Comments on
Guideline on the Evaluation of Anticancer Medicinal Products in Man
(CPMP/EWP/205/95 Rev. 3, Draft, 17 March 2005)

German Region of the International Biometric Society

Comments:

1. 'Windows of opportunity study'

The term 'windows of opportunity study' is mentioned several times throughout the document, but a formal definition of this type of study is missing.

2. page 5, II.1.1 2nd paragraph

'It is accepted that the dose initially is administered per body surface area. Whether this reduces interpatient variability in exposure should be investigated in the exploratory studies programme and alternative dosing, e.g. per body weight, by gender or simply a non-adjusted dose should be examined.'

It should be made more precise what this means exactly. Does this imply that in a study with different doses per body surface area, the analysis should also describe the corresponding doses on another scale (as e.g. body weight), or is it required that several studies using different dose escalation scales are performed.

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3. page 6, II.1.1 Objectives 6th bullet

'Fr orally administered drug, food-drug interaction should be studied.'

This requirement should be made more precise.

4. page 6, II.1.1 Objectives 7th bullet

'Mass balance studies are encouraged.'

The term 'mass balance studies' should be defined.

5. page 12, II.2.2 Exploratory trials with time-related endpoints, 4th bullet

The wording of this paragraph should be re-considered, since its meaning is difficult to understand.

6. page 14-15, III.1.1 2nd paragraph

It should be made clear whether the whole paragraph refers to non-inferiority trials.

7. page 18, III.2 3rd paragraph, last sentence

'In cases where the treatment effect has been underestimated in the planning of the study, this may create a dilemma if statistically convincing effects have been demonstrated too early, but mainly if the difference relates to survival.'

It is not quit clear what is meant by this sentence.

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8. page 18, III.2 7th paragraph

'For non-inferiority studies it may be appropriate to present, in addition to PFS, sensitivity analyses investigating effects of censoring or not treatment withdrawal/change of therapy/death.'

It is not clear what a 'not treatment withdrawal' means.

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