This format has been agreed and adopted at the 15th ASEAN Consultative Committee for Standards and Quality (ACCSQ)- Pharmaceutical Product Working Group (PPWG). Starting from 1st January 2009 (as agreed upon at the meeting of Jawatankuasa Kerja Bioekuivalens Kebangsaan (JKKBE) 2/2008), submission of bioequivalence reports should comply to the following format.

Bioequivalence Study Reporting Format

1. Title Page

1.1 Study Title

1.2 Name and address of Sponsor

1.3 Name, person in charge and address of Institution

1.4 Name and address of Principal Investigator

1.5 Name of Medical/ Clinical Investigator

1.6 Name, person in charge and address of clinical laboratory

1.7 Name, person in charge and address of analytical laboratory

1.8 Name, person in charge and address for Data Management, Pharmacokinetics and Statistical Analysis

1.9 Name and address of Other Investigator(s) & study personnel

1.10 Start and end date of clinical and analytical study

1.11 Signature and date of investigator(s), (medical writer, QA Manager – if applicable)

2. Study Synopsis

3. Table of Contents

4. Abbreviation and Definition of Terms

5. Introduction

5.1 Pharmacology

5.2 Pharmacokinetics

5.3 Adverse events

6. Objective

7. Product Information

7.1 Test Product Information

- Trade Name
- Active Ingredient, Strength, and Dosage Form
- Batch Number, Manufacturing Date and Expiry Date
- Batch size compliance (can be directly provided by sponsor)
- Product Formulation (can be directly provided by sponsor)

- Finished Product Specifications (can be directly provided by sponsor)
- Name and Address of Manufacturer

7.2 Reference Product Information
- Trade Name
- Active Ingredient, Strength, and Dosage Form
- Batch Number, Manufacturing Date and Expiry Date
- Name and Address of Manufacturer
- Name and Address of Importer or Authorization Holder

7.3 Pharmaceutical Equivalence Data
- Comparing content of Active Ingredient / Potency
- Uniformity of Dosage Units

7.4 Comparison of Dissolution Profiles (can be directly provided by sponsor)

7.5 Letter with a signed statement from the applicant/sponsor confirming that the test product is the same as the one that is submitted for marketing authorization

8. Investigational Plan

8.1 Clinical Study Design
- Study design (crossover, parallel)
- Fed, fasted
- Inclusion, exclusion, restriction
- Standardization of study condition
- Drug administration
- Removal of Subject from Assessment
- Health screening
- Subject detail, no of subjects, deviation
- Sampling protocol/time, sample preparation/handling, storage, deviation
- Volume of blood collected
- Subject monitoring
- Genetic phenotyping (if applicable)

8.2 Study Treatments
- Selection of Doses – single, multiple
- Identity of Investigational Products, dosing
- Randomization
- Blinding
- Washout period
- Water intake volume

8.3 Clinical and Safety Records
- Adverse Event
- Drug related Adverse Drug Reaction

8.4 Pharmacokinetic Parameters and Tests
- Definitions and calculation

8.5 Statistical Analyses
- Log transformed data analysis (AUC, Cmax)
- Sampling Time Adjustments
- t max,
- t ½
- Acceptance Criteria for Bioequivalence
- ANOVA presentation
- Power

8.6 Assay Methodology and Validation
- Assay method description
- Method of detection
- Validation procedure and summary results
  - Specificity;
  - Accuracy
  - Precision;
  - Recovery;
  - Stability;
  - LOQ
  - Linearity

8.7 Data Quality Assurance

9. Results and Discussion

9.1 Clinical Study Results
- Demographic characteristics of the subjects.
- Details of clinical activity.
- Deviation from protocol, if any.
- Results of drug/alcohol/smoking usage, medical history and medical examination, vital sign and diagnostic laboratory test of subjects.
- Adverse event/reaction reports for test product and reference product.

9.2 Summary of analytical results

9.3 Pharmacokinetic Analyses
- Drug levels at each sampling time, descriptive statistics
- Table of individual subject pharmacokinetic parameters, descriptive statistics
- Figure of mean plasma or urine concentration-time profile
- Figure of individual subject plasma or urine concentration-time profile

9.4 Statistical Analyses

- Statistical considerations
- Time points selected for Kel, $t_{1/2}$
- Summary statistics of pharmacokinetic parameters: AUC_t, % AUC extrapolated, AUC_{inf}, C_{max}, t_{max}, $t_{1/2}$
- Summary of statistical significance for AUC and C_{max} (based on log-transformed data calculated as 90 % CI of test/reference Geometric Means) and for t_{max} (based on non-transformed data calculated as p value).
- Similar calculation for urine data: Ae and dAe/dt (Ae corresponds to AUC, $(dAe/dt)_{max}$ corresponds to C_{max}).
- Intra-subject variability
- Power of study
- Assessment of sequence, period and treatment effects
- Table - Analysis of Variance, Geometric least-squares means for each pharmacokinetic parameters.
- Table - Calculation of 90% confidence interval for the ratio of pharmacokinetic parameters under consideration in logarithmic transformation.

10. Conclusions

11. Appendices

11.1 Protocol and Approval

- Letter of approval from DRA (if applicable)
- Study protocol and its amendments together with Institutional Review Board/Ethical Committee approvals
- Informed Consent Form
- Protocol deviation listing
- Adverse Event listing
- FP specification and CoA

11.2 Validation Report (including 20% of raw chromatograms)

11.3 Analytical Report (including 20% of raw chromatograms)

11.4 Certificate of Clinical Facility, Clinical Laboratory and Certificate of Analytical Laboratory (if any)

11.5 Dose proportionality comparative dissolution profiles between various strengths (when BE study investigating only one strength but application for registration consists of several strengths (from sponsor).

* Bioequivalence Centres, MOPI & PhAMA has been informed on this requirement during Mesyuarat Jawatankuasa Kerja Bioekuivalens Kebangsaan (JKKBE) 2/2008 (04/12/2008) .