MEDICHEM

NEWSLETTER

November 2003

Medichem 2003 Board Elections

With the Medichem Board Meeting on October 6th in Ludwigshafen, the term of office ended for the former Board Member Miroslav Cikrt (Czech Republic). After a written ballot held in July 2003, **Peter S. Nmadu** (Nigeria) became a newly elected Board Member. Owing to the fact that there was no General assembly at this time, Peter could not be introduced and greeted in the usual manner. The Medichem Board, however, offers him a warm welcome. We are looking forward to a fruitful collaboration in the future.

On behalf of Medichem, the Board again thanks Miroslav Cikrt for his contributions in the past. He was the organizer of a wonderful congress in 2001 in Prague. We trust that he will continue to support Medichem in the future.

Dr. Michael Nasterlack
(Ludwigshafen, Germany)

New Internet Homepage for Medichem

Several Members have already seen the new Medichem website, which is graciously maintained and hosted by Don Cook from Shoreland Inc. At the last Medichem General Assembly in February, it had been decided to amend the Medichem website through enhanced features. To this end, Noel Humphry and his assistant Kerry Campbell, who had done an outstanding job in setting up and running the previous site up to now, cooperated with Stephen Borron and Don Cook. The new website, which has a "members only" section with news alerts, literature reviews, future electronic voting options etc., is still developing. Nevertheless, I am sure that you will like this new concept. Please refer to my accompanying letter to find the password for the "members only" section.

If you cannot yet access the URL (www.medichem.org.au), please try entering the IP address in the browser (207.67.24.195). You may also have to clear web cache files as some intranet DNS servers may not be refreshed. In this event, you may have to contact your IT Department.

Another internet event currently in preparation is a special website set up by Stephen Borron for the XXXII. Medichem Congress in Paris in September 2004. By the time you receive this Newsletter, it will be accessible at www.medichem2004.org .

Dr. Michael Nasterlack
(Ludwigshafen, Germany)

MEDICHEM - Occupational and Environmental Health in the Production and Use of Chemicals

The Nova Scotia Court of Appeal has overturned a Nova Scotia worker's claim for sleep disorder benefits. A Michelin employee had been granted workers' compensation benefits for sleep disorder syndrome in which the Tribunal had ruled that working shift work constituted a compensable injury. Here is an article from the Halifax Herald, Tuesday December 31, 2002, by Amy Smith.

Michelin prevails in shift work appeal. Worker's problem with hours not company's problem, court rules

Tire giant Michelin isn't to blame for a worker's disabling sleep loss Due to shift work, the Nova Scotia Court of Appeal ruled Monday. The Decision says Richard Ross's intolerance to shift work was "a personal characteristic" and not "caused or aggravated by the requirements of the job." Michelin North America (Canada) Inc. had appealed a Jan. 25 Workers' Compensation Appeals Tribunal decision that found years of working the back shift caused Mr. Ross to suffer severe insomnia constituting a compensable injury. Mr. Ross said despite sleeping pills and other measures, he could sleep only a few hours between shifts at Michelin's Bridgewater plant and worried about his safety on the job. Michelin's three Nova Scotia Plants run 24 hours a day and most of its 3,500 employees work shifts. Company spokeswoman Norma Nixon said Monday's decision was a very good outcome. "From our perspective, we're very pleased with the decision. "If the decision had held, it could have increased costs for Michelin and other organizations. It could have set a precedent." Jane Spurr, one of Mr. Ross's lawyers, refused comment, saying she was awaiting instructions from her client. The appeal court said the tribunal decision was unique in Nova Scotia in that it was the first time it had awarded compensation to a worker whose injury - lack of sleep leading to disabling symptoms - "occurred when he was off duty, on his own time and away from the work site." Mr. Ross, 34, of Bridgewater, started rotating shifts full time in June 1987. After seven years on that schedule he said he started having trouble sleeping and missed work several times due to severe sleeplessness. He considered himself disabled by his diminished alertness, which he said made it unsafe for him to work with industrial equipment. In 1999, Mr. Ross filed a workers' compensation accident report claiming he suffered from shift-work maladaptation syndrome, a sleep disorder recognized by the American Psychiatric Association. Michelin argued Mr. Ross took the job knowing it involved shift work and for nine years it wasn't an issue. The company said shift-work maladaptation is a personal condition that made shift work inappropriate for Mr. Ross. Michelin said, for example, a window washer afraid of heights would have to find a different line of work. The appeal court ruling by justices Gerald Freeman, Thomas Cromwell and Jill Hamilton said there are no regulations under the Workers' Compensation Act referring to shift-work maladaptation syndrome or any other type of insomnia. "It must be acknowledged that compensation for the state of being 'very tired,' as (Michelin) characterized (Mr. Ross's) cognitive deficit, does not appear to fit readily into the traditional pattern of workers' compensation for personal injuries caused by accident," the court ruled.

Dr. Sol E. Sax, Mississauga (Canada)

You can find more information about the case if you search the web with the keywords "Ross, Michelin, Bridgewater".

The proposed New Chemicals Policy of the European Union has stirred quite a bit of interest even outside Europe. Many, especially those concerned with environment and safety questions, see it as an example for other countries to follow. While the aim of improving chemical safety, for producers as well as for consumers, is beyond discussion, the methods to achieve this goal, and the arguments used, are not. The following editorial, where the arguments used by the General Directorate Environment of the European Commission are critically reviewed, was published in the International

Archives of Occupational and Environmental Health (2003) 76: 553-555

Where should the Chemicals Policy go?

The Commission of the European Community (CEC) is currently preparing an extensive review of its chemicals policy, the aim of which will be to create a new regulatory system for existing and new substances, through a Registration, Evaluation and Authorisation of Chemicals (REACH) system. The new chemicals policy is based on a "White Paper" forwarded by CEC's Commissioner Margot Wallström, head of the European Directorate-General (DG) Environment. The Commission believes that one of the benefits of REACH will be improved occupational health. Industry groups, whilst not disagreeing with the aim to reduce workplace-related health risks, are worried that the design of this system could lead to major disadvantages for the European chemical industry and its employees. One of the key arguments in this discussion is the cost-effectiveness of REACH. It is assumed by the CEC that the estimated direct and indirect costs of 18 – 32 billion euros following the implementation of REACH would be compensated, at least partially, by considerable cost savings through the reduction of the number of cases of chemical-related disease in Europe [Liikanen and Wallström 2003].

In her speech „Beyond REACH“ (European Voice Conference, 31 March – 1 April 2003, in Brussels), Commissioner Wallström provided such estimates of expected cost savings. They should amount to 18 – 54 billion euros over a time period of 30 years. This should mainly be achievable through a reduction of the number of occupationally induced cancer cases by 2,200 – 4,300, annually, over the same time period.

These figures originate from a study by the Risk & Policy Analysts UK (RPA), which had been contracted by DG Environment [RPA 2003]. In short, the authors of the RPA study come to their conclusions by attributing an estimated 32,500 new cancer cases per year to occupational exposure to known or suspected carcinogens. Of this figure, 20%, i.e. 6,500 new cancer cases per year, are then assumed to stem from exposures to hitherto unknown chemical carcinogens. From these, one third (2,167) and two thirds (4,333) are then proposed, respectively, as lower and upper bound estimates of the number of cases assumed to be prevented in the future through REACH.

The methods on which these estimates are based do warrant a second look.

The RPA study uses the total number of cancer cases occurring in Europe, to which they apply estimated occupationally attributable proportions published elsewhere [Doll and Peto 1981, Morrell et al. 1998, ILO 2000]. The main mistake in their approach is the simplistic assumption of “occupational exposures” equal “hazardous substances” equal "chemicals". They disregard the fact that most of the cancers included in these proportions are not related to industrial chemicals and thus to substances which would fall under the regulation of REACH. This apparently led the authors to interpret, erroneously, some of their sources. The following quotation makes this obvious: "The Australian study [Morell et al. 1998] utilises the Doll and Peto percentages of cancer deaths that can be attributed to occupational exposures and then makes assumptions on the number of cancer deaths due to occupational exposure to chemicals" [RPA 2003]. As a matter of fact, Morrell and co-workers never made this mistake but constantly referred to cancers caused by "hazardous substances". This is in line with Doll's and Peto's approach which explicitly includes cancers resulting from exposure to asbestos, combustion products, and other substances that are not "industrial chemicals" [Doll and Peto 1981]. Thus, the assumed number of 32,500 cancer cases attributed by RPA to "chemicals" is ill-founded, and so is the arbitrarily derived number of 6,500 cancer cases that are attributed to "unknown chemical carcinogens".

The magnitude of this error becomes apparent if reported occupational cancer cases are used as a basis for extrapolation. For instance, a total of 112 occupational

cancer cases were reported in Finland in 1999, 109 (97%) of which were caused by asbestos [Karjalainen et al. 2001]. The respective figures from Germany in the year 2000 were 1,022, including 933 (91%) asbestos cases and excluding ionising radiation [Bundesministerium für Sozialordnung (BMA) 2001]. The extrapolation of these figures at the EU level on the basis of the size of the respective workforces results in 7,518 and 4,276 occupational cancer cases per year, respectively. From these, 91 – 97% are related to asbestos. Only 3 – 9% are related to industrial chemicals, which results in an estimated 128 to 526 chemical-related cases per year. Although this result may be biased by some underreporting of occupational cancers, the anomaly between these figures and the above estimates is striking.

But, even if RPA's figures were not based on flawed assumptions, we would have to ask the question: Can we expect to predict validly the future possible savings in cancer cases on the basis of today's cancer incidence rates?

All estimates of the occupationally induced fraction of total cancer cases necessarily relate to workplace exposures and conditions in the past. In the case of the groundbreaking study by Doll and Peto this was between the 1940s to 1970s [Doll and Peto 1981]. The relevant exposures during this time, like asbestos, aromatic amines, and other important, known carcinogens, contribute to today's cancer rates only due to the long latency periods between exposure and disease onset. In most of Europe they are "settled cases", from the regulatory point of view. Thus, actual cancer incidence rates provide no clues to actual workplace exposures.

This statement is often countered by the argument that "only a small number of the many thousands of industrial compounds used in modern workplaces have been thoroughly investigated" [Kraut 1994]. However, it is unlikely that today's workplace chemicals pose as yet undetected risks comparable to those from asbestos or aromatic amines. Since 1981, new chemicals within the EU have been at least basically tested before being registered [Allanou et al. 1999]. So-called existing chemicals have been on the market for more than twenty years. Among these are the ones, which, the RPA study alleges, cause thousands of cancers today, of up-to-now unknown origin. There are no indications, however, from occupational epidemiology studies or current occupational medical experience, which point to risks in today's workplaces comparable to those from asbestos, benzene, and certain aromatic amines at workplaces in the past [Goldberg and Hémon 1993, Greenberg et al. 2001, Peto 2001]. The majority of studies establishing a link between an increased risk of cancer and a particular working environment were published between 1950 and 1975. Relatively few occupational carcinogens have been identified in the past 25 years [WHO, IARC 2003]. The reason for this paucity of new discoveries is, obviously, not a lack of new exploratory studies during this period of time, but the absence of, or drastically reduced, exposures to potent carcinogens comparable to benzene, asbestos, etc. in today's workplaces [Goldberg and Hémon 1993]. Thus, the proportion of total cancer cases attributable to occupational chemicals is likely to be smaller today than it used to be, and further decreasing.

Of course, we do not want to propose that there are no relevant health risks in today's workplaces. According to a press release on behalf of the "First pan-European campaign to combat risks of dangerous substances at work", more than 350 million working days are lost each year due to work-related ill health [OSHA 2003]. This number relates to some 7.7 million people throughout the EU who are estimated to suffer each year from work-related health problems (7.4 million accidents not counted). Among these, musculoskeletal problems account for 4.1 million (53%), stress, depression and anxiety account for 1.4 million (18.2%), and pulmonary disorders make up another 7.6% of cases (Dupré 2001). In the press release it is further stated that only 12% of firms were aware of their regulatory duties and that 20% of safety data sheets supplied by manufacturers of hazardous substances contained errors.

We firmly believe that the solution to these problems lies in the implementation of already existing legislation and the application of readily available knowledge in ergonomics and workplace safety and hygiene. Therefore, we propose to assign the limited available resources to such projects where firms are guided, supported and encouraged to employ the best available technology in order to improve existing workplaces. This would more reliably lead to economic benefits and prevention of human suffering than would a more rigorous system for testing, classification and labelling, the implication of which is justified with poorly founded benefit assumptions.
(References available on request).

Prof. Andreas Zober
Dr. Michael Nasterlack
(Ludwigshafen, Germany)

Of course, we have forwarded this paper also to the General Directorate Environment of the European Commission. The answer we received was not exactly satisfying: the receipt of our letter was acknowledged.

Occupational Health Status of Workers Exposed to Female Hormones in a Pharmaceutical Plant

A large number of highly hazardous substances are handled in the pharmaceutical industry. One of the fundamental features of the control of hazard arising from therapeutic materials is to identify the foreseeable effects of the agents under conditions of use through a health surveillance system. A workplace can only be safe when both those who are responsible for it and those who work in it fully understand both the risks involved and the systematic approach to controlling them within acceptable limits.

An occupational health study was conducted in a pharmaceutical industry engaged in the manufacture of contraceptive pills with a view to evaluate the health status of workers exposed to female hormones. The sample included 11 workers from the steroidal section, 16 from the non-steroidal area and 11 control subjects. The findings revealed that all the workers exposed to the hormones showed various manifestations attributable to the toxic effects of exposure to high levels of airborne sex steroids in the work atmosphere as well as suppression of endogenous hormones. The levels of norgestrel and ethinyl oestradiol and the dust containing the steroids in the work environment were far exceeded the prescribed dose for contraception warranting urgent interventional strategies to safeguard the health of the workforce.

The authors came to the following conclusions:

1. All the workers exposed to the sex steroids, showed the various steroid induced manifestations attributable to exposure to high levels of airborne steroids in the working atmosphere as well as suppression of endogenous hormones in the workers exposed to norgestrel and ethinyl oestradiol.
2. The levels of norgestrel and ethinyl oestradiol and the dust contraining the above steroids were far higher than the prescribed dose for the contraception i.e. Norgestrel with a minimum airborne level of 1.35 mg/m^3 to a maximum level of 8.9 mg/m^3 and the ethinyl oestradiol with a minimum level of 1.67 mg/m3 to a maximum level of 6.25 mg/m^3. The normal dose prescribed for contraception is 0.3 mg. norgestrel and 0.03 mg of ethinyl oestradiol per day (for women only).

(T.V. Ranga Rao et al., Indian J. Occup. Environ. Med. 7: 17-22, 2003)

Dr. Thirumalaj Rajgopal, Mumbai (India)

Styrene exposure and ischemic heart disease: A case-cohort study

Epidemiologic studies have consistently reported increased daily mortality and hospital admissions for ischemic heart disease related to daily changes in ambient particulate levels. One theory is that substances adhering to particulates might have a cardiovascular effect. Styrene has been found in very low doses in air and has chemical characteristics that would cause adherence to particles. Industrial studies have found an increase in cardiovascular disease among styrene-

exposed workers. To explore a possible dose-response relation between styrene exposure and ischemic heart disease, the authors of this case-cohort study included 498 cases that died from ischemic heart disease and a 15 % random sample (n = 997) of all male workers who were employed during 1943-1984 in two styrene-butadiene rubber-manufacturing plants in the United States. Proportional hazards models showed that recent styrene exposure was significantly associated with acute disease for exposure during the most recent 2 years among active workers with 2 or more years of employment was 2.95 (95% confidence interval: 1.02, 8.57) at a time-weighted styrene concentration of 0.2-<0.3 ppm and 4.30 (95 % confidence interval: 1.56, 11.84) at ≥0,3 ppm for the same exposure period, respectively.
(G.M. Matanoski and X.G. Tao, Am. J. Epidemiol. 158: 988-995, 2003)

I confess that this article puzzled me somehow. Firstly, the basis for the hypothesis tested was far from conclusive from my point of view. First, there are other substances which have been discussed in the context of particulate matter. Second, the exposures reported for these workers seem almost negligible compared to the current MAK of 20 ppm, and compared to exposures of up to 100 ppm which were associated with the use of styrene e. g. in boat or tank building. Third, mortality from ischemic heart disease appears not to be the optimal parameter for the assessment of the general risk of developing ischemic heart disease (bearing in mind that the factors which ultimately lead to survival of, or death from, heart attack may have nothing to do with the factors that caused the underlying disease). If anybody wants to comment on this, I would be very interested in their views.

Dr. Michael Nasterlack
(Ludwigshafen, Germany)

Perceived Treatment Efficacy for Conventional and Alternative Therapies Reported by Persons with Multiple Chemical Sensitivity

Multiple chemical sensitivity (MCS) is a condition in which persons experience negative health effects in multiple organ systems from exposure to low levels of common chemicals. Although symptoms experienced from particular chemicals vary across persons, they are generally stable within persons. The sensitivities often spread over time, first to related chemicals and then to other classes of chemicals. This study examined self-reported perceived treatment efficacy of 101 treatments used by 917 persons with self-reported MCS. Treatments examined included environmental medicine techniques, holistic therapies, individual nutritional supplements, detoxification techniques, body therapies, Eastern-origin techniques, newer therapies, prescription items, and others. The three most highly rated treatments were creating a chemical-free living space, chemical avoidance, and prayer. Both creating a chemical-free living space and chemical avoidance were rated by 95 % of respondents as helpful. Results for most therapies were mixed. Participants had consulted a mean of 12 health care providers and spent over one-third of their annual income on health care costs. We discuss this drain on personal resources and describe respondents' attitudes toward the possibility of healing from MCS.
(P.R. Gibson et al., Environ Health Perspect. 111: 1498-1504, 2003)

Dr. Michael Nasterlack
(Ludwigshafen, Germany)

Somebody is caught in his car drunk, and tells the police and the judge that his positive breath or blood test is not due to alcohol drinking, but to a long working day in a job where alcohol was used as a solvent. At least in Germany, I am aware of several court cases where this argument had been brought up, but had been perceived as a nice try, and turned down. If you ever have to deal with this question, here is the solution (not the first experiment of that sort, but always a pleasure to read). So, don't even try to use this argument for yourself...

Neuromotor effects of acute ethanol inhalation exposure in humans: a preliminary study

Ethanol (ETOH) is added to unleaded gasoline to decrease environmental levels of carbon monoxide from automobiles emissions. Therefore, addition of ETOH in reformulated fuel will most likely increase and the involuntarily human exposure to this chemical will also increase. This preliminary study was undertaken to evaluate the possible neuromotor effects resulting from acute ETOH exposure by inhalation in humans. Five healthy non-smoking adult males, with no history of alcohol abuse, were exposed by inhalation, in a dynamic, controlled-environment exposure chamber, to various concentrations of ETOH (0, 250, 500 and 1,000 ppm in air) for six hours. Reaction time, body sway, hand tremor and rapid alternating movements were measured before and after each exposure session by using the CATSYS™ 7.0 system and a diadochokinesimeter. The concentrations of ETOH in blood and in alveolar air were also measured. ETOH was not detected in blood nor in alveolar air when volunteers were exposed to 250 and 500 ppm, but at the end of exposure to 1,000 ppm, blood and alveolar air concentrations were 0.443 mg/100ml and 253.1 ppm, respectively. The neuromotor tests did not show conclusively significant differences between the exposed and non-exposed conditions. In conclusion, this study suggests that acute exposure to ethanol at 1,000 ppm or lower or to concentrations that could be encountered upon refueling is not likely to cause any significant neuromotor alterations in healthy males.
(V. Nadeau et al., J. Occup. Health 45: 215-222, 2003)

Prof. Alfred Thiess, Ludwigshafen (Germany)

The following reached me just the other day. Because I was just preparing this Newsletter, I thought it a good idea to forward this to the whole Medichem community. The immediate treatment of chemical burns is certainly a relevant topic for most of us, and many will have their own experience and views on it.

Question from a Medichem member: Treatment of chemical burns

I am a recent member to Medichem. For the last several years I have been Medical Director for Millennium Chemical Company. It is a chemical manufacturer with plants in the States, Europe, South America and the Pacific. Recently one of the sites has been promoting a specific product to prevent chemical burns and I have been asked to evaluate it for more general distribution and use.

I am trying to get some feedback from corporate medical directors or occ doc consultants regarding their experiences, if any, with this French product used often in Europe as a first wash to prevent chemical burns. Specifically the products are Diphoterine and Hexafluorine. The web site of the company is "http://www.prevor.com/Prevor-us/SITE/Index%20US.htm".

I would like to poll the relevant membership of Medichem to get some real life experience anecdotes, protocols and implementation approaches.

By way of brief background,Diphotérine® is an amphoteric and chelating molecule formulated into a liquid hypertonic solution which reportedly works much better than water washes in preventing chemical burns to skin and eyes. Hexaflourine is a similar product formulated specifically for use in HF exposures.

Dr. Kevin Trangle, Cleveland (USA)

The following is my answer to this question, where of course my personal views and those of my experienced colleagues are expressed. This is not an official BASF position, nor does BASF legally support this view. I do not wish to claim that these views are necessarily correct, but they are intended as a contribution to a discussion among colleagues.

Let me first state BASF's medical department's position regarding the treatment of acute chemical burns. We acknowledge the buffering and chelating properties of this (and similar) products. However, the small volumes available and thus the limited

time and intensity of applicable (and only laminar) flow counteract these advantages over simple water (provided, this comes from a tap, shower, hose etc., and not out of eye-wash bottles).

To our opinion:

- decontamination is more effective than neutralisation
- a high concentration gradient can be achieved and maintained through high flow only
- a turbulent flow is better than a laminar flow, to mechanically remove even non water-soluble substances
- high flow guarantees the immediate reduction of heat caused by chemical reactions
- water is universally applicable (acids, caustics, water-soluble and non-soluble substances), almost everywhere available, cheap and effective

To the best of my knowledge, there are several case series or treatment reports distributed by the company, but no conclusive evidence is available which shows the ultimate advantage of these solutions over (correctly applied) water.

Dr. Michael Nasterlack
(Ludwigshafen, Germany)

Dear Medichem members, if you are experienced in the treatment of chemical burns and want to contribute to this discussion, I would very much appreciate if you sent a mail to Kevin at ***ktrangle@att.net*** *(and copy me on it). Also, if you disagree with my statement, please let us know. If new aspects arise from this discussion, I would like to take up this issue again in the next Newsletter and provide you with the different opinions.*

Recently, our Chairman Stephen Borron was contacted by a Forensic Medicine & Clinical Toxicology Lecturer from Egypt, who wrote:

My name is Mohamed Farid Ibraheem, a lecturer of Clinical Toxicology & Forensic Medicine in Benha Faculty of Medicine.

The Medical College of Benha is a New Collage and we try hard to develop our Department's Library. However, we do not have enough money to do so, as you know we are a developing country. While I was searching the Net I found your web site.

FOR THE SPIRIT OF SCIENCE, I am asking if you can donate us with any COMPLIMENTARY Copy(ies) (New, Old, Used, hardbound, or even Xerox Photocopy) of toxicology and/or forensic books or Journals to put it/them in our Library.

This/These Book(s) definitely will help us in developing our library and our department staff. At the same time we can direct our under and post graduate to read and buy the right books. In addition, the other Forensic and Toxicology Departments in different medical collages in Egypt can benefit and be informed by this/these book(s) as we are trying to exchange our information about the recent publications that concern forensic and toxicology.

If you decided to help us please send the books by a such a way that we can avoid the CUSTOM COST, as it is high here in Egypt.

Stephen passed this request on to the Board, and I decided to forward it here to you. If you have something of interest to our Egyptian colleague, please send it to

Mohamed Farid Ibraheem.
Benha Faculty of Medicine.
Forensic Medicine & Clinical Toxicology Dept.
Benha
Kaluiobia 13
EGYPT

Welcome to New Members

Dr. **Elke Verwerft**, BASF Antwerpen N.V., Antwerpen (Belgium),

Dr. **Peter Thakurdas**, Medicanz Ltd., Newmarket, AKLD (New Zealand),

Forthcoming Events

XXXII. Medichem 2004 - Paris

The XXXII. Medichem Congress will take place **September 1 – 3, 2004** at the Sofitel Paris Rive Gauche Hotel. The 1st announcement and call for papers are underway.

Please check our website at **www.medichem.org.au** or **www.medichem2004.org** for further information.