

NEWSLETTER

Medichem 2004 Board Elections – Call for Candidates

This year, the following Medichem Board members arrive at the end of their term of office:

Stephen W. Borron, Andreas Flückiger, Oswald Jahn, Michael Nasterlack, Todor Popov, Thirumalai Rajgopal, Konrad Rydzynski, Sergio Salomon, and Friedrich W. Schmahl.

Thus, eight seats on the Medichem Board plus the Chairman's seat are to be distributed.

The following have declared to stand again as candidates for a further term of office: Stephen Borron, Andreas Flückiger, Michael Nasterlack, Todor Popov, Thirumalai Rajgopal, Sergio Salomon, and Friedrich W. Schmahl.

You, Medichem members in good standing, are now asked to nominate candidates for the Board, if you want to do so.

According to Article 5 Sect. 4.1 of the Medichem Constitution, each Board member shall be from a different country. This rule does not apply for those holding the offices of Chairman, Vice Chairman, Secretary, Treasurer, and immediate Past Chairman.

Members from Canada, France, Nigeria, South Africa, Taiwan, The Netherlands, United Kingdom, or USA cannot be candidates in this year's Board election, unless they run as candidate for Chairman.

All candidates must be Medichem Members in good standing, and also ICOH members in good standing, or at least agree to join ICOH if elected. Furthermore, the nomination shall only be valid if it is sent in along with written acceptance of the nomination from the candidate himself or herself. Additionally, according to Article 5, section 2 of the Constitution the candidate for Chairman has to be approved by ICOH. This approval will be obtained through the secretary. Nominations must be sent to the Secretary of Medichem, Dr. Michael Nasterlack, by mail or fax (+49 621 60 43322). They must be in possession of the secretary no later than May 31st, 2004. **Please indicate clearly, whether the nomination is for a regular seat on the Board or for the position of Chairman.**

The ballot form for the election will be sent out along with the next Newsletter in July 2004.

Dr. Michael Nasterlack
(Ludwigshafen, Germany)



March 2004



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

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Dr. Leslie M. Yee (USA)

Factors Affecting the Extent of Dermal Absorption of Solvent Vapours: A Human Volunteer Study

Jones et al., in a recent evaluation of vapor exposures to butoxyethanol (EGBE) submitted volunteers to a variety of conditions, including a simulated work environment. The authors demonstrate that an increase in environmental temperature, in combination with wearing of Tyvek coveralls increased skin absorption significantly. The

solution on the surface of the skin which may increase the apparent permeability coefficient (Wilkinson and Williams, 2002)] and opening of skin pores under conditions of increased temperature and/or humidity. The studies showed that clothing had a minimal effect on the dermal contribution to total body burden with neither minimal clothing nor overalls having a significant effect on the amount absorbed through the skin. This could be because the rate of gas exchange through the clothing exceeds the

humid than the ambient environment.

(K. Jones et al., Ann. Occup. Hyg. 47: 145-150, 2003)

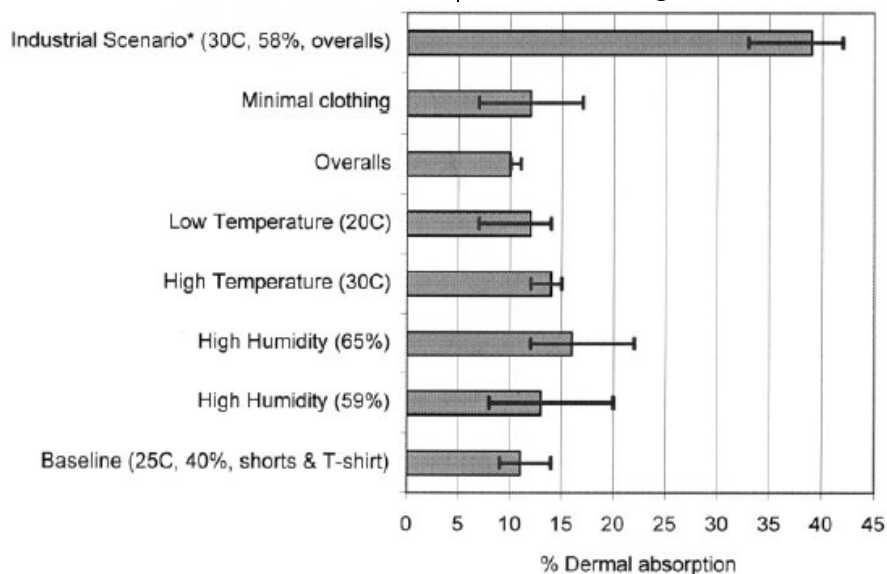
Take home message:

Protective equipment isn't always.

Dr. Stephen Borron (Paris, France)



Environmental contamination with persistent organic pollutants invariably leads to the presence of these substances in human breast milk. Several of these POPs, especially the PCBs, have been linked to neurodevelopmental deficits, notably reduced IQ in children. Although the alleged IQ losses have been marginal for the individuals on one side, and authorities and regulatory bodies have never stopped to recommend breastfeeding for its undoubted beneficiary effects on the other side, these findings understandably lead to concern and uncertainty in many mothers. The following study, although not originally aimed at this question, adds an interesting aspect to this dilemma.



authors conclude that their studies have shown that both increased temperature and increased humidity increase the percentage dermal absorption and this is statistically significant for increased temperature ($P = 0.03$, $30\text{ }^{\circ}\text{C}$). This is likely to be due to increased surface blood flow (as reported, for example, by Vanakoski et al., 1996), increased skin hydration (as observed by Schafer et al., 2002) and perspiration [aiding dissolution of 2-butoxyethanol, forming a

absorption rate of 2-butoxyethanol through the skin. Combining high temperature, high humidity and the wearing of overalls had a significant impact on the percentage dermal absorption, resulting in a mean dermal contribution to total body burden of 39% (range 33–42%). This may be due to the overalls generating a microclimate next to the skin (as observed by Schafer et al., 2002) where the environment is significantly hotter and more

Influence of Breastfeeding on Cognitive Outcomes at Age 6-8 Years: Follow-up of Very Low Birth Weight Infants

The relation between breastfeeding and childhood cognitive development was examined in 1991-1993 among 439 school-age children weighing <1,500 g when born in the United States between

1991 and 1993. Measures of cognitive function included overall intellectual function, verbal ability, visual-spatial and visual-motor skill, and memory. Higher test scores for each domain of cognitive function except memory were observed among children who were breastfed directly. After covariate adjustment for home environment, maternal verbal ability, a composite measure of parental education and occupation, and length of hospitalization, the authors found that breastfed children evidenced an advantage only for measures specific to visual-motor integration (5.1 intelligence quotient (IQ) points, 95% confidence interval: 1.0, 9.2). Differences in test scores between breastfed children and those who did not receive any breast milk feedings were 3.6 IQ points (95% confidence interval: -0.3, 7.5) for overall intellectual functioning and 2.3 IQ points (95% confidence interval: -3.0, 7.6) for verbal ability. Indicators of social advantage confound the association between breastfeeding and cognitive function, but careful measurement can reduce residual confounding and may clarify causal relations. (M.M. Smith et al., *Am. J. Epidemiol.* 158: 1075-1082, 2003)

Thus, even if an adverse effect of POPs ingested with mothers' milk occurred on the children's IQ, this effect would undoubtedly have been smaller than the beneficiary influence on the intellectual development

of skin-contact, love and care associated with breast-feeding. This aspect should also be borne in mind in discussions about interventions to improve the health prospects of the next generation, especially against the background of growing concern about e. g. Attention Deficit Hyperactivity Syndrome, violence, and other phenomena often discussed in the context with environmental influences. Investing in the improvement of the psychosocial situation of young families might well yield a much higher reward for our societies than frantic attempts to remove even the last bit of "chemical contamination" from the environment.

Dr. Michael Nasterlack
(Ludwigshafen, Germany)



No Evidence for an Impact of Selenium Supplementation on Environment-associated Health Disorders - a Systematic Review

In addition to vitamin C (and other vitamins/antioxidants), clinical ecologists (functional medicine) recommend selenium supplementation as a fundamental therapeutic remedy for the treatment of environment associated health disorders. This recommendation is based on the postulation that the trace element selenium inhibits oxidative stress generated during endogenous detoxification of xenobiotics (phase 1) by increasing selenium-dependent glutathione

peroxidase activity, and that it counteracts heavy metal toxicity by forming inert metal complexes. The objective of this review was to investigate whether there are any valid studies providing reliable evidence of the therapeutic benefits of selenium supplementation in potentially environment associated health disorders. A systematic review was conducted based on the rigorous and well-defined methods developed by the Cochrane Collaboration. To achieve the demanding standards for systematic review set by the Cochrane Collaboration, study selection, quality assessment and data abstraction were performed independently and in duplicate using a standardized protocol. Overall, 1290 studies were identified as being eligible for inclusion. Twelve of these met the inclusion criteria and their quality was evaluated individually. None of the studies included in the analysis provided evidence of the therapeutic benefits of selenium supplementation in environment associated health disorders. (M. Lacour et al., *Int. J. Hyg. Environ. Health* 207: 1-13, 2004)

Two things really strike me in this article. One is that there appears to be no scientific support for a therapy which is widely sold to people mostly with diseases, the diagnosis of which is usually equally weakly founded (o.k., I confess that I almost expected this). The other one is the fact that among a host of 1290 studies

only 12 were considered to be of sufficient quality to enter into the final analysis. What a waste of resources, and what a blow into the faces of many "researchers" in this field!

Dr. Michael Nasterlack
(Ludwigshafen, Germany)



There is not much in environmental medicine that has been more intensely debated than the possible association between certain environmental factors and reduced male fertility, lowered sperm counts and other "gender bender" effects. Here is another contribution to this discussion.

Association of in Utero Exposure to Maternal Smoking with Reduced Semen Quality and Testis Size in Adulthood: a Cross-sectional Study of 1,770 Young Men from the General Population in Five European Countries

Between 1996 and 1999, the authors invited all young men from five European countries who were undergoing compulsory medical examination for possible military service to participate in a study on male reproductive health. The participation rate was 19% in two cities in Denmark (n = 889), 17% in Oslo, Norway (n = 221), 13% in Turku, Finland (n = 313), 14% in Kaunas, Lithuania (n = 157), and 19% in Tartu, Estonia (n = 190). Each man provided a semen sample, was examined by a

physician, and, in collaboration with his mother, completed a questionnaire about general and reproductive health, current smoking habits, and exposure to smoking *in utero*. After adjustment for confounding factors, men exposed to smoking *in utero* had a reduction in sperm concentration of 20.1% (95% confidence interval (CI): 6.8, 33.5) and a reduction in total sperm count of 24.5% (95% CI: 9.5, 39.5) in comparison with unexposed men. Percentages of motile and morphologically normal sperm cells were 1.85 (95% CI: 0.46, 3.23) and 0.64 (95% CI: -0.02, 1.30) percentage points lower, respectively, among men exposed *in utero*, and exposed men had a 1.15-ml (95% CI: 0.66, 1.64) smaller testis size. The associations were present when data from the study centers were analyzed separately (though not in Lithuania, where only 1% of mothers smoked during pregnancy), although the strength of the association varied. Maternal smoking may have long-term implications for the reproductive health of the offspring. This is another good reason to advise pregnant women to avoid smoking.

(T.K. Jensen et al., *Am. J. Epidemiol.* 159: 49-58, 2004)

Dr. Michael Nasterlack
(Ludwigshafen, Germany)



Having had to deal with a specific question, I came across the following (although somewhat older) study, which as a "side effect" yielded a

probably spurious result on ALS. This still enigmatic disease entity has repeatedly been associated with various exposures, to the best of my knowledge mostly without proper scientific basis. Does anybody know more?

Mortality in Chemical Workers Potentially Exposed to 2,4-Dichlorophenoxyacetic acid (2,4-D) 1945-94: an Update

The study was carried out to update and add to a previously identified cohort of employees potentially exposed to the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D). The putative association between 2,4-D and non-Hodgkin's lymphoma has been debated for more than a decade.

Cohort members were male employees of The Dow Chemical Company who manufactured or formulated 2,4-D any time from 1945 to the end of 1994. Their mortality experience was compared with national rates and with more than 40 000 other company employees who worked at the same location.

330 Deaths were observed among 1517 people compared with 365 expected (standardised mortality ratio (SMR)=0.90, 95% confidence interval (95% CI) 0.81 to 1.01). There were no significantly increased SMRs for any of the causes of death analyzed. When compared with the United States rates, the SMR for non-Hodgkin's lymphoma (NHL) was 1.00 (95% CI 0.21 to 2.92). The

internal comparison with other Dow employees showed a non-significant relative risk of 2.63, (95% CI 0.85 to 8.33). Death was attributed to amyotrophic lateral sclerosis (ALS) for three cohort members. Compared with the other company employees, the relative risk was 3.45 (95% CI 1.10 to 11.11). The cases were employed in the manufacture or formulation of 2,4-D at different periods (1947-9, 1950-1, and 1968-86), and for varying durations of time (1.3, 1.8, and 12.5 years).

There was no evidence of a causal association between exposure to 2,4-D and mortality due to all causes and total malignant neoplasms. No significant risk due to NHL was found. Although not an initial hypothesis, an increased relative risk of ALS was noted. This finding is unsupported by other animal and human studies.

(C.J. Burns et al., *Occup. Environ. Med.* 58: 24-30, 2001)

Dr. Michael Nasterlack
(Ludwigshafen, Germany)



There is a multitude of epidemiological studies which link "pesticides" to adverse health effects in children. Some of these studies may well indicate real risks, but due to the lack of specificity of the exposure term are not useful for the derivation of real-life consequences. Animal experiments with specific substances may well provide clues, where a second epidemiological look is warranted.

Developmental Exposure to Chlorpyrifos Elicits Sex-selective Alterations of Serotonergic Synaptic Function in Adulthood: Critical Periods and Regional Selectivity for Effects on the Serotonin Transporter, Receptor Subtypes, and Cell Signalling

Organophosphate pesticides kill insects by allowing the neurotransmitter acetylcholine to build up at nerve endings. This short-circuits the cholinergic system, which governs involuntary processes. Low organophosphate doses given to rats *in utero* are associated with neurodevelopmental effects and impaired behavior in adult animals, and in the past, researchers assumed these adverse effects arose from disruption of the cholinergic system. But recently Justin E. Aldridge and colleagues at Duke University Medical Center found that one organophosphate, chlorpyrifos, appears to affect brain development through other, additional mechanisms, and at doses lower than those that perturb the cholinergic system. Now Aldridge and colleagues report that fetal and newborn rats exposed to chlorpyrifos during particular developmental windows undergo changes in their brain serotonin systems that persist into adulthood, possibly contributing to the neurodevelopmental effects of this particular pesticide.

Chlorpyrifos was once one of the most widely used

pesticides in the United States. Due to concerns about its neurologic effects in children, chlorpyrifos was banned from home and garden use in June 2000 under an agreement between the U.S. Environmental Protection Agency and pesticide manufacturers. But it is still used in the United States to protect commercial fruit and vegetable crops and worldwide it remains one of the most heavily used pesticides.

Aldridge and colleagues injected pregnant rats daily with 1 or 5 milligrams of chlorpyrifos per kilogram body weight (mg/kg) for 3 days either early (when the brain is first being formed) or late in gestation. These doses bracket the threshold for maternal toxicity and fetal cholinesterase inhibition. They also injected non-previously exposed 1-week-old pups with 1 mg/kg and 2-week-old pups with 5 mg/kg over a 3-day period.

The researchers allowed the young rats and the offspring of the pregnant rats to mature, then harvested the adult animals and measured biomarkers of serotonin system function in their dissected brains. These biomarkers included a number of serotonin receptors and transporters that the researchers had earlier found to be altered shortly after chlorpyrifos exposure. Although statistically significant effects were seen at all exposure intervals and for both doses, treatments during the late gestational period and the first week after birth – a stage in the rat that parallels the

second trimester of human fetal development – had the maximum effects, with increases in receptors and transporters as great as 30 - 80 % above control values in some brain regions. The greatest of these elevations occurred in male rats in the striatum region, which is generally thought to be involved with motor control.

It appears that later in development, the treatment affects males more than females. Other studies of chlorpyrifos's neurodevelopmental effects also have found that sex differences emerged only when exposure occurred late in gestation or in the neonatal period, but those studies did not follow rats to adulthood, nor did they focus on serotonin disruption by chlorpyrifos.

The authors suggest that perturbations in cell differentiation and brain architecture may be one of the contributors to non-cholinergic mechanisms of chlorpyrifos-induced neurobehavioral anomalies. Because serotonin is involved in controlling appetite and modulating depression, these results also lend support to the idea that environmental exposures may increase the risk of these problems, according to the authors.

(J.E. Aldridge et al., Environ. Health Perspect. 112: 148-155, 2004)

Dr. Michael Nasterlack
(Ludwigshafen, Germany)



Proposed UK Exposure Limits Framework

This consultative document gives proposals for a simplified system of UK Occupational Exposure Limits (OEL) that should be much easier for small firms to understand and use. The aim is to help the wide spectrum of firms using chemicals to properly protect their workers. The proposal in this Consultative Document is to replace the current poorly understood system with a single type of OEL, to be called a Workplace Exposure Limit (WEL). This will impose a single duty on employers – the amount of a chemical in their workplace air must not exceed the WEL.

This change is also important for countries like Australia which base their Exposure Standards on the UK system. The consultation document can be obtained from:

<http://www.hse.gov.uk/consult/condocs/cd189.htm>

There is also a supporting Research Report RR172 - The Role of Occupational Exposure Limits in the Health and Safety Systems of EU Member States at <http://www.hse.gov.uk/research/rrhtm/rr172.htm>.

(Hazmat & Environment Notes – Nov / Dec 2003)

Jeff Simpson (Ashburton, Australia)



In the November 2003 Newsletter, I forwarded Kevin Trangle's question regarding the use of Diphotérine® or other amphoteric and chelating agents in the treatment of chemical burns,

and provided my own (sceptical) view on this. Our Medichem colleague Goran Adevik contributed some additional points to this discussion, which I want to share with you.

Treatment of Chemical Burns - Additional Views

The discussion in the latest issue of Medichem Newsletter is interesting and important. Strong acids and caustics are ubiquitous throughout chemical industries.

Among my customers is a chlorine alkali plant producing and NaOH and handling large amounts of sulphuric acid and also hydrochloric acid. Three other chemical plants, which are our customers, handle considerable amounts of strong caustics and in almost every lab in those industries use strong acids and strong caustics.

Two of those plants have earlier had nasty accidents with NaOH causing severe burns and permanent blindness. That was however before my time. There has been many less dramatic cases every year.

Since I began at this work, about four years ago, I have worked to introduce Diphotérine as a personal sanitation agent. Thus in the chlorine alkali plant, everyone carries a 100 ml bottle in his belt for immediate sanitation.

My argument for this is that time is critical. Emergency showers, taps and hoses should be found, maybe with caustic in your eyes and panic in your

mind. Taking the lid off ones personal container and putting it to ones eye is something that could be practiced and could be performed at once.

It does certainly not replace water as the main sanitation agent. Absolutely not! However it is a valuable complement. Fortunately we have not so far got any extensive practical experience. However from the chlorine plant I recall two different incidents where workers had got a sprinkle of strong caustic (NaOH) in the face and in one eye. They booth used their Diphoterine first themselves and then got help from coworkers with physiologic NaCl solution flushing. Some ten minutes later I saw them in our medical center. In both cases they reported nearly immediate relief of pain in the eye when using Diphoterine. They were flushed for some time by us. pH as tested with indicator paper, was neutral.

Inspection showed no sign of damage to cornea or any other structure of the eye. One of them had some red spots on the skin in the face, but they had faded off the day after.

Those two cases, I admit, are not much of a proof for the benefits of Diphoterine. However this experience seems to confirm what the manufacturer claims about the effectiveness of it.

I strongly agree with Dr. Nasterlack that decontamination is important and that water cannot be replaced. However Diphoterine has an advantage as a first remedy in that it works fast. It not only neutralizes very effectively. It

also chelates the OH^- and H^+ ions, but also chelate-binds them.

I think this is especially important in caustic burns. I have been taught that in an acid burn proteins coagulate and become some barrier to penetration of the acid. Caustics make proteins hydrolyze and thus open the way for deeper damage of tissue, that can go on even if the surface is cleared of the substance. If that is correct it is especially urgent to neutralize, bind and what ever to stop and disarm the harmful agent.

FH is not common enough among our customer companies that we have seen reason to introduce Hexafluorine. I got aware of BF_3 used as component in a catalyst by one customer. In an incident it leaked out into the atmosphere where it obviously reacted with water in the air forming HF and B_2O_3 . We decided it was not enough to introduce one more sanitation agent and thus I have no experience of Hexafluorine. By another plant an entrepreneur was engaged for cleaning reactors. For this they were using HF among else. I noticed that their workers were equipped with Hexafluorine.

Dr. Nasterlack also has a point in that water is cheap and abundant. Everyone knows how to use it and turbulent flow is effective for removing most substances. There is also a practical disadvantage having a whole battery of specific sanitation remedies. In case of emergency the most obvious things seem to become complicated.

However, I think Diphoterine is not complicated to use. It works with acids and caustics as well. It is never less effective than water (in laminar flow, to say). It works fast and that could maybe save vision if you have it at hand. It seems to relive or stop pain, maybe enough to open the eyelids in spite of blepharospasm thus enhancing effectiveness of flushing and you might eventually regain orientation enough to get to the emergency shower.

In summary, to my opinion Diphoterine has a place in chemical environments where strong acids and caustics are used, especially as a personal equipment always near at hand. This, I think, is a splendid example where Medichem could be of great benefit to us. Fortunately it is uncommon that a single doctor gets enough personal experience from chemical burns to become an authority. But if we contribute with our scattered cases we might perhaps get wiser together.

Dr. Goran Adevik
(Stenungsund, Sweden)

*Our colleague Andreas
Flückiger wrote*

...it is with great interest that I read your article in the latest Medichem Newsletter. Our company's attitude (again with the same disclaimers Michael Nasterlack made for BASF) is exactly the same as the one of BASF. We recommend tap water in abundant quantities, and for some exceptional cases, also provide Polyethylene Glycol 400.

In the Basel area, there are still rumors of one or two (non-Roche) cases of ocular contamination treated with buffer solutions (possibly quite different from the stuff in the Prevor products) where there was precipitation of material in the cornea as a result of a chemical reaction between the contaminant and the buffer. This made the situation very much worse and the patient/s ended up blind until he/they got corneal transplants. So here the feeling is clearly that whilst this is very rare, if buffers are used potentially for any and all chemical contaminations, an adverse reaction between chemical and buffer can never be fully excluded.

We have also made the following pragmatic reflection: if we have a severe case of burn, we will not be the ones to treat the patient from A to Z, i.e. the patient will be handed to a hospital for further treatment. If everything goes well, no-one will question the initial treatment. If it does not, the question will invariably be raised whether everything possible was done to limit the damage - from immediate first aid to decontamination procedures and solutions to the final treatment in the hospital. If the hospital will ultimately get our severe cases, we want to be able to deliver the patients to the hospital with a pre-treatment that the hospital is in agreement with. We got together with them, and they clearly stated that they did not want any buffers used.

Dr. Andreas Flückiger (Basel, Switzerland)

I am very grateful for these real-life examples although, as Goran pointed out, they are certainly not enough to draw firm conclusions regarding the use of Diphoterine®. Nevertheless, they provide useful additional and alternative views to the position taken by myself. Thanks very much, Goran and Andreas!



Welcome to New Members

Dr. **Tomotaro Dote**,
Dr. **Hiroyasu Shimizu**,
Dr. **Kan Usuda**,
all Dept. of Hygiene and Public Health, Osaka Medical College (Japan),
Dr. **Adriaan Combrinck**,
Elixir Health Consultants,
Montana Park (South Africa)



Forthcoming Events

Hazmat 2004 Conference, 5-6th May, Melbourne

Will cover Dangerous Goods, Hazardous Substances, Global Harmonisation, NICNAS, Prescribed Waste Disposal, Emergency Response, Security, Liability Issues, etc. With good networking opportunities with the speakers.

Cost \$770, Members of Supporting Organisations \$660, All Distance Attendees \$550. Contact Fire Protection Association of Australia (FPAA)

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XXXII. Medichem 2004 - Paris

The XXXII. Medichem International Congress will take place on September 1-3, 2004 in Paris, France at the Sofitel Paris Forum Rive Gauche Hotel. The main theme for the Congress is "Toward Global Sustainable Best Practices for Chemical Safety & Health." Each day will be devoted primarily to a different aspect of this goal. Day 1 will cover Protecting Ourselves (worker health and safety), Day 2 will focus on Protecting Our Neighbours (Community preparedness, prevention and response) and Day 3 will highlight Protecting Our Future (children and the environment). **Deadlines for reduced early registration fees as well as for abstract submission have been extended to April 15th.** Complete information on the Congress may be obtained at <http://www.medichem2004.org>

