



1 16 February 2012  
2 EMA/CHMP/965150/2011  
3 Committee for Medicinal Products for Human Use (CHMP)

4 **Concept paper on the need to revise the points to**  
5 **consider on adjustment for baseline covariates**

6 Draft

Agreed by Biostatistics Working Party	December 2011
Adoption by CHMP for release for consultation	16 February 2012
Start of public consultation	29 February 2012
End of consultation (deadline for comments)	30 May 2012

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Keywords	<i>Baseline covariates, statistical analysis, allocation methods</i>
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## 12 **1. Introduction**

13 The CHMP points to consider on adjustment for baseline covariates came into operation in 2003. Since  
14 then, it has been widely used by both, industry and regulators when planning and assessing  
15 confirmatory clinical trials. However, since the release of this PtC document the position of the PtC on  
16 specific treatment allocation methods has been debated. Meanwhile, methodological advances have  
17 been made that allow for more in depth insight into the impact such methods might have (for example  
18 on the validity of conventional statistical tests).

## 19 **2. Problem statement**

20 Within the framework of the CHMP policy of a regular review of guidance documents, it is proposed to  
21 revisit the recommendations. Since it was first drafted, new aspects with regard to the impact of  
22 treatment allocation procedures on the statistical analysis have emerged in the scientific literature and  
23 might influence the acceptance of such methods in certain situations. Therefore, changes to the  
24 current text are intended to reflect the current state of scientific knowledge in this document which  
25 could evolve in a guideline.

## 26 **3. Discussion (on the problem statement)**

27 The topics to be discussed when revising the guidance document should cover the recent  
28 developments and discussions as given in section 1. Questions and topics to be discussed relate to

- 29 • design and analysis considerations with regard to treatment allocation procedures

## 30 **4. Recommendation**

31 It is proposed to revise the current CHMP Points to Consider on adjustment for baseline covariates. The  
32 scope of the revision is detailed above.

## 33 **5. Proposed timetable**

34 It is anticipated that a new draft CHMP guidance document will be available 9 months after adoption of  
35 this document for 6 month release for external consultation.

## 36 **6. Resource requirements for preparation**

37 The preparation of this revision of the guidance document will involve the BSWP. It is anticipated that  
38 at least one plenary session discussions at the BSWP will be needed.

## 39 **7. Impact assessment (anticipated)**

40 The handling of baseline covariates in study design and statistical analyses are important issues in  
41 most marketing authorisation applications. It is anticipated that this document will lead to an improved  
42 standard of regulatory assessment of confirmatory trials and improve planning of confirmatory trials by  
43 sponsors.

44 **8. Interested parties**

45 External consultation: pharmaceutical industry, academic networks and patient organisations.

46 **9. References**

47 CPMP/EWP/2863/99: "Points to Consider on Adjustment for Baseline Covariates".

48 CPMP/ICH/363/96: "ICH E9 Statistical Principles for Clinical Trials".