EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 October 2013
CHMP/PKWP/EMA/423732/2013
Committee for Medicinal Products for Human Use (CHMP)

Capecitabine Product-Specific Bioequivalence Guidance

Draft

Draft Agreed by Pharmacokinetics Working Party	**October 2013**
Adoption by CHMP for release for consultation	24 October 2013
Start of public consultation	15 November 2013
End of consultation (deadline for comments)	15 February 2014

Comments should be provided using this template. The completed comments form should be sent to PKWPsecretariat@ema.europa.eu.

Keywords	***Bioequivalence, generics, capecitabine***

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Capecitabine Product-Specific Bioequivalence Guidance

Disclaimer:

This guidance should not be understood as being legally enforceable and is without prejudice to the need to ensure that the data submitted in support of a marketing authorisation application complies with the appropriate scientific, regulatory and legal requirements.

Requirements for bioequivalence demonstration (PKWP)*

BCS Classification**	**BCS Class:** ☐ **I** ☐ **III** ☒ **Neither of the two** **Background:** Capecitabine is an unstable compound in acidic medium. Absorption is almost complete. The available data on solubility does not allow its BCS classification.
BE Study design	**single dose** **cross-over**
	patients

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	☐ **fasting** ☒ **fed** ☐ **both** ☐ **either fasting or fed** Fed state recommended to minimise the risk of vomiting.
	Strength: 500 mg because it is the highest strength **Background:** linear PK
	Number of studies: one single dose study
Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** AUC_{0-t}, Cmax
	90% confidence interval: 80.00– 125.00 Widening of the usual acceptance criteria for Cmax is not accepted because capecitabine is considered a "critical dose" drug.

16 * As drug variability has not been reviewed, this guidance is not applicable to highly variables drugs.

17 ** The BCS classification should be confirmed by the Applicant at time of submission based on available data (solubility experiments, literature, etc.). If
18 a drug substance has been classified as BCS class II or IV, no further solubility investigations are needed.