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Chaldhorn Research Institute

INTERNATIONAL CENTRE FOR ENVIRONMENTAL AND INDUSTRIAL TOXICOLOGY (ICEIT)

CRI's ICEIT has been designated as a "UNEP Centre of Excellence for Environmental and Industrial Toxicology".

THE THIRD PRINCESS CHULABHORN SCIENCE CONGRESS

The International Congress on Water and Development: Water is Life

December 11-15, 1995 Bangkok, Thailand



To mark the most auspicious occasion of the commemoration of the Fiftieth Anniversary (Golden Jubilee) of His Majesty King Bhumibol Adulyadej of Thailand's accession to the throne, the Chulabhorn Research Institute organized this international congress on the theme "Water and Development: Water is Life" since His Majesty has long promoted the importance of the sustainable development of water resources.

The Congress provided a forum for scholars, researchers, engineers, and decision makers from around the world to discuss and exchange knowledge on all aspects of water resource development

and utilization. Specialist areas in the Congress program included science and technology, economics, law, health; and the environmental, social and political sciences, in relation to their contribution to the sustainable development of water resources.

The opening ceremony of the Congress was graced with the presence of His Majesty King Bhumibol Adulyadej, Her Majesty Queen Sirikit, Her Royal Highness Princess Sirindhorn and Her Royal Highness Princess Chulabhorn who, as Chairman of the Organizing Committee, gave the address of welcome.

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THE THIRD PRINCESS CHULABHORN SCIENCE CONGRESS

(Continued from page 1)

In the keynote lecture delivered at the opening ceremony, UN Assistant Secretary General, Dr. Nay Htun paid tribute to the innovative projects undertaken by His Majesty King Bhumibol of Thailand to improve the management and utilization of water.

Dr. Nay Htun's address, entitled "Water: Past, Present and Future", emphasized the multi-faceted and all embracing role of water in every aspect of development, giving as examples of the critical role of water, the provision of food, livelihoods, energy, transportation and recreational opportunities, improving health, sanitation and the quality of life; modulating nutrient flows in the biosphere and geochemical cycles; influencing the hydrosphere, climate and weather systems.

Dr. Nay Htun concluded that water, historically, currently, and in the future, will continue to play a pivotal role in all aspects of human life and endeavours. With decisive actions









now, to protect, prudently manage and use water, this life giving and supporting resource will continue to provide all the benefits expected for present and future generations.

The ninety five plenary, symposium and free communication sessions that constituted the Congress program were divided into six main technical sessions: Water and Health; Integrated Management of River Basins; Engineering and Scientific Aspects of Management; Economic, Social and Cultural Aspects; Legal and Institutional Aspects; and Environmental Aspects.

At the end of the Congress the chairman of each technical session produced a synopsis of the main deliberations that took place during the program of presentations and discussions.

The Princess Chulabhorn _ Gold Medal Award _

The Third Princess Chulabhorn Science Congress was the occasion for the presentation of this year's prestigious Gold Medal Award to three internationally renowned scientists and academics who have given outstanding support to the activities of the Chulabhorn Research Institute.

This year the awardees were Dr. Nay Htun, UN Assistant Secretary-General; Dr. Frederick Becker, Vice President for Research at the University of Texas M.D. Anderson Cancer Center, Houston, U.S.A.; and Dr. Ronald Shank, Professor of Toxicology, University of California, Irvine, U.S.A. The presentations were made by Her Royal Highness Princess Chulabhorn in a special ceremony on 15 December 1995 prior to the closing of the Third Princess Chulabhorn Science Congress.

The Princess Chulabhorn Gold Medal Award honors and acclaims persons or organizations of world renown who have made significant contributions to the success of the academic achievement of the Institute.

The 1995 Awardees:-

Dr. Nay Htun



For the last 28 years, Dr. Nay Htun has been closely involved with international development and environmental issues not only in helping to create policies and strategies but also at the level of technical implementation. After heading the industrial, commercial and retail business department at Exxon Thailand from 1968 to 1978, he served as Associate Chairman and Professor of Environmental Engineering at the Asian Institute of Technology. His experience in these positions became the foundation upon which, beginning in 1978, he began his long association with the United Nations, helping to establish the Industry and Environment Office in Paris, France, for the review of policies, strategies and technologies needed for the environmentally sound management of major industrial sectors. From 1983 to 1990 he served in Bangkok as UNEP Regional Director and Representative for Asia and the Pacific, and in 1994 he accepted the post of UNDP Assistant Administrator and Regional Director in the bureau for Asia and the Pacific and serves with the prestigious rank of UN Assistant Secretary-General. From May 1990 to August 1992 he was seconded to the Secretariat of the United Nations Conference on Environment and Development (UNCED) in Geneva, Switzerland, where he served as Director of Programme and as a special advisor in organizing the Earth Summit. His commitment to assisting in maintaining the health of the environment as part of sustainable growth and development is emphasized by his presence on the board of non-profit organizations including the Advisory Committee on the Environment, at the International Council of Scientific Unions in Paris, France, the Dow Chemicals Advisory Council on the Environment, the World Business Council for Sustainable Development in Geneva, and the Chulabhorn Research Institute.

Dr. Nay Htun's contributions to the Chulabhorn Research Institute have been of immeasurable importance. He has enthusiastically served on the International Advisory Board of the Institute from the time of its formation. His background and experience provide him with a sensitive understanding of the problems of protecting the environment while, at the same time, encouraging sustainable development. His expertise, advice and wisdom in this regard have helped the Institute to identify goals that are attuned to the special needs of the region.

Dr. Frederick Becker



Since he was appointed Scientific Director of the University of Texas M.D. Anderson Cancer Center in 1988, Dr. Frederick Becker, through his vision and leadership has been responsible for establishing the reputation of this institution as one of the foremost cancer research centers in the world. In addition to his administrative achievements. Dr. Becker's research contributions have also been remarkable. His pioneering insights into the nature of heterogeneity in cellular responses to carcinogens, the expression of alpha-fetoprotein, the hypomethylation of nuclear DNA in the premalignant state, and the effects of carcinogenic adducts and photodimers have helped shape subsequent research around the world. He is author of more than 200 research papers and his 6volume work "Cancer: a Comprehensive Treatise" is not only a vital source in the field but has served as the model for subsequent cancer literature.

Dr. Becker has been a member of the International Advisory Board of the Chulabhorn Research Institute since 1987 and has initiated on behalf of the Institute contacts with eminent scientists abroad and has made important contributions to the Institute's research, helping through his advice and support in the priority area of chemical carcinogenesis. In keeping with his philosophy of maintaining a balance between basic and applied research, Dr. Becker has encouraged and supported collaborations with M.D. Anderson Cancer Center that have made cutting-edge technologies of high potential benefit available to the Chulabhorn Research Institute.

Dr. Ronald Shank



Professor Ronald C. Shank is currently Director of the Environmental Toxicology Graduate Training Program at the Department of Community and Environmental Medicine, University of California at Irvine, where he also has the chair in Toxicology. He is an internationally renowned toxicologist whose work has had an important influence on scientists both in the United States and throughout the world.

His influential activities on numerous task forces, study groups and committees, including the United States Environmental Protection Agency and the National Academy of Sciences, and his many international engagements, demonstrate his energetic commitment to creating and implementing solutions for environmental toxicological problems around the world.

His interests include the biochemical mechanisms of toxicology, the metabolic activation of toxicants, the interaction of cytotoxic agents with DNA, and chemical carcinogenesis. His studies on aflatoxin and nitrosamine liver toxicity have helped create a widespread awareness of the consequences of these environmental toxins in Thailand as well as abroad. More recently his focus has been on the mechanisms of liver toxicity and carcinogenesis and this research has established the important role that alterations in the methylation state of DNA play in these processes. Dr. Shank's outstanding body of research work, which encompasses more than 50 published articles and 22 book chapters, embodies the ideals of environmental toxicology, starting with the identification of toxins in the field and then reaching an understanding of their mechanisms of action.

Reinforcing his long-standing support for environmental toxicology in Thailand, Dr. Shank joined the International Advisory Board of the Chulabhorn Research Institute at its inception in 1987. Since then, his efforts on the Institute's behalf have been tireless and of inestimable importance. From the very beginning, he has shared the Institute's vision for a far-reaching Environmental and Industrial Toxicological Program and has used his wide experience to help forge a realizable design.

CRI/ICEIT Newsletter

TRAINING COURSES ON APPLICATIONS OF NMR SPECTROSCOPY AND MASS SPECTROMETRY TO ORGANIC CHEMISTRY AND DETERMINATION OF ENVIRONMENTAL POLLUTANTS

From 27 November to 1 December 1995, the Chulabhorn Research Institute with the support or Deutsche Gesellschaft fuer Technische Zusammenarbeit (GTZ) under the Institute's program "Application of Science and Technology to Improve the Quality of Life" organized concurrently a training course on NMR Spectroscopy and Mass Spectrometry, and a training course on Determination of Environmental Pollutants.

100 Participants were accepted tor the course on Applications on NMR Spectroscopy and Mass Spectrometry to Organic Chemistry, and 45 on the course on Determination of Environmental Pollutants.

The Faculty members for the two courses were Professor H. Budzikiewicz, University of Koln; Dr. H.M. Helbich, University of Heidelberg; Dr. J. Nair, German Cancer Research Institute; Dr. G. Schilling, University of Heidelberg; Professor G. Spiteller, University of Bayreuth; and Dr. B. Spiegelhalder, German Cancer Research Institute.

In the part of the program devoted to applications of NMR spectroscopy and mass spectrometry to organic chemistry, Professor Budzikiewicz gave sessions on CImass spectrometry and its applications, FAB and spray techniques and LC-MS coupling; Dr. Nair gave an introduction to high performance liquid chromatography (HPLC); Dr. Schilling presented sessions on NMR spectroscopy both 1-D and 2-D techniques and their practical applications, as well as an introduction to advanced NMR spectroscopy; and Professor Spiteller gave presentations on EImass spectrometry and GC-MS cou-

The second part of the program focused on the determination of environmental pollutants. In this course, Dr. Nair gave an introduction to ³²P-postlabelling and its applications in separation of nucleotides in ³²P-postlabelling assay and in experiments using B (a) P adducted DNA; Dr. Helbich gave sessions on detection of polychlorinated biphenyls in the environment and in human samples by





GC-ECD or GC-MS, and also an analysis of PCB in fish, soil and waste water; Professor Spiteller dealt with biomedical application of MS; and Dr. Spiegelhalder presented a session on detection of environmental organic nitro compound using new analytical techniques, using Bangkok air samples for analysis.

The main emphasis of the training was on the various techniques used in NMR Spectroscopy and Mass Spectrometry for the determination of structures in organic chemistry and the application of Mass Spectrometry in the biomedical fields including high performance liquid chromotography.

Regional Workshop on Risk Assessment and Risk Management in Biotechnology

September 30 – October 4, 1996 Bangkok, Thailand

The workshop is organized to provide a background on risk assessment and management processes in biotechnology for those engaged in research and development or involved in regulatory agencies.

The program covers fundamental principles of risk assessment and risk management for GMO's as well as general background on biosafety issues such as development, commercialization and trade implications.

Topics and activities:

- Overview of trends in biotechnology
- Principles and methods of risk assessment and risk management for GMO's with illustration of key principles as applied to one case from initial development to marketing
- Key issues in risk assessment and risk management
 - Gene flow
 - Monitoring
 - Problem genes
 - Food safety
 - Wastes and discharges
 - Pharmaceuticals from transgenic plants and animals
 - Problems of controlling research and development
 - Labellina
- Effect of public perception on development and marketing
- Creating the right regulatory climate at the national, regional and international level
- Case studies: a number of case studies from the United States, the European Union and from the Southeast Asian region will be presented and examined by working groups of participants and resource persons
- Visit to a field trial of transgenic tomato, outside Bangkok

RESOURCE PERSONS

Course Coordinator: M. Ruchirawat

S. Attathom, Plant Genetic Engineering Unit, Kasetsart University, Thailand.

J.E. Bcringer, School of Biological Sciences,

University of Bristol, U.K.

V.L. Giddinge, Biotechnology, Biologies & Environmental Protection (BBEP).

United States Department of Agri-

culture, USA.

H.K. Marquard, Biotechnology Unit, Chemicals and Biotechnology Division, De-

partment of the Environment, U.K.

S. Mongkolsuk, Head of Laboratory of Biotechnology, Chulabhorn Research Institute, Thailand.

M. Schectmann, United States Department of Agriculture, USA.

COURSE FEE

- 1) Registration fee and accommodation:
 - sharing a double room US\$468 (including breakfast)
 - single room US\$580 (including breakfast)
- 2) Registration fee only US\$300

For further information, please contact:

CHULABHORN RESEARCH INSTITUTE
Office of Scientific Affairs
Vipavadee Rangsit Highway
Bangkok 10210, Thailand
Tel: (66-2) 247-1900, 247-5757
Fax: (66-2) 247-1222, 574-0616

CRI/ICEIT NEWSLETTER

The Safe Use Project:

Raising Awareness in the Thai Agrochemical Industry

The agrochemical industry world-wide plays a vital role in protecting food supplies and, for the foreseeable future, agrochemicals will play a major role in protecting crops and ensuring sustainable yields. However, a lack of awareness and understanding of the safe and effective handling and use of agrochemicals can lead to overusage, and contamination of soil, water-courses and crops, presenting a serious hazard to human and animal life, and to the environment.

The high level of agrochemical use in many countries today presents both short and long term risks to farmers and to the quality of human and animal feeds. Poor understanding among farmers of how best to protect themselves and their crops contributes to the seriousness of the situation.

agrochemical The industry. through its global representative, the International Group of National Associations of Manufacturers of Agrochemicals (GIFAP), in 1989 recognized that it must play a more active role in raising safety standards in production. distribution and use of agrochemicals. Accordingly, in 1991 three 3 year pilot projects were started (in Kenya, Guatemala, and Thailand) at a cost of US\$4 million. The objectives of these Safe Use Projects were to draw attention to the need for joint action between the public and private sector, to demonstrate progress, and to draw up a model for the future.

In Thailand, the Safe Use Project was implemented through the Thai Pesticide Association (TPA), in cooperation with the Royal Thai government.

Launched on 30 October 1991, Thailand's Safe Use Project had as its specific objectives:

- To reduce the incidence of pesticide-related casualties.
- Raise awareness of safe handling, storage and use of pesticides within the industry, medical profession and farming communities.
- Assist government and non-government agencies with resources, expertise and training.

- Improve compliance with the FAO International Code of Conduct on the Distribution & Use of Pesticides, and with national law.
- 5. Protect the environment.

Among the key activities undertaken under the project were:

- Training of trainers, retailers and farmers.
- 2. Schools education.
- 3. Medical programme.
- Implementation of industry standards.
- 5. Model farm concept.
- 6. Safe use awareness campaign.

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A STUDY OF CHLORDANE EXPOSURE

Chlordane is a chlorinated cyclodiene pesticide introduced in 1948 and used extensively as a termiticide until 1988 when it was banned in the United States for most uses. It is considered to act as a toxicant with many of the signs and symptoms of poisoning produced by DDT. One striking difference, however, is the ability of chlordane and other chlorinated cyclodienes to induce convulsions. Other frequent findings are headaches, nausea, vomiting, dizziness and chronic, jerking movements.

It is thought that the cyclodiene interacts with the picrotoxin receptor in the nervous system, releasing excitatory transmitters and interfering with the y-aminobutyric acid neurotransmission system. The primary target appears to be synapses with the highest number of converging presynaptic elements, so that the threshold for excitation is lowered and increases the number and frequency of action potentials. This is a process that potentiates through the nervous system via postsynaptic pathways, producing responses 10 to 100 times more intense than normal. Researchers from the Environmental Sciences Laboratory, University of Southern California School of Medicine, have now published the findings of an epidemiological study of 216 adult occupants or former residents of an apartment complex in Houston. Texas, where in April 1987, the outside wooden surfaces of the buildings were sprayed for termites with chlordane. Later in 1987 and in 1988, chlordane combined with clorpyrifos was again sprayed on these surfaces. The apartment units were tested for chlordane residue in 1990 and 1991 when 85 per cent of 81 samples from wooden surfaces were found to have chlordane at 0.5 µg/929 cm² or more.

The subjects in the study were examined using a pretested neurobehavioral battery and questionnaires. The exposed group of 109 women and 97 men, ages 17 to 70 years, was compared with 174 unexposed Houston referents who matched the exposed subjects in age and educational level.

Neurobehavioral function, pulmonary function and symptomotology were compared as were subjects' histories for occupational, personal, and residential confounding factors.

Examination of subjects exposed in their homes to chlordane as compared to referent subjects showed significant impairment of both the neurophysiological and psychological functions including mood states. Accompanying these changes were significant differences in symptom frequency and in respiratory rheumatic and cardiovascular disease symptoms. The most notable changes were slowing of reaction time, balance dysfunction as revealed by increased sway speed, reductions in cognitive function, perceptual motor speed, and delayed verbal recall.

Source: Abridged from "Protracted Neurotoxicity from Chlordane Sprayed to Kill Termites", K.H. Kilburn and J.C. Thornton. Environmental Health Perspectives, Vol. 103, Number 7-8, July-August 1995.

ASBESTOS AND COLON CANCER: A WEIGHT-OF-THE-EVIDENCE REVIEW

here is a persistent belief that exposure to asbestos increases the risk of gastrointestinal (GI) cancer. originated from a study by Selikoff et al of asbestos insulation workers which found a threefold excess risk of cancer of the stomach, colon and rectum. However, it is now recognized that many deaths ascribed to GI cancer up to the early 1960s were wrongly diagnosed: necropsy and histological studies revealed that several of these deaths were due to lung cancer or mesotheliomas. Selikoff later concluded that about one half of the pancreatic cancers in the original study were misclassified. There have been many other studies and reviews of the putative link between asbestos and GI cancer with contradictory conclusions. John Gamble of Exxon Biomedical Sciences, Inc., New Jersey, U.S.A. evaluated the evidence, concentrating on colorectal carcinoma and, where possible, on colon cancer. The known risk factors for colon cancer are overweight and inactivity, which have a modest influence. If these two factors are confounding the results of studies, their effect will be to decrease the perceived risk (assuming the more exposed workers are more active and less overweight). In the studies that assessed exposure-response relationships confounding is considered least likely. Neither alcohol nor smoking has a significant association with colon cancer.

As well as misclassification of lung cancer as GI cancer, a comparison of causes of death or death certificates with hospital diagnosis found that colon cancer was overreported and rectal cancer was underreported. The problem should be greatest where asbestos exposure is highest because the proportion of asbestos-related cancers will be higher. For low-exposed groups, the effect is not considered significant.

Another possible source of error is "diagnostic suspicion bias". When a person is known to have been exposed to asbestos, there may be an increased tendency to diagnose colon cancer. Whether this occurs is not known.

Latency is an important factor because both colorectal cancer and lung cancer are considered to take

about 20 years to develop after exposure to an aetiological agent. Thus a restriction to at least 20 years latency should exclude some or all of the nonoccupational cases. The standardized mortality ratio (SMR) is the number of observed cases divided by the number of expected cases in the general population. In the asbestos studies reviewed, the SMRs for colon and colorectal cancers were similar when latency was not considered. When the cohorts were stratified for latency, the SMR for colorectal cancer was about 25% higher than for colon cancer. Therefore the studies that did not consider latency could have overestimated the risk for colon cancer.

Lung cancer shows a linear relationship to asbestos exposure and the risk of lung cancer is used as a surrogate estimate of such exposure. There is no control for smoking, but this is assumed not to influence the results. The proportion of mesotheliomas can also serve as a surrogate measure for asbestos exposure but it is more affected by type of asbestos. The classification of asbestos exposure by lung cancer SMR and proportion of mesothelioma is broadly consistent.

Gamble reviews 19 cohort studies that have reported SMRs for lung cancer and colorectal cancers among asbestos workers with at least 10 years latency. These were divided into cohorts with lung cancer SMR < 2 or \geq 2. In the low lung cancer group there was no convincing increased risk of colorectal cancer. In the high exposure group, only two of seven studies clearly showed a large increased risk of colorectal cancer.

Analysis of asbestos exposiveresponse relationships in individual studies found that four of six showed an association for lung cancer, one found no association for either type of cancer and are given an apparent association for colorectal cancer, but only in the high exposure category. The advantage of these analyses is that the exposive-response relationship for lung cancer is less likely to be confounded by cigarette smoking and exposure classification is more accurate. The most appropriate study design for determining causality is a nested case-control study, in which colon cancer cases are compared with controls within a cohort of asbestos workers. Four such studies showed no apparent association. Two studies observed a nearly doubled excess risk: one did not control for potential confounders or consider the degree of exposure; the second contained a large number of workers exposed to other carcinogens.

The biological basis for asbestos action has been investigated in animal experiments, mainly using rats. None of these, including long-term ingestion studies, found an increased risk of Gl tumors. Physiological studies indicated that only a small fraction of asbestos fibres penetrate the gut wall, with no evidence of associated intestinal damage. One study saw an increase in DNA synthesis but this was not correlated with tumor incidence.

Examination of asbestos workers with colon cancer revealed asbestos resident in about one third of these workers but associated equally with normal tissue and tumors.

Summary

Three factors detract from the hypothesis that exposure to asbestos increases the risk of colon cancer.

- The consistent lack of an association between low exposure to asbestos and colorectal cancer. Although workers with higher exposure show an increased risk of colorectal cancer, this may be due to misdiagnosis.
- The lack of a clear exposiveresponse relationship for colon cancer, whereas there is one for lung cancer.
- The negative results from studies on animals. Gamble concludes "asbestos exposure does not appear to increase the risk of colon cancer".

Source: Environmental Health Perspectives, Vol. 102, No. 12, December 1994.

The Safe Use Project

(Continued from page 6)

Working alongside the Thai Government Departments of Agriculture and Agricultural Extension, the TPA's existing retailer and training programmes were upgraded by improving training materials, audio-visual aids and safety handbooks. In the 3 year period

up to 1994, 749 trainers, 413 retailers and 329,000 farmers had received training in pesticide safety under the project.

Included under the educational programme was the thrust to extend awareness via high school students through curriculum materials and also through informal methods. A project-related medical programme recognized that one of the challenges in the

diagnosis and treatment of pesticide poisoning in Thailand is lack of fast, easy access to relevant information. Thus to facilitate improvements in availability of information, the project contributed to a joint programme conducted by the Ministry of Public Health, Food and Drug Administration, and the Thai Toxicological Society, in the training of 1,300 doctors and nurses nationwide, in first aid, diagnosis and treatment of pesticide poisoning.

The project also provided all doctors nationwide with reference texts, information posters, and a trade/common name index, which is also available on diskette.

An important aspect of the project was to ensure that industrial standards are met. Thus, the project assisted manufacturers, formulators and repackers to meet the standards set out in the FAO International Code of Conduct on the Distribution and Use of Pesticides, industry guidelines, and national law.

This programme involved free expert advice to all companies; plant audits by expert advisory groups; information bulletins and safety guidelines; and industry cooperation on safety and disposal issues.

SECOND ANNOUNCEMENT

The Second International Conference on Environmental and Industrial Toxicology: Research and Its Application

Bangkok, Thailand 9 – 13 December 1996

Symposium Topics:

- Oxidative stress, signal transduction and cell-cell communication: mechanisms of epigenetic toxicology
- 2. Chemical prevention of cancer
- Biomarkers for exposure and susceptibility
- 4. Applied environmental toxicology
- New approaches to detecting environmental toxicants
- Evaluation of toxicity and assessment of risks to human health
- 7. Hazardous waste management

Call for Submitted Papers:

- 1. Toxicology of environmental and industrial chemicals and pollutants
 - Industrial chemicals and chemical mixtures
 - Pesticides
 - Air pollution
 - Water pollution
 - Food-borne agents
 - Solvents/gas/vapours
 - Heavy metals
- 2. Mechanisms of toxicity
 - Biochemical toxicology
 - Biotransformation
 - Oxidative damage
 - Target organ toxicology
- 3. Cancer risks by environmental factors
 - Environmental carcinogens
 - UV and ozone
 - Chemoprevention of cancer risks
- 4. Factors modifying toxicity
 - Nutrition, diet and lifestyle fac-
 - Genetic susceptibility and other host factors

- 5. Evaluation of toxicity
 - Models for toxicological studies
 - Short-term toxicity testings
 - New techniques for detection of pollutant-induced toxicity
 - Biomarkers for exposure and susceptibility
 - Evaluation of environmental and toxicological hazards
- 6. Detection and detoxification of chemicals in the environment
 - Detoxification of industrial chemicals and hazardous wastes
 - Technology for detection of environmental toxicants
 - Monitoring of toxicants in the environment
 - Management of toxic/hazardous wastes
 - Bioremediation
- 7. Risk assessment and risk management
 - Human exposure, risk assessment and management
 - Regulatory aspects and international issues of environmental toxicology with special reference to developing countries

For further information please contact:

The Secretariat – ICEIT II Chulabhorn Research Institute Office of Scientific Affairs Vipavadee Rangsit Highway Bangkok 10210, Thailand Tel: (66-2) 247-1900, 247-5757 Fax: (66-2) 247-1222, 574-0616

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Correspondence should be addressed to:

ICEIT NEWSLETTER Chulabhorn Research Institute Office of Scientific Affairs

c/o Faculty of Science, Mahidol University Rama 6 Road Bangkok 10400, Thailand Telex: 84770 UNIMAHI TH

Telefax: 647/0 UNIMAHI Telefax: (662) 247-1222 Tel: (662) 247-1900