had been so close and later complained to IARC for not having made such disclosure (4). There have been other expressions of concern over the participation of observers affiliated with financially interested parties (1). We feel that limiting who can come as observers has in practice limited participation to corporate representatives. Allowing observers to sit at the table with members of the IARC Task Groups, unidentified (with different-colored tags) as observers, and participating in the meetings as equals has exacerbated this problem. WHO expert meetings should be open to the public or closed; and if open, there should be an effort by WHO to financially assist the participation of scientists representing environmental NGOs and trade unions.

Dr. Rice commented on how IARC has applied the WHO Disclosure Guidelines in a recent message to Dr. B. Castleman. "Each case of a declared interest is decided on its own merits. In any case, declared interests (if any) are stated by each person at the opening session of the meeting. If we

decide that some one with essential expertise has too close a tie to industry, we either decline his/her participation with thanks; or offer him/her observer (non-voting) status; or require that they recuse themselves from an evaluation that involves a conflict. We have 'disinvited' individuals, yes, after receiving their statement of interests." We have not heard of any participants with vested interests recusing themselves from voting.

Dr. Rice offered to meet with NRDC when he returns to Washington at the end of February, and NRDC in response asked to be provided with the following in advance of the meeting:

-- recent figures on how many Working Group members had financial conflicts-of-interest, how many were asked not to take part, how many recused themselves, and how many had conflicts but were allowed to participate

-- copies of the declarations by participants in the Monographs for which there have been "apparent" conflicts of interest (e.g., for styrene, butadiene, saccharin, atrazine, methyl t-butyl ether, glass wool).

Under the WHO Guidelines, the experts' declarations may be made publicly available in cases where the objectivity of the meeting is being questioned.

In his message this month to Dr. Castleman, Dr. Rice wrote, "It is getting very difficult to find individuals who have contributed significantly to the scientific literature on specific chemicals and who have no research funding or other connection with industry." While we share the concern that the high scientific quality that characterized the IARC Monographs in the past should be preserved, we feel that there are sufficient independent scientists with expertise in carcinogenesis available in governments and academia; and we see this attitude at IARC as a capitulation to corporate influence rather than a proper implementation of the WHO Guidelines.

We feel that it is very important that the WHO Director-General's Office establish implementation procedures for the Guidelines at all WHO institutions. In order to protect the integrity of WHO institutions, it is necessary that genuine efforts be made to assure that financial conflicts of interest are fully disclosed and analyzed. If an individual has such a conflict of interest, it should be presumed that s/he cannot be totally objective and therefore should not be a member of the scientific panel. While it is appropriate to open Task Group meetings with discussions of potential conflicts and biases of panel members, we feel that it is also important to exercise judgment in the selection of panel members, based on their disclosure forms and relevant information on the chemicals to be studied and related business interests, in selecting who is invited to participate in the first place.

Transparency is essential to the process, as WHO clearly realized in establishing the Guidelines. There should not be a high threshold for the release of disclosure forms by WHO and WHO agencies, when questions of scientific objectivity and balance of expert groups are raised. We accordingly request that, first of all, IARC be instructed to comply with the above-mentioned request from NRDC for declaration forms immediately.

These matters may be properly taken up by the World Health Assembly and at the next meeting of the IARC Governing Council.

We look forward to hearing from you soon. Please respond to Dr. Barry Castleman

Sincerely,

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3.

An open letter from Natural Resources Defense Council, New York, USA, to Dr. Paul Kleihues, Director, International Agency for Research on Cancer about Concern that Working Group members who will be assessing styrene have financial conflicts of interest.

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February 12, 2002

Dr. Paul Kleihues
Director
International Agency for Research on Cancer
Re: Concern that Working Group members who will be assessing styrene have financial conflicts of interest

The Natural Resources Defense Council (NRDC) is a non-profit public interest group using the law, science, and the support of more than 500,000 members nationwide to works towards a healthier environment. We are writing to express our concern regarding the current meeting of the *IARC Monographs Working Group on the Evaluation of Carcinogenic Risks to Humans, Vol. 82: Some traditional herbal medicines, some mycotoxins, naphthalene and styrene*, in Lyon on February 12-19, 2002. Our concerns stem from the evident conflict of interest surrounding the toxicologists who will provide opinion on styrene. The three toxicologists, James A. Bond, Gary P. Carlson, and George Cruzan each have financial relationships with groups representing the interests of the styrene manufacturers. Both Carlson and Cruzan are paid scientific consultants for SIRC, the Styrene Information and Research Center. Bond was employed by CIIT (Chemical Industry Institute of Toxicology), representing chemical manufacturers. The evident conflicts of these three experts is likely to undermine the credibility of the IARC work product on styrene.

Dr. Marcia Angell, senior lecturer at Harvard Medical School, and former editor-in-chief of the *New England Journal of Medicine*, defines a financial conflict as any financial association that may cause a researcher to prefer one outcome over another. Financial conflict, Dr. Angell points out, is a function of the situation, not the investigator's response to it; there is nothing "potential" about it. Angell has spear-headed an important reform movement in medical journals that addresses conflict of interest issues, and her working definition of financial conflict is as applicable to IARC as to other scientific research.

The IARC Monographs are one of the most valuable assessments available to risk assessors and government policy-makers world-wide. NRDC has often cited and quoted the Monographs, and considers IARC a leader in cancer assessment. However, we note that all deliberations of the IARC

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Working Group are made "behind closed doors", and that no transcripts of the deliberations are publicly available. Most significant, the voting of the Working Group members is never made public. This lack of transparency, and lack of public oversight makes peer-review impossible. This situation would be intolerable except for the respect, credibility, and scientific integrity which has characterized the IARC...until recent times.

Recently, scientists with tremendous credibility have begun to question the scientific integrity of IARC decision-making frameworks as well as the outcomes of particular deliberations. A recent article by Dr. Lorenzo Tomatis, former Director of IARC, suggests that IARC has begun a new trend, towards downgrading carcinogens as follows:

Additional criteria for evaluating carcinogenicity which are related to mechanism(s) of action were originally introduced [by IARC] with the aim of further strengthening the scientific solidity of the evaluations. Unfortunately, such information has not been necessarily used to ensure better protection of public health. During the past few years, atrazine, saccharin, d-(2-ethylhexyl)phthalate, glasswool, rockwool and slagwool were downgraded from "possibly carcinogenic to humans" (group 2B of the IARC classification) to "not classifiable as to its carcinogenicity to humans" (group 3 of the IARC classification), and 1,3-butadiene was classified as "probably carcinogenic to humans" (group 2A of the IARC classification), while the National Toxicologic Program of the USA has classified it as a recognized human carcinogen. Evidence for carcinogenicity provided by the results of experimental bioassays has been disregarded on the basis of unproven mechanistic hypotheses. If those hypotheses are shown to be incorrect once they have been tested experimentally, or if they do not account adequately for the wide range of susceptibility that is known to exist in human populations, very serious consequences for public health may follow.

This new trend towards downgrading carcinogens, coupled with Working Group members with obvious financial conflicts of interest, and the overall lack of transparency in the decision-making and voting processes, threatens to rob IARC of its credibility as an impartial and expert scientific agency.

IARC's recent deliberations on butadiene have also raised controversy. Dr. Benedetto Terracini, was Chair of the IARC 1998 Working Group in which Butadiene was classified as a Group 2A carcinogen. This classification was decided in a very unusual second vote, in which the final count was 14 votes for Group 1 v. 15 votes for Group 2A. Dr. Terracini points out, in a letter to Administrator Christine Whitman, US Environmental Protection Agency, that:

"Multidisciplinary groups of experts are a vital and irreplaceable tool in the exercise of evaluating scientific data (such as that undertaken by IARC, which remains a unique worldwide reference for scientists and public health authorities). Nevertheless, it must be acknowledged that occasionally the end point reflects their composition and the criteria for selecting its members."

Dr. Terracini's statement captures a fact that IARC does not seem to officially recognize; the composition of the panel members will affect the outcome of the decision. By choosing panel members whose financial ties with the industry are obvious, it is just as obvious that the decision will be biased towards favoring industry interests. Is IARC allowing the styrene industry to assess its own product, using the good name of IARC to lend credibility to the affair?

A consortium of a dozen prominent medical journals, including Lancet, the New England Journal of Medicine, JAMA, and others have recently responded to the problems of conflict of interest in medical research with progressive policies that will minimize undue influence of sponsorship on research agendas and results. These efforts include a new policy prohibiting researchers with financial conflicts of interest from authoring review articles, which, like IARC reviews, pick and choose among research findings for salient results for policy-making. In addition, the US EPA Science Advisory Board, which has been widely criticized for undue industry influence in its external reviews of EPA science, is currently addressing the problems of having industry scientists and industry-paid consultants acting as "independent" scientific reviewers. The results of financially conflicted scientific advisors is widely recognized to create undue bias and industry favoritism.

The WHO/IARC have now issued guidelines for disclosure of potential conflicts of interest by scientific experts selected to serve on task groups. Those who worked for adoption of these guidelines hope that they will be fully applied, and that to the extent possible panel members will be chosen who do not have financial conflicts of interest of any kind (particularly with the chemical industry and other business interests). It is hoped that efforts will also be made to assure that, to the extent that biases exist in panels, there will be an attempt by IARC to assure that there is a balance of viewpoints.

NRDC requests that IARC, in the interests of preserving the credibility and scientific integrity of the premiere international body of cancer assessment, remove from its Working Group any members with a financial conflict of interest. We appeal to the IARC as scientists, as persons of integrity, and as protectors of public health.

Respectfully,

Jennifer Beth Sass, Ph.D.

Senior Scientist

Natural Resources Defense Council

Linda Greer, Ph.D.

Senior Scientist and Director, Health and the Environment Program

Natural Resources Defense Council

cc. to

Dr. Jerry M. Rice

Programme Head

Carcinogen Identification and Evaluation

International Agency for Research on Cancer

David Longfellow

Chief, Chemical and Physical

Carcinogenesis Branch

Division of Cancer Biology

National Cancer Institute

4.

An open letter to Jerry M. Rice, Chief, Unit of Carcinogen Identification and Evaluation International Agency for Research on Cancer

Jerry M. Rice, Ph.D.
Chief, Unit of Carcinogen Identification and
Evaluation
International Agency for Research on Cancer
150 cours Albert Thomas
69372 Lyon Cedex 08
FRANCE

our ref: iarc/ot/wp
date: 10 October 2002
contact: Owen Tudor
direct line: 020 7467 1325
email: otudor@tuc.org.uk

Dear Dr Rice,

Reform Needed at the International Agency for Research on Cancer.

We write to register our grave concern at recent developments at the International Agency for Research on Cancer. We are alarmed to read US Natural Resources Defense Council (NRDC) reports of conflicts of interest, bias toward industry and of questionable evaluation practices at IARC. Clearly any weakening of the IARC standard setting process has dangerous ramifications for those working with the substances in question. We note also that the NRDC concerns are shared by many eminent scientists, including Dr James Huff of the US National Institute of Environmental Health Sciences, who headed IARC's programme on evaluating carcinogens from 1977 until 1980 and Dr Lorenzo Tomatis, IARC's director from 1982 to 1993. Both are signatories to a February 2002 letter to the World Health Organisation highly critical of IARC for using 'research openly or surreptitiously sponsored by industrial concerns.'

As international and national union organisations representing tens of millions of workers worldwide, we call on you to address as a matter of urgency the issues raised by NRDC, particularly its charge that meetings can be dominated by an industry perspective that 'has not historically represented the interests of public health, worker safety, or environmental protection.'

Further, we feel at this time it is particularly important IARC distances itself - and is seen to distance itself - from any suggestion of improper corporate influence.

We await your urgent response on these matters.

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Cancer & mineral wool

Yours sincerely

Owen Tudor, Senior Policy Officer for Prevention, Rehabilitation and Compensation, Trades Union Congress

and the following:

Silvana Cappuccio. International health and safety officer. International Textile, Garment and Leather Workers' Federation (ITGLWF)

Reg Green, International health and safety officer, International Federation of Chemical, Energy, Mine and General Workers' Unions (ICEM)

Fiona Murie. International health, safety and environment officer, International Federation of Building and Woodworkers (IFBWW)

Rory O'Neill, International health, safety and environment officer, International Federation of Journalists (IFJ)

Ron Oswald, General Secretary, International Union of Food, Agricultural, Hotel, Restaurant, Catering, Tobacco and Allied Workers' Associations (IUF)

Sue Pennicuik, Health and safety director, Australian Council of Trade Unions

Marc Sapir, Director, ETUC Trade Union Technical Bureau for Health and Safety

Margaret Seminario, Safety and health director, AFL-CIO, USA

This letter is being copied to:

Paul Kleihues, Director of IARC, Lyon

Gro Harlem Brundtland, Director-General, World Health Organization

Guy Ryder, General Secretary, International Confederation of Free Trade Unions (ICFTU)

Lucien Royer, International health, safety and environment officer, International Confederation of Free Trade Unions (ICFTU)

5.

No Effect or No Information? - Comments on a Nested Case–Control Study of Lung Cancer among European Rock and Slag Wool Production Workers

From International Journal of Occupational and Environmental Health, Volume 8, Number 3; July/September 2002, pp 281-283:

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Resumé

The author considers the validity of a recent study of lung cancer among European rock and slag wool workers. The study failed to demonstrate an association between lung cancer and exposure to man-made vitreous fibers and also did not manage to demonstrate a relationship between lung cancer and asbestos exposure, an odd finding that casts doubt on its validity. This article deals with bias towards the null and other aspects of the reviewed study that may explain its failure to demonstrate an effect of asbestos, concluding that the study does not add to knowledge about a possible carcinogenic effect of rock and slag wool fibers, the apparent null results simply being non-informative because of the study's poor ability to detect existing associations. *Key words:* bias; man-made vitreous fibers; methodology; null results; validity.

In October 2001, the International Agency for Research on Cancer (IARC) decided to alter the classification of rock and slag wool fibers from class 2B (possibly carcinogenic to humans) to class 3 (not classifiable as to carcinogenic effects in humans).⁽¹⁾ This decision may have been influenced by the results obtained by Boffetta and co-workers in a nested case-control study of lung cancer among workers in the European man-made vitreous fibers (MMVF) industry, a study that was published in an internal IARC report in December 2000. ⁽²⁾

According to Boffetta and co-workers, their “. . . study offers no support to the notion that MMVFs, as experienced by workers in the modern European RSW production industry, are carcinogenic to humans”² (“RSW” stands for rock and slag wool). I find this conclusion acceptable, but I would be extremely reluctant to infer from this study that MMVF exposure does not increase the risk of lung cancer. In particular, I find it alarming that the study by Boffetta and co-workers also failed to demonstrate an effect of asbestos (**Table 1**), notwithstanding the manifest indications of asbestos exposure: four cases of mesothelioma were observed, and a total of 87 cases (65%) and 357 controls (70%) were classified as having been exposed to asbestos, about half of them for 12

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years or more.² This inability to demonstrate an effect of asbestos casts serious doubt on the validity of the study by Boffetta and co-workers. (2)

TABLE 1. Asbestos Exposure and Lung Cancer: Smoking-adjusted Odds Ratios (ORs) and 95% Confidence Intervals (95% CI)*

<u>Asbestos Exposure Category</u>	<u>OR (95% CI)</u>
Ever exposed	0.86 (0.52–1.42)
Ever high exposure	0.64 (0.31–1.31)
Duration of exposure 1–11 years	0.74 (0.41–1.35)
Duration of exposure 12–56 years	0.82 (0.44–1.53)

*Source: Boffetta et al.,² tables VI and 3.4.

Various forms of flaws in study design and data may reduce a study's ability to detect existing associations, the consequence being a bias towards null results. (3) In the following, I elucidate some aspects found in the Boffetta et al. study 2 that may have brought about the strange null results seen for asbestos and lung cancer.

ASCERTAINMENT OF THE CASE DIAGNOSIS

In this study, a considerable number of the lung cancer cases were identified from death certificates, e.g., all the German cases were identified in this way.² Generally, death certificate diagnoses are of low validity, about one third of them proving to be incorrect when compared with autopsy findings. (4-5) The fact that many malignant neoplasms spread to the lungs makes it likely that "lung cancer" is being overdiagnosed as cause of death where no histologic evidence is available. In the Boffetta et al. study, histologic data are lacking for 55 of a total of 133 cases, and it seems noteworthy that the odds ratios based solely on histologically verified cases differ consistently from the odds ratios based on all cases (**Table 2**). These findings substantiate the assumption that the case series may comprise a number of people without primary lung cancer, a feature producing null-biased estimates. (3)

TABLE 2. Exposures to Man-made Vitreous Fibers (MMVF) and Lung Cancer, Analyses Based on All Cases and on Histologically Verified Cases, Respectively: Smoking-adjusted Odds Ratios (ORs) and 95% Confidence Intervals(95% CI)

<u>MMVF Exposure Category</u>	<u>All Cases OR (95% CI)</u>	<u>Verified Cases Only OR (95% CI)</u>
Ever exposed	0.59 (0.23–1.54)	0.97 (0.20–4.78)
Duration of exposure 1–2 years	0.59 (0.20–1.72)	1.36 (0.24–7.67)
Duration of exposure 3–11 years	0.32 (0.11–0.99)	0.66 (0.11–3.94)
Duration of exposure 12–53 years	0.40 (0.13–1.22)	1.00 (0.16–6.18)

*Source: Boffetta et al.,² tables V and 6.9.

SELECTION OF THE CONTROL SERIES

The study design was that of a (cohort) nested case-control study with two control series, one of the series being restricted to people who died before the procurement of exposure data. The controls were sampled from the risk sets of the cases, and individually matched to the cases. Within some of the match strata the data appear sparse, seeing that 44 subjects were selected as controls for more than one case.

When controls are selected with replacement (as in this study), cases should also be candidates for the control series, and in a situation characterized by sparse data some cases would expectedly have been selected as controls. However, none of the cases were selected as controls, a feature indicating that in the study under consideration controls were selected among non-cases only. If restricted to non-cases, control sampling with replacement leads to inconsistent estimates, in particular when the data are sparse. (6,7)

In this study, the controls were, allegedly, selected by density sampling. (2) This implies that apart from random error the control series should represent the exposure distribution of the person-years at risk accumulated by the cohort during the period in which any new case would have been included in the case series. Unfortunately, none of the control series employed in the present study seem to represent relevant population-time:

First, people suffering from a number of tobacco-related diseases were excluded as controls, a restriction that makes the control series underestimate the share of (heavy) smokers in the cohort. In consequence, the lung cancer risk brought about by tobacco smoking is overestimated at the expense of effects of occupational agents, e.g., asbestos. Introducing a "smoking adjustment" concept in the analysis cannot solve this bias.

Second, the control series that was restricted to deceased people hardly represents the person-years at risk accumulated by the cohort members, many of whom were still alive at the end of the follow-up period.

Additionally, the study employed several measures of cumulative exposure, but the sampling of controls did not account for the fact that many cohort members had been accumulating exposure during the follow-up.

These workers contributed person-years at risk to alternating categories of cumulated exposure, "moving" from lower towards higher categories during the course of the study. Where a relationship between cumulated exposure and the studied disease does exist, it is unlikely that the risk sets of the cases represent the underlying person-years with respect to cumulated exposure - they would, rather, tend to represent the exposure distribution of the case series. Thus, for cumulative exposure measures, the employment of a control series sampled from the risk sets of the cases is likely to have blurred existing associations.

PROCUREMENT OF EXPOSURE DATA

Cases and controls were classified according to history of exposure by the times of diagnosis (cases) and sampling (controls), respectively. A subset of the workers was classified as being free from MMVF exposure and served as standard of reference. It seems, however, questionable to classify a worker as unexposed to MMVF if he or she has at any time been employed in a MMVF production plant. Therefore, the exposure gradient may have been more level than indicated by the report, and existing associations may have been overlooked.

Non-differential Exposure Misclassification

The great difficulties in assessing historical exposure data make misclassification inevitable, and despite the trouble taken over exposure assessment, the study under consideration is likely to have suffered from this scourge. An indication of this problem is found in the range of the individual exposure scores (as assessed in the study), which is much wider than that of comparable hygienic data. (2)

Were the Expert Panels Effectively Blinded?

For each case and control, information about exposure history was obtained from expert panels set up in the MMVF plants, supplemented by interview with the index person or a next of kin. The assessment of a subject's exposure within the MMVF industry was predominantly based on the information provided by the expert panels. These panels included experienced managers, foremen, and workers, and they provided information not only about occupational exposures, but also about individual smoking habits.

It seems likely that the blinding of the expert panels proved impossible: the panel members must have known many of the study subjects, and may also have known whether a particular worker was still alive, maybe still employed. That the members of the expert panels were able to recognize the workers studied was demonstrated by the following: for a subset of cases and controls, the researchers sent a second inquiry to the expert panels in order to compare the data from the first and second inquiries. However, the second inquiry could not be carried through as the panel members recognized the workers concerned and thus considered it pointless to repeat the inquiry.(2)

The validity of the elaborate exposure assessment employed by Boffetta and co-workers depends heavily on the validity of the information provided by the expert panels in the MMVF plants. A failure of blinding is likely to have resulted in outcome-dependent misclassification of exposure.

TIME FROM EXPOSURE TO DISEASE

The reviewed study applied a set of analyses that disregarded exposure within the 15 or 30 years preceding diagnosis. However, none of the analyses accounted for the fact that an occupational lung cancer does not occur within the very first years of exposure to an occupational agent. By including also the first years of exposure in the risk period, the study may have included a number of lung cancer cases that - for biological reasons - cannot be related to MMVF. Such "noise," i.e., inclusion of irrelevant cases, will blur existing associations.

DOCUMENTATION

The documentation section of the IARC report 2 contains a multitude of results, whereas the basic methods and data are rather poorly documented. Unfortunately, the documentation available also suffers from the inclusion of numerous errors and oddities.

CONCLUSION

In conclusion, the study 2 does not add to our knowledge about a possible MMVF-lung cancer relationship. Flaws in the study design and data make it likely that the apparent null results are simply non-informative because of the study's poor ability to detect existing associations.

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