EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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3 Committee for Medicinal Products for Human Use (CHMP)

4 Sorafenib Product-Specific Bioequivalence Guidance

5 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

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

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Keywords	***Bioequivalence, generics, sorafenib***

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Sorafenib 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:** Sorafenib is a low solubility compound.
BE Study design	**single dose** **cross-over**
	healthy volunteers
	☒ **fasting** ☐ **fed** ☐ **both** ☐ **either fasting or fed**

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	Strength: 200 mg **Background:** There is only one strength available i.e. 200 mg. Sorafenib exhibits non-linear pharmacokinetics with a less than dose-proportional increase in AUC with increasing doses within the dose range 400-800 mg. The non-linearity is proposed to be due to limited solubility. Hence, the highest and the lowest strength should be studied.
	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_{0-72h} and Cmax
	90% confidence interval: 80.00– 125.00

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.