



International Society for Clinical Biostatistics

News

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Editor: David W. Warne

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Editorial

You may have noticed some small changes in the appearance of this newsletter. Articles were originally typed into Word, WordPerfect 5.1 or into a Psion Series 3 palm-top computer. I was in a state of mild panic in mid-April as my old Series 3 decided it didn't want to work, but fortunately the people at Psion, London replaced it within 3 days, and all was well again. The articles were then arranged in WinWord 2 running under a new OS/2-2 operating system. Expect further cosmetic changes in the next few issues as I get to grips with the huge number of facilities of this word processor cum desktop publishing program.

One benefit of WinWord 2 (part of Microsoft's Office set of programs) is that the list of wordprocessing file systems that can be read is now much longer: please send me articles in the following formats: ASCII (text), WinWord (1, 2), PMWord (1.1 - OS/2), Word for DOS (4, 5.0, 5.5), Word for Mac (4, 5), Works for Windows, Works 2 for DOS, WordStar (3.3, 3.45, 4, 5.0, 5.5), Lotus 1-2-3 (2, 3), Excel (2, 3), dBase (II, III, III+, IV), WordPerfect (4, 5.2, 5.1) or RTF. Also graphics files in WMF, EPS, TIF, CGM, HGL, WPG, DRW, PCX, BMP, DXF, PLT or PIC can be used.

There's not much more space for a long editorial this issue due to the unusually large number of articles which I hope you will find interesting. If you have any article or announcement, please send it to the editor: the more articles, the more interesting each newsletter will be. The issue is 2/3 larger than each of the previous 5 issues and, if a few more articles are contributed, it is likely that an extra edition or two could appear in 1994. It's up to YOU, the members of ISCB. Please send all contributions (e.g. trip reports from ISCB14 - Cambridge'93) to the editor by the beginning of November 1993.

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ISCB Membership

The ISCB membership reached a peak of 563 towards the end of 1992 when many people joined when attending the ISCB13-Copenhagen Meeting. Hopefully 1993 will see many new members joining and taking advantage of reduced fees for ISCB14-Cambridge.

#	Country	31/Dec/92	09/Jun/93
1	UK	90	65
2	Germany	67	45
3	Sweden	51	42
4	France	52	38
5	Italy	33	26
6	USA	45	26
7	Denmark	58	24
8	Netherlands	30	23
9	Hungary	1	21
10	Belgium	22	18
11	Norway	18	18
12	Switzerland	25	16
13	Canada	12	12
14	Poland		11
15	Spain	12	11
16	Australia	9	8
17	Austria	9	5
18	Finland	7	5
19	Japan	6	4
20	Portugal	3	3
21	Ireland	2	2
22	Israel	3	2
23	Czech Rep.		1
24	Hong Kong	1	1
25	India	1	1
26	Slovenia	1	1
27	South Africa	1	1
28	Kenya	1	
29	New Zealand	1	
30	Thailand	1	
31	Turkey	1	
	TOTAL	563	430

Questions & Answers

Perhaps not surprisingly given that I had failed to find hardly any references to the subject in statistical journals when I reviewed the subject in August 1992, no contributions were received on the Question of **N-of-1s**.

If a "definitive article" is required, the publication in *Controlled Clinical Trials* (**14:1-5, 1993**) of "Suspended Judgement: n-of-1 Trials" by the ubiquitous Stephen Senn would be a good starting point for a statistician or medical adviser wanting to learn about the subject. Such designs may have merits, but one should be very careful as the non-statistical papers contain many flawed arguments.

A Question that arose in my mind when I took over editing ISCB News was "who are the ISCB members: what do they do and which other journals and newsletters do they subscribe to?". Over the past few years, ISCB has asked itself what its role should be. In particular, should it aim to do more than hold a conference each year? I intend to send out a questionnaire with the next newsletter, to be returned with the invoice, asking for a little information about the ISCB membership. Questions that spring to mind are which other societies and publications are subscribed to, which software packages are used, and does anyone use any unusual hardware for their work. If you have suggestions for what to else to ask, please send them to the editor by the beginning of November 1993.

Aims of ISCB

The Society was founded to stimulate research on the principles and methodology used in the design and analysis of clinical research, to increase the relevance of statistical theory to the real world of clinical medicine, and to provide a common forum through meetings and publications for the exchange of knowledge, experience and ideas among clinicians, statisticians and members of related disciplines (e.g. epidemiologists, clinical chemists and clinical pharmacologists) working or interested in the field of clinical biostatistics.

TURNING STATISTICS INTO A PROFESSION: A PERSONAL VIEW

Stephen Senn

According to George Bernard Shaw, any profession is a conspiracy against the laity. Let us consider the matter.

In the language of economics a profession is a cartel. Supply is restricted to drive up the price. In the language of religion it is a priesthood. Those who have not been initiated and anointed are not allowed to talk about the mysteries. In the language of science it is an attempt to set up an authority, whereas scientific research is the process of challenging dogma.

The consequence of professionalism is the establishing of orthodoxy. One only has to look at the medical profession to see this. Rightly or wrongly, osteopathy, homeopathy and naturepathy have been marginalised. The phenomenon continues and it has even been suggested that it will see the eventual world-wide triumph of Anglo-Saxon medicine. Would this sort of process be impossible were statistics to be turned into a profession? Is there not a danger, for example that frequentist views would become part of an official canon and Bayesianism outlawed as a heresy?

Why is this suddenly an issue? The reason is that moves are being undertaken both in Europe and America to turn statistics into a profession. The Royal Statistical Society (RSS) and the Institute of Statisticians (IOS) have merged into one society. The RSS had a statutory right, which it never exercised, of appointing "chartered" statisticians. The IOS had a programme of examinations leading to the award of professional qualifications. Now that the two have merged, suitably qualified and experienced statisticians may be awarded the designation *chartered statistician* (CStat).

Similar moves are being undertaken in the USA. I attended the recent joint meeting of the Eastern North America Region of the Biometrics Society, The American Statistical Association (ASA) and the Institute of Mathematical Statistics in Philadelphia (22-24 March 93). The ASA organised an open meeting on certification which attracted considerable interest. Although no definite decision in favour of certification has yet been taken, a proposal for implementation has been worked out in considerable detail.

Closer to home (in my case) the Swiss Statistical Association debated the matter at their annual general meeting in May.

What are the advantages of certification? It is tempting to state that it issues a guarantee that a statistician with the qualification possesses some minimal competence. As statisticians, however, we know that we have to think critically about screening procedures and that any such process will have false positives (and false negatives) and misclassify individuals. I think the most that one can say (and I do not claim that it is not worth saying) is that the probability that a certified statistician will be generally incompetent will be fairly low. (This does not mean, however, that such a person will be competent to give an opinion on each and every statistical topic.)

A further advantage from my point of view will be that it will eliminate a source of irritation. I resent the way in which certain persons who have never studied statistics set themselves up as statistical consultants. All too often such people are indeed incompetent, if for no other reason than that they underestimate the extent to which statistics is a difficult subject. I resent the way also in which some such persons have a tendency to sell the subject short: by suggesting that more subtle methods are unnecessary refinements and that statistics is a matter of simple common sense. Statistics is a matter of common sense but it is the subject of *advanced* common sense.

It would be wrong to suppose, however, that all persons who have not undergone a formal study of statistics are necessarily incompetent statisticians. Our science is young and although its modern foundations were laid only in this century or the last decades of the previous century, those who undertook this work, of necessity, had not studied statistics themselves. Some of them had not even studied mathematics. Edgeworth, for example was a barrister who studied classics and was self-taught in mathematics¹ and Student's major area of study was chemistry². Fisher, was of course, a mathematics wrangler at Cambridge³ but the extent to which statistics as a subject of study is a modern phenomenon may be judged by the fact that he never held a chair in statistics. Finally, as an example, of the importance of amateurs to the history of our science, we may cite Galton, who flirted with mathematics at Cambridge but found it too difficult and eventually took a poll degree (not honours) in medicine⁴. This did not stop him becoming a statistical amateur par excellence and discovering empirically the phenomenon of correlation (which he called regression).

How and why does all this affect ISCB? One way, certainly, is because of our interest in drug regulation. We are currently (via SEDREG) trying to persuade the commission of the EC to recognise the importance of statisticians to the drug regulatory process. But this begs the question "who or what is a statistician?". There is no debate as to who is a physician. Is it not a necessary prerequisite to having statisticians involved in drug regulation that we should have a means of defining such persons? Maybe a qualification such as CStat is not enough. Maybe we need to go further and define Medical Statistician as has, indeed, been done in Germany where the GMDS and the German region of the Biometric Society have developed a qualification which has been recognised by the authorities.

What I think on this issue is not important. What is important is what ISCB as a whole thinks. If you have an opinion on the subject, now is as good a time as any to write a letter to the editor of the *ISCB Newsletter*.

References

- 1 Stephen Stigler, *The History of Statistics*, Belknap Harvard, Cambridge Massachusetts, 1986.
- 2 Pearson, E.S. *'Student' a Statistical Biography of William Sealy Gosset* (Edited by R.L. Plackett and G.A. Barnard), Clarendon Press, Oxford, 1990.
- 3 Box, J. Fisher, R.A. Fisher, *The Life of a Scientist*, John Wiley and Sons, New York, 1978.
- 4 Forrest, D.W. *Francis Galton, The Life and Work of a Victorian Genius*, Paul Elek, London, 1974.

"European" FDA Workshop in Basel

Ruth Amstein, Julian A. Gray* and Fritz R. Bühler
ECPM, Department of Research, University Hospitals, Basel
and * Pharma Research Clinical, F. Hoffmann-La Roche Ltd. Basel

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The European Course in Pharmaceutical Medicine which is supported by funding from the European Community invited four FDA Directors from the Center for Drug Evaluation and Research (CDER) for a special Workshop at the Basel Convention Center on October 8, 1992. A total of 320 participants - delegates and faculty from the European Course in Pharmaceutical Medicine, staff from the pharmaceutical industry and regulatory authorities as well as members from universities - attended this excellent meeting on "Innovations in drug development and evaluation: The FDA perspective" with emphasis on new regulatory initiatives and harmonization. Professor Fritz R. Bühler, Head of Roche PRC and Chairman of the Board of the European Course in Pharmaceutical Medicine pointed out in his introduction that it was a European premiere and a rare opportunity to welcome four directors of the FDA together,

Reduced delay for NDA approval

Dr. Carl Peck, Director, CDER, opened the meeting by announcing that the delay for NDA approvals will be reduced to one year on average and six months for urgent cases. The FDA drug regulatory staff would need to be increased by 600 officials on the costs of the pharmaceutical industry. In particular FDA is interested to hasten the regulatory process for drugs treating serious life-threatening conditions i.e. fatal cancer or AIDS. This can be achieved by the **Subpart E Regulation** which requires early consultation with the agency who may contribute with their own research facilities to optimize the development program. **Accelerated approval regulation** may involve the use of **surrogate endpoints** (presumed markers of the drug's action). Approvals will be conditional and require post-marketing trials to establish the relationship between the surrogate endpoint and clinical efficacy.

New aspects in the early clinical phases of drug development are **individualization of dosage** taking into consideration different dosage schedules for women, elderly and ethnic subgroups and **informative clinical trial design**. The latter aims at reducing drug development time by setting up appropriate dose-response/ concentration-response studies and by early identification of pharmacokinetic/ pharmacodynamic interrelationships.

Placebo controlled trials are pivotal in the USA

The interpretation of active control trials can often be misleading, said Dr. Robert Temple, Director, Office of Drug Evaluation I, CDER, therefore a placebo control is inevitable to prove efficacy. However, active control trials are discussible in fields like duodenal ulcer, chemotherapy induced nausea and AIDS; they are clearly acceptable for infectious diseases, good responsive tumors and the development of NSAIDs. Placebo control is an issue of discussion in the international harmonization process since European authorities take a different position in diseases like depression taking into consideration ethical aspects.

Warning to perform interim analyses

Dr. Robert O'Neill, Director, Division of Biometrics, CDER, explained the activities of his division. They review the statistical methods, conclusions and interpretation of a submitted study. Their own research is aimed at critical trial issues like subgroup analyses and surrogate endpoints. A problem often confronted is interim analyses. They should be avoided unless ethically required in life threatening conditions since they bear risks like potential bias from early unblinding, premature study termination or overstatement of treatment effects. An interim analysis has to be defined prospectively in the protocol with the appropriate adjustments for loss of statistical power. Dr. O'Neill encourages the use of **meta-analysis** in particular for the interpretation of safety data or as supportive information for efficacy studies.

Harmonization in Post Marketing Surveillance (PMS)

Dr. Charles Anello, Acting Director, Office of Epidemiology and biostatistics, CDER, reviewed the growing area of PMS and pharmacoepidemiology. Reports on adverse drug reactions (ADR) have increased to a great extent during the past years. Between 1970-1980 the FDA received approximately 10,000 reports/year, in 1991 the number exceeded 80,000. ADRs must be quickly verified and the population at risk has to be identified. This often occurs under the observance and pressure of the public. The international cooperation of health authorities is best established in the field of ADR reporting using the channels of WHO and CIOMS (Council for International Organizations of Medical Sciences).

Biometry Fund

Marken, 4th May 1993

Dear Stephen,

The Biometry Fund is most grateful for the contribution of UK £100 received from ISCB in 1992. The enclosed brief annual report provides you with an impression of the progress made with the fund. Although its means are modest, the often heart warming responses show how much the work of the fund is appreciated by the recipients of the aid provided. However, the deserving causes that the fund cannot support for lack of money are reason enough to continue the efforts to sustain modest growth. It is our hope that ISCB will again be willing to provide support in 1993.

Yours sincerely,

Arend Heyting, Treasurer Biometry Fund, Moeniswerf 7-8, NL-1156DA MARKEN, Netherlands

BRIEF ANNUAL REPORT 1992

During 1992, the number of private donors remained relatively stable. The number of institutional sponsors grew to eighteen:

Astra Hässle AB
Agricultural University Wageningen
Agricultural Mathematics Group DLO, Wageningen
Avery Materials Group Europe
Biometric Society Netherlands Region
Centre for Biostatistics, Univ. of Utrecht
Dept. Medical Statistics, Leiden University
Dept. of Mathematics, Agricultural University, Wageningen
Erasmus Univ. Pub. Health & Soc. Med., Rotterdam
Hoffmann-La Roche
International Society for Clinical Biostatistics
Med. Stat. Section of the Netherlands Soc. for Stat.
Netherlands Society for Statistics and Operations Research
Organon International B.V.
PSI, Statisticians in the Pharmaceutical Industry
ROMERES: Rotterdam Medical Research Foundation
Solvay Duphar B.V.
Univ. of Nijmegen, Fac. of Med. Science, Med. Stat. Dept.

The annual income rose slightly to about US\$4000. The operational costs remained stable at US\$100 leaving 97.5% of income available to support worthwhile causes. The following paragraphs describe the aid that was provided (end of year exchange rates).

The Biometric Conference in New Zealand provided a good opportunity for biometricians in that part of the world to attend. The Biometry Fund contributed US\$1700 towards their travel expenses. An important event of the Biometric Conference was the invited session "Statistical Needs for Developing Countries" organised by Norman Goodchild, well-known for his work in the initiation of the Biometric Networks in S.E. Asia and Africa. This provided a unique opportunity to bring the biometrical problems in the developing countries to the attention of the international biometric community. The Biometry Fund paid US\$1200 of the organisational expenses.

A student of Zimbabwe received US\$1300 to complete his MSc studies at Diepenbeek, Belgium. Having obtained his degree, he has now started work in Zimbabwe.

Finally, the Biometry Fund acted as intermediary in finding an appropriate destination for the last 22 volumes of

JASA and Technometrics. These were donated by a Dutch biometrician, who will also pass on the newly appearing issues in the coming years. The generous donor delivered the journals personally to the Polish statistical institute where they are now a welcome addition to the library.

Looking towards the future, moves are on the way to install a board of trustees to help with the promotion of the Biometry Fund. Further discussions have been initiated with the Award Fund Committee of the Biometric Society, with the aim of improving international coordination of biometric aid to developing countries. Finally, the Biometry Fund has increased its efforts to establish a comprehensive network of local contacts with biometricians in the developing countries. All help with this is welcome.

In 1992 J. Jansen joined the board. The other members are J. Hermans (chairman), P.H. van Ewijk (secretary) and A. Heyting (treasurer).

P.H. van Ewijk, Secretary Biometry Fund, P.O. Box 900, NL-1380 DA Weesp, Netherlands
Biometry Fund Bank account number 34.31.20.550 at the Rabobank, Pr. Irenelaan 6, NL-1381 NA Weesp, Netherlands

ISCB Accounts

At the 1992 AGM in Copenhagen, it was asked if the members could have a statement of the society's accounts. The then treasurer, Doug Wilson, promised he would produce a statement up to the end of 1991. Unfortunately we are still waiting... This also has the unfortunate effect of making it impossible for Karsten Schmidt to produce accounts to the end of 1992. It is hoped that the situation can be solved in time for the next newsletter. Karsten will be able to produce accounts for the year to the end of 1993.

In contrast, the accounts for ISCB13-Copenhagen are now available:...



13 - Copenhagen

Preliminary¹⁾ Account of ISCB 13, Copenhagen 1992

<u>Income</u>	Total DKK ²⁾
Conference fees	754,075
Sponsor support	228,922
Exhibitions and adds	89,020
Interest, exchange gains, and commission	51,829
<hr/>	
	1,123,893
<hr/>	
<u>Costs</u>	
Administration	279,474
Conference facilities and consumptions	374,846
Postage, advertisement, and transportation	51,122
Conference materials	73,357
Travel and accommodation	135,280
Membership fees, 190 ³⁾ new members transferred to ISCB	26,697
<hr/>	
	913,793
<hr/>	
Net income ISCB 13	210,100
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1) Account not yet audited.

2) 1 DKK ~ 0.105 £ ~ 0.154 \$.

3) Participants who were not members of ISCB.

May 24, 1993

Susanne Møller
Treasurer, ISCB 13

Karsten Schmidt
Chairman of Organizing Committee,
ISCB 13

SEDREG: Progress Report

from Karsten Schmidt

The chairmanship of the ISCB Working Party on Statistics in European Drug Regulation (SEDREG) was passed to Professor John A. Lewis of Kent University in the Autumn of 1992. The ISCB is grateful to Professor Roel van Strik for his hard work in chairing SEDREG during its initial years.

The formation of an Executive Team of SEDREG was endorsed by SEDREG and ISCB Executive Committee (excom) at the Copenhagen conference. This four-person team was formed in November 1992. Besides John Lewis (JL) the team consists of David R. Jones (DJ), Professor of Medical Statistics, University of Leicester, U.K., Bernhard Huitfeldt (BH), Head of Biostatistics, Kabi Pharmacia Therapeutics AB, Sweden, and Karsten Schmidt (KS), President of Spadille Biostatistik ApS, Denmark. The individual remits of the team members are: JL chairman, DJ representative of academia and regulatory contact, BH representative of industry and contact to other statistical societies, KS representative of ISCB excom and CROs and contact to ISCB and SEDREG.

The Executive Team met on January 22, 1993, in London. Earlier initiatives of SEDREG were sorted out and the tasks reformulated as follows:

- 1) Continue to monitor the statistical expertise employed in or available to European Drug Regulatory Bodies, including the proposed European Medicines Evaluation Agency (EMA).
- 2) Establish the case for such statistical expertise and define the level and nature of the resources required.
- 3) Define, promote, and execute a strategy for achieving the said two objectives.

Although a precise time-scale was not fixed, it was agreed that SEDREG was supposed to work within a limited time frame.

Opportunities should be sought to use the media in order to promote people's perception about the need for statisticians in regulatory work. In this context hard evidence of adverse consequences of the current situation would be extremely valuable.

Since it was anticipated that details regarding the structure of the European Medicines Evaluation Agency would be decided soon, the Executive Team agreed to send as soon as possible a personal letter to CPMP and the other regulatory bodies with a brief summary of the RSS report on Statisticians in European Regulatory Agencies, along with the report itself. Support for the said letter should subsequently be sought from all relevant statistical societies in Europe and communicated to the CPMP when achieved.

The letter to CPMP was sent on February 12, 1993, and a reply from the Commission of the EC Directorate-General, International Market and Industrial Affairs (DGIII/C-3) was received on April 27, 1993. This reply says that the letter and report received *"were transmitted to the CPMP and to the CPMP's Working Party on Efficacy of Medicinal Products where the members noted them with great interest"*.

The letters to the individual EC Medicines Licensing Authorities were sent on April 29, 1993, and a reply was received on May 25, 1993, from Dr. A.W. Broekmans, Executive Director of the Medicines Evaluation Board of the Netherlands, saying that one of the members of the Marketing Authorization Granting Board is a statistician and that *"it is not envisaged that statisticians will be employed by the EMA"*. In a letter sent to Dr. Broekmans on June 3, 1993, the SEDREG Executive Team has asked for a clarification as to whether the said statistician acts as an adviser to a Government Department or as a Government employee. This letter also explains that the primary interest is *"to increase the number of statisticians employed on a full-time basis by Government Regulatory Agencies, routinely involved in the full regulatory review process, and available for dialogue with industry statisticians."* Further, it is stated, *"If it transpires that EMA does not employ technical experts for review purposes, then there is no case to be made for statisticians in this body. But this state of affairs would not be very satisfactory: Use of outside experts alone would impair communication with industry during the review process; consistency of approach may suffer. However, if EMA does employ some qualified reviewers, e.g. medically qualified personnel, then I think the case for statisticians is still open."*

Support from relevant statistical societies in Europe has been sought by a letter sent on May 7, 1993. Replies will be forwarded to the CPMP when received.

A SEDREG meeting is scheduled to take place in the evening of September 21 during the ISCB 14 conference in Cambridge.

Books and Software for Review

Books

The following books have been sent to my predecessor, Jørgen Seldrup, and are available for review. Please contact the editor if you would like one or more of them. Reviewers are allowed to keep the book(s) that they reviewed.

Wiley, London:

Senn SJ (1992)
Cross-Over Trials in Clinical Research

Marcel Dekker, New York & Basel:

Balakrishnan N (1992)
Handbook of the logistic distribution

Chow SC & Liu JP (1992)
Design and analysis of bioavailability
and bioequivalence studies

Cottman RJ (1993)
Total engineering quality management

Guarino RA (ed) (1993)
New drug Approval process

Kocherlakota S & Kocherlakota C (1992)
Bivariate discrete distributions

Lutz EW (ed) (1991)
Future demographic trends in Europe
and North America: What can we assume
today ?

Mathai AM & Provost SB (1992)
Quadratic forms in random variables:
Theory and applications

Peace KE (1992)
Biopharmaceutical sequential statistical
applications

Ratkowsky DA, Evans MA & Alldredge JR
(1993)
Cross-Over Experiments

Singer DC & Upton RP (1993)
Guidelines for laboratory quality auditing

Wang C (1993)
Sense and nonsense of statistical
inference: controversy, misuse and
subtlety

Software

"RANDOM v5.0", a commercially produced program for generating randomization lists and labels for a variety of designs has been sent to the editor for review by Dr. Wiedey GmbH, Konstanz, Germany.

It comes on a 3.5" or 5.25" diskette and runs only in German. A 20 page manual accompanies the disks and is also in German.

Since this is a commercial package (not shareware or public domain software), the reviewer will be offered the chance to purchase the program for a reduced price; normally it costs DM 625 (about £250).

Reminder

**International Society
for Clinical Biostatistics**



Fourteenth International Meeting

Cambridge UK 21-24 September 1993

For information about the meeting and the Society, please contact:

ISCB 14 Secretariat
Conference Contact
42 Devonshire Road
CAMBRIDGE CB1 2BL
ENGLAND - UK
Tel: +44 223 323437
Fax: +44 223 460396

NOTICE OF THE ANNUAL GENERAL MEETING 1993

The annual general meeting of the International Society for Biostatistics for 1993 will be held on the afternoon of Thursday 23 September 1993 starting at 16.00 in Lady Mitchell Hall, Sidgwick Site, Cambridge, UK. All members of the Society are hereby invited to attend.

Items for the agenda should be communicated in writing to the Honorary Secretary, Dr. Stephen Senn, Medical Department, CIBA-GEIGY, CH-4002 Basel, Switzerland by the 27 August 1993 or to him personally at the annual conference prior to the annual general meeting.

NOMINATIONS FOR THE INTERNATIONAL SOCIETY FOR CLINICAL BIostatISTICS

Nominations are sought for two places as members of the executive committee. For a nomination to be valid it must be received by the Nominations Committee and passed to the Honorary Secretary not later than 24 hours before the annual general meeting. Nominations must be accompanied by the name of the proposer and the seconder and the written consent of the nominee to stand for the said position. Professor Stephen Evans, Department of Epidemiology & Medical Statistics, London Hospital Medical College at QMW, Mile End Road, London E1 4NS, UK has agreed to act on behalf of the nominations committee. Nominations should be addressed to him.

Nominations are also sought for two persons prepared to audit the accounts of the Society and for one person prepared to serve as a member of the nominations committee.

Stephen Senn, Honorary Secretary

Guidelines

Members may be interested to know that PSI (Statisticians in the Pharmaceutical Industry) has produced guidelines for Good Statistical Practice.

EC-CPMP

Recently, the European Community has issued a "Note for Guidance on Biostatistical Methodology in Clinical Trials in Drug Licence Applications" (III/3630/92-EN, Draft 4, DE/UK, March 1993). Comments should be sent to CPMP before 15 November 1993.

At the ISI meeting to be held in Florence (25 August - 2 September), there will be a contributed papers session on "Global Harmonization of Good Statistical Practice in Clinical Trials". The session to be held on 1 September, 09.00-12.00, is organised by Dr. Satya D. Dubey of the FDA.

The following abstract is by Karsten Schmidt, an Executive Team member of the ISCB's SEDREG working party:

AN APPRAISAL OF THE PROPOSED STATISTICAL GUIDELINES FOR DRUG LICENSE APPLICATION IN THE EC

Karsten Schmidt
President, Spadille Biostatistik ApS
EFSPI Council Member
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The European Community Good Clinical Practice (GCP) Guidelines came into force in July 1991. These guidelines emphasize the necessity of experienced and appropriately qualified statisticians being involved in clinical trials in order to assure high quality allowing for an efficient and fast new drug approval process. However, the GCP guidelines do not give details as regards statistical methodology, and therefore preparation of a supplementary statistical guideline was initiated at the beginning of 1992. A proposal: "Guideline on Biostatistical Methodology in Clinical Trial in Drug License Applications" is now available for discussions, [having been formally released by the CPMP in May 1993]. Although experienced statisticians could have given valuable input during the long process of developing the proposal, it has been classified as confidential, and therefore specific comments must wait for the formal release.

For the experienced statistician who knows generally accepted appropriate statistical practice it may be important that a guideline expresses what the regulatory agencies prefer in complex and/or controversial areas, where an established appropriate practice is not agreed upon, without thereby excluding innovations and reasonable alternatives. To promote harmonization contradictions with other guidelines and international standards should be avoided.

The European Federation of Statisticians in the Pharmaceutical Industry (EFSPI) is an umbrella organization for 7 national European biostatistical organizations, having a total membership of more than 1000 biostatisticians with particular interest in the new statistical guidelines that are hopefully directed towards an audience of experienced biostatisticians in industry and regulatory agencies. Each member organization will discuss the new proposal, and at a full day meeting of the EFSPI Council Members the various views will be coordinated. This paper will summarize the views with special emphasis on the potential impact of the proposal on the global harmonization process. In addition, the paper will address other key issues important for the harmonization of statistical practice such as e.g. the need of having statistical expertise within the European regulatory agencies for providing statistical review, dialogue with and feedback to industry statisticians, a need that will pertain regardless of any guidelines as currently debated in the ISCB Working Party on Statisticians in European Drug Regulation (SEDREG).

Other potential problems regarding harmonization from the industry statisticians' perspective will be identified and discussed.

Résumé

Cette présentation résumera le point de vue de la Fédération Européenne des Statisticiens de l'Industrie Pharmaceutique (EFSPI) sur un projet de texte intitulé "Recommandations sur la méthodologie statistique des essais cliniques réalisés pour les demandes d'enregistrement des médicaments". Il s'agira tout particulièrement d'évaluer l'impact potentiel de ce texte sur le processus d'harmonisation des pratiques dans le domaine des essais cliniques, processus actuellement en cours. D'autre part, des points considérés comme très importants, relativement à l'harmonisation des pratiques proprement statistiques, seront également discutés.

RANDOM HARVEST

A Muesli of Quotations Culled by Guernsey McPearson
(First helping)

In support of the role of doubt in experimentation (survival analysis in this case): *When a duel begins it is supposed that there may be equality; because it is not always skill that prevails.*
Samuel Johnson

On medicine and the quality of life: *C'est une ennuyeuse maladie que de conserver sa santé par un trop grand régime.* (Free translation: *a slavish concern for one's health is itself a troubling illness.*)
La Rochefoucauld

The trialist's philosophy: *Faithfully we experiment, assuming that death is a still undetected virus.*
Robert Graves

On transforming data. *The Fraction of Life can be increased in value not so much by increasing your Numerator as by lessening your Denominator.*
Carlyle (Sartor Resartus)

On trials whose size has been determined on practical grounds. *Nothing will come of nothing.*
Shakespeare (King Lear)

On statistics and measuring the quality of life: *A calculation of consequences is no more equivalent to a sentiment, than a seriatim enumeration of square yards or feet touches the fancy like the sight of the Alps or Andes.*
Hazlitt

On the logical superiority of mathematics compared to biology: *God can make an ass with three tails but not a triangle with four sides.*
Paracelsus

The statistics of balding ?
*Thy sinnes and haire may no man equal call
For as thy sinnes increase thy haire doe fall.*
Donne

In praise of data bases: *La mémoire est nécessaire pour toutes les opérations de la raison.*
(Free translation: *Logic requires memory*)
Pascale

Do you find statistics difficult ? *The cause of obscurity and confusion in the mind of man is threefold. Dull organs, dear sir, in the first place. Second slight and transient impressions made by the objects, when the said organs are not dull; and, Thirdly a memory like unto a sieve.*
Sterne (Tristram Shandy)

On perfect balance:
*Intra due cibi, distanti e moventi
d'un modo, prima si morria di fame,
che liber uomo l'un recasse ai denti.*

*(Between two foods distant and appetising
in like measure, a free man would die of hunger
ere he put either to his teeth.)*
Dante (Il Paradiso)

Why every statistician should remember to show respect to the medical profession
*For there was never yet philosopher
That could endure the tooth-ache patiently
However they have writ the style of gods
And made a push at chance and suffering.*
Shakespeare (Much Ado About Nothing)

Organise an ISCB Conference ? Yes, no problem.

Simon Day

The editor asked me to fill a page or three of this Newsletter with some information about this year's conference. Given that you should have already received at least one copy of the Call for Registration before now - and there is another copy enclosed with this mailing I thought that rather than just put in a page of advertising, you might like to hear of some of the fun and games that have gone into trying to get the thing together.

It was Stuart Pocock's big idea in the first place and, to my mind, he has got a lot to answer for. Especially when he declined to be on the Organising Committee, preferring instead to suggest to me in a very flattering way that it was a job better suited to 'a younger man'. Very flattering indeed, Stuart, but my few remaining hairs are going grey ! Anyway, I started things off by contacting a few conference organising companies. This is a delicate operation. You have to ask them to put forward their plans for a conference whilst explaining that you have not got any money to pay them and that the ISCB Executive Committee may even decide that they don't want the conference in this country after all. I guess that is a common problem such companies face and I must say I got very helpful comments from several of them.

I first met the people at 'Conference Contact' in April 1991 although my first contact with other companies was back in November 1990 (nearly three years ahead of time ! In that April, we made a provisional booking (i.e. one that does not cost anything!) for the conference rooms in the Sidgwick Site at Cambridge after a long walk around many options. Booking a room that will seat 500 and has nearby parallel rooms that seat about 150 each is not easy. In April 1991, we booked the only set of such rooms that Cambridge had available throughout June - October 1993. This is how far in advance everyone else is booking up their conferences so it is obviously important to get going well ahead of time.

It was at this time that I began to panic. Were the rooms suitable ? Was the cost reasonable ? Were the fees being charged by the organising company reasonable ? I needed to share the blame for things so appointed the infamous Local Organising Committee. 'Local' is merely a relative term. It means 'based in the same country as the conference will be held'. So who have we got ?

Deborah Ashby said she 'might' be able to help - so I took that as a 'Yes' and asked her to keep an eye on the financial side of things. The budget for the meeting is about £125,000 (excluding accommodation costs) so a constant supply of batteries in her calculator are essential.

Tony Johnson said there are lots of statisticians based in Cambridge so it would seem reasonable that some help should be offered to the organisers. Got him too ! He is helping me out by providing 'local insight'. He has got a fair idea about where different places are in relation to each other so can offer some advice and confirmation about suitability of conference rooms and accommodation etc. (I live about 150 km from Cambridge and only get there about once a month.)

Alan Phillips does a lot of work for the organisation PSI (Statisticians in the Pharmaceutical Industry) in organising their short courses. He must have about twenty course texts sitting on his book-shelf so I gave him a call and asked him what he could come up with. 'International Society of who ?' he asked. But his enthusiasm and willingness came through and he agreed to help. I think we have a really interesting and popular group of courses that will appeal to pharmaceutical and academic statisticians. The choice of putting them on the day before the conference rather than the day after was purely driven by availability of rooms but I hope that many of you will feel an extra day in Cambridge could be worthwhile and support these courses.

Organise an ISCB Conference (continued)...

And then there is me. I once heard someone say that the chairman of anything shouldn't have to do too much - just make a lot of noise and enthuse others to do things. Maybe I don't delegate enough..... I certainly get everything done by my team (of 'younger men') that I ask of them..... but I still end up with A LOT to do.

Of course, no-one cares about the things that go on behind the scenes. What everyone really wants to know about is the scientific programme. I'm not sure how Doug Altman's name got put forward. That may have been engineered into the same conversation I originally had with Stuart Pocock. When I asked Doug if he would chair the Programme Committee he was not sure. He had all sorts of other commitments and wanted to think about it for a while. A while later I found some excuse to call him and broached the subject again. His response was something like '... of course I'll do it. I really ought to say "No" but you know how it is with these things'. 'Good', I thought: Got him ! We started talking about who should be on the Scientific Programme Committee and I said that it was important that there is close liaison between him and the Organising Committee. 'Right', he said, 'you walked into that one, didn't you ?'. I was his first recruit.

Doug and I pondered friends, enemies and useful contacts. Choosing a committee to work with is a great way to regain contact with past colleagues or to get to know people better with whom you have never had much to do with but have often wanted to work. We were biased towards the UK simply because the conference is to be held here, but were also conscious of trying to get good international representation (a point that proved particularly important later on). Unlike the Local Organising Committee, I cannot begin to describe the process by which each name was decided upon - it was a very multivariate decision - but the list we ended up with is as follows: Doug, myself, Per Kragh Andersen, Mike Campbell, Giuseppe Gallus, Nancy Geller, David Machin, Martin Schumacher, Stephen Senn, Hans Wedel and Andreas Zipfell.

Deciding on topics was the first task of the Programme Committee whilst the Organising Committee was frantically trying to get the Call for Papers finalised and distributed. We needed to decide on themes to publish there. That was not so difficult, although a lot of care and thought was put into it. Having recently made a move from academia to industry I am acutely aware of the different needs and interests of the two groups and wanted to ensure the Conference would be equally interesting to both groups. Hence, we picked topics such as Statistics, Medicine and the Law. This is important in public health issues and in pharmaceutical liability cases, as well as simply being fascinating in its own right. We picked the topic of Measurement and Evaluation of Risk Factors which is important to epidemiologists and clinical trialists alike. Each topic was carefully thought about and we hope virtually all of them will be useful to all delegates - and if not directly useful, then certainly very interesting.

Deciding on who to invite was difficult. Again, a very multivariate decision: trying to balance countries (and hence potential travel costs) was important. Naturally, some topics had dozens of potential speakers, others very few. Here we have made a great deal of use of the Programme Committee members. They are the ones who know best about the people in their countries - or are in a position to find out - so there were a lot of faxes back and forth between the various Committee members regarding specific individuals.

We also wanted to wait for some of the submitted Abstracts to arrive to see what you wanted to talk about. A couple that arrived early and looked particularly interesting we reviewed and considered worth 'upgrading' to invited papers. Maybe if next year's organisers do the same it will be an incentive to submit early. The Local Organisers were, meanwhile, busy preparing the Call for Registration and wanted as much detail of the programme and invited speakers as was possible from the Programme team.

Organise an ISCB Conference (continued)...

Waiting for the Abstracts to arrive in the post was a little nerve-wracking. You may recall the deadline for submissions was 1st March.... by the first week of February we only had five Abstracts submitted ! Where were you all ? We have ended up with about 130 in total, many of which will have to be rejected through lack of time in the programme. This is the wrong reason for rejecting some very good and interesting work. But I don't think I could organise a ten day conference !

Doug has sent each of the Abstracts to two of the Programme Committee to review and make a recommendation. In addition, he and I have each read them all and formed opinions. How did we decide which to accept and which to reject ? It will be difficult not least because it is not simply a question of ranking them on scientific merit. We need a balance in the programme and we feel inclined towards a variety of presenters rather than the same faces cropping up too often: so if you are one of the people who submitted a handful of Abstracts, thanks, but I expect we will not accept them all - however good they are.

So what next ? My hope is that things should go quiet for a while now. All that should happen is that your cheques should start arriving stating your willingness and enthusiasm to attend the conference. I would put in a plea for you to register early. At the very least it will help tremendously with cash flow. We have already received over £5000 in sponsorship money and 'borrowed' over £10,000 from the Society - and spent the lot ! So before we have to borrow much more, some of your registration fees would really help.

Apart from waiting to receive money from you, our next task is to prepare and print the final timetable of sessions and the programme with all the Abstracts and additional information. We have used previous years' publicity material as a guide to what we should produce and I suspect we will use the layout and style of previous Programmes to design ours. The proof reading is a task that I do not relish.

So that is about all there is to it, really. Why not offer to organise one yourself ? You don't have to wait until you are asked. You get to know lots of people although it does take up a lot of time. Sufficient time, in fact, that I need to put in a big 'Thank You' to my boss for supporting me throughout all of this (promise I'll do some work next year !) and my wife (promise I'll decorate the house next year! Thanks also go the rest of my Local Organising Committee, the Programme Committee and all their respective employers who are supporting them by giving their time. Further thanks to Peter, Cathy and the other staff at 'Conference Contact'.

And finally, it is not too early to acknowledge the sponsorship being offered to us (cash or otherwise) by Lilly Research Ltd, PSI (Statisticians in the Pharmaceutical Industry), Roche Products Ltd, The Royal Statistical Society, Scotia Pharmaceuticals Ltd, Spadille Biostatistik ApS, Sterling Winthrop Research and The Wellcome Foundation. I shall repeat these words of thanks as often as I feel I can get away with it. Until we know how many people plan to attend the meeting, we cannot know how much to charge. If we do not make the break-even number of participants then the Conference will make a loss and ISCB will have to make up the difference. That would be embarrassing ! If anyone else who reads this works for a company who may wish to offer some kind of sponsorship to the meeting then I would be very pleased if you called me to discuss any options.

I hope to see as many of you in Cambridge as are able to come.



Membership Information

THE INTERNATIONAL SOCIETY FOR CLINICAL BIostatISTICS

The International Society for Clinical Biostatistics (ISCB) was founded in 1978 to stimulate research into the principles and methodology used in the design and analysis of clinical research and to increase the relevance of statistical theory to the real world of clinical medicine.

The ISCB organises an annual scientific meeting which members and non-members are able to attend. The main objective of the annual scientific meetings is to create an opportunity for the exchange of knowledge, experience and ideas among clinicians, statisticians and members of other disciplines, such as epidemiologists, clinical chemists and clinical pharmacologists, working or interested in, the field of clinical biostatistics.

The scientific meetings cover a broad spectrum of biostatistical interests and regularly include sessions on the design and analysis of clinical trials, epidemiology and statistical methodology, as well as from time to time considering more specialist issues such as, for example, education of biometricians and biometrics users, pharmacokinetics, medical data-bases and pharmacoepidemiology. Each meeting includes a mini-symposium devoted to a particular medical or statistical field. Recent examples have been Organ Transplantation, Regulatory Affairs in Europe and North America and Quality of Life.

Previous meetings in recent years have been held in Cardiff (1986), Gothenburg (1987), Innsbruck (1988), Maastricht (1989), Nimes (1990), Brussels (1991), Copenhagen (1992). The 1993 meeting will be held in Cambridge and Basel will play host in 1994.

The proceedings of these scientific meetings are published in *Statistics in Medicine*. The ISCB benefits from a special journal concession from John Wiley & Sons Limited, the publishers of *Statistics in Medicine*, so that members are able to subscribe to the journal at preferential rates.

The ISCB also organises courses to cover particular statistical topics. These are run to precede or follow on from the annual scientific meeting and are given by the foremost researchers in the field. Recent courses have included Non Parametric Methods in Medical Research, Decision Analysis in Early Phase Drug Trials, Analysis of Longitudinal Data, Martingales in Survival Analysis, Issues in the Design of Clinical Trials.

The annual general meeting of the ISCB is organised to coincide with the scientific meeting. Membership of the Society is drawn from over 25 countries worldwide and the number of members is over 550.

The current composition of the executive committee is as follows: President, Dr Jørgen Seldrup (France), Past President, Professor Claude Chastang (France), Vice-President, Dr Marc Buyse (Belgium), Treasurer, Dr Karsten Schmidt (Denmark), Honorary Secretary, Dr Stephen Senn (Switzerland), Newsletter Editor, Dr David Warne (Switzerland). and Members, S Day (UK), Dr E Gehan (USA), Professor J van Houwelingen (Netherlands), Dr B Huitfeldt (Sweden), Dr A Johnson (UK), Professor W Köpcke (Germany), and Dr M Valsecchi (Italy).

The ISCB also has special working groups dealing with particular aspects of biostatistics. A particular focus in recent years has been statistics in drug regulatory affairs. The chairman of the ISCB working party on Statistics in European Drug Regulation (SEDREG) is Professor John Lewis of the Institute of Mathematics and Statistics, University of Kent, Canterbury, CT2 7NF, UK.

The Society publishes a newsletter twice a year. The current editor is Dr David Warne, CIBA-GEIGY, Medical Department, K-490.3.32, CH-4002 Basel, Switzerland. Items for inclusion in the Newsletter should be sent to him.

Membership of the Society is open to all with an interest in biostatistics. The current annual (to 31 December 1993) Ordinary membership fee is £15. The Full-time Student Membership fee is £7.50. Members can also choose to receive *Statistics in Medicine* at a reduced cost.

Applications for membership should be addressed to:
The Treasurer ISCB, Dr Karsten Schmidt, Spadille Biostatistik ApS,
NW Gadesvej 4, DK-3480 Fredensborg, Box 25, Denmark.

INTERNATIONAL SOCIETY FOR CLINICAL BIostatISTICS

1993

MEMBERSHIP SUBSCRIPTION

Surname Initials Occupation (please tick):
Title (Prof./Dr./etc.) Post held Statistician
Business address Medical Doctor
Both
Neither
Postal code and country

SUBSCRIPTION: £ 15.00 Ordinary membership of ISCB (to December 31, 1993).
(please tick one only) £ 7.50 Full-time Student Membership of ISCB (to December 31, 1993).
£ 110.00 Ordinary Membership of ISCB (to December 31, 1993) +
subscription to *Statistics in Medicine*, 1993.

Payment is made by:

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Card Number (13 or 16 digits) Expiry date

The following cheques, made payable to the *International Society for Clinical Biostatistics*, are acceptable:
A British Bank cheque, a Sterling Eurocheque, or any cheque drawn in Sterling and payable in London on a named London Bank.

This form is to be sent to the ISCB Honorary Treasurer at the following address:

Karsten Schmidt,
Spadille Biostatistik ApS,
N.W. Gadesvej 4,
P.O. Box 25,
DK-3480 Fredensborg,
Denmark.
Phone: +45 42 284100,
Fax: +45 42 284200.



*First announcement of ISCB-15
in Basle, Switzerland*

The fifteenth meeting of ISCB will take place 25-28 July 1994 in Basle. In addition a course day on 29 July is envisaged. The programme Chairperson is Amy Racine. The members of the Local Organising Committee are Jakob Schenker, Uwe Ferner, Walburga Rieser, and Stephen Senn.

Beside the scientific programme of the conference there are other good reasons to attend the congress. The Swiss city of Basle is located on the upper Rhine and has borders with France and Germany. The old city with its Middle Ages character is a charming place, especially in summer, and it is a good starting point for excursions to other parts of Switzerland as well as to France and Germany. With its airport (only 6 km from the centre) and its excellent railway connections it offers good possibilities for travelling.

Basle was founded 2000 years ago by the Romans and became the centre of the upper Rhine region. With its university, founded in 1460, its fair and congress centre, its advanced chemical and pharmaceutical industry and its French and German neighbours, Basle has developed an approach of international openness. Basle is also proud of its place in the history of statistics and of medicine: Paracelsus and James Bernoulli were here. We hope that you too will be amongst us at ISCB-15 and form part of the continuing association of the city with these two subjects.

Barl or Barzel ?
Brushing up your Pronunciation for ISCB 15
Stephen Senn

People tend to get rather confused in pronouncing the name of this city on the Rhine. The situation is, however, perfectly simple. *Barl* is the pronunciation to be used when speaking English and (approximately) when speaking French. The spelling in these two languages is Basle (English) and Bâle (French). In German the spelling is *Basel*, pronounced *Barzel* (In this phonetic representation the letter z should be pronounced in the English way.)

There is an increasing tendency amongst English speakers to pronounce the city in the German way. This is not very complimentary. Provided that a place is important enough English speakers always pronounce things in an English way. Nobody says *Paree* for *Paris* except when joking and I bet that all of you who attended ISCB13 (even Jørgen Seldrup and Karsten Schmidt) described themselves (when speaking English) as being in Copenhagen.

So, if you want to pay the locals a compliment, say *Barl* not *Barzel*. After all we like to regard ourselves as being citizens of Switzerland's second city and the rivalry for this status is with Geneva. Now hands up all of you who say *Genève* when speaking English.

(Editorial Note: S.Senn is a Swiss statistician who sounds more English than most English people. This insistence of Anglicising place is rather strange to the English editor who would prefer to use the local place names !)

The Fourth International Conference on Teaching Statistics

ICOTS 4

*25-30 July 1994
Congress Palace
Marrakech, MOROCCO*

For further information, write to:

Mr. EL GHAZALI Abdelaziz
Chairman of the Local Organizing Committee
I.N.S.E.A.
P.O.Box 6217, Rabat- Instituts,
Rabat, MOROCCO

or

Prof. Y. Escofier
Chairman of the Programme Committee
Université Montpellier II,
Science et Technique du Languedoc,
Place E Bataillon
F-34095 Montpellier
Cédex 5, FRANCE

CALL FOR PAPERS

The International Statistical Institute (ISI) and l'Institut National de Statistique et d'Economie Appliqué (I.N.S.E.A.) are pleased to announce that the **Fourth International Conference on Teaching Statistics** will be held in Marrakech, Morocco, from 25-30 July 1994.

The main objectives of the Conference are:

promoting the exchange of ideas about teaching materials, methods and content
fostering international co-operation amongst teachers of statistics.

The programme will include invited lectures, contributed papers and working groups.

People who are intending to present a paper or take part in a working group should get in contact with the organiser before 30th December 1993. After this date, and until 31st May 1994, additional contributed paper proposals may be sent to the chairman of the Programme Committee. The abstract should be limited to a single A4 page before being submitted for acceptance. A proceedings document will be available at the beginning of the conference. It will include abstracts of contributed papers and texts (8 pages) of the invited papers.

ISCB Advertising Rates

The current costs are:

Full A4 page: £180

Half A4 page: £100

Quarter A4 page: £ 60

Additionally, we will include loose flyers with the distribution of the newsletter at an initial handling cost of £25. However, if the addition of the flyer(s) increases the postal charges, the advertiser will also be charged the difference in distribution costs. For further information, please contact the editor.

Calendar

5-9 July 1993	Leuven, BELGIUM
8th International Workshop on Statistical Modelling Info: E. Lesaffre, Biostatistical Centre, UZ St. Rafael, B-3000 Leuven, BELGIUM. Tel: +32 16 336896, Fax: +32 16 336663	
17-20 August 1993	Innsbruck, AUSTRIA
International Symposium on Statistics with Non-Precise Data Info: Prof. R. Viertl, Institut f. Statistik u. Wahrscheinlichkeitstheorie, Technische Universität Wien, A-1040 Wien, AUSTRIA.	
24 August - 1 September 1993	Montreal, CANADA
22nd General Population Conference Info: International Union for the Scientific Study of Population, rue des Augustins 34, B-4000 Liège, BELGIUM. Tel: +32 41 224080, Fax: +32 41 223847	
25 August - 2 September 1993	Firenze, ITALY
49th Session of the International Statistical Institute Info: ISI-Firenze'93, c/o CMO-Newtours, I-50144 Firenze, ITALY. Tel: +39 55 366969, Fax: +39 55 333505 [including on 1 Sep., 09.00-12.00: a contributed papers session on "Global Harmonization of Good Statistical Practice in Clinical Trials".]	
29 August - 1 September 1993	Washington, USA
9th International Conference on Pharmacoepidemiology Info: International Society for Pharmacoepidemiology, University of Kansas Medical Center, Department of Preventative Medicine, 3901 Rainbow Boulevard, Robinson 4004, Kansas City, KS 66160-7313, USA.	
6-7 September 1993	Paris, FRANCE
International Meeting on Statistical Methods in Biopharmacie Info: D.Serrurier, Laboratoires CIBA-GEIGY, 2&4 rue Lionel Terray, F-92506 Rueil Malmaison, Cédex, FRANCE.	
12-15 September 1993	Bristol, UK
PSI Annual Conference Info: PSI Executive Secretary, P.O. Box 37, Ely CB6 3XY. ENGLAND-UK. Tel: +44 353 648740	
21-24 September 1993	Cambridge, UK
14th Meeting of the International Society for Clinical Biostatistics Info: ISCB 14 Secretariat, Conference Contact, 42 Devonshire Road, Cambridge CB1 2BL, ENGLAND - UK. Tel: +44 223 323437, Fax: +44 223 460396	
25-27 April 1994	Edinburgh, UK
5th European Workshop on Statistical Methodology in Clinical Research and Development Info: S.Senn, CIBA-GEIGY, CH-4002 Basel, SWITZERLAND.	
25-30 July 1994	Marrakech, MOROCCO
ICOTS-4: The Fourth International Conference on Teaching Statistics Info: ISI Permanent Office, 428 Prinses Beatrixlaan, P.O. Box 950, NL-2270AZ, Voorburg, NETHERLANDS. Tel: +31 70 3375737, Fax: +31 70 3860025	
8-12 August 1994	Hamilton, CANADA
17th International Biometric Conference Info: IBC Local Organising Committee, Dep't of Mathematics and Statistics, McMaster University, Hamilton, Ontario L8S 4K1, CANADA. Tel: +1 416 5297070, Fax: +1 416 5220935	
14-16 September 1994	Newcastle-upon-Tyne, UK
RSS International Conference Info: I.J.Goddard, Executive Secretary, Royal Statistical Society, 25 Enford Street, London W1H 2BH. ENGLAND-UK. Tel: +44 71 7235882, Fax: +44 71 7061710	