Pharmacokinetic (PK) Comparability for Biosimilars: Anvisa Perspective

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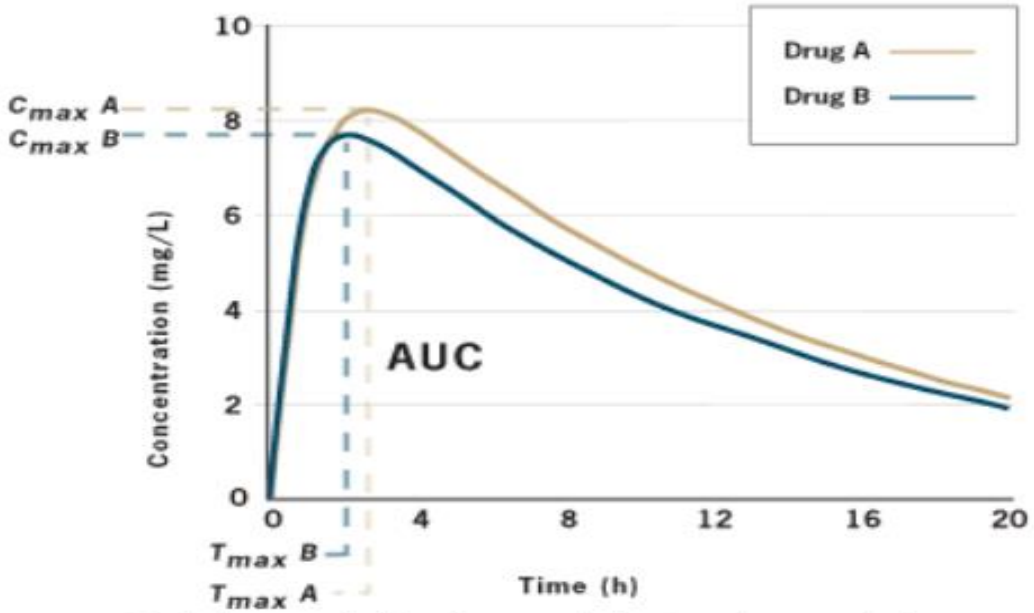
Clarification Note n. 002/2015

- **PK Studies for Biosimilars:**
  - Evidence of similarity;
  - Needed for conclusion of the assessment of application.
  - Should be submitted *in digital format* simultaneously with the application by the code 10846.

Comparative Pharmacokinetic Studies

Oral Absorption

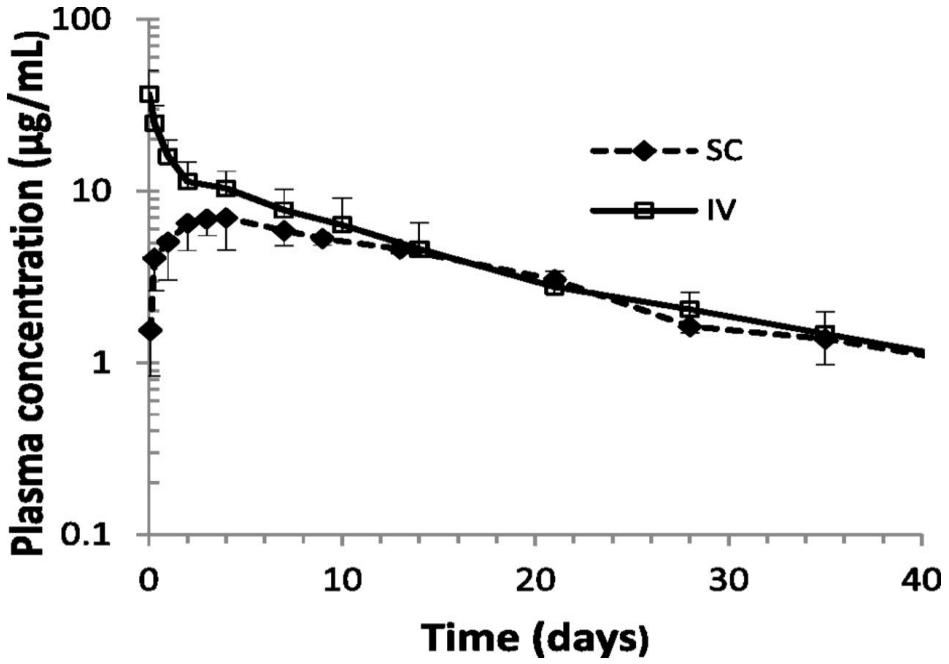


Typical concentration-time graph for two drug products

Source: http://www.bpac.org.nz/BPJ/2007/March/bioequiv.aspx

Comparative Pharmacokinetic Studies

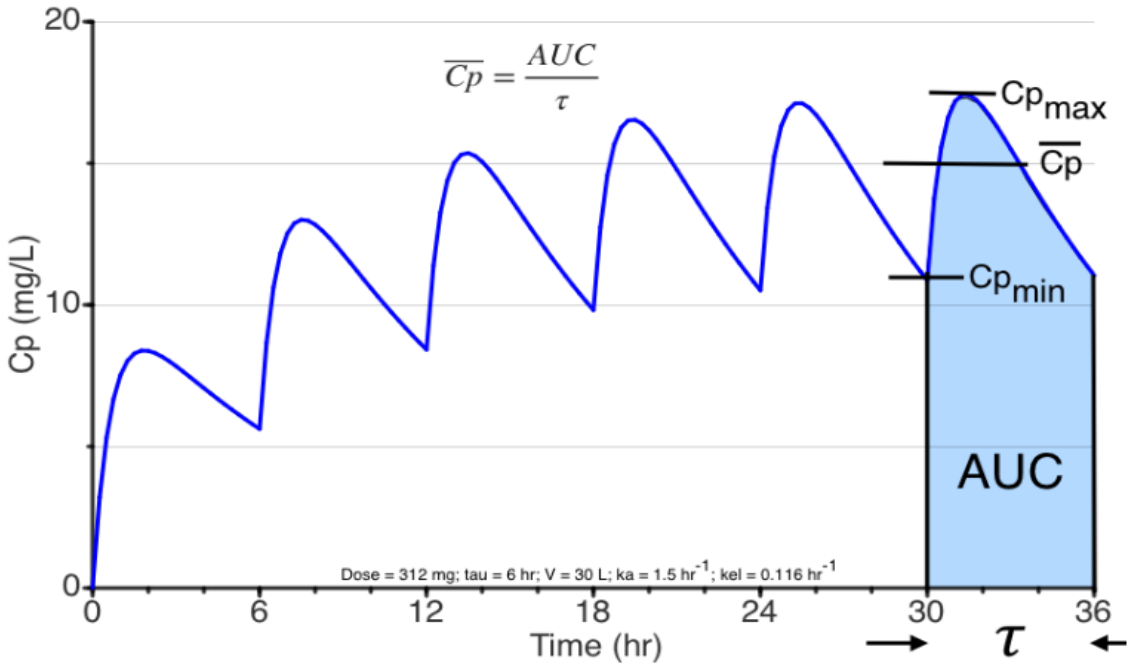
Intravenous (IV) and Subcutaneous (SC) Absorption



Source: Wolfgang F. Richter, and Björn Jacobsen Drug Metab Dispos 2014;42:1881-1889

Comparative Pharmacokinetic Studies

Multiple Oral Administration



Source: https://www.boomer.org/c/p4/c15/c1504.html

Clarification Note n. 002/2015

- **Documentation based on RE nº 895/2003:**
  - General Information (product, CRO, signature list);
  - Clinical report (study design, administration, population, hospilatization);
  - Bioanalytical report (methodology, validation, calculated concentrations, procedures);
  - Statistical report (PK and statistical analysis, data according to Technical Note n. 04/2016).

Clarification Note n. 002/2015

- **Recomendations for Design of Comparative PK Studies for Biosimilars:**
  - Justifications for inclusion of patients or healthy subjects;
  - Intra and Inter-Subject variability for determination of number of subjects;
  - PK linearity for selection of dose;
  - Approval of IEC.

Clarification Note n. 002/2015

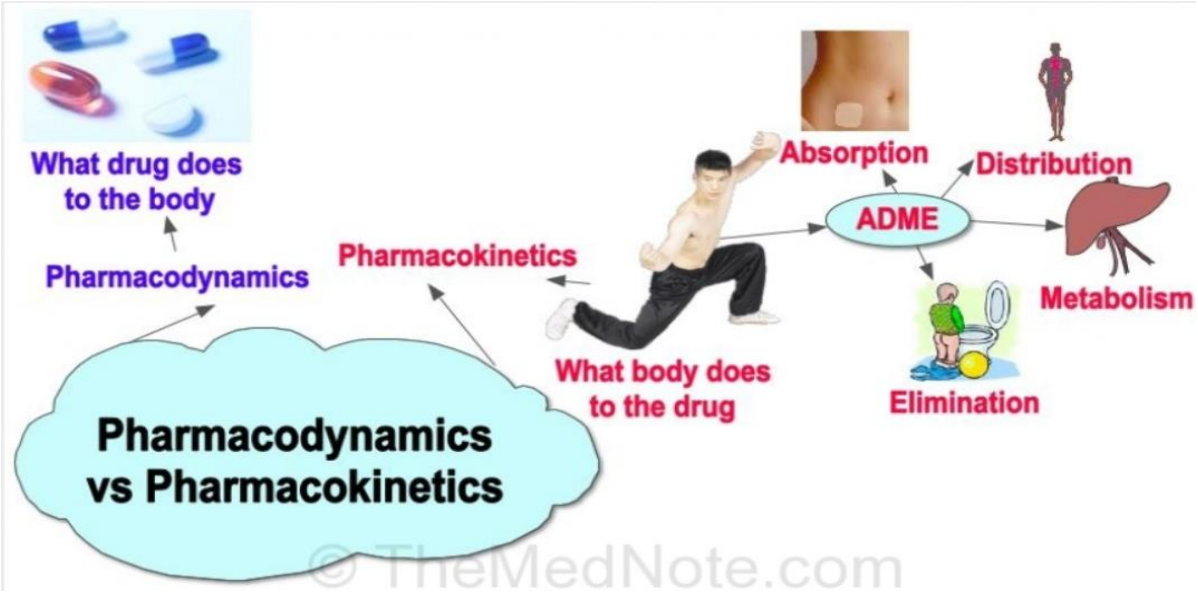
- **Recomendations for Design of Comparative PK Studies for Biosimilars:**
  - Bioanalytic Method Validation based on RDC n. 27/2012;
  - For each PK parameter: log-transformed with each individual value, SD, CV and ANOVA
  - For AUC_{0-t} and C_{max}: 90% of Confidence Interval.

Clarification Note n. 002/2015

- **Recomendations for Design of Comparative PK Studies for Biosimilars:**
  - Bioanalytic Method Validation based on RDC n. 27/2012;
  - For each PK parameter: log-transformed with each individual value, SD, CV and ANOVA;
  - For AUC_{0-t} and C_{max}: 90% of Confidence Interval;
  - Similarity criteria: 90% GMR between 0.8 and 1,25.

Technical Note n. 118/2016

- **Comparative PK Studies for Biosimilars should be submitted simultaneously with the application to DDCM:**



Source: http://www.themednote.com/2011/07/10/pharmacodynamics-vs-pharmacokinetics/

Technical Note n. 118/2016

- **Major Considerations:**
  - Submission code 10900;
  - 45 days for the first comunication if prioritization is approved;
  - If CETER assess this documents during DDCM, it isn't necessary to submit again during biosimilar application.

Source: http://www.themednote.com/2011/07/10/pharmacodynamics-vs-pharmacokinetics/

Common queries by CETER

- **Format of the Report;**
- **Laboratorial exams for subjects;**
- **Raw data and results of the bioanalytical report (validation, batch runs);**
- **Stability of drug in plasma;**

Source: http://www.themednote.com/2011/07/10/pharmacodynamics-vs-pharmacokinetics/

Thank you!

Source: http://shenlinlab.com/Blog%20Topics%20html/FDA%20Law%20Blog%203%20Biosimilars.html