Dear Professor Jelliffe,

Your idea for the organization of an International IMIA Conference on the "Use of Pharmaco-kinetic and Pharmacodynamic Modeling for Optimal Drug Therapy", which you addressed to Dr. Marion Ball on March 18th, 1991, has received a favorable reply from the Board of IMIA.

Hereby enclosed you will find some general guidelines and recommendations for IMIA Meetings which might help you in the planning of your meeting.

I am convinced that you will be able to come up with an interesting programme and set of speakers. Your proposal has to be approved by the Board which will meet in Washington DC on November 15-16th, 1991 just preceding SCAMC.

Sincerely Yours,

Prof. Dr. Jos L. WILLEMS
President of IMIA

cc. : Dr. Marion Ball
Prof. Dr. R. Salamon
Dear Professor Jelliffe,

As a follow-up of my letter dated April 15th, I am sending you hereby a copy of the latest IMIA Information Bulletin in which you can find the membership list of IMIA from which you should solicit participation and representation in order to make your conference a truly international event.

I look forward to receiving from you a carefully worked out plan indicating the scientific contents of the Conference, the proposed venue and funding to carry out this mission.

Please, use the IMIA guidelines which were enclosed with my letter of April 15th to draft this plan.

Your proposal should reach me by August 1st at the latest, since it has to be circulated to the IMIA Board in preparation of their meeting prior to the AMIA/SCAMC meeting in Washington DC, on November 15, 1991.

We very much want to welcome you to work very closely with us, and look forward to adding your working conference initiative to our IMIA Agenda.

Most Sincerely,

Prof. Dr. Jos L. Willems
President of IMIA
Dear Dr. Jelliffe,

I have well received your FAX of August 12th, 1991. I was pleased with the progress you have made.

Your idea of an Open Conference is quite reasonable and will increase general interest in the subject.

I will ask Prof. J.H. van Bemmel, whether Elsevier Science Publisher - North Holland would not be interested in publishing the Proceedings.

To this end the computer application aspects will have to be put more in the forefront, I believe.

Sincerely Yours,

Joël L. WILLEMS, M.D.
President, IMIA

cc. : Prof. dr. ir. J.H. van Bemmel
    Dr. Marion Ball

This three-hour workshop will be directed toward physicians, clinical pharmacologists, and clinical pharmacists with an interest in Medical Informatics and in the study of drug behavior and its application to individualized drug therapy.

This workshop will be organized jointly by Roger W. Jelliffe, M.D. of the Laboratory of Applied Pharmacokinetics of the University of Southern California School of Medicine (phone 213/342-1300, fax 213/223-7474), and Pascal Maire, Pharm.D., Chief of Pharmacy at the Hospital Antoine Charial, Hospices Civils de Lyon, France (phone 011-33-78-346161, extension 3393, fax 011-33-78 346161, extension 3326). The workshop, designed for 30 - 50 participants or more, will include informal presentations of key concepts necessary to the understanding of the kinetic behavior of drugs and the utilization of these concepts in the individualization of drug dosage regimens for patients. In addition, demonstrations of software used in the management of common clinical problems in this area will be provided. Participants will also be encouraged to attend the continuation of this workshop at the above satellite conference in Lyon.

Key Concepts. Dr. Roger Jelliffe

1. An Introduction to Pharmacokinetic Models
2. Accommodating the Model to Changes in Renal (and other) Function. The Use of ClinicalDescriptors.
3. Fitting the Model to Serum Level Data. The Use of Bayes' Theorem.
4. Selection of Therapeutic Goals
5. Achieving them by Adaptive Control of the Model.

Demonstration of the USC Software. Dr. Jelliffe and Dr. Pascal Maire

6. Application to Aminoglycoside and Vancomycin Therapy
7. Application to Lidocaine and Digitalis
8. Application to Cancer Chemotherapy, and to Control of Large Pharmacodynamic Models

Participants are also encouraged to attend the IMIA - ADCAPT - FIP - USC satellite working group conference in Lyon, France, on September 21 - 23, 1992, to obtain further practical experience with the software.
Part II - A Three-Day Satellite Working Group
Conference on Clinical Applications and Advanced
Research Concepts in Pharmacokinetics, in Lyon,
France, at the Claude Bernard University,
September 21 - 23, 1992

Monday, September 21, 1992 An Introduction for New Participants

Morning: Key Concepts and Demonstration.

9:00 AM - Registration
9:30 AM - Welcome and Introductions - Dr. Roger Jelliffe
1. Individualizing Drug Therapy: an Overview.
2. Setting Individualized Therapeutic Goals.
to Individualizing Drug Dosage Regimens?
4. What structural type of Pharmacokinetic Model?
5. Estimation of Creatinine Clearance.
6. Determining the Assay Error Pattern.
7. The Bayesian Fitting Procedure.

11:00 AM - Break

11:15 AM - More Concepts - Dr. Jelliffe
8. Optimal Times to Obtain Serum Levels.
9. Nonpharmacokinetic Sources of Error in Drug Therapy. Contributions of the
Ward Care, the Pharmacy, the Laboratory, and the Phlebotomy Service.

12:00 Noon - Demonstrations of the Programs - Dr. Pascal Maire
1. The Amikacin Program. Planning the Initial Regimen.
2. Entering past doses and levels. Fitting the data.
3. Editing and Resaving past data.

1:00 PM - Lunch

Afternoon: Hands-on Use of the Software

2:30 PM - The Amikacin Program
Case 1. Setting Therapeutic Goals. Developing the Initial Regimen - Dr. Maire.
Case 2. Entering past data and Fitting it - Dr. Maire.
Case 3. Editing and Updating a past data file - Dr. Maire.

3:15 PM - Break

3:30 PM - Beginning the MB program for general Modeling with Bayesian fitting.
Vancomycin Therapy:
Case 1. Developing the Initial Regimen
Use of Dosing Option #9 - Dr. Maire
Case 2. Entering, Storing, and fitting Vancomycin data - Dr. Maire
Devise, manage, and discuss your own cases. Dr. Jelliffe
Review and Questions - Drs. Jelliffe and Maire

4:45 PM - Review and Discussion. Drs. Jelliffe and Maire.

5:00 PM - Adjourn
Tuesday, September 22, 1992
New Things for Old Users of the USC Software

Continuing with the Clinical Software

8:30 AM - Registration
9:00 AM - Introduction: Estimation of Variability. Use of Population Models: Types of Bayesian Priors. Control of Patient Variability: Bayesian Posteriors and their Control by Individualization of Dosage Regimens. Dr. Jelliffe
9:30 AM - Use of 2 - Compartment Models in Clinical Therapeutics: Dr. Jelliffe Problems with Traditional Approaches. Application to Lidocaine and Digitalis.
10:00 AM - Lidocaine: Controlling the Central Compartment. Dr. Jelliffe
Case 1. Developing the Initial Regimen. Use of Dosing Option #5. Case 2. Entering, Storing, and fitting Lidocaine data.
10:30 AM - Digitalis: Controlling the Peripheral Compartment for Digoxin and Digitoxin. Case 1. Developing the Initial Regimens. Use of Dosing Option #6. Dr. Jelliffe

11:00 AM - Break

Modeling of Population Pharmacokinetic and Pharmacodynamic Behavior
11:15 AM - Demonstration of the NPEM Program for Population Modeling in your Center. An Example using Routine USC Clinical Amikacin Patient Data Files. Dr. Maire
11:45 AM - Parameter Estimation, Model Simulation, and Effect Models in Clinical Research
12:15 PM - Demonstration of the BOXES Program for Making a PK Model
Making a PK - PD Effect Model
Example: A Model of Hematologic Toxicity. Dr. Jelliffe

1:00 PM - Lunch

2:00 PM - New Clinical Applications. Dr. Roger Jelliffe, Chairperson
2:00 PM - Adaptive Control in Cancer Chemotherapy of Childhood Leukemias. Dr. John Rodman
2:30 PM - Adaptive Control in Chemotherapy of Infectious Disease. Dr. George Drusano.
3:00 PM - Optimal Adaptive Control of Pharmacodynamic Effects with Aminoglycoside Antibiotics. Dr. Rodolphe Garraffo.
3:30 PM - Pharmacokinetics of Cyclosporine. Dr. Brian Whiting

4:00 PM Break

4:15 PM - Oral Presentations of Work by USC Software Users. Dr. Bruno Lacarelle, Chairperson
4:15 PM - A Selected Oral Presentation from a Current User
4:30 PM - A Selected Oral Presentation from a Current User
4:45 PM - A Selected Oral Presentation from a Current User
5:00 PM - A Selected Oral Presentation from a Current User

5:15 PM - An Evening Poster Session of Work by USC Software Users.

7:00 PM Adjourn

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AN EVENING GET-TOGETHER
IN OLD LYON! (To be announced)
**********************************************************************
Wednesday, September 23, 1992.

Estimation of Population Variability.
Dr. Jean-Louis Brazier, Chairperson

9:00 AM - Welcome and Introductions - Dr. Brazier
9:05 AM - Why Make Population Models? Why are Population Models and Bayes' Theorem Relevant to Drug Development and to Individualizing Drug Dosage Regimens?
Dr. Jelliffe
9:15 AM - Population Modeling with the NONMEM program. Dr. Lewis Sheiner
10:00 AM - Hierarchical Bayesian Approaches to Population Modeling. Dr. Adrian Smith

10:45 AM - Break

Estimation and Experimental Design
Dr. France Mentre, Chairperson

11:00 AM - Nonparametric Maximum Likelihood Population Modeling. Dr. Alain Mallet
11:45 AM - Nonparametric EM algorithms for Population Modeling. Dr. Alan Schumitzky
12:15 PM - Optimal Experimental Design and Therapeutic Drug Monitoring. Dr. Luc Pronzato

1:00 PM - Lunch

Adaptive Control of Dosage Regimens
Dr. Jean-Pierre Boissel

2:00 PM - Adaptive Control Using the Theory of Optimal Command. Dr. Athanasios Iliadis
2:30 PM - Adaptive Control of Large Kinetic and Effect Models, with Side Constraints. Dr. Schumitzky

3:00 PM - Break

Optimal Adaptive Control
Dr. Alain Venot, Chairman

3:15 PM - Multiple Model Adaptive Control and Approximate Optimal Closed-Loop Control of Drug Regimens. Dr. Mark Milman
4:00 PM - Optimal Adaptive Control and Monitoring Strategies by Iterations in Policy Space. Dr. David Bayard
4:30 PM - Panel Discussion on Population Modeling, Adaptive Control, and Experimental Design. Dr. Jean-Louis Steimer, Dr. Maire, and all participants.
5:00 PM - Closing Remarks. Dr. Jelliffe

5:15 PM - Adjourn
### Organizing Committee

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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<tbody>
<tr>
<td>Pascal Maire, Pharm.D.</td>
<td>Chairperson</td>
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<td>Roger Jelliffe, M.D.</td>
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<td>Bruno Charpiat, Pharm.D.</td>
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<td>Alain Laffont, Pharm.D.</td>
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<td>Eliane Vermeulen, Pharm.D.</td>
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<td>Valentine Breant, Pharm.D.</td>
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<td>Christine Pivot, Pharm.D.</td>
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<td>Valerie Cogoluenhes, Pharm.D.</td>
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### Scientific Committee

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<th>Name</th>
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<tr>
<td>Roger Jelliffe, M.D.</td>
<td>Chairperson (USA)</td>
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<td>Pascal Maire, Pharm.D.</td>
<td>(F)</td>
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<td>Alan Schumitzky, Ph.D.</td>
<td>(USA)</td>
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<td>Philippe Courpron, M.D.</td>
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<td>Patrice Degoulet, M.D.</td>
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<td>Francois Talabart, M.D.</td>
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<td>France Mentre, Ph.D.</td>
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<td>Barry Woodcock, M.D.</td>
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<td>K.C. Lun, Ph.D.</td>
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<td>Joaquim Bonal, Pharm.D.</td>
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### Faculty

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<tr>
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<td>Athanasios Iliadis, Ph.D.</td>
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### Supported by (we hope)

- Bristol Laboratories
- Eli Lilly Laboratories
- Sandoz Laboratories
- Roussel Laboratories
- Roche Laboratories
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- IMIA
- AMIA
- Hospices Civils de Lyon
- Claude Bernard University - Lyon I
- Micro Informatique Diffusion
- MRES
- Region Rhone-Alpes
- INBIOMED
- ADCA/P - EJG

and others...
Registration Fees

For Part I, with the Medinfo '92, there is no separate registration fee other than that of the Medinfo '92.

For Part II, the Satellite meeting to both the Medinfo '92 and the FIP World Congress, for those registrants not employed by universities or hospitals, there will be

a registration fee of $800, or 5600FF.

However, for those employed by universities and hospitals, there will be 2 lower registration fees, each with a discount for AMIA, IMIA, ADILOW-EUG, and FIP members, as shown below.

Early registration (before April 1, 1992) will also receive a discount as described below.

<table>
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<tr>
<th>Days 1 and 2</th>
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<th>Early Reg</th>
<th>Discount</th>
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<td>Days 2 and 3</td>
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<td>$275 or 1925FF</td>
<td>$250 or 1750FF</td>
<td>$225 or 1575FF</td>
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<td>Days 1, 2, and 3</td>
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<td>$325 or 2275FF</td>
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<td>$275 or 1925FF</td>
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<td>Days 1, 2, and 3</td>
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<td>$425 or 2975FF</td>
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These fees include all conference material, the publication of the proceedings, attendance at the conference, mid-session breaks and luncheon on the days registered. It does not include hotel expenses. A list of hotels to consider using will be provided. A conference dinner, on Tuesday, September 22, 1992, also not included in the registration fee, is planned in addition. Tickets for registrants and their guests may be ordered at the same time as the registration for 300FF ($40) each.

Registration is limited to 50 participants on Day 1, 100 on day 2, and 150 on Day 3. Because of these limitations, applications will be accepted in the order they are received.

The Proceedings

Preprints of the proceedings will be edited by Drs. Jelliffe, Schumitzky, and Maire, with the other members of the scientific committee acting as auxiliary reviewers. It is anticipated that they will be available at the conference, and included in the registration fee. The final proceedings, not included in the registration fee, will be published later by Springer-Verlag or Elsevier, and may be ordered at the conference.

Our proposed schedule is as follows. All speakers must submit complete written papers to the scientific committee by March 1, 1992. This must be done in order for the speaker to be on the program. All authors must follow the recommendations set by Springer-Verlag or Elsevier for camera-ready material. We currently favor the use of Microsoft Word on the Macintosh and either
that or Wordperfect or Chi-Writer for the PC. All authors must send their material both as a printout and as a floppy disk.

It may also be possible to include the USC software in the final book, probably as a CD. There will be an auxiliary program so the one can take the CD to a CD reader and copy out the software on conventional floppy disks. This will probably require approximately twenty 360K floppy disks for all the software.

**Oral Presentations and the Poster Session**

For the poster session and the oral presentations, abstracts must also be submitted to the committee by March 1, 1992. Those presentations accepted will also be published in the proceedings. Presenters must be registered for the conference for the abstract to be published.

**Addresses for Further Information**

Further information may be obtained from the USA from:

Roger W. Jelliffe, M.D.
Laboratory of Applied Pharmacokinetics
University of Southern California School of Medicine, HMR805
2011 Zonal Ave.
Los Angeles CA 90033
Phone (213)342-1300, Fax (213)223-7474

and from Europe from:

Pascal Maire, Pharm.D.
Department of Pharmacy
Hospital Antoine Charial, Hospices Civils de Lyon
40, Avenue de la Table de Pierre
69340 Francheville
FRANCE
Phone 78-34-61-61 ext 3393, Fax 78-34-61-61 ext 3326