

## STANDARDS OF LABORATORY PRACTICE (SLP) COMMITTEE

### Interim report

Since its inception in 1997 at the Vancouver congress under the chair of Dr. Ester Zylber-Katz, its founding chair, and under Professor Pierre Marquet, the next chair, the SLP committee has taken enormous strides towards developing guidelines for international standards of practice in TDM and CT.

During ICTDMCT Louisville in April 2005, the SLP committee organised its first workshop under the chairmanship of Professor Marquet. The topics for the workshop and the speakers were:

- 1) Pierre Marquet (Professor of Pharmacology, Dept of Pharmacology-Toxicology, Limoges University Hospital, France):  
*Presentation of the new definition of therapeutic drug monitoring proposed by the committee. Review of the national and international guidelines for TDM laboratories.*
- 2) Tai Kwong (Professor of Pathology and Laboratory Medicine, Dept of Pathology and Laboratory Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York):  
*Review of the national and international guidelines for toxicology laboratories.*
- 3) Philip Walson (Professor of Paediatrics and Pharmacology, University of Cincinnati; Director, Clinical Pharmacology Division and Clinical Trials Office, Cincinnati Children's Hospital Medical Center):  
*Panic Values and what they mean for TDM.*
- 4) Alison Thomson (Area Pharmacy Specialist, Pharmacy Department, Western Infirmary, North Glasgow University Hospitals Division, Glasgow):  
*Education of Physicians on TDM and CT. What should they know and how should we teach them?*

Here are very brief summaries of two of the speakers:

### **Review of guidelines for Therapeutic Drug Monitoring**

Pierre Marquet, Department of Pharmacology-Toxicology,  
University Hospital, Limoges, France.

#### **Summary:**

After a reminder of the new definition of TDM proposed by the Standard of Laboratory Practice Committee and approved by the Executive Committee, this talk reviewed the internationally available guidelines for TDM, i.e. those issued by the National Academy of Clinical Biochemistry (USA), the French Societies of Pharmacology and Analytical Toxicology, the World Federation of Societies of Biological Psychiatry (WFSBP), the IATDMCT Clinical Pharmacokinetics Committee and by Dutch IATDMCT members together with the Society for Clinical Pharmacology and Biopharmaceutics and the Poison Information Center. Three lists of drugs to test in TDM labs were proposed, to be discussed by the committee: one for drugs used in the general population (first-line drugs), one for those used in special populations (second line) and one for drugs that require TDM in special cases and can probably be assayed in reference labs only (third line).

#### **Education of physicians on TDM & CT, what should they know and how do we teach them?**

Alison H Thomson, Pharmacy Dept, Western Infirmary, Glasgow, Div of Cardiovascular & Medical Sciences, University of Glasgow

#### **What is the problem?**

Doctors (pharmacists, microbiologists, biochemists) don't like "equations" and don't understand basic clinical pharmacokinetics. Drug analysis is misused, drug concentrations are misinterpreted, actions are inappropriate. Some of the common misconceptions were described with case or literature examples to illustrate the main points.

#### **Concentration-effect Relationships: common misconceptions**

- "The sicker the patient, the higher should be the dose (and/or) concentration"
- "A concentration measurement above the therapeutic range is toxic"
- "Poor response and/or low concentrations always indicate that a dosage increase is required"

*Drug concentration vs response relationships usually show a log-concentration effect profile so that there is a point beyond which an increase in dose will not increase response but may increase toxicity, e.g. ciclosporin (AUC data), bendrofluazide in hypertension.*

#### **Basic clinical pharmacokinetic principles**

The aim is to describe the profile of drug concentration in the body by considering absorption, distribution and elimination and use the information to decide - "how much" and "how often"?

#### **Drug Absorption**

Bioavailability: the proportion of the administered dose that reaches the systemic circulation; absorption rate constant describes the speed of absorption from e.g. gut

to the systemic circulation.

### **Drug Distribution – common misconceptions**

- “Patients with renal impairment should always receive reduced loading doses of drugs or they will become toxic”
- I forgot to measure the trough and had just given the IV dose so I ran round to the other side of the patient as fast as I could and took a sample”

*Loading dose (mg) = Target Conc (mg/L) x V (L) therefore liver/hepatic function does not affect the loading dose required to reach a target concentration. Samples taken during distribution or ignorance of protein binding abnormalities can lead to misinterpretation of results.*

### **Drug Elimination – common misconceptions**

- “The prescription has been discontinued... so the drug is no longer present”
- “Elimination half-life involves equations and is therefore not clinically relevant”
- “The prescription has been discontinued... so the drug is no longer present”.
- “If a drug has an elimination half-life of 2 hours, it will disappear from the body in 10-12 hours”

Examples of misinterpretations included digoxin samples taken before steady state had been achieved, leading to toxicity; insufficient monitoring of a patient with unstable renal function; and discontinuation of one antibiotic and therapy started with another (similar) one despite therapeutic concentrations of the first remaining for a further week.

*Drug clearance determines the average steady state concentration. Elimination Half-life depends on clearance and volume of distribution and determines the time taken to achieve steady state and to eliminate a drug from the body. “Drugs don’t have half-lives, patients have half-lives”*

### **What do clinicians need to consider?**

- **Starting dose:** disease state, route, size, elimination route, loading vs maintenance dose
- **Evaluation of response:** duration of therapy, steady state?
- **Drug analysis:** sample time, dosage history, clinical response and targets?
- **Dose adjustment:** clinical targets, appropriate interpretation of concentration and response?

**Other factors:** PD relationships, drug interactions, protein binding, changing clinical condition

As joint chairs, we met at the University of Mainz in December 2005 to discuss our plans for the SLP committee leading to ICTDMCT 2007 in Nice. It is quite a formidable task to follow in the footsteps of Dr. Ester Zylber-Katz and Professor Pierre Marquet, and so we feel it is appropriate there are two of us to share the burden.

In 2007, we propose to conduct another workshop. A tentative title would be “TDM in theory and practice, state of the art”. Details of the workshop including speakers will be published later. We also aim to prepare a leaflet containing relevant information on important aspects of TDM and CT.

The SLP committee at present comprises of 28 members. It is our intention to encourage active participation of the members in the affairs of the committee and to encourage others to join.

**Professor Christoph Hiemke and Dr. Edgar P. Spencer**  
*Joint Chair, SLP Committee, 2005-2007*