

**STC**

**NEWS/NOUVELLES**

**OFFICIAL  
NEWSLETTER**

**OF THE SOCIETY OF TOXICOLOGY OF CANADA**

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C.P./P.O. Box 517, Beaconsfield, Quebec, Canada H9V 1W1 <http://meds.queensu.ca/stcweb/>

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When we moved into our Sechelt home, we spent a lot of time digging out *Hypericum perforatum*, which had spread throughout a border along the edge of the house, to the detriment of some special tulips. St. John's wort, as it is commonly known, is a five petalled yellow flower, described by Galen as having neurological and vulnerary (wound healing) properties. It was found to be significantly more effective in controlling mild to moderate depression, with fewer side effects than low-dose tricyclics (Linde K, Gilbert R, Murlow C, Pauls A, Weidenhammer W, Melchart D. St. John's wort for depression: an overview and meta-analysis of randomized clinical trials. *Brit. Med. J.* 313:253-257. 1996). The putative antidepressant mechanism may be hypericin, which has high affinity for gamma-aminobutyric acid, the stimulation of which is known to have antidepressant effects. Hypericin activates dopamine receptors but inhibits serotonin receptor expression (Muller W. Effects of *Hypericum* extract on the suppression of serotonin receptors. *J Geriatr Psychiatry Neurol.* 7:S63-S64, 1994). This altered receptor regulation is consistent with the multi-week lag period between dose initiation and clinical effect, seen also in other antidepressants.

One of the first things I learnt as an undergraduate about St. John's wort was its side effect of photosensitivity, especially in fair-skinned people. This characteristic is being exploited with other drugs in photodynamic therapy. Light-sensitive molecules are activated by laser beams to destroy unwanted tissues, such as neoplasia, atherosclerotic lesions and invasive blood vessels in the eye, etc. For example, Dr. Julia Levy, a researcher at the University of British Columbia and head of QLT PhotoTherapeutics, has developed verteporfin based on two naturally-occurring porphyrins (Medicinal light-swords. *Economist* Feb 13: pp 77-79, 1999). Porphyrin derivatives are but one of the many classes of phototoxic chemicals. These cause non-immunological light-induced toxic reactions, an example of which is sunburn. Phototoxic

and photo-allergenic compounds include psoralens (8-methoxypsoralen), sulphonamides, sulphonureas, phenothiazine, tetracyclines (demethylchlortetracycline ), aminobenzoic acid, 6-methylcoumarin, musk ambrette, and ragweed (Compositae). I used to think the Star Wars trilogy was fiction, now we have medicinal light-swords! But will health care accept my claim for sessions under the tanning lamps if I call them photodynamic therapy?

More seriously, the world of medicinal herbs is often viewed with scepticism, though they have been widely used for centuries. There are concerns about efficacy, content, labelling, dosage, and interaction with other plant remedies and pharmaceuticals. Some recent articles review this field of interest to toxicologists (O'Hara MA, Kiefer D, Farrell K, Kemper K. A review of 12 commonly used medicinal herbs. Arch. Family Med.7: 523-536, 1998; Miller LG Selected clinical considerations focusing on known or potential drug-herb interactions. Arch. Internal Med. 158:2200-2211, 1998). For example, there are over 1,600 references to St. John's wort on MEDLINE. We hope to have an article on the safety and regulation of herbal medicines in a future issue of STC NEWS/NOUVELLES. On page 21 of this issue of our newsletter is a brief summary of the International Workshop to Evaluate Research Needs on the Use and Safety of Medicinal Herbs, held in Raleigh, NC, USA in September 1998.

Once, when I was in veterinary practice, a client told me that he had taken the medication prescribed for his dog. Why? To cure his hangover. His partner said that there had been no adverse effects, save a difficulty getting him to walk past lamp standards and fire hydrants. Well, once again, fact has caught up with fiction. Clomicalm a human anti-depressant, is now available for veterinary treatment of *canine clinical separation anxiety*, or what happens when you leave your dog alone in the home all day whilst you are at work. In addition, there is Anipryl, used for the treatment of *human Parkinson's disease*, as it increases the level of dopamine, and for *canine Cushing's disease*, in which overactivity of the adrenals which leads to urinary incontinence. Now is it available for the veterinary treatment of *canine cognitive dysfunction*, which may be demonstrated by "inappropriate urination". One wonders which pharmaceutical for human use the equine stud farms will appropriate to prolong the breeding life of stallions.

**NOMINATION AND ELECTION OF STC VICE-PRESIDENT, TREASURER AND ONE COUNCILLOR - Gail Bellward, Past President STC, University of British Columbia, Faculty Of Pharmaceutical Sciences, 2146 East Mall, Vancouver, BC V6T 1Z3. Canada**

Please send nominations for the following positions **as soon as possible** to Gail Bellward (Past-President and Chair of the Nominating Committee):

**Vice-President:** This person automatically becomes President at the end of the two-year term as V.P. Besides filling in for the President when necessary, the V.P.'s duties are to oversee the development of the plans for the Annual Symposium and to function as the liaison to CFBS regarding requests for toxicological expertise. We are particularly looking for nominations of people from the government sector.

**Treasurer:** The term of office is three years for treasurer, who functions as the financial director of the Board. The treasurer authorizes expenditures, collects dues and sends their receipts, interacts frequently with the Executive Director, prepares financial statements, arranges for audit of the books, collects and files G.S.T. and Q.S.T., etc.

**Councillor:** during a three-year term of office, the Councillor participates in meetings of the Board of Directors, providing advice and counsel, acts as liaison with specific committees as directed by the President, updates the STC Orientation Guide and Policy Manual (for one year) and is a member of the Awards Committee (for one year). In addition, the Councillor may be assigned a specific task by the President to assist in the management of the Board. This year we are particularly looking for nominations from the academic sector.

## **BOOK REVIEW #1 - Don Ecobichon**

*"Occupational and Environmental Neurotoxicology" by Robert G. Feldman, Lippincott-Raven, Philadelphia, PA. 1999. pp500 CDN\$160.00*

This is a well-written and much needed text devoted to agent-induced neurological anomalies, crafted together by one of the most practical neurologists at work today. Short chapters on exposure, recognizing the chemically exposed individual and approach to diagnosis, lead into succinct chapters on metals and metalloids (lead, arsenic, mercury, thallium, aluminum, tin and manganese), organic chemicals (tri- and tetra-chloroethylene, 1,1,1-trichloroethane, toluene, xylenes, n-hexane, MnBk, styrene, carbon disulphide, and acrylamide), gases (ethylene oxide, carbon monoxide) and pesticides (organophosphorus and carbamate esters). There is an extremely useful Appendix - the Boston Occupational and Environmental Neurology Questionnaire - to assist in making the discovery and diagnosis of neurological impairment(s).

While one could quibble about not finding one's favourite chemical of the moment, e.g. ethylene glycol monomethyl ether, the propionitriles (DMAPN, IDPN), etc, but one has to call a halt somewhere. More can go into the next edition when there is a better database. The chapters are written in a consistent, systematic order, easily accomplished when there is only one author, and the chapters are well illustrated with charts, diagrams relating biochemical and physiological effects and exposure, and photomicrographs of neuropathology. Don't let the price scare you. This is a monumental, up-to-date volume that should be on your reference shelf. It will remain current for some time to come.

## **SOCIETY OF TOXICOLOGY OF CANADA (STC)**

### **32nd Annual Symposium**

### **Toxicology In The New Millennium**

**December 2-3, 1999**

# Holiday Inn Montréal Midtown

**Thursday, December 2, 1999**

8:45 AM Introduction/Opening Remarks Len Lillie, President STC

## **Session I - Toxicology: Personal Reflections Chairperson: Len Lillie**

8:55 AM Introduction

Len Lillie, Parke-Davis Research Institute, Mississauga ON

9:00 AM Historical Landmarks in Toxicology Research

Gabriel Plaa, Université de Montréal, Montréal QC

9:45 AM Henderson Award Lecture

Speaker TBA

## **Session II - Genomics and Proteomics in Toxicology Chairperson: David Riddick**

10:55 AM Introduction

David Riddick, University of Toronto, Toronto ON

11:00 AM An Introduction to Genomics and Proteomics

Alan Bernstein, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto ON

11:45 AM Poster Session and Lunch

## **Session II - Genomics and Proteomics in Toxicology (continued)**

2:00 PM An Update on Genome Projects: Human and Model Organisms Lap-Chee Tsui, Hospital for Sick Children, Toronto ON

2:30 PM The Environmental Genome Project F. Peter Guengerich, Vanderbilt University, Nashville TN

3:30 PM Genomics and Proteomics: New Directions in Toxicology James Beall, Consultant in Toxicology, Jefferson MD

4:00 PM Discussion and Chairperson's Concluding Remarks

### **4:15 PM STC Annual Business Meeting**

6:30 PM President's Reception

8:00 PM Dinner

## **Friday, December 3, 1999**

### **Session III - Emerging Technologies in Toxicology Chairperson: John Clement**

8:55 AM Introduction

John Clement, BioChem Pharma Inc, Laval QC

9:00 AM Gene Arrays for Toxicology

Spencer Farr, Phase-1 Molecular Toxicology Inc, Santa Fe NM

9:30 AM Use of GeneChip Arrays for Gene Expression Monitoring and Genotyping

Tom Ryder, Affymetrix Inc, Santa Clara CA

10:30 AM Combinatorial Libraries and High Throughput Metabolism Data Acquisition Methods

Paul Erhardt, University of Toledo, Toledo OH

11:00 AM High Throughput Toxicity Evaluation

Roger Ulrich, Abbott Laboratories, Abbott Park IL

11:30 AM Discussion and Chairperson's Concluding Remarks

11:45 AM Poster Session and Lunch

**Session IV - New Directions in Molecular Toxicology Chairperson: Genevieve Bondy**

12:55 PM Introduction

Genevieve Bondy, Health Canada, Ottawa ON

1:00 PM Proteomic Analysis in Molecular Toxicology

Sandra Steiner, Large Scale Biology Corp, Rockville MD

1:30 PM Molecular Technologies in Forensics

Speaker TBA

2:00 PM Identification of Disease Susceptibility Genes

Speaker TBA

2:30 PM Discussion and Chairperson's Concluding Remarks

3:00 PM Conclusion

*Ed. Note: For the latest information about the 32<sup>nd</sup> STC Annual Symposium, please contact:*

*David S. Riddick, PhD*

*Associate Professor*

*Department of Pharmacology*

*Medical Sciences Building*

*University of Toronto*

*Toronto, Ontario, Canada*

*M5S 1A8*

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## **SOCIETY OF TOXICOLOGY OF CANADA/SOCIÉTÉ DE TOXICOLOGIE DU CANADA (STC)**

### **STC AWARD OF DISTINCTION**

#### *Purpose:*

The purpose of the STC Award of Distinction is to honour those individuals who have made outstanding and sustained contributions to the science of toxicology in Canada and/or the Society of Toxicology of Canada.

#### *Selection Committee:*

Recipients shall be chosen by a committee of four members drawn from the Society: the Past-President who will act as chairperson, one of the Councillors, and two members appointed by the Board from the general membership and who are not members of the Board.

#### *Nominations:*

Nominations must be made by two regular members of STC, in good standing, but no member may nominate more than one candidate during any one year. Nominations for the Award shall be made to the Chairperson of the Selection Committee before July 1 of the year of the award. Nominations must be accompanied by:

- 1 A summary, not to exceed two pages, describing the nominee's contribution to the science of toxicology and/or to the STC;
- 2 Copies of no more than five manuscripts and other documents considered by the sponsor to be pertinent to the award.
- 3 The nominee's curriculum vitae and a brief biographical sketch suitable for press release.

Nominees who are not granted the award in the year of the nomination will be automatically included among the nominees in the two subsequent years unless the sponsors explicitly express otherwise. Sponsors will be invited to update previously submitted information.

*Award and Presentations:*

The award will be in the form of a plaque or other suitable memento. Presentation of the award will be made at the President's Reception during the Annual Meeting.

*Criteria:*

The following criteria will guide the Selection Committee:

- 1 The recipient should have demonstrated outstanding and sustained contributions to the science of toxicology in Canada and/or the recipient should have provided outstanding and sustained service to the Society of Toxicology of Canada
- 2 The Selection Committee will exercise discretion regarding the relative contribution of the recipient to the science of toxicology in Canada and service to the Society of Toxicology of Canada.
- 3 The decision of the Selection Committee shall be final. Only one award may be made annually, and there is no obligation or duty to make the award when, in the opinion of the Selection Committee, there is no qualified candidate.

Information about STC's activities, awards and/or membership application forms may be obtained by contacting

Secretary STC

CP/PO Box 517,

Beaconsfield, Québec

H9W 5V1

## **SOCIÉTÉ DE TOXICOLOGIE DU CANADA/SOCIETY OF TOXICOLOGY OF CANADA (STC)**

### **STC PRIX DU MÉRITE**

#### *But:*

Le but du Prix du mérite est d'honorer les personnes qui ont apporté une contribution remarquable et soutenue au domaine de la toxicologie au Canada ou à la bonne marche de la Société de toxicologie du Canada.

#### *Comité de sélection:*

Les récipiendaires seront choisis par un comité de sélection formé de quatre membres de la Société: le président sortant de la Société qui présidera le comité, l'un des conseillers, ainsi que deux membres réguliers choisis par le bureau de direction, mais qui ne font pas partie du bureau de direction.

#### *Candidatures:*

Les candidatures doivent être soumises par deux membres réguliers de la Société; aucun membre ne peut soumettre plus d'une candidature chaque année. Les candidatures doivent être déposées auprès du président du comité de sélection avant le 1<sup>er</sup> Juillet de l'année de la remise du Prix. Les documents suivants doivent être soumis à l'appui des candidatures:

1 un résumé de deux pages décrivant la contribution du candidat ou de la candidate au domaine de la toxicologie ou au fonctionnement de la STC;

2 des copies d'au plus cinq manuscrits ou documents pertinents produits par le candidat ou la candidate;

3 un curriculum vitae du candidat ou de la candidate, ainsi qu'une notice biographique à l'intention du monde de la presse.

À moins que les parrains des candidats ou des candidates ne souhaitent qu'il ne soit autrement, les candidatures non retenues l'année de leur dépôt seront réactivées automatiquement lors des deux années suivantes. Les parrains verront alors à mettre à jour les dossiers soumis.

*Le Prix et sa remise:*

Le Prix consistera en une plaque ou en toute autre marque tangible de reconnaissance. La remise du Prix se fera lors de la réception du président, à l'occasion du Colloque annuel de la Société.

*Critères:*

Le comité de sélection se basera sur les critères qui suivent:

1 le ou la récipiendaire devra avoir apporté une contribution remarquable et soutenue au domaine de la toxicologie au Canada; à ceci pourrait se substituer une contribution sous la forme d'états de service remarquable et soutenues au sein de la Société de toxicologie du Canada;

2 c'est au comité de sélection qu'il incombera de porter un jugement éclairé sur le mérite de la candidature;

3 la décision du comité de sélection sera finale et un seul prix sera remis chaque année. Si, de l'avis du comité de sélection, aucune candidature n'est méritante, le Prix ne sera pas remis.

On peut obtenir des informations sur les activités et les prix de la STC ainsi que sur la façon de joindre les rangs de la Société, en écrivant à l'adresse suivante:

Secrétaire de la STC

CP/PO 517,

Beaconsfield, Québec

H9W 5V1

## **SOCIÉTÉ DE TOXICOLOGIE DU CANADA/SOCIETY OF TOXICOLOGY OF CANADA (STC)**

### **STC PRIX VEYLIEN HENDERSON**

Par ce Prix, la STC cherche à reconnaître l'importante contribution à la toxicologie d'un chercheur ou d'une chercheuse œuvrant au Canada. Les conditions d'éligibilité sont les suivantes:

1 être citoyen(ne) canadien(ne);

2 être âgé(e) de moins de 45 ans en date du 1<sup>er</sup> Juillet de l'année de l'obtention du Prix;

3 être mis(e) en nomination par un membre régulier en règle de la Société. Ce membre devra faire parvenir au secrétaire;

a une lettre d'appui à sa recommandation;

b un résumé de deux pages soulignant la contribution remarquable du candidat ou de la candidate;

c un curriculum vitae complet et une liste des publications du candidat ou de la candidate;

d des tirés à part d'au plus cinq (5) publications reflétant bien les activités de recherche du candidat ou de la candidate.

Le tout doit être transmis au secrétaire, à l'adresse habituelle de la société, avant le 1<sup>er</sup> Juillet de l'année de la remise du Prix.

Secrétaire de la STC

CP/PO 517,

Beaconsfield, Québec

H9W 5V1

**STC VEYLIEN HENDERSON AWARD**

This STC Award honours an individual who has made a significant contribution to the discipline of toxicology in Canada. The conditions of the award are as follows:

1 the candidate must be a Canadian citizen;

2 the candidate must be under 45 years of age as of July 1 of the year in which the award is given;

3 the candidate must be nominated by one ordinary member of the Society (in good standing) who will supply the Secretary with:

a a supporting letter of recommendation;

b a two page resume describing the significant contribution made;

c a complete curriculum vitae and publication list; and

d reprints of not more than 5 papers best reflecting the candidate's research.

All of the above should be sent to the Secretary, at the STC address by July 1 of the year of application for this award.

Secretary STC

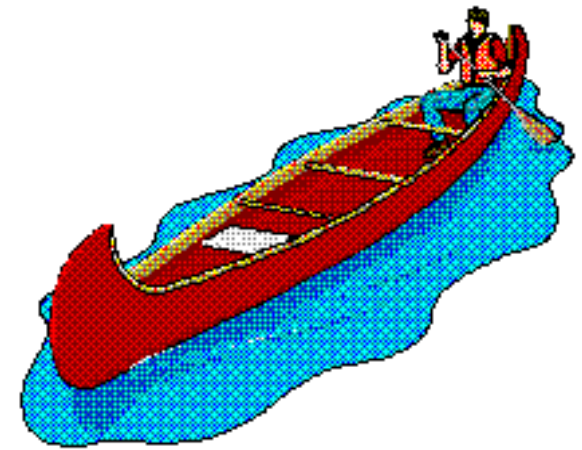
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**THE VIEW FROM MY CANOE - Don Ecobichon**

Spring has come. For much of April, the daily event was skeins of Canada geese winging northward, with some remaining on a near-0by marsh for a few days of rest., generating lots of noise and cackling until they got their act together to continue onward. For a few days, we had a solitary trumpeter swan (sex unknown) in the company of a pair of Canada geese. Max, our yellow Labrador, was most interested in this huge bird although the bird was less than impressed by the dog. While the canoe is not in the water yet, the time is approaching with the pike and pickerel seasons now open. Perhaps, I shall soon have some time to cogitate and ruminate.



I managed to get to the SOT meeting in New Orleans this March, after a few years' absence, to renew acquaintances and to learn what is new in the discipline, spending time mostly in seminars, workshops and plenary lectures. It was good to meet old friends, most of whom knew that I had retired (I don't know how). I was present to see my colleagues and friends Jules Brodeur and Michel Charbonneau receive the SOT Awards for Education and Achievement, respectively. Well deserved, both of them. In addition, Canadian graduate students in toxicology programs did exceptionally well - Jacqueline Walisser, a student with Rob Thies (UBC, Pharmacy) received the prestigious Carl C. Smith Award from the SOT Mechanisms Specialty Section and Graeme Smith and Andrew Tan, students with Tom Massey (Queen's U) received awards of Merit from the SOT Carcinogenesis Specialty Section. Congratulations to one and all! It is nice to see Canadians making their mark internationally.

A great story was told in one of the plenary lectures, the Burroughs Welcome Lecture, given by Dr. Boekelheide (Brown University) on male reproduction. I wrote notes furiously and think that I can reconstruct the story faithfully. It concerns a discussion between God, St. Michael and St. Gabriel, who were designing the evolving world and introducing mammals. Saint Michael claimed that there might be a problem since internalized gonads would be susceptible to the proposed increase in body temperature. Saint Gabriel suggested hanging them outside. Saint Michael was concerned that, dangling on a couple of tubes, they could be ripped off easily and "there goes spontaneous reproduction". St. Gabriel countered by suggesting that they could be placed in a bag. God said "yes, I like it". Saint Michael was still concerned that. Since the human was to stand erect, the gonads would be out in front with no protection at all. God said "you guys are just wasting time and we have a whole universe to create. The humans will just have to order something from consumer's support".

The relationship between scientists and news media reporters has always been at odds since neither understands the other. Scientists must learn to communicate with the public and reporters have to stop thinking of scientists in terms of weird "geeks" who can not communicate. Scientists are often portrayed as deranged individuals conducting unethical, even dangerous, experiments. Examples: Dr. Jekyll and Mr Hyde., Dr. Strangelove, Sphere, even Jurassic Park. Scientists believe that reporters are only interested in news that is bad, otr at least twisting it so that it appears to be bad. Michael Crichton, the author of Jurassic Park and the sequel, wrote an essay in Science (March 5, pp1461-1463) that explores the issues of communication, interpretation and missed opportunities, using films as examples of heroes and villains. Worth reading.

Speaking of reading, on a recent, long flight to Chile, I read Robin Cook's "Toxin", a thriller about the meat industry, the virulent strain of E. coli (O157:H7) and HMOs control over hospitals. The description of meat processing, from cows to hamburger patties is guaranteed to

make you a vegetarian. The science is accurate. Cook being a physician-writer who is meticulous in his research, and has an axe or two to grind. I cannot imagine that he made many friends in certain circles, including the US FDA who he accuses of being in bed with the beef industry and having a mandate that does not protect the public's health. Read the book - this movie will never be made.

In my search for published papers with the most authors, I have found one entitled "Respiratory Health Hazards in Agriculture" (Am J Resp. Crit. Care Med 158/5 II, S1-S76, 1998) with 32 authors. A second paper, entitled "Decay of the GRB 990123 OptiAfterglow: Implications for the Fireball Model" (Science 283:2069-2072, 1999) involves 52 authors from 24 different institutions from Tenerife to Iceland and the USA to China.

### **NEWS FROM OTTAWA - Rekha Mehta, Health Protection Branch, Health Canada**

To continue along with the theme of natural health products, on March 29<sup>th</sup>, 1999, the creation of the Office of Natural Health Products (ONHP) in Health Canada was announced by the Health Minister, Mr. Allan Rock. This new Office is expected to be responsible for the regulation of natural health products in Canada, and it was created in response to 53 recommendations by the Standing Committee on Health's report "Natural Health Products: A New Vision". The establishment of this Office reflects Health Canada's commitment to ensure that natural health products are safe, of high quality and properly labelled and advertised. As neither food nor drug, natural health products may require a unique regulatory structure.

The Standing Committee's recommendations, developed to address the distinct nature of natural health products, will be used in defining the policy framework, within which the ONHP will operate. The Office reports directly to the Assistant Deputy Minister, Health Protection Branch (HPB) who has named Dr. Colin Broughton from HPB Toronto to head a Transition Team to establish this Office. For further information and future developments visit the ONHP information page on the Health Canada web site, at [GOTOBUTTON BM\\_1\\_ www.hc-gc.ca](#). A toll free number is also available, 1-888-774-5555 for general information, Teletypewriter (TTY) for hearing impaired: 1-800-465-7735.

One of the first tasks that ONHP is undertaking is the investigation into products containing blue-green algae, a problem that recently came to the forefront. As a precaution, Health Canada is advising consumers that products containing blue-green algae may contain toxins known as microcystins that are toxic to the liver and, despite recent, unfounded reports that they can be used as a treatment for Attention Deficit



Disorder(ADD), these products should not be given to children who with their lower body weights, are at greater risk of developing serious liver damage. Adverse symptoms from long-term use of these products (weeks to months) may not be obvious, but could range from a feeling of general malaise or gastro-intestinal discomfort, to jaundice. In children the toxic effects are more likely to present as acute gastro-intestinal symptoms (nausea, vomiting, diarrhea, etc.). In order to determine the extent of this potential problem, Health Canada, through the Office of Natural Health Products, Therapeutic Products Programme, and the Food Directorate of the HPB, is surveying products containing blue-green algae to determine the frequency and forms of such products on the market, and the levels of microcystins in these products. Many products containing blue-green algae sold in Canada through both retail outlets and direct-sellers, are in tablet, capsule, or powder forms as food supplements, particularly as a natural source of minerals. Due to the potential health risk, consumers who choose to use products containing blue-green algae, especially those from natural lakes, have been advised to do so only for short periods of time, as required, and discontinue their use in children.

In other news from Ottawa, two new senior management appointments took place. Soon Dr. Marc Le Maguer will be joining Health Canada under the Government of Canada Executive Interchange Program as the Director General, Food Directorate, HPB. Dr. Le Maguer has held positions in the area of food research with the Universities of Guelph and Alberta. He is expected to play a key role in implementing the government's commitment to enhance and develop its food safety and nutrition policies and programs in Health Canada through the three year, \$65 million additional investment into the Food Program announced in the 1999 federal budget.

The second appointment took place as part of the Department's effort to enrich its scientific and policy capacity. Dr. Robert McMurtry, currently Dean of Medicine and Dentistry at the University of Western Ontario with speciality training in orthopaedic surgery, has been appointed as the first G.D.W. Cameron Visiting Fellow at Health Canada. Dr. McMurtry's duties will be to advise the Minister, the Deputy Minister and the Department on a wide range of emerging health issues and to participate in policy development from a health expert's viewpoint. The new Chair is named after Dr. George Donald West Cameron who served as Deputy Minister of National Health between 1946 and 1965. Those appointed to the post are expected to be eminent individuals in the field of health and health care who can make a significant and lasting contribution to the development of policy and knowledge within Health Canada on a wide range of subjects. Appointments will normally be of one to two years duration.

On the national front, following the February 1999 Federal Budget which provided a largest single new investment of \$12.9 billion into health, Minister Rock has been on the road, attending events and news releases in Toronto, Vancouver, Montreal, Quebec City, Edmonton, Moncton, Halifax, and Dakota Tipi (Manitoba). Additional news releases still keep pouring in with such announcements as funding allocations for First Nations and Inuit Health initiatives, the new Canadian Diabetes Prevention and Control Strategy, prenatal nutrition programs, National Children's Agenda, Canadian Strategy on HIV/AIDS, the NURSE fund, a national network of information about health and health services, Medicare and the Canadian Institutes of Health Research (CIHR). To date, CIHR funding has been allocated for the Canadian Neurotrauma Research Program which is a one-year partnership of eight Canadian organisations, including the Rick Hansen Institute, to find cures for brain and spinal cord traumas. The second CIHR funding was provided to the Vancouver General Hospital to develop and establish a centre of excellence for prostate cancer research in Canada. (Additional information on these news releases is available at <http://www.hc-sc.gc.ca/english/news-arc.htm#rel>).

To touch base on HPB Transition from where my predecessor (Doug Arnold) left off, more than 800 people across the country took part in last fall's National Consultations into the renewal of the federal health protection legislation, risk management and public involvement. To a certain extent in agreement with the viewpoints expressed by HPB scientists, the consensus among the participants was the need: (a) for health and safety to come before economic and other considerations with issues such as cost recovery raising concerns of conflicts of interests; (b) for the Department's activities and decision-making processes to be more transparent to the public and various stakeholders with greater accountability of Health Canada to Canadians; (c) for regulations for industry to be better adapted to suit the current trends with greater consistency in the way they are being enforced; (d) for improved legislation to reflect the realities of contemporary society and science (categorization of products through definitions, advertising, etc.); and (e) for a fundamental review of the Health Protection Program, including its legislative component in order to establish the principles for the responsibilities of the Minister of Health.

In April, 1999, the Canada Food Safety and Inspection Bill was introduced in the House of Commons by the Honorable Lyle Vanclief, Minister of Agriculture and Agri-Food. The Canadian Food Inspection Agency (CFIA) and the Departments of Health Canada and Industry Canada worked in partnership to consolidate and modernize five food Acts (the Canada Agriculture Products Act, the Meat Inspection Act, the Fish Inspection Act, and the food related aspects of the Food and Drugs Act and the Consumer Packaging and Labeling Act) and the three agricultural input Acts (Feeds Act, Seeds Act, Fertilizers Act) into this single statute. The Food and Drugs Act, as a result of removal of the food provisions, will now be known as the Health Products Safety Act. This renewal of the legislation seems a logical step after creating the CFIA with the Bill clarifying and reaffirming the Minister of Health's authority for establishing policies and standards respecting any matter that may affect the safety and nutritional quality of food. The Minister of Health is also given the authority to create an emergency food standard which would enable him to rapidly respond to a serious public health problem not covered by existing standards. The proposed new Act will maintain the current system of checks and balances with the Minister of Health assessing the effectiveness of the Agency's activities related to food safety, and the Minister of Agriculture and Agri-Food responsible for enforcement through the CFIA.

## **LE MERCURE À LA BAIE JAMES : PLUS DE DIX ANS DE GESTION DU RISQUE.**

**Gaston Chevalier, Université du Québec à Montréal, directeur du CIRTOX, et Président du Comité mercure de la Baie James.**

*Mercury contamination in Northern Quebec as a result of hydroelectric activities has resulted in widespread contamination of certain ecosystems, and exposure of aboriginal populations to levels that have generated public health concern. Dr. Chevalier, University of Quebec in Montreal, reflects on the lessons learned during the past 10 years in the risk management and on the efforts made to communicate these risks to the populations involved.*

## **LE PROBLÈME**

Les écosystèmes nordiques du Canada (entre 50° et 55° de latitude) contiennent naturellement une certaine teneur en mercure en plus des apports atmosphériques d'origine industrielle. Suite à la mise en eau des barrages du nord québécois, la contamination de la chaîne alimentaire a nettement augmenté par la mise en disponibilité du carbone organique de la végétation riveraine inondée. Celle-ci a favorisé l'activité de méthylation bactérienne du mercure inorganique dans l'eau en méthyl-mercure. Quatre ans après l'inondation (1984), les taux de mercure méthylé des poissons piscivores comme le brochet ont atteint 3-4 mg/kg alors qu'ils sont de l'ordre de 1 mg/kg dans les lacs naturels voisins. La concentration du méthyl-mercure dans l'eau est de l'ordre du nano g/li (ppt). Le benthos et le plancton ont des niveaux d'environ 1 µg/Kg (ppb) et les poissons non-piscivores qui s'en nourrissent présentent des teneurs de l'ordre du mg/Kg (ppm), alors que certains oiseaux piscivores recèlent des niveaux de méthyl-mercure de plusieurs dizaines de mg/kg dans leurs plumes. Certains habitants des communautés indiennes qui se nourrissent traditionnellement de poissons ont aussi vu la concentration en méthyl-mercure de leurs cheveux atteindre des teneurs élevées (plus de 30 mg/Kg) au début des années 80.

## LES SOLUTIONS

La signature en 1986 de la convention Mercure de la Baie James entre le Gouvernement du Québec, les autorités régionales crie et Hydro-Québec visait par la mise en place de programmes de suivi et recherche à mieux comprendre la nature et l'étendue du problème causé par la présence de mercure sur le territoire de la Baie James, en particulier le bassin du complexe du fleuve La Grande.

De manière spécifique, la convention visait à évaluer le phénomène de contamination environnementale dans ce milieu nordique, de définir des actions en vue de minimiser le risque potentiel d'effets sur la santé des populations crie, exposées au contaminant par l'alimentation ainsi que sur leur mode de vie traditionnel et d'identifier toute mesure propre à remédier à la contamination.

Le suivi des concentrations de mercure, après 18 ans de mise en eau du réservoir La-Grande-2, montre que les niveaux de mercure demeurent plus élevés dans les poissons des réservoirs que ceux des lacs naturels voisins, mais ces niveaux sont maintenant en phase décroissante tant chez les poissons piscivores ex.: (brochet) que chez les non-piscivores ex.: (corrégone). Plus de 15,000 poissons ont été analysés.

Le programme de surveillance biologique de l'exposition au mercure chez les populations indiennes crie a été orienté dès le début vers les segments de population les plus à risque, à savoir les personnes de plus de 40 ans et les trappeurs, qui sont des consommateurs réguliers de poissons, de même que les femmes en âge de procréer, en raison du risque élevé que présente le mercure pour le développement du fœtus.

Les concentrations acceptables de mercure dans les cheveux ont été fixées entre 0 mg/kg et 30 mg/kg pour la population en général et entre 0 mg/kg et 15 mg/kg pour les femmes en âge de procréer (15 à 39 ans), soit des seuils qui tiennent compte des effets bénéfiques reconnus des poissons dans le régime alimentaire (source de protéine, vitamines et d'antioxydants).

Depuis quelques années, les taux de contamination alarmants chez les humains sont devenus faits rarissimes . Les teneurs diminués et maintenant stabilisés chez la plus grande partie de la population (moins de 2 mg/kg) ne présentent plus de risque à la santé humaine. La diminution de l'exposition des populations consommatrices de poissons peut être attribuées à une baisse de consommation des poissons les plus contaminés, suite aux avis sanitaires du Comité recommandant de manger les espèces non-piscivores. Une diminution significative de la consommation globale de poissons est aussi à considérer, ce qui pose la question de communication du risque auprès des populations autochtones, question à laquelle le comité a aussi œuvré par de nombreuses actions d'information (affiches, brochures, vidéo, radio) en trois langues.

Par ses programmes d'études et d'action, le Comité Mercure a procédé pendant dix ans de 1986 et 1996 à évaluer et gérer les impacts environnementaux et sociaux de la contamination accrue du mercure due à la construction des barrages hydroélectriques. La nature de la contamination de la chaîne alimentaire, l'étendue du territoire considéré, les programmes de surveillance environnementale et biologiques mis sur pied, les processus d'évaluation et de gestion du risque adoptés par notre Comité, les activités interculturelles de communication du risque auprès des populations concernées, ainsi que les moyens techniques et financiers déployés au Québec sont d'intérêt pour d'autres sociétés elles aussi aux prises à des problématiques très semblables, comme celles des pays de l'Amazonie.

## **SECRECY AND THE CORPORATIZATION OF SCIENCE - David Josephy**

### **Dept. of Chemistry and Biochemistry, University of Guelph**

"Chemical and Engineering News" (C&EN; April 19, 1999) reports on a meeting held at M.I.T. in March, on the subject of "Secrecy in Science". This forum was sponsored by the AAAS Committee on Scientific Freedom and Responsibility.

One focus of the forum was on government-imposed secrecy. According to Sen. Moynihan of New York, a speaker at the forum, the U.S. government classified 6,620,154 secrets in 1997. Apparently, the total number of secrets is not itself a secret.

The impact of government regulation on science has been the subject of a lot of debate in the U.S., in recent months. A tiny clause in the latest U.S. budget legislation stipulates that anyone can now request, through the Freedom of Information Act (FOIA), the raw data from any project funded by the U.S. government. This far-reaching change was slipped through Congress, apparently, without anyone noticing. The implications are yet to be seen. One can envisage some nasty tactics, such as harassing one's scientific competitors by demanding that reams of old data be turned over: the task of complying with the paperwork could bring research to a grinding halt. As one professor noted, "*Complying with FOIA is exorbitantly expensive, and that cost is going to come out of your research budgets.*" Even worse, there is concern that the new federal regulations permit individuals to demand access to still-unpublished data. This could have a destructive effect on the process of peer review, if researchers are forced by the courts to make data public before it has been submitted for publication. U.S. scientific societies are now scrambling to work out a strategy for dealing with these legislative changes.

Another facet of the changing climate in academic science is, of course, the growing impact of commercial interests on the universities. C&EN notes that about 20% of research at MIT is now funded by industry, and I expect the numbers are similar at many Canadian universities. The trend will continue to increase: many of the new "government" funding opportunities in Canada, such as the Canada Foundation for Innovation (<http://www.innovation.ca/english/about/index.html>) have an explicit requirement for private "matching" funds.

What impact does such corporate involvement have on the academic research enterprise? It's a big question; I will just relate a couple of personal anecdotes. A few years ago, I had a grant application for work with bacterial strains expressing recombinant human enzymes turned down. The panel commented that the same work could be accomplished using human lymphoblastoid cell lines instead. These cell lines that had already been described in the open literature by a group of academic scientists in the U.S., who were supported by corporate funding. What the grant panel did not know is that these "published" cell lines were, in practice, unavailable to academic researchers. I had already tried to obtain these cells. My polite request was answered by a pile of legal documents which explained that I would have to pay US \$10,000 for each cell line, and I would have to agree in writing not to modify the cell lines in any way --- a restriction which ruled out the experiments which I wanted to perform. How can one reproduce (let alone extend) published experiments, if the reagents themselves are made unobtainable? When the researchers have a direct financial interest in their work, the temptation to present results in the most favourable light becomes that much greater, and so does the need for independent confirmation and verification of the published claims.

In some cases (e.g., transgenic animals, which must be bred and maintained at substantial expense), it may be appropriate to ask for reimbursement of the cost of supplying the reagents, since grant funds may not be available for this specific purpose. In fact, I ask persons requesting bacterial strains from my lab. to make a small contribution, for this reason; if they are unable to do so, I send the strains anyway. But it is quite another matter for scientists to demand large sums of money, in the interest of maximizing corporate (and personal) profit.

The second example arose last month. Our latest research is looking at structure-function relationships in human cytochrome P450 1A2. There is no crystal structure available for this enzyme, but two academic groups in Europe have published theoretical models of the structure. I thought that it would be useful to analyze our data in light of these models, especially since there are some significant differences between them. So, I asked each of the groups to send us the computer data file corresponding to their proposed structure. One group replied immediately, by E-mail, and attached the complete data set. In contrast, the principal investigator for the other group wrote that "files of my models are not currently available to the public domain due to contractual agreements with the companies who fund my work. However, I would be delighted to collaborate with you in this area ... [if] we can find some way of working together without me giving away commercially sensitive information." I replied that I felt that this was an unreasonable attitude: the data were published (in 1996) and should be made available to other researchers. But, of course, no data were ever sent to me.

Now, the work in question occupies about 20 pages of an academic journal, complete with close-up figures of drug-protein interactions at the active site, and claims of the accuracy and importance of the model. Without access to the crystallographic-coordinate data, however, it is almost impossible to assess the scientific value or validity of the model. When I discussed this question with colleagues, they suggested that I write to the editor of the journal in which the article was published. The editor turned out to be the chair of the department in which the principal investigator works!

I think that scientists have to make a choice. You can go the "corporate" route: obtain commercial funding for your work; protect your discoveries by filing patents, requiring licence agreements, and imposing other legal restrictions, and do your best to make a profit. Or you can publish your results in the "open" (one wishes quotation marks were not necessary here) literature, and allow other researchers to replicate, test, and extend your results, in the interests of science, not profit. But if researchers try to have it both ways at once, then the integrity of science is seriously threatened.

Have other readers of News/Nouvelles encountered similar situations? I'm sure the editor would be interested to hear about your experiences, as would I.

## **BOOK REVIEW #2 - Don Ecobichon**

*"The Killing Factory" John Parker. Smith Gryphon Publishers, London, UK. Obtainable through the Barnes & Noble Catalogue. CDN\$10*

With the interest generated in the Gulf War Syndrome that has afflicted some 60,000+ allied military personnel, a clear picture has never been available because of government incompetence, stalling tactics along with an unwillingness to admit that there was a problem.

Being an English journalist, Parker focuses on the Porton Down chemical and biological research station, its inception during the gas attacks in WWI and the development of both offensive and defensive capabilities before and during WWII. A mini-history of the station. It explores the use of "volunteers" to test equipment (not all that good) as well as various toxic materials including mustard gas, phosgene, HCN, CS and,. Of course, both the chemical nerve gases (sarin, soman, tabun) and biologicals (anthrax, plague, botulism, etc) known to be in Iraq's arsenal. It catalogues the chronic illnesses suffered by these volunteers and personnel.

Enter the Gulf War Syndrome with the documented physical and mental health problems, the plethora of vaccines administered (the anthrax vaccine had never been cleared by regulatory agencies), the antibiotics administered, the "antidote" for nerve gas intoxication (pyridostigmine bromide, again not cleared by any health regulators), the pyrethroid esters and DEET used to protect against biting insects, the wind-driven sand, aviation and diesel fuel, the nerve gas decontaminant (ethylene glycol monomethyl ether), the highly toxic chemical resistant coating sprayed on combat vehicles,(no personnel protective equipment was used), the oil fires and , last but not least, the depleted uranium used to harden warheads to penetrate weapons-grade steel. The term "atmospheric overload" was coined to describe the environment into which the military were thrown.

The tragic medical cases, both US and UK soldiers, are well described as are their battles to claim compensation from governments reluctant to acknowledge these men and women. Cancer as well as severe neurological problems and birth defects (spousal) continue to exert a costly toll on these people. Recognition has been slow.

Parker raises the issue of animal experimentation to frequently, quoting numbers of animals and species used to provide little valid information on chemical and biological toxicities, thereby exposing himself to criticism as an animal rights activist. This foray detracts from the main story, an expose of human suffering and government indifference to what can only be described as tragic circumstances. The book provides what might be claimed to be a relatively complex account of the "exposures", with much more information given than has ever been delivered piecemeal at a reasonable price through the catalogue of Barnes and Noble, Mississauga, Ontario.

**AN OVERVIEW AND STATUS REPORT OF THE ICH GUIDELINES WHICH RELATE TO THE PRECLINICAL SAFETY EVALUATION OF NEW DRUGS AND BIOTECHNOLOGICALS Jon Daniels, Ph.D., DABT<sup>1</sup>, Randall Leeder, Ph.D.<sup>2</sup>, and Rick Stewart, Ph.D.<sup>3</sup> <sup>1</sup>CanTox Health Sciences International; <sup>2</sup>Leo Pharma Inc.; <sup>3</sup>ITR Laboratories Canada Inc.**

Since discussions between industry and regulatory representatives from the United States, Europe, and Japan began in 1990, the mission for the International Conference of Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use has been to achieve consensus on a set of internationally acceptable toxicity testing guidelines for medicinal products. The tripartite harmonized technical guidelines published by ICH provide the required scientific and technical guidance to the pharmaceutical industry for development of testing procedures while ensuring the safety, quality, and efficacy of the tests performed, as well as, the predictive value of the data generated. Harmonization of testing requirements on a global basis is expected to provide the consistency needed for efficient drug development, and as a result, is expected to reduce the delay in time experienced in the process of product development and registration. As observer to the ICH process, Canada (*i.e.*, as represented by the Therapeutic Products Programme of Health Canada) has agreed to adopt the consensus guidelines as they become finalized.

The ICH has provided a dynamic and unique platform for dialogue to be conducted between industry representatives and regulatory authorities. The identification, collection, and analysis of data are considered paramount to developing the necessary scientific and regulatory rationale to support the proposed changes in the current registration protocols for the participating regions. However, the inability to effectively search the available databases, the time for development of new databases and/or the existence of confidentiality constraints, in many instances, have been shown to impede adequate disclosure of the required data. These apparent limitations have proven to hinder the progress toward consensus on a number of specific topics and topic areas. Throughout the process of overcoming these barriers, the actual and perceived differences in technical requirements between the regions have become further characterized and defined. Most of all, this process has relied heavily on a continued commitment to communication within industry organizations and within and between the regulatory agencies involved.

### **Use of ICH Guidelines by Industry**

To assess the use of the ICH guidelines by the pharmaceutical industry to date, two independent industry surveys have been commissioned by the ICH Steering Committee. The surveys were designed to provide an indication of the current use level of the ICH guidelines by industry during the drug development process. Aside from providing an indication of the acceptance and use of the ICH guidelines within

regions, the results have been used to assess the impact of these guidelines with respect to a number of different topic areas. Overall, the results were reported to show an apparent increase in the number of companies that are using ICH guidelines in their protocols for new drug research.

Based on the results of these surveys, it was not unexpected that a lag in regulatory review would be experienced in a number of studies developed using the new guidelines. In many instances, especially for products intended for use in chronic indications, the preclinical data to support such studies would likely have been obtained several years prior to the submission of the current marketing application. The use of these guidelines during the design of safety evaluation programs for pharmaceuticals, in particular new chemical entities, was most apparent in regions where there had been an opportunity for discussion of specific test protocols to be used during the investigational stage of clinical development. Although the impact of the ICH guidelines is difficult to assess at such an early stage, the increase in the number of additional topics proposed by industry to be considered for future harmonization is encouraging.

### **Status of ICH Safety Guidelines**

The progress made as a result of the ICH process is evidenced by the list of safety topics/subtopics and their status (see table below). To date, 12 topics relating to the preclinical safety evaluation of pharmaceutical products have been finalized and adopted, in addition to a multidisciplinary topic which covers the timing of toxicology studies in relation to the conduct of clinical trials. A more recent advancement has been the adoption at the ICH Steering Committee meeting in September 1998 of *Safety Pharmacology Studies* as a new ICH Topic. The aim is to harmonize the guidance, which is currently under development in the three ICH regions, and reach agreement on the definition, objectives and scope of safety pharmacology studies. The guideline will also address which studies are needed before initiation of Phase 1 clinical trials.

The ICH guidelines have focused for the most part on defining the technical data requirements for the safety evaluation of pharmaceuticals. Since the guidelines for each of the safety topics have been written to support a more flexible approach compared to the previously existing guidelines within regions, the specifications or principles described within each, for the most part, are also applicable to biopharmaceuticals. However, the ICH has recognized that conventional toxicity testing programs developed for pharmaceuticals, in particular, the need for similar types and durations of studies, would not be deemed as being appropriate for most biopharmaceuticals (*e.g.*, traditional biologics such as blood products), vaccines and biotechnology-derived pharmaceuticals). The similarity of these biological products to molecules produced naturally in humans and/or the high potency or unique species specificity of these agents has been determined to be the important considerations in this regard. As such, it was proposed that an independent safety guideline was needed to provide more relevant guidance for these types of products. As a result of these initial efforts, Safety Topic S6, *Safety Studies for Biotechnological Products*, was finalized and adopted as a tripartite harmonized guideline in July of 1997.

### **Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals**

Since a number of guidance documents were already published in the United States, Europe, and Japan with regard to biotechnology-

derived products and to specific aspects of incorporating safety considerations into the development of testing programs, a tripartite guideline was proposed for this topic to overrule any inconsistencies between the established guideline and any previously existing guidance documents. The finalized guideline addresses the preclinical safety testing requirements for biotechnological products and investigates such diverse topics as, the use of animal models of disease, the determination of when genotoxicity assays and carcinogenicity studies should be performed, and the impact of antibody formation on the duration of toxicology studies.

The guideline provides the basic framework for the design of preclinical programs; however, it is not a list of detailed study protocols and/or standardized study designs which are definitive for safety evaluation purposes. The biotechnology products considered within the guideline, include but are not completely limited to, products which have been derived using expression systems in bacteria, yeast, insect, plant and mammalian cells which are used as *in vivo* diagnostics, therapeutics or prophylactics. In these products the active ingredient may include proteins and peptides, and their derivatives or products of which they are components. Products recently considered "specified biologics" would also be considered under the scope of this document. Although not specifically included, the guideline may also be applicable to other known biological products, such as recombinant DNA protein vaccines, blood plasma extracted factors or endogenous proteins extracted from human tissue.

Biological products which are not specifically considered within this guideline include allergenic extracts, cellular blood components, conventional bacterial or viral vaccines, DNA vaccines or cellular and gene therapies. However, considerable interest has been focused on the harmonization and development of internationally acceptable guidelines for the preclinical safety assessment of these biotechnology products, particularly in the case of DNA vaccines, and cellular and gene therapies. As such, in the future it can be assumed that as discussions continue to be held within the ICH, a review of available databases will likely lead to the development of tripartite guidelines for these additional types of biopharmaceutical products.

As mentioned previously, the ICH guidelines have been developed to provide guidance while allowing more flexibility than what has been experienced in the past, especially with regard to toxicity testing requirements. The key to developing preclinical safety assessment programs for biotechnology-derived pharmaceuticals has been to be dynamic and flexible, employing a case-by-case, science-based approach to the design of product specific testing programs. With an increased level of flexibility, however, there is an associated increase in the risk for the potential misinterpretation of what truly is required.

<b>Status of ICH Safety Topics and Guidelines</b>		
S1A	Guideline on the Need for Carcinogenicity Studies of Pharmaceuticals	Step 5 (Adopted - November 1995)
S1B	Carcinogenicity: Testing for Carcinogenicity of Pharmaceuticals	Step 5 (Adopted - July 1997)
S1C	Dose Selection for Carcinogenicity Studies of Pharmaceuticals	Step 5 (Adopted - October 1994 Addendum (S1C (R)) was adopted in July 1997)
S2A	Genotoxicity: Guidance on Specific Aspects of Regulatory Tests for Pharmaceuticals	Step 5 (Adopted - July 1995)

S2B	Genotoxicity: Battery of Genotoxicity Tests	Step 5 (Adopted - July 1997)
S3A	Toxicokinetics: Guidance on the Assessment of Systemic Exposure in Toxicity Studies	Step 5 (Adopted - October 1994)
S3B	Pharmacokinetics: Guidance for Repeated Dose Tissue Distribution Studies	Step 5 (Adopted - October 1994)
S4	Single and Repeated Dose Toxicity Testing	Step 5 (Adopted - November) 1991
S4A	Repeated dose Toxicity Testing in Non-Rodents	Step 4 (Adopted - September 1998)
S5A	Detection of Toxicity to Reproduction for Medicinal Products	Step 5 (Adopted - June 1993)
S5B	Reproductive Toxicology: Toxicity to Male Fertility	Step 5 (Adopted - November 1995)
S6	Safety Studies for Biotechnological Products	Step 5 (Adopted - July 1997)
S7	Safety Pharmacology Studies	Step 1 (Accepted as a new topic - September 1998)
M3	Timing of Pre-Clinical Studies in Relation to Clinical Trials	Step 5 (Adopted - July 1997)

ICH Home Page: <http://www.ifpma.org/ich1.html>

**UNE CHAIRE EN ANALYSE DE RISQUES TOXICOLOGIQUES À L'UNIVERSITÉ DE MONTRÉAL. Gaétan Carrier**  
**Université de Montréal, Département de médecine du travail et d'hygiène du milieu, Faculté de médecine.**

*Dr. Gaetan Carrier was recently appointed Chairman of the newly created program in Risk Assessment at the University of Montreal. In this article, Dr. Carrier summarises the historical context of this initiative, the goals and objective of the Program, partnerships, and the outlook for the future.*

Le 11 mars dernier, le département de médecine du travail et hygiène du milieu de l'Université de Montréal lançait sa nouvelle chaire en analyse des risques toxicologiques pour la santé humaine. Initiative du directeur du Département, le docteur Claude Viau, cette chaire devrait s'imposer comme le centre de référence en la matière au Québec. En fait, le Département d'accueil de cette chaire est déjà fortement impliqué dans ce domaine depuis plusieurs années. D'ailleurs, sa position au sein du secteur des sciences de la santé publique de la Faculté de médecine lui confère une caractéristique unique le rapprochant *de facto* des milieux d'application des résultats de ses recherches. Des organismes comme le ministère de la Santé et des services sociaux, des directions de santé publiques de Régions régionales, Santé Canada et la Commission de la santé et de la sécurité du travail font régulièrement appel à l'expertise de ses professeurs.

**Motifs ayant favorisé la création de cette chaire**

Les risques à la santé humaine associés à une menace environnementale font maintenant partie des préoccupations courantes de notre société. Les spécialistes de la santé et de l'environnement sont de plus en plus appelés à répondre à des questions concernant ces préoccupations du public. Ils doivent posséder les connaissances et les outils qui leur permettent de documenter et de caractériser ces risques à la santé. Les problèmes posés sont complexes. Ces risques présentent des caractéristiques intrinsèques qui rendent difficile leur mise en évidence et leur quantification. L'essentiel des problèmes à gérer concerne la toxicité chronique provoquée par de faibles expositions, répétées dans le temps. Les risques sont difficiles à objectiver pour des raisons méthodologiques : l'intensité des effets est faible, la caractérisation de l'exposition est délicate, les signes apparaissent après un délai de latence qui peut atteindre plusieurs années pour les maladies comme le cancer ou les atteintes du système nerveux, les maladies ne sont pas spécifiques aux contaminants, elles sont multifactorielles avec une intrication de facteurs endogènes et exogènes. La question qui se pose aux scientifiques est la suivante : les avantages que nous tirons des progrès technologiques, pourraient-ils, au-delà de certaines limites, être contrebalancés par d'insidieux dangers ? Quelle est la limite à ne pas franchir ?

L'incertitude scientifique est véritablement le dénominateur commun à de nombreuses questions de santé environnementale. Cette incertitude nous place dans un dilemme « Agir sans être parfaitement sûr ». Ce qui oblige les gouvernements à proposer des critères de décision en matière de gestion de risques qui, tout en s'appuyant sur les connaissances scientifiques, intègrent des dimensions économiques, politiques et sociales pour fixer des normes ou limites considérées acceptables socialement à une période donnée et dans un pays donné. L'incertitude scientifique, en plus d'être la donnée de base du travail du professionnel en même temps qu'elle en est le premier enjeu, est une contrainte réelle pour nos décideurs, ces derniers ne peuvent l'ignorer. C'est dans ce contexte que cette chaire a été créée dans le but de répondre aux préoccupations qu'expriment tant les professionnels de santé en charge de l'évaluation des risques que les décideurs administratifs ou politiques en charge de la gestion des risques au Québec. La raison d'être de la chaire est l'amélioration des connaissances sur les effets que l'environnement peut avoir sur la santé humaine et la formation de spécialistes en analyse des risques toxicologiques.

## **Partenaires financiers**

Les partenaires financiers dans cette chaire sont : la Société d'électrolyse et de chimie Alcan , Hydro-Québec, Noranda, la Régie régionale de la santé et des services sociaux de Montréal-Centre (Direction de la santé publique) et l'Institut de recherche en santé et en sécurité du travail, le ministère de la Santé et des Services sociaux du Québec (Direction générale de la santé publique) ainsi que le Conseil International sur les métaux et l'environnement. La chaire peut déjà compter sur des engagements totalisant 1 265 000\$.

La vocation de la chaire en analyse des risques toxicologiques à l'Université de Montréal

Par définition, une chaire en analyse des risques à la santé respectera la vocation première d'une université, soit la recherche et l'enseignement. Ces deux entités devront se développer avec le souci de servir la société aux prises avec des problèmes environnementaux reliés à ses activités humaines. Nous résumerions comme suit les objectifs poursuivis à travers les activités de la chaire

## **La recherche**

L'analyse des risques à la santé associés à l'exposition à un agent environnemental nocif étant le processus qui conduit à estimer dans la population exposée, l'incidence ou la probabilité d'altérations de la santé attribuable à cet agent. La recherche doit donc viser à réduire les incertitudes associées à l'évaluation de l'exposition et à l'évaluation de la relation « dose-réponse » pour la population exposée. Dans cette optique, nos recherches porteront sur les aspects suivants :

- Définir quels sont les meilleurs déterminants des agents environnementaux potentiellement nocifs pour l'humain sur l'incidence de problème(s) de santé.
- Améliorer les méthodes d'analyse de l'exposition en développant des bons marqueurs biologiques de l'exposition et des protocoles d'intervention qui augmentent la qualité et la précision de l'estimation de l'exposition d'une population.
- Augmenter la spécificité de la mesure des effets, en développant des marqueurs biologiques d'effets spécifiques à l'agent environnemental à l'étude.
- Développer des modèles toxicocinétiques qui permettent d'estimer, avec une bonne valeur prédictive, la charge corporelle ou la concentration de ces substances aux organes cibles en tout temps et ce pour n'importe quel scénario d'exposition.
- Améliorer les connaissances actuelles sur les mécanismes d'action par lesquels ces agents produisent leurs effets physiologiques et pathologiques et sur la relation « dose - réponse de ses effets » dans l'organisme humain.
- Développer des modèles de « relation dose - réponse » qui s'appuient sur ces connaissances.
- Développer des moyens qui nous permettent de vérifier la validité de modèles proposés pour estimer des risques chroniques, tels le cancer, par les organismes de contrôles de la qualité de l'environnement ou par des chercheurs internationaux.
- Etudier les interactions de plusieurs substances potentiellement nocives présentes au même moment dans l'organisme humain et définir l'influence de ces interactions sur la cinétique et la relation dose-réponse aux organes cibles de ces substances dans notre organisme.

## **L'enseignement**

Former des chercheurs de pointe dans ce domaine. Former de bons analystes (experts) en risques toxicologiques pour l'humain. Développer des programmes d'enseignement pour des clientèles particulières : spécialistes en santé publique, journalistes, etc.

## **Sur le plan social**

Sur ce plan, l'université entend jouer un rôle d'éducateur auprès de la population générale et de publics cibles sur la problématique de l'analyse et de la gestion des risques environnementaux auxquels la population est confrontée. Elle veut créer des lieux d'échanges et de discussions sur divers enjeux de l'analyse et la gestion du risque.

## **Associations et collaborations**

Le titulaire de la chaire a déjà l'assurance de la collaboration des chercheurs du département de médecine du travail et d'hygiène du milieu et de chercheurs d'autres départements et facultés de l'Université de Montréal ainsi que des collaborations avec la direction de la Santé publique de Montréal-Centre et de la Montérégie. Nous chercherons à faire en sorte que la chaire devienne un projet où les intérêts de plusieurs organismes québécois et canadiens convergent pour le bénéfice de tous.

## **WELCOME TO NEW MEMBERS OF STC - Gordon Krip, Executive Director, STC**

We welcome the following new members of STC and wish them well in their careers and lives.

**Regular Category** George C. Becking Ph.D. Phoenix OHC Inc. Kingston; Ugis Bickis Ph.D., Kingston; Jacques Bernier Ph.D.\* ; Michael Brown Ph.D. Northern env. Chem Toronto; Ian Dean Ph.D. Southern res. Inst Birmingham Alabama; Daniel Cyr Ph.D.\*; Denis Girard Ph.D.\*; Edouard Kouassi Ph.D.\*; Flora Raptan Ph.D. Nova Chemicals Calgary; Mohammed Tariq Ph.D. Armed Forces Hospital Riyadh, Saudi Arabia; Glen Van Der Kraak Ph.D. Univ. Guelph; Haiwang Tang Ph.D. Univ. Oklahoma; James Z. Xing Ph.D. Univ Alberta, Edmonton.

**Associate Category** Bernard Cornet Ph.D. Pasteur Mériex Connaught Toronto; Philippe Desaulniers B.Sc.\*; Muhammed Z. Khan Ph.D. Univ Toronto; Terence R.S. Ozolins Ph.D. Wyeth-Ayerst Res Labs Chazy, NY; Pietro Sgro Ph.D. Univ Toronto

**Students Category** Mélanie Audet B.Sc.\*; Craig Bailey B.Sc. (Hons.) Queens Univ; Myriam Binet B.Sc.\* Phillipe Desharnais B.Sc. \*; Régina Escarné B.Sc.\*; Malcolm Gibson B.Sc. (Hons.) Queens Univ; Jeff Naylor B.Sc. Queens Univ; Nhi Nguyen B.Sc. \*; Martin Pelletier B.Sc.\*; Danielle Poirier B.Sc.\*; Rajan Puri B.Sc. (Hons.) Queens Univ; Anik Savoie B.Sc.\*

\*INRS - Institut Armand Frappier, Centre de recherche en santé humaine, Pointe-Claire, Québec

**BOTANICALS AND HERBAL MEDICINES - NOT A ROSE GARDEN - Michael Prior**

A workshop to "*Evaluate research needs on the use and safety of medicinal herbs*" was held in Raleigh, NC, USA, in September, 1998. This was sponsored by several American organizations, including several member agencies of the National Institutes of Health, as well as the Department of Health and Human Services, Food and Drug Administration (FDA), and the Society for the Advancement of Women's Health Research.

At the present time, in the USA, an American manufacturer of botanicals can state that a product can claim to "*promote regularity*" or "*help maintain cardiovascular health*". It cannot state it "*alleviates constipation*" or "*lowers cholesterol*".

About a year ago, the US FDA issued a proposed rule "*Regulations on statements made for dietary supplements concerning the effect of the product on the structure or function of the body*". Under this proposal, any dietary supplement that expressly or implicitly claims to diagnose, treat, prevent or cure a disease means that the product will be regarded as a drug, and have to meet the safety and effectiveness standards for drugs under the US Food, Drug and Cosmetic Act. What is "*disease*"? The US FDA proposes the following definition:

*"Any deviation from, impairment of, or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of one or more signs or symptoms. For purposes of this definition, 'signs and symptoms' include laboratory or clinical measurements that are characteristic of a disease, such as elevated cholesterol fraction, uric acid, blood sugar, and glycosylated hemoglobin, and characteristic signs of disease, such as elevated blood pressure or intraocular pressure."*

The American Botanical Council is concerned that this will push botanicals under more stringent FDA oversight; whilst the American Medical Association supports the definition and would like to expand it to include states of health leading to deviation, impairment, or interruption.

There were many questions. What is the information base upon which these are made, and can these be substantiated? What is meant by "good manufacturing practices"? Can there be standards for something for which there is no current and generally available analytical methodology? Do we need safety standards for products that have been around and used for hundreds if not thousands of years? Can we use the German research on botanicals?

## **CANADIAN INSTITUTES OF HEALTH RESEARCH**

*This is a copy of the letter signed by Dr. Len Lillie, President of the STC, on behalf of the STC Board, and sent to Dr. Henry Friesen of the Medical Research Council of Canada*

Dear Dr. Friesen:

As outlined in my letter of February 28, 1999, the Board of Directors of the Society of Toxicology of Canada would like to confirm our continuing interest in the development of the Canadian Institutes of Health Research (CIHR) and in our participation in its implementation.

### **Background Information**

The Society of Toxicology of Canada/La Société de Toxicologie du Canada (STC), founded in 1964, is the scientific and professional organization of toxicologists in Canada. STC is a member of the Canadian Federation of Biological Societies (CFBS) and the International Union of Toxicology (IUTOX). STC currently has approximately 350 members working in universities, federal and provincial governments, and industry in every province of Canada and in the Northwest Territories. STC members are also located in 17 U.S. states and 9 other foreign countries. The Society held its 31<sup>st</sup> Annual Scientific Symposium, *Advances in the Scientific Basis of Safety and Risk Assessment/Progrès Récents en Matière D'Evaluation du Risque et de L'Innocuité*, December 3 and 4, 1998 in Montreal.

Toxicology is the study of the adverse effects of chemicals on living organisms. The role of toxicologists is to identify and describe the potentially harmful effects of naturally occurring and man-made chemicals, physical agents, and energy, to investigate the mechanisms by which harmful effects may occur, and to determine the relative risks of these agents to man, animals, plants, and the environment. Toxicologists in Canada work in many different milieu including clinical medicine, pharmacology, pathology, occupational health, veterinary medicine, forensic sciences, regulatory toxicology, chemistry, environmental sciences, wildlife and aquatic biology, agriculture, and others. Our interests encompass numerous areas in the biomedical sciences based on effects on potential target organs such as the nervous system, lung, kidney, liver and reproductive organs; specific toxic agents such as lead, asbestos, persistent organic chemicals, or mycotoxins; or components of the human and animal environment such as air and water pollution, occupational and industrial contaminants and forensic toxicology.

Canada's toxicologists serve in a wide variety of sectors such as basic and applied biomedical research and teaching, pharmaceutical discovery and development, environmental toxicology, occupational health and safety and regulatory toxicology. STC members are consistent recipients of Medical Research Council (MRC) grants and serve as members and chairs of grant selection committees. STC members are also recipients of grants from other major funding agencies such as the Natural Sciences and Engineering Research Council of Canada (NSERC), the Canadian Network of Toxicology Centres (CNTC), and various health charities. STC members include many recipients of significant international awards recognizing excellence in research.

### **The CIHR Concept**

CIHR represents a significant new concept in the organization and funding of biomedical research in Canada. STC would like to commend the Task Force for its efforts in the conception and promotion of this initiative and, in particular, the comprehensive, flexible, and inclusive nature of the concept.

Intrinsic to the CIHR proposal is the establishment of ten to fifteen Institutes, each encompassing four principle divisions of basic and applied health research. Lists of possible Institutes are given on the CIHR website and in the document "*A New Approach to Health Research for the 21<sup>st</sup> Century*". While the lists of proposed Institutes are not complete nor the suggested intra-Institute mix of diseases and research topics fixed, the titles, nature, and orientation of the Institutes which are ultimately decided upon will affect the direction of biomedical and related research in this country for many years to come.

## **STC's Position**

### *Emphasis on Clinical Disease Categories:*

As representatives of basic and applied scientists in an intrinsically multidisciplinary biomedical science, we note and would like to express our concern with the very strong orientation of the proposed list of Institutes towards major categories of specific clinical diseases. Much of our work in toxicology concerns the broad spectrum of effects exerted by a particular molecule, rather than a particular disease model. Therefore, although some toxicological research can be classified into categories based on specific diseases or target organs, many research projects cannot.

Examples of research that are difficult to classify according to specific disease conditions or organ systems include: 1) disposition of toxicants throughout the body (toxicokinetics); 2) studies of the mechanism of toxicity of chemicals that affect multiple target organs (such as carcinogens and developmental toxicants); 3) molecular mechanisms of toxicity of specific toxic agents at the cellular and subcellular level (e.g., pesticides or metals), and 4) assessment of risk to the population of exposure to specific agents and mixtures.

Another way to look at human health and disease is as an interaction among individual susceptibility (genetics), age and environmental factors (e.g., toxic agents). Toxicology, through multidisciplinary approaches, seeks to decrease human illness and dysfunction from environmental and occupational chemicals by understanding their interrelationships with age and genetics.

### *Institute of Drug Research:*

We support the concept of an Institute of Drug Research as suggested by the Association of the Deans of Pharmacy of Canada. In addition to research involving drug discovery and development, we suggest that the mandate of this proposed Institute should be expanded to include drug and chemical safety and should encompass all research on biologically active chemicals, including those not considered "drugs" in the therapeutic sense. For example, environmental contaminants would be an important group of disease causing agents to be included in one of the institutes.

### *Institute of Public and Population Health:*

The proposed Institute of Public and Population Health includes a number of very important areas. We support strongly research in areas such as addiction, food safety, and comparative medicine and animal health. Epidemiology, nutrition and preventative medicine would also fit well within this Institute. However, this proposal should not become a kind of catch-all category for anything that does not fit within a specific disease grouping.

We believe a very strong case can be made for a separate Institute of Environmental Health. Both environmental and occupational diseases have become increasingly important issues of public concern, affect the majority of Canada's population in one way or another, and do not easily fit within a specific organ system based disease category. In the U.S. these concerns have resulted in the establishment of the National Institute of Environmental Health Sciences (NIEHC) and we believe a similar emphasis is warranted in Canada

### **The Need for a National Toxicological Perspective**

Because of the downsizing of the role of active researchers in Health Canada, many of whom have been involved in food safety and drug evaluation, we believe that it is imperative that a strong toxicological component be included as part of at least one of the Institutes. This would establish a base to link toxicologists across the country and become an essential national resource for the food and pharmaceutical industries, and for governmental regulatory agencies. We believe that with an MRC oriented toxicology network focusing on human health via the CIHR vehicle, the goal of synergistic, interdisciplinary research would be achieved. Furthermore, we believe that such an approach would elicit considerable interest from potential industrial partners. Finally, we believe that the increasingly global nature of industrial and regulatory toxicology demands a strong national presence so that Canada can continue to have a seat at this important international table.

### **Issues of Governance**

A key element in the proposed governance structure for CIHR is the setting of priorities at the level of both the Governing Council and the Institute Advisory Boards. The funding of Canadian science may now be "managed" to a far greater extent than ever before. It has been indicated that each Institute would encompass four principle divisions of health research, i.e., Basic Biomedical, Applied Clinical, Health Services and Health Systems, and Society, Culture and the Health of Populations. STC stresses the importance of establishing an appropriate balance between the funding of basic and applied research. The focus of the proposed Institutes on clinical disease and pressures to assess productivity on immediate applicability must be balanced with the requirement that a significant proportion of government funds continue to support investigator directed basic research, which has been shown, time and again, to provide the basis for discoveries that impact directly on human health in a nonpredictable manner.

### **STC Participation**

Implementation of CIHR will require a significant contribution from the biomedical community at large, including members of Canadian scientific societies such as STC. STC, directly or in cooperation with other major Canadian scientific organizations such as CFBS, is prepared to nominate worthy individuals from among its members to participate in the work of developing the Institutes and the policies

and procedures which will be needed to make them function. We would appreciate being kept informed of the development of the CIHR and of the need for participation by members of the Canadian biomedical community.

## **Summary**

The Society of Toxicology of Canada supports the concept of the Canadian Institutes of Health and, in particular, the comprehensive, flexible and inclusive nature of the concept.

We would like to express our concern with what we believe to be the excessively strong orientation of the proposed Institutes towards categories of clinical disease, an orientation which may well be in conflict with the objectives of comprehensiveness and inclusivity. We expect that this concern will be shared by other disciplines encompassing basic and applied biomedical sciences.

We believe that it is essential to maintain a balance between centrally managed research programs and individual investigator directed research.

We support the formation of an Institute for Drug Research. We also believe there is considerable merit in an Institute encompassing environmental and occupational health.

We believe that a strong toxicological presence is an essential component of at least one of the Institutes.

We wish to contribute to the further development of the CIHR concept through the nomination of worthy individuals to participate in the implementation of CIHR and its constituent Institutes.

We look forward to continued participation in CIHR and to developing the best possible format for toxicological research in Canada.

Yours sincerely,

Leonard E. Lillie, DVM, PhD

*for* The Board of Directors

The Society of Toxicology of Canada

*Ed. Note: For sources of new information on the governance of CIHR, go to the websites of MRC <[www.mrc.gc.ca](http://www.mrc.gc.ca)> and CIHR <[www.cihr.org](http://www.cihr.org)>.*

**FROM THE DESK OF THE PRESIDENT - Len Lillie, Parke Davis Research Institute, Mississauga, Ontario, and President of STC,**

Today in southern Ontario is as nice an early summer's day as any of us have any right to expect and tomorrow is the first long weekend of the summer. The urge to take the afternoon off is almost (emphasis on almost) overwhelming. Our senses here are being assailed on all sides by pre-election hype (the election here is June 3<sup>rd</sup>). I have just returned from a long delayed March break to (among other places) Savannah, Georgia piqued by curiosity about the minor phenomenon which is Midnight in the Garden of Good and Evil or "the Book" as it is referred to there. It even includes a little toxicology as one of the minor characters claims to have possession of a vial of sodium flouroacetate which locals fear he will dump into the water supply if he has a bad day. An interesting diversion and a good read (and movie) if you have not seen it.

The Board met March 27<sup>th</sup> in Montreal. A major item on the agenda was consideration of the Canadian Institutes of Health (CIHR) initiative. As I mentioned in the last issue of News/Nouvelles, we sent an initial letter (a sensitizing dose?) to Dr. Henry Friesen the chair of the CIHR Task Force in February. Quite a bit of effort has since been invested in developing a more detailed STC position on the CIHR initiative. This was sent to Dr. Friesen in early May. A copy of the text is included with this Newsletter. Thanks especially to Heather Durham and Gail Bellward for the work on this important issue.

We are also trying to interest other groups in this issue as STC by itself is a relatively small (if eloquent) voice in the Canadian medical research universe. The Board would welcome your thoughts on this issue. If you want to know more about CIHR, consult their website at <http://www.cihr.org>.

The Board also reviewed plans for the 1999 Scientific Symposium which is scheduled for December 2, 3, 1999 in Montreal. The details are provided elsewhere but the concensus is that this will be an excellent program with an end-of -millenium retrospective on the development of toxicology in Canada and an in depth and very forward looking focus on genomics, proteomics and related technologies as they apply to toxicology. Thanks to David Riddick and the Scientific Program Committee.

The ICT XI pot continues to simmer quietly . Gaston Chevalier, Doug Arnold and the Bid Committee are busy with the necessary background work. I am happy to be able to confirm that I have received written confirmation that NRC will back our bid for ICT XI and verbal confirmation of participation by the Palais des Congrès de Montréal. I look forward to working again with Laurier Forget and Alain Carboneau on this project. Sometime around the middle of this year, we will send a letter to the IUTOX Executive confirming our intent to submit a bid for ICT XI. The work of the Bid Committee will intensify progressively as we move into the year 2000.

The Board is continuing with the work of reviewing and revising the STC committee structure. New Terms of Reference were accepted for an integrated Awards Committee. Gail Bellward and Suzanne Desjardin will form the nucleus of this committee and two non-Board members will be added. The membership Committee has also been restructured. Malle Jurima-Romet has agreed to Chair this committee and several additional members will be added in the near future.

Congratulations to Sheldon Roth on his re-appointment as Head of the Division of Toxicology in the Department of Pharmacology and Therapeutics at the University of Calgary. Sheldon is a former Board member and is currently Chair of the Education Committee and editor of the STC slide set on Principles of Toxicology.

Some of you may be wondering about the status and/or fate of the Canadian Federation of Biological Societies. STC has traditionally been a strong supporter of CFBS. CFBS which has certainly been struggling in the last few years, has been pretty quiet since the departure of previous Executive Director Paul Hough. Paul had done an excellent job representing the Canadian biological/biomedical community until taking the position of Vice-president of BIOTEC Canada in September of last year. We have received news that Dr. Bruce Sells, Professor Emeritus (biochemistry) of the University of Guelph has accepted the position of Executive Director of CFBS. We look forward to working with Bruce. Heather Durham will be representing STC at the CFBS meeting in Winnipeg in early June and will be able to provide us with an update on the status of CFBS at that time.

Elsewhere in this newsletter you will find information soliciting nominations for STC awards and notice of Board positions coming open for election this year. The Board has made a special effort to get this information out to members very early this year so that you have plenty of time to consider nominations/applications.

Have a great summer .

## **JOB OPPORTUNITY: ACADEMIA**

## **TOXICOGENOMIC POSITIONS**

Post Doctoral/Research Associate and Graduate Student positions are available to investigate the effect of gestational and lactational exposure to estrogenic chemicals (i.e. estrogenic endocrine disruptors) on testicular gene expression and spermatogenesis in mice. This multi-disciplinary project will test the hypothesis that exposure to endocrine disruptors during development compromises male fertility as a result of alterations in testicular gene expression profiles. This position will provide an opportunity to acquire experience in a wide variety of areas including animal handling, sperm assessment, in vitro fertilization, in situ hybridization, cDNA array technology, bioinformatics and the statistical analysis of gene expression data. Further information regarding research activities in the laboratory are available at [www.bch.msu.edu/~zacharet/tzlab.htm](http://www.bch.msu.edu/~zacharet/tzlab.htm).

This is a multifaceted position that will require a highly motivated and well organized individual with excellent written and oral communication skills. Knowledge of molecular biology and/or biochemistry is essential. Experience with animal handling, statistical analysis, genomics, bioinformatics and database management is highly desirable. Competitive salary, including benefits, will be based on training and experience.

Michigan State University (MSU) is located in East Lansing, Michigan approximately 2 hours drive west from either Windsor or Port Huron. MSU is a land grant university with an enrollment of approximately 42,000 students in a greater community of approximately 300,000. The positions will be within the Department of Biochemistry and the recently completed National Food Safety & Toxicology Center. Both provide excellent research facilities and a dynamic training environment.

Interested individuals are requested to submit a cover letter outlining their research experience and career aspirations, a curriculum vitae and copies of relevant reprints to:

Tim Zacharewski, Ph.D.

Michigan State University

Department of Biochemistry

419 Biochemistry Building

Wilson Road

East Lansing, Michigan 48824-1319

USA

Office Tel: (517) 355-1607

Lab Tel: (517) 353-1944

Departmental Fax: (517) 353-9334

e-mail: [tzachare@pilot.msu.edu](mailto:tzachare@pilot.msu.edu)

## **DAILY EXERCISES FOR THE NONATHLETIC - Michael Prior**

### **Exercise Calories burned off**

Beating around the bush 75

Jumping to conclusions 100

Passing the buck 25

Making mountains out of molehills 500

Bending over backwards 75

Jumping on the bandwagon 200

Running around in circles 350

Opening a can of worms 50

## **CONFERENCES, MEETINGS AND WORKSHOPS**

### **1999**

July 4-10 7<sup>th</sup> International Neurotoxicology Association Meeting, University of Leicester, UK. Contact: Dr David Ray, MRC Toxicology Unit, Hodgkin Building, Lancaster Road, Leicester LE1 9HN

July 14 - 16 Scientific Meeting on Biomarkers in Environmental Toxicology. Christchurch, New Zealand. Contact: Dr. David Ray, MRC Toxicology Unit, Hodgkin Building, Lancaster Road, Leicester LE1 9HN, UK. E-mail: der2@le.ac.uk

August 22-26 7<sup>th</sup> European ISSX Meeting, Budapest, Hungary. Contact: ISSX Office, PO Box 3, Cabin John, MD 20818, USA. Fax: 301-983-5357.

Sept 14 - 16 British Toxicology Society, Congress. University of Oxford, UK. Contact: Secretary, Mr. AB Wilson, Inveresk Research

International Trament EH33 2NE, Scotland. Tel: 1875-614-545; Fax: 1875-614-555; E-mail: sandy.wilson@iri.iri.bex400.co.uk

Sept 28-Oct 5 1999 North American Congress of Clinical Toxicology. La Jolla, CA, USA. Contact: Registrar, Contemporary Forums, 11900 Silvergate Drive, Dublin CA 94568-2257, USA

Oct 10 - 13 7<sup>th</sup> International Symposium on Particle Toxicology, Maastricht, The Netherlands. Contact: Conference Agency Limburg, P.O. Box 1402, 6201 BK Maastricht, The Netherlands. Tel: +31-(0)43-361-91-92 Fax: +31-(0)43-361-90-20 e-mail: cal.conferenceagency@pi.net

Oct 17 - 20 17<sup>th</sup> International Neurotoxicology Conference, Little Rock, Arkansas, USA. Contact: Prof. Joan Cranmer, Department of Pediatrics, University of Arkansas for Medical Sciences, 1120 Marshall Rm. 302, Little Rock, AR 72202, USA. Tel: 501-320-2986; Fax: 501-320-4978; e-mail: CranmerJoanM@exchange.uama.edu

Oct 24-28 9<sup>th</sup> North American ISSX Meeting, Nashville, Tennessee, USA. Contact: ISSX/ACT-DCT Meeting, PO Box 3, Cabin John, MD 20818, USA. Fax: (301) 983-5357; Web site: <http://www.louisville.edu/medschool/biochemistry/ISSX-ACS>

Nov 6-10 4<sup>th</sup> Congress of Toxicology in Developing Countries, 4<sup>th</sup> CTOX-DC, Antalya, Turkey. Contact: Prof. Dr. Semra ardas, (4<sup>th</sup> CTOX-DC), Gazi University-Faculty of Pharmacy Toxicology Department (Eczacilik) Hipidrom 06330 Ankara, Turkey

Nov 14-18 SETAC 20<sup>th</sup> Annual Meeting, Sustaining Global Environmental Integrity. Philadelphia, PA, USA. Contact: SETAC, 1010 North 12<sup>th</sup> Avenue, Pensacola, FL 32501-3367, USA; Tel: 850-469-1500; Fax: 850-469-9778; E-mail: setac@setac.org

December Thirty-Second Annual Symposium, Society of Toxicology of Canada, Montréal, Québec. Contact: Society of Toxicology of Canada, P.O. Box 517, Beaconsfield, Québec H9W 5V1. Tel: 514-428-2676, Fax: 514-428-4946

## **2000**

March 13-16 Society of Toxicology Annual Meeting, Philadelphia, Pennsylvania. For information or registration, contact: SOT HQ, Tel: 703-438-3115 or Fax: 703-438-3113

June 24-28 15<sup>th</sup> International Symposium of the Society of Toxicologic Pathologists. Reproductive Biology/Endocrine Disrupters. Phoenix, Arizona, USA. Contact: STP Registration, 19 Mantua Road, Mt. Royal, New Jersey 08061, USA

July 15 - 20 CPT 2000. VII World Conference on Clinical Pharmacology and Therapeutics. Florence, Italy. Contact: CMO S.r.l. - Conventions Meetings Organizations, Via San Donato 22, 51027 Florence, Italy.

Sept 17-20 38<sup>th</sup> Congress of the European Societies of Toxicology. Eurotox 2000. Contact: Alan Boobis, Imperial College, London W12 0NN, England. Tel: 44 181 383 3221; Fax 44 181 383 2066; e-mail [aboobis@rpms.ac.uk](mailto:aboobis@rpms.ac.uk)

## **2001**

March 25-29 Annual Meeting of The Society of Toxicology. San Francisco USA. Contact: SOT, 1767 Business Centre Drive, Suite 302, Reston, Virginia 22090-5332, USA

June 24-28 20<sup>th</sup> International Symposium of the Society of Toxicologic Pathologists. Orlando, Florida USA. Contact: STP Registration, 19 Mantua Road, Mt. Royal, New Jersey 08061, USA

July 8 - 13 Ninth International Congress of Toxicology, ICT-IX, Brisbane, Australia. Contact: Congress Secretariat, Intermedia Convention and Event Management, 11/97 Castlemaine Street, P.O. Box 1280, Milton, QLD 4064 Australia. Tel: +61-0-7-3369-0477; Fax: +61-0-7-3369-1512; E-mail: [ictix2001@im.com.au](mailto:ictix2001@im.com.au) Web site: <http://www.uq.edu.au/ICT9>

## **2004**

July Tenth International Congress of Toxicology, ICT-X, Tampere, Finland.