



SCRIBE

THE INTERNATIONAL SOCIETY FOR PHARMACOEPIDEMIOLOGY

President's Message

By Susana Perez Gutthann, FISPE

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Deadline for
Winter 2004 Issue
December 20th 2003

Over 740 delegates and 24 exhibitors participated in the 1st International Conference on Therapeutic Risk Management and 19th International Conference on Pharmacoepidemiology (ICPE) in Philadelphia! The meeting set a new attendance record -- a target for next year's ICPE to exceed! The success of this year's meeting is attributable to the strong program resulting from the hard work of the Scientific Program Committee chaired by **Sean Hennessey**, and the Local Host Committee chaired by **Brian Strom**. Also, we should not forget the significant contributions of ISPE members who volunteered their time and energy by serving on councils and committees, and the ISPE staff. A special thanks goes out to the members of the re-energized Development, Education, Membership and Publications committees for their combined efforts, which have raised the Society's visibility and the ICPE. A big thank you to all of you!

Therapeutic Risk Management

Consistent with the Board's decision to embrace therapeutic risk management as part of the Society's mission, the Board charged the Scientific Program Committee to highlight therapeutic risk management at the 2003 annual conference. This was accomplished. Therapeutic risk management was evident throughout the meeting, from **Robert Califf's** keynote address, workshops and symposia, through podium presentations and posters. The panel sessions on the US Food & Drug



Administration concept papers were particularly well attended and provided a unique opportunity for ISPE members to discuss how the field should be shaped as we move forward.

2003 Annual Meeting

As always there are too many meetings and sessions to attend and too little time to accomplish everything we would like to do at ICPE. But be assured ISPE members take their volunteer roles seriously and participated in committee and council meetings and the annual meeting sessions. We began promptly at 9:00am on August 20 with a Finance Committee meeting, followed by the Strategic Planning Task Force, and a Board meeting.

On Thursday, we participated in the Introduction to Pharmacoepidemiology and the Advanced Topics in Pharmacoepidemiology course organized by **Jacques LeLorier**. Both sessions were heard by standing-room only crowds. And we are pleased the US Centers for Education and Research in Therapeutics (CERTs) decided to hold its annual steering committee meeting on Thursday afternoon at the conference hotel. Several ISPE members play key roles in the CERTs program. ISPE hosted the third annual CERTs roundtable discussion breakfast Sunday morning.

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Annette Stenhagen and **Sam Lesko** organized the first of what should be another annual event – the Academic Showcase – held in conjunction with the Welcome Reception. Ten academic programs participated. **Cees Schep** and **Stephen Evans** will be organizing the Academic Showcase in Bordeaux.

And another ISPE first – the induction of the first class of Fellows of the Society or FISPEs. **Tom MacDonald**, who championed the establishment of a Fellow program, introduced the 37 new FISPEs. (Although the Board approved the applicants' status as Fellows at the April 2003 Board meeting, formal induction is held at the ICPE.) Any

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member who would like to apply for Fellow status must submit an application by December 15, 2003. Forms are posted on the ISPE website.

Many of us had the usual hard time choosing from among the concurrent sessions and posters: epidemiology methods – with propensity scores as a frequent topic, sources of data, pharmacogenomics, pharmacoconomics, pharmacovigilance, risk benefit, drug utilization, devices, vaccines, pregnancy outcomes and those focusing on specific classes of therapeutics agents. And yes, we still have sessions on NSAIDs; it appears NSAIDs are here to stay. For those of us who stayed until the end, the Hot Topic Session on Smallpox Vaccination was a unique opportunity to learn about and discuss large-scale therapeutic risk management in all aspects ranging from policy to implementation, epidemiological work and risk communication.

The success of this year's meeting was evidenced by the large attendance, and increased coverage by the media. *The New York Times*, *Wall Street Journal*, *Pink Sheet*, and *Health News Daily* reported on a session. **Yola Moride's** Public Relations Committee is off to a great start!

ISPE's Strategic Plan

In 2002, the Board with the assistance of the Ad Hoc Strategic Planning Task Force prepared a long term Strategic Plan to guide the Society towards a desired future, which also would result in a stronger and more visible Society. Implementation of the goals and objectives is promising and encouraging. Thanks to the commitment of volunteers and increased staff support, a number of key committees and councils have been revamped and

became increasingly active this past year. In particular, the Membership Committee (chaired by **Annette Stenhagen**), Finance Committee (chaired by **Judith Jones**), Development Committee (co-chaired by **Nancy Dreyer**, The Americas; **Cees Schep**, Europe, and **Kuni Hayashi**, Japan) Publications Committee (chaired by **Daniel Fife**), and **Education Committee** (chaired by **Jacques LeLorier**). These committees are working on strengthening educational programs at our meetings, increasing the numbers of individual and institutional/organizational members worldwide, developing communications about ISPE, redesigning the website, raising funds, and strengthening links with organizations, institutions and other professional societies.

We would like you to be part of ISPE's plan implementation efforts. Committee rosters are posted on the Members Only section of the ISPE website. Just send an email to the committee chair or ISPE office indicating your interest to join a committee.

Recent Board Actions

The Board of Directors took the following actions at its August 2003 meetings in Philadelphia.

- Expressed appreciation to the following Board members whose terms expired for their dedication and commitment to the Society: **Jacques LeLorier**, Past-President; **Frank May**, **Peter Gruer**, **Yola Moride**, **Susan Sacks**, and **Bruno Stricker**.
- Welcomed **Jerry Faich**, President-Elect, **Frank May**, Vice-President Finance-Elect, **Sean Hennessy**, **David Lilienfeld**, **Stephen Lanes**, **Miriam Sturkenboom**, and **Panos Tsintis** to the Board.

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SCRIBBLES – EDITORIAL

Dear Colleagues,

Recently I received a call from **Daniel Fife**, Chair of ISPE Publication Committee, who said the ISPE Board would like me to serve as the Editor of Scribe. Daniel said this is an important position in ISPE that had been filled by some of the Society's most prominent members. I said I had to think about assuming the responsibilities of editor and needed to get clearance from my superiors at FDA to serve ISPE in this new capacity. I am glad to report my bosses supported me and the ethics folks at FDA approved this "outside activity" -- so I willingly accepted this challenging job.

I was told the responsibility of an editor is to solicit and edit articles for the newsletter. Editorship is a tough job in itself and perhaps more difficult

for me since I have to maintain the high standards set by past editors namely **Alec Walker** and **Jacques LeLorier**. As you know, Alec and Jacques are leaders in the field and past-presidents of ISPE as well.

As editor of Scribe, I have some ideas to make this newsletter more lively and interesting. Towards this end, I have decided to start a new column, Scribeline. This column is based on the British journal *Lancet's* Lifeline column. To sustain Scribeline, I will send out a set of questions to people in our field and hope to receive their answers in a timely fashion.

I realize many ISPE members would like updated information on developing issues related to drug safety and some would like to exchange and share information with other

members. As part of the Website Task Force, which is another arm of the Publications Committee, I encourage you to regularly visit the ISPE Bulletin Board in the Members Only section, and to make use of this tool for information exchange. Incidentally, this Task Force will be recommending ways the website might become the Society's hub for information exchange.

These are changing times for *Scribe*. The Board decided *Scribe* would go to an electronic format only with the next issue. Please let us know if this transition will create any problems for you, especially for our members in developing countries some of whom may not have easy access to the Internet.

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- Agreed to extend the staff time dedicated to plan implementation for two months; i.e., through the end of FY 2003, and asked staff to include time for plan implementation in the draft FY 2004 budget after considering the progress described in the Annual Report of Strategic Planning and Plan Implementation Efforts.
- Accepted the following revised mission statement: "ISPE is an international forum for the open exchange of scientific information among academia, government and industry, and for development of policy, a provider of education, and an advocate for the fields of pharmacoepidemiology and therapeutic risk management."

- Agreed *Scribe* will move to an electronic format, and ISPE members will receive *PDS* in electronic format only with an option to purchase the paper copy in 2004. The decision was predicated on the results of the members' preference survey, which **Ken Rothman** directed.
- Endorsed the proposal of the new Ad Hoc Committee on Good Pharmacoepidemiology Practices, chaired by **Stephen Lanes**, to develop two sets of guidelines Good Pharmacoepidemiology Practices and Good Risk Management Practices. We expect to see a draft set of guidelines at the April 2004 Board meeting.
- Accepted report from **Sue West** on the Mid Year Symposium,

Changing Behaviors: How Do We Do It? How Do We Know When We've Done It? which will be held April 19, 2004 in Baltimore, Maryland. **Judith Jones** agreed to coordinate the Introductory Course to Pharmacoepidemiology, which will be offered April 20, 2004.

- Accepted report from **Nicholas Moore**, Chair, 2004 Scientific Program Committee on the *20th International Conference on Pharmacoepidemiology and Therapeutic Risk Management*, which will be held August 22-25, 2004 in Bordeaux, France. The Core Committee will include **Nicole Hartnell**, Chair of the Student

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SYMPOSIUM

Managing Risk of FDA-Regulated Products

By Lois La Grenade MD, MPH, Medical Epidemiologist, Division of Drug Risk Evaluation, Center for Drug Evaluation & Research, US Food & Drug Administration

The concurrent sessions of the 19th International Conference on Pharmacoepidemiology (ICPE) got off to a lively start on Friday morning, August 22, 2004, with representatives from three key centers of the US Food and Drug Administration (FDA) providing varying perspectives on risk management at the Agency.

The first speaker introduced by moderator **Dr. Hugh Tilson** was **Dr. Steven Galson**, Deputy Center Director, Center for Drug Evaluation and Research (CDER). Dr. Galson focused his presentation on current FDA Risk Management policy as mandated by the Prescription Drug User Fee Act of 2002 (PDUFA III). He hailed PDUFA III as a major milestone for public health, with the objective of evaluating whether drug products are being used in a safe way, as early as possible in the drug development process. To meet this objective, CDER is in the process

of developing Guidances on Risk Assessment, Risk Management and Pharmacovigilance. Concept papers were published in March 2003, and the center is currently working on draft guidances, incorporating comments from the public into the concept papers. It is expected that the draft guidances will be published this Fall with the Final Guidance published in September 2004.

Dr. Susan Ellenberg, Director of the Office of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research (CBER) addressed the problems CBER faces with competing priorities -- making new products available as quickly as possible, while at the same time ensuring that these products are safe. There are special issues with biologics; many are novel products, used to treat or prevent serious illnesses. Risk-benefit considerations for such products might therefore lead to rapid

approval, with a subsequent need for more critical post-marketing surveillance to balance the relatively small pre-licensing body of data. For the more traditional biologic products such as blood products and vaccines, there was a higher standard of safety expected by the public -- 100% safety. Many products required long-term surveillance for safety issues such as transmission of genetic and infectious diseases.

Jay Crowley, Principal Human Factor Engineer, Center for Devices and Radiological Health (CDRH), gave the final presentation of this symposium. He pointed out that much of managing the risk of medical devices had to be done at the local level. One of CDRH's main roles is to guide manufacturers to improve design, labeling and training to address known risks and to help the device user and patient to understand the risks and benefits. Crowley outlined some of the unique problems of devices -- they have long lives, and are often used for purposes other than the initial intended use, by users other than the original ones; often the link between the device and the adverse event is not easily detected; different manufacturers made the same device but with slight modifications that were not readily apparent, and could alter risk. He outlined the role of the Medical Device Surveillance Network (MeDSuN) in rapid detection and understanding of previously unknown and serious problems with devices. CDRH would continue to improve MeDSuN and to communicate findings to manufacturers and users so that corrective action could be speedily implemented.

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I am grateful to all those who agreed to write articles for this issue of *Scribe*, which focuses largely on the 19th ICPE in Philly. I need your continued support to make my job easier. *Scribe* is your newsletter and I urge you to contribute. You can send a report on new happenings in your country in the area of drug safety, which may be of relevance to others, news about any award that you have won, or if you have been named to a committee or task force of interest to ISPE, or any other item of interest, please email me (ahmads@cdcr.fda.gov) the details so it can be highlighted in *Scribe*. The

deadline for the Winter 2004 issue is December 20. You can also write to me if you have suggestions about issues/topics that we should cover in future *Scribes* as well as your thoughts about *Scribeline*. Finally, all constructive criticism is welcome in an effort to improve *Scribe*.

With peace,
Rizwan
 (Ahmads@cdcr.fda.gov)

The views expressed in this editorial are those of the author and not necessarily those of the FDA.

SYMPOSIUM

Issues in Implementation of Risk Management Plans

By Jackie Gardner, PhD, University of Washington

A panel chaired by **Anne Trontell**, Deputy Director of FDA’s Office of Drug Safety (ODS), addressed issues in implementing risk management plans. Speakers included **Gretchen Dieck**, Vice President of Safety Evaluation and Epidemiology at Pfizer, **Susana Perez Guthann**, Senior Director of Global Epidemiology and Safety, also at Pfizer, and **Judith Kramer**, Principal Investigator of the Duke University Center for Education and Research in Therapeutics (CERT).

Dr. Trontell described FDA’s three draft guidances for industry on risk management (www.fda.gov/cder/meeting/riskManageII.htm), for which public comments were sought in 2003. (ISPE comments are available at www.pharmacoepi.org). She focused the panel’s attention on the Risk Management Programs guidance, and cautioned that any discussion of risk must keep benefit in mind as well. Speaking of the appropriate time to consider a risk management plan as whenever risk reduction needs emerge either pre- or post-marketing. Dr. Trontell described tools for risk management currently employed by FDA:

- Targeted education and outreach, such as Dear Health Care Professional (HCP) letters, MedGuides, Patient Package Inserts (PPI)
- Guiding systems applied to prescribing, dispensing, or patient use, such as patient agreements or consents, prescription stickers
- Restricted distribution, such as restriction of types of prescribers or central pharmacy dispensing.

Selection of tools is influenced by factors such as scientific evidence

of their effectiveness, stakeholder input and burden, and consistency with existing and accepted tools. Dr. Trontell pointed out that evidence of tool effectiveness is limited, and that historical education and outreach efforts, such as labeling changes and Dear HCP letters have shown mixed effectiveness in the literature. She asked for feedback on how FDA can best use evidence to improve the selection and effectiveness of risk management tools.

Dr. Dieck presented the perspective that risk management should be a global and dynamic process, spanning the product life cycle, and should benefit both prescribers and patients. She urged that in all cases the risks being managed must be established rather than theoretical risks, using validated tools. She called for a partnership between industry and regulators, and between FDA’s preapproval review divisions and the ODS, to determine when a program is needed, what the program goal is, and how success will be measured. Dr. Dieck proposed that early application of risk management practices by sponsors might offset the need for major risk management programs later.

Dr. Perez-Guthann echoed the call for management only of established risks, and voiced the sentiment that most products will not need a risk management plan beyond labeling. She reviewed the international initiatives currently in progress and referred interested parties to the EU Summary Report of Heads of Agencies Ad Hoc Working Group (www.heads.medagencies.org/summary). She described the feedback ISPE had provided to FDA on the draft guidance, including

consideration of the impact on health systems of proposed tools, establishment of class balance; i.e., new vs. old products, and the need for coordination with international as well as US stakeholders. She, too, stressed the dynamic nature of the risk management process, suggesting that it begins at the initiation of drugs into humans and continues through various developmental milestones through approval and pharmacovigilance. Her suggested action plan included

- Benefit-risk quantification using modeling and simulation techniques
- Implementation to minimize impact on health care systems, both locally and internationally
- Seamless multidisciplinary collaboration in implementation
- A plan for evaluation.

Dr. Kramer, bringing forth information gleaned from a series of five “Think Tank” workshops on the subject of risk assessment, communication, and management mounted by the CERTs, expressed a different view: that every prescribed agent should have a risk management plan. She agreed that risk management should be a continuum across a product life cycle, but that risks should be categorized by severity in the context of benefits. The CERT sessions have called for

- More outcomes studies under conditions of normal use
- More public scrutiny of risk data
- Active surveillance rather than waiting for signal to emerge
- A strong focus on benefits in the context of risk

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SYMPOSIUM

Elements of Good Pharmacovigilance Practice

By Julie Beitz, MD, Deputy Office Director, Office of Drug Evaluation III, Center for Drug Evaluation and Research, US Food and Drug Administration

Of the many facets of pharmacovigilance that we could choose from, we selected three topics to discuss in depth at this symposium. First, **Dr. June Almenoff**, GlaxoSmith-Kline, spoke of the advances in data mining techniques as they are applied to large adverse event databases. She described some fundamental principles, potential data mining applications, and her company's approach to incorporating data mining into pharmacovigilance activities. Almenoff also described some of the advantages and limitations of data mining.

Dr. Kasia Petchel, Pfizer, updated the participants on the status of International Conference on Harmonization (ICH) guidance development

with regard to planning effective pharmacovigilance activities. She provided background on the structure and process of ICH itself, and then discussed the guideline on pharmacovigilance planning currently under consideration at ICH. Petchel described the guideline's purpose, scope and key concepts as they evolved at the July ICH meeting in Brussels.

Lastly, **Dr. Sue West**, University of North Carolina, summarized challenges in developing a training program for staff engaged in pharmacovigilance activities. Some of these challenges include choosing educational topics to be covered, deciding who should be trained, determining what organizations should perform the training, deciding

whether to provide academic credit, certification or neither, and deciding on the format (e.g., distance learning modules) that would best accommodate busy schedules. The audience was asked to complete a short written survey to provide comments on these issues.

There were two major themes throughout the presentations: Carefully planned and executed pharmacovigilance activities can minimize toxicity and maximize benefits of products; and the best method to address a specific product-event association will vary depending on the product and event of interest, on the population being treated, on the specific question that needs to be answered, and on the inherent strengths and limitations of the method.

Invited Plenary Lecture

By Wei Dong, MD, PhD, Senior Epidemiologist, Genentech

Dr Samuel Shapiro, who is currently a visiting professor in the Department of Epidemiology at Columbia University, gave the invited lecture addressing common flaws in drug epidemiology and approaches to reducing the risk of repeating these mistakes at the 2003 ICPE.

He first reviewed the significance of drug epidemiology to public health such as demonstrating the role of aspirin in reducing the risk of myocardial infarction. Shapiro said 'good science should be a skeptical science'. As an example, he listed the finding of a spurious association between calcium channel blockers and the risk of breast cancer reported in earlier studies. For younger researchers, his advice was that 'making enough errors in one's career early on' is not a bad thing if the lesson is learned.

Dr. Shapiro challenged the commonly accepted hierarchy in making causal inference, ranking from high to low: randomized controlled trial (RCT), cohort study, case-control study, case-cohort or time series, cross-sectional study followed by ecological study. He insisted there is no inherent superiority of the cohort design over case-control design (or vice versa). He was of the opinion that the blinded RCT should not be taken as error-proof due to limitations such as short-term observation and/or loss of blinding. Typically, after initial blinding, a longer-term RCT gradually becomes equivalent to an open-label trial as intended and unintended medication effects make each patient's assignment increasingly clear, therefore, it is not qualitatively different from a drug epidemiology (observational) study and it may be subject to the same biases. He urged people to 'abandon the hierarchy'.

Shapiro argued that while statistics is absolutely critical in drug epidemiology, the interpretation of results should be guided by clinical and biological considerations. To further illustrate this point, he gave this quote "John Snow is a pathologist first, a clinician second, and an epidemiologist third" from the latest book on Snow [Cholera, Chloroform, and the Science of Medicine: A Life of John Snow by Vinten-Johansen P, et al. 2003; Oxford University Press].

Dr. Shapiro concluded by urging the audience to return to the skeptical thinking of epidemiology, and to understand that epidemiological research is good at interpreting a large relative risk, but not a small risk.

[Editor's Note: Dr. Shapiro's slides are posted in the Members-Only section of the ISPE website].

AWARDS

Best Prize awarded for Papers Published in 2002 (Volume 11) in Pharmacoepidemiology and Drug Safety (PDS)

By Judy Kinman, Regional Managing Editor, *Pharmacoepidemiology & Drug Safety*

The ISPE-Pharmacoepidemiology & Drug Safety (PDS) Prize is awarded annually to the author of the best paper published in PDS.

The selection committee for the Best Paper Prize is comprised of the two editors of *Pharmacoepidemiology and Drug Safety* (Drs. Ron Mann/Brian Strom) and a past ISPE President. This year's ISPE representative was Dr. H. G. M. (Bert) Leufkens.

If there was a conflict of interest created by a committee member being a co-author or in some other way tied to a paper under consideration, that judge did not evaluate that paper, and the first author was automatically disqualified from receiving the \$1,000 award, generously donated by the publisher John Wiley & Sons, Inc. However, the paper was still eligible to receive a Certificate of Distinction.

The awards were based on four criteria: originality, clarity of presentation, methodological soundness, and public health importance. A 25-point system was devised, of which 10

points were allocated for public health importance. Only original reports were eligible for the prize.

The quality of papers published in the journal dramatically improved in this past year, and the selection committee, with difficulty, selected five papers for the award, which are presented in alphabetic order.

Certificates of Distinction were awarded to:

Janine A. Blackman, MD, PhD. Estrogen Replacement Therapy and Risk of Lung Cancer. Volume 11 Issue 7:561-7, Oct-Nov. 2002. Co-authors: Patricia F. Coogan, Lynn Rosenberg, Brian L. Strom, Ann G. Zauber, Julie R. Palmer, Patricia Langenberg, Samuel Shapiro.

James Cross, MS. Postmarketing Drug Dosage Changes of 499 FDA-Approved New Molecular Entities, 1980-1999. Volume 11, Issue 6:439-46, September 2002. Co-authors: Howard Lee, Agnes Westelinck, Julie Nelson, Charles Grudzinskas, Carl Peck

Eibert R. Heerdink, PhD.

Changes in Prescribed Drug Doses after Market Introduction. Volume 11, Issue 6:447-453, September 2002. Co-authors: John Urquhart, Hubert G. Leufkens.

Stephen Kimmel, MD, MSCE.

Parenteral Ketorolac and Risk of Myocardial Infarction. Volume 11, Issue 2: 113-119, March 2002. Co-authors: Jesse A. Berlin, Judith L. Kinman, Sean Hennessy, Harold Feldman, Jeffrey L. Carson, Brian L. Strom.

The \$1000 cash prize winner and a Certificate of Distinction was awarded to:

John P. Mullooly, PhD. Wheezing Lower Respiratory Disease and Vaccination of Full-term Infants. Volume 11, Issue 1:21-30, Jan-Feb. 2002. Co-authors: John Pearson, Lois Drew, Roberleigh Schuler, Julie Maher, Paul Gargiullo, Frank DeStefano, Robert Chen, and the Vaccine Safety Datalink Working Group.

ISPE Member Receives Prestigious 2003 Queen's Birthday Award

Dr. John McEwen, Principal Medical Adviser, Therapeutic Goods Administration (TGA) – the Australian drug regulatory agency – received a Public Service Medal at the Queen's Birthday Honours Awards. The Governor-General presented the medal to Dr. McEwen on September 19, 2003. The citation on the award reads "for outstanding public service in advocating drug safety through the monitoring and reporting of adverse reactions".

John McEwen, PSM, MBBS, MSc, MPS, graduated in Pharmacy at the Victorian College of Pharmacy and ob-

tained an MSc in Neurophysiology at Melbourne University. After a period as lecturer in Physiology, he completed medical training and house positions at Royal Melbourne Hospital. From 1979 to 1989, John McEwen was Secretary of the Adverse Drug Reactions Advisory Committee and subsequently Head, Drug Evaluation Support Branch in the forerunner organisation to the TGA. During this time he was a member and later Chairman of the Advisory Board to the WHO Collaborating Centre for International Drug Monitoring, Uppsala, Sweden, and also acted as Editor of *Australian Prescriber*.

McEwen spent five years as Medical Director, CSL Limited, Melbourne, before returning to the TGA in August 1994. He has in turn worked for the TGA as Head, Clinical Evaluation Unit 2, Drug Safety and Evaluation Branch (TGA) and Head, Adverse Drug Reactions Unit before taking up his current position in January 2002.

Congratulations John!

ERRATUM: In the Spring/Summer 2003, we incorrectly published the name of an Academic Showcase Sponsor. The correct name of the program is the Slone Epidemiology Center at Boston University.



Scene

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An



es from the
003
ISPE
Annual Meeting



IN APPRECIATION

The Board of Directors, members and staff of the International Society for Pharmacoepidemiology (ISPE) would like to acknowledge the following volunteers and organizational supporters of the society. Their contributions contributed to the success of the 1st International Conference on Therapeutic Risk Management & 19th International Conference on Pharmacoepidemiology.

Sean Hennessy, FISPE, Chair, ICPE Scientific Program Committee

Brian Strom, FISPE, Chair, Local Host Committee

Annette Stemhagen, FISPE & **Samuel Lesko**, Co-Chairs, Academic Showcase Members, ICPE Scientific Program Committee Members, Local Host Committee
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Uppsala Monitoring Centre

MedDRA and SNOMED - ISPE's Informal Conversation with FDA

By Robert P. Wise, MD, MPH, Epidemiologist, Center for Biologics Evaluation & Research, US Food and Drug Administration

A special session to discuss MedDRA and SNOMED issues was held at the 2003 ICPE. In the recently published proposed SADR rule (Safety Reporting Requirements for Human Drug and Biological Products), FDA announced plans to employ MedDRA in conformance with agreements of the International Conference on Harmonisation. However, in the aftermath of the July 1 announcement of SNOMED licensure by HHS (<http://www.hhs.gov/news/press/2003pres/20030701.html>), this session offered "an opportunity...to share views about current plans and anticipated developments along with the merits of the two systems, the spectre of competing standards, and practical questions, such as implementation issues. Representatives from FDA explained that the proposed SADR rule is still open for comments from the public.

Among multiple concerns voiced by meeting attendees was that few people if any in the field of pharmacoepidemiology appeared to have sufficient recent first-hand experience with SNOMED to form an assessment of its adequacy for safety surveillance. The vocabulary's development was apparently directed to pathological classification and detailed coding of disease, since it was originally developed and is still owned by the American College of Pathologists. Discussion suggested that this coding system might be acceptable for data entry, but safety surveillance requires getting data out, too. The question was raised, "Does SNOMED offer the kind of flexibility achieved by MedDRA for querying at various levels of specificity?" One participant argued that SNOMED CT is incomplete, despite having

over 340,000 terms. He said, by way of example, that the code for amputation of a toe is the same as that for loss of a foot.

Other concerns included the relationship between SNOMED CT and MedDRA, the burden of training costs that might be imposed by adoption of SNOMED CT, and the question of who would be responsible for maintenance. Would user input be accommodated over time? One experienced epidemiologist, reflecting on the differences between ICD-8 and ICD-9CM pointed out that discontinuities in data across any change in coding system could introduce analytic artifacts, and translations between coding systems frequently introduce inaccuracies or data loss. Would ICH agreements require translation of SNOMED CT into other languages, imposing additional costs and risks of inaccuracies?

FDA attendees reiterated that the proposed FDA rule for postmarketing reporting (<http://www.fda.gov/OHRMS/DOCKETS/98fr/03-5204.html>) would adopt MedDRA as the standard vocabulary for adverse event reporting, but the final rule would only emerge after study of all submitted comments. Participants emphasized that input from ISPE members on the potential impact for the proposed rule of a new terminology, such as SNOMED CT, would be welcomed. These comments may be "submitted to the docket" by e-mail to FDADockets@oc.fda.gov.

FDA's Internet web site provides a series of questions and answers on this initiative. One is particularly germane:

Q7. On July 1, 2003, Secretary Thompson announced that the Department of Health and Human Services (DHHS) entered into a licensing agreement to make a clinical terminology database, SNOMED, available without charge to the U.S. health care industry. How does this announcement affect FDA's proposal to require that postmarketing safety reports from industry be coded in the ICH agreed international drug regulatory terminology (MedDRA)?

A. The SNOMED initiative announced by DHHS is for standardization of electronic medical records in the United States. For purposes of postmarketing safety reporting to FDA and other international drug regulatory authorities, FDA has proposed to require that the reports from industry be coded in the ICH agreed international drug regulatory terminology (MedDRA). This remains the Agency's proposal. We believe these initiatives are not necessarily incompatible and the two terminologies effectively could coexist to advance public health goals both nationally and internationally.

Public comment on this particular issue is welcome, as well as specific comment requested in the proposed rule on potential strategies and approaches for facilitating seamless, cross-standard drug regulatory communications, such as mapping between alternative terminologies. (Source: <http://www.fda.gov/oc/initiatives/barcode-sadr/qa-sadr.html>)

Sub Scribe

RESULTS -- ELECTION 2003

Congratulations to ISPE's new officers -- **Gerald Faich**, FISPE, President-Elect, **Frank May**, Vice President Finance-Elect, and to the newly elected directors -- **Stephen Lanes**, Industry North America; **Sean Hennessy**, FISPE, Academic North America; **David Lilienfeld**, FISPE, Industry Non-North America; and **Miriam Sturkenboom**, Academic Rest of World, and **Panos Tsintis**, Government Rest of World. Thanks to all ISPE members who stood for election.

CALL FOR NOMINATIONS 2004

The ISPE Nominations Committee invites your participation to identify qualified members to serve on the ISPE Board of Directors. The Committee will be working to fill five director positions (Industry – North America; Industry – Rest of World; Academic – North America; Academic – Rest of World; and Government-North America), and the President-Elect position.

If you would like to nominate someone, if you are interested in serving, or if you have questions about the responsibilities of serving, please contact Tom MacDonald, FISPE, Chair of the Nominating Committee (tom@memo.dundee.ac.uk).

MEMBERS ONLY SECTION OF WEBSITE

The Members Only section of the website has several components of interest to members:

-- Selected PowerPoint presentations and pictures from the 2003 Annual Meeting

-- An ISPE bulletin board. The Website Task Force is seeking to make the bulletin board serve as a communication tool for as many members as possible. Suggestions are welcome and can be addressed to **Daniel Fife** at dfife2@prdu.s.jnj.com
 -- Update Member Information Form. Use this electronic form to inform the office of any change in your contact information. Maintaining current information on ISPE members is a continuous task. It is in your interest to inform the ISPE office of any changes; we don't want to lose any member.

-- Committee rosters. If you would like to join a committee, or if you are a member of a committee and your name is not listed, please send an email to ISPE@paimgmt.com

MEMBERSHIP BILLING 2004

Invoices for 2004 membership dues will be mailed to all members in November – so be on the lookout for your dues invoice. You will be able to renew your membership by mail, by fax or online at the ISPE website.

FELLOW STATUS

The ISPE Board of Directors created a special elected category of membership for its outstanding leadership. Elected members are designated 'ISPE Fellows'. Fellowship Status is awarded upon election as Fellow by the board on the recommendation of a committee of peers. Consideration for election to fellowship is open to those who are recognized as having leadership roles in the Society.

A FISPE application form is posted in the "Join Us" section of the ISPE website. The Fellowship

Subcommittee will consider all completed applications received in the ISPE Office by **December 15, 2003** for Fellow status to be conferred in 2004. The Subcommittee will submit its recommendations to the ISPE Board of Directors for consideration at the Board's Mid-Year Meeting, April 2004. All applicants approved for FIPSE status will be inducted at the 2004 Annual Meeting in Bordeaux, France.

INVITATION TO REVIEW ABSTRACTS FOR 2004 ANNUAL MEETING

Nicholas Moore, Chair of the ISPE Scientific Program Committee, invites ISPE members to review abstracts submitted for presentation as oral presentations and poster presentations at the 2004 Annual Meeting.

To review abstracts, your dues must be current, you must be available to review abstracts in mid-March 2004, and you must return a completed Reviewer Questionnaire by **December 15, 2003** to the ISPE Office. The questionnaire will be posted in the 2004 Annual Meeting section of the ISPE website.

ISPE MOVES TO ELECTRONIC PUBLICATIONS

The ISPE Board decided to disseminate electronically both the newsletter (*Scribe*) and the journal (*Pharmacoepidemiology and Drug Safety*) effective in 2004. Members will have the option to purchase at an additional cost a subscription for the hard copy version of PDS.

2004 ANNUAL MEETING

The International Society for Pharmacoepidemiology and
the European Drug Utilization Research Group
announce the

20th International Conference on Pharmacoepidemiology & Therapeutic Risk Management

Visit the ISPE website,
www.pharmacoepi.org, 2004 Annual Meeting for information about the online abstract & workshop/symposia submissions, meeting agenda, housing information, and other meeting-related news. The online abstract submission form is expected to be operational by mid-December 2003.

SPONSORSHIPS, EXHIBITS & ACADEMIC SHOWCASE

ISPE offers organizations and academic institutions opportunities to support the 20th Annual Meeting through sponsorships and by displaying their products and services to conference attendees. Contact ISPE at ISPE@paimgmt.com or 301-718-6500 for more information.

STUDENT AWARDS

To recognize and encourage excellence in the scholarship of students in pharmacoepidemiology, the ISPE Board of Directors grants several student awards annually. The Scientific Program Committee oversees the selection and presentation of awards, which will be presented at the 2004 annual meeting.

SCHOLARSHIPS

A limited number of scholarships (expense reimbursement) will be available to assist with attendance. Scholarships may be used for registration, lodging, and travel to the conference. Researchers from developing countries, those in genuine financial need, and students who otherwise would be unable to attend ICPE are invited to submit an application form, which will be posted on the 2004 Annual Meeting website.

August 22-25, 2004
Bordeaux Conference Centre
Bordeaux, France

CALL FOR ABSTRACTS
ISPE invites your abstracts for oral/poster presentations and workshop & symposia.

SUBMISSION DEADLINE
February 20, 2004



ScribeLine

David Coulter

David Coulter received his medical degree from Otago University, Dunedin, New Zealand in 1959. For more than a quarter century he has been investigating the safety and efficacy of drugs. David until recently directed the Intensive Medicines Monitoring Program (IMMP), which undertakes prospective, observational, cohort studies on selected new medicines.

Which patient has had most effect on your work, and why? A baby who died after receiving an improper dose of chloroquine by injection. Drugs can be toxic and there are certain patients who are at

greater risk than others.

What is your best-published work? Coulter DM, Edwards, IR. Cough associated with captopril and enalapril. *BMJ* 1987; 294:1521-3.

What is the best piece of advice you have received? Encourage your staff by example.

What is the best advice that you can give to a new person in the field? Consider that you know nothing. Then you will look more carefully at your work.

What is your greatest regret? That we haven't had the resources to provide adequate staff to achieve the

full potential of the IMMP.

What apart from your partner is the passion of your life? This is the hardest question because living is a passion. All of the following (not necessarily in order of priority): Pharmacoeconomics (this has had the most time), music (singing and playing the organ), running, and traveling (with my partner). The last three have been given too little time.

What is your greatest fear? That misguided people in a position of power can destroy the work that we are doing.

What are you currently reading? Everything on COX-2 inhibitors.

Which is your favorite country? New Zealand.

What do you think is the most exciting field of science at the moment? Pharmacogenetics.

What part of your work gives you the most pleasure? Reviewing the adverse events as they come in from monitoring studies of new drugs. Much of it is new stuff.

What is your favorite journey, and why? Driving north on the motorway out of Dunedin, because it means I am going on holiday, and it's nice to arrive in the south of France, though we can't drive all the way!

What is your favorite saying? Observe, remember, compare.

What is the least enjoyable job you've ever had? Picking brussel sprouts in a market garden in the middle of winter (as a student).

continued from page 3

Council, to ensure students' interests are considered in planning for the annual meeting.

- Selected Lisbon, Portugal as the site for ICPE 2006. We are grateful for the efforts put forth by the **Corrine de Vries** (England) **Salvo Mannino** (Italy), and **Magda Melo** (Portugal) to showcase possible venues for the ICPE. We are looking for volunteers interested in proposing venues to host the 2007 ICPE and 2008 ICPE. Please contact the ISPE office if you would like to host an ICPE in your area.

The Future

Epidemiology is the established science of public health research. It has been and continues to be key for the evaluation of public health interventions. More specifically, epidemiology also has a well-established role in the fields of therapeutic R&D and

safety, and ISPE has long been recognized as a key forum for the advancement of epidemiology methods and applications in the area of therapeutics.

External focus on risk management activities increases. If we look at *Therapeutic Risk Management* as a Public Health Intervention, it follows that epidemiology is the key science underlying safety risk ascertainment and risk management evaluation. As reflected in the Society's initiatives and the conference program this year, many ISPE members are among the most experienced in developing and implementing risk management activities beyond what could be expected as leaders of epidemiological studies and methods. This is an exciting time to further expand and strengthen ISPE's contributions in the scientific and policy community. I look forward to working with you this year to make it happen.

CALENDAR

[Visit the ISPE website, www.pharmacoepi.org for updated information.]

2004

- **February 20, 2004**
Deadline for submitting abstracts for 2004 Annual Meeting. Online submission site will be operational by mid-December 2003.
- **April 17-20, 2004**
ISPE Mid-Year Meeting
Baltimore, Maryland. USA
- April 17*
ISPE Board of Directors Meeting
- April 18*
ISPE Scientific Program Planning Committee

April 19
Mid-Year Symposium:
Changing Behaviors: How do we do it? How do we know when we've done it?

April 20
Introduction to Pharmacoepidemiology: An Intensive Workshop

- **August 22-25, 2004**
20th International Conference on Pharmacoepidemiology & Therapeutic Risk Management
Bordeaux Convention Center
Bordeaux, France

2005

- **August 21-24, 2005**
21st International Conference on Pharmacoepidemiology & Therapeutic Risk Management
Nashville, Tennessee. USA

2006

- **August 2006**
22nd International Conference on Pharmacoepidemiology & Therapeutic Risk Management
Lisbon, Portugal

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- Patient input in risk management plan development
- Evaluation of risk management plans and placement of the evaluations in the public domain

A critical policy issue expressed by Dr. Kramer is who pays for design, testing, conduct and evaluation of risk management plans? Recognizing that risk management plans may limit the market size of a product, she noted that industry might choose not to develop drugs with any safety issues, thus reducing innovation in needed areas. The CERTs have called for an Institute of Medicine (IOM) study to review the U.S. system for assessing effectiveness and safety of approved drugs, for

example, rationalizing the use of older, off-patent drugs in elderly patients.

[Editor's Note: The PowerPoint presentations for this session are posted in the Members Only section of the ISPE website, www.pharmacoepi.org.]

FIPS: The Unique Role of the International Professional Society in Advancing Health Services Research

By Hugh Tilson, FISPE, and Mark Epstein

Representatives of the eight member organizations that together comprise the Forum of International Professional Societies (FIPS) recently shared their views on several issues, which served to highlight similarities and differences among the societies and underscored the value of these international organizations. The panel discussion was held as a formal peer-reviewed session in conjunction with the 5th *International Conference on the Scientific Basis of Health Services: Global Evidence for Local Decisions*, September 21, 2003, in Washington, DC. ISPE was a Collaborating Organization of the conference.

Hugh Tilson, FISPE and ISPE designated liaison to the FIPS, organized and moderated the session. Representing the FIPS members were **Judith Jones**, FISPE, ISPE; **Marilyn Dix Smith**, ISPOR; **David Ballard**, International Society for Quality in Health Care (ISQua); **Thomas Getzen**, International Health Economics Association (iHEA); **W. David Helms**, AcademyHealth; **Chris Henshall**, Health Technology Assessment International (HTAi); **John Wong**, Society for Medical Decision Making (SMDS); and **Albert Wu**, International Society for Quality of Life Research (ISOQOL).

A summary of several issues addressed by FIPS members follows.

Nurturing membership from the developing world: All participants voiced interest in and mentioned

efforts toward this objective. Among efforts of interest were: outreach and formal mentoring programs (mentioned by only one or two of the FIPS members); encouraging local chapters and meetings; encouraging special sessions at annual meetings for invitational papers about and from the developing world (even providing scientific help to ensure abstracts meet the minimum level of scholarship to make the meeting worthwhile); and providing special discount fees for membership (several) and scholarships for attendance at annual meeting.

Ensuring balanced governance: Several formal organizational approaches were presented: quotas and mandatory 'assigned' seats for the various estates and geographies; wide distribution of information and recruitment of candidates from otherwise under-represented bodies or geographies; no more than a fixed number of members from any single country.

The ability and mechanism to influence policy (including funding) for health services research (or our related areas of expertise) internationally or in a given country: Four (and a tentative half-raised fifth hand) of FIPS members reported that they take formal public policy positions; the others ensure that members are aware and apprised of positions and will undertake presentation of scholarly research related to positions for the advocacy positions of others. Of those, which do not take such public positions, fundamental logic

is the organization does not wish to be divisive among its members or distracted from its primary scholarly mission. Those, which do take such positions, range in level of activism from those taking broad policy positions on matters affecting the ability of the sector to conduct its work (e.g. data privacy) to narrowly focused national advocacy for practice improvement (e.g. advocating for accreditation standards) and may do so via direct advocacy (within the permitted restrictions of conditions of incorporation) or through a 'fire-wall protected' affiliate (e.g. the coalition for health services research advocacy organization for funding and the AHRQ budget). The virtues of a 'high hurdle' for organizational policy positions were espoused, including a possible 'best practice' of a 2/3 majority required of the Board before such a public position could be taken.

FIPS is a consortium of organizations whose scope and membership include health care researchers worldwide. The Forum seeks to explore issues of common interest, opportunities for possible cooperation or collaboration, or possible projects or work products of mutual interest. ISPOR and ISPE sponsored the creation of the Forum, which held its initial meeting January 10, 2000. Members rotate in providing voluntary support for annual face-to-face meetings of the Forum. For 2004, ISPE will collaborate with iHEA as convener and host.