

**EMEA/EFPIA WORKSHOP ON
ADAPTIVE DESIGNS (AD) IN
CONFIRMATORY CLINICAL TRIALS**

December 14th, 2007

Summary of key positions from the
discussions

Regulatory (dis)agreement

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1. Introduction

<i>Agreement</i>	<i>Disagreement</i>	<i>Open questions</i>
Cost of R&D is a public health issue Growing patient pressure Interim analysis can be ethical/mandatory	Cost of R&D as main driver for AD Need to save time <i>per se</i>	AD brings better information
AD \neq rescue remedy Some uncertainty remains in Phase III Control of type I error is feasible Early stopping will reduce totality of evidence	Complete blurring of exploratory and confirmatory phases	AD only in difficult setting AD main improve dose selection (but no trade-off) AD and conditional approval AD and single pivotal trial Selection of (BM-defined) target population How to determine the success of AD

2. Seamless design

<i>Agreement</i>	<i>Disagreement</i>	<i>Open questions</i>
Some reassuring examples of seamless design exist There is a need for replication		Real benefit of seamless design Potential benefit of long-term follow-up of Phase II patients

3. Sponsor involvement

<i>Agreement</i>	<i>Disagreement</i>	<i>Open questions</i>
<p>Trial integrity is primary goal</p> <p>Risk of operational bias is obvious</p> <p>Justification for sponsor involvement is not impossible</p>	<p>Sponsor involvement should be the rule</p>	<p>What are « unanticipated complexities » (need examples)</p> <p>How to prove absence of bias (probabilistic approach)</p> <p>Timing of paediatric studies</p>

4. Heterogeneity

<i>Agreement</i>	<i>Disagreement</i>	<i>Open questions</i>
AD means improved transparency Price to pay: mutiplicity and increased awareness of heterogeneity	How to quantify (and tolerate) heterogeneity	How to assess information leakage

5. Future steps

<i>Agreement</i>	<i>Disagreement</i>	<i>Open questions</i>
Industry/regulators need to work together A discussion framework will be created within Scientific Advice		

NB. Scientific advice is available for broader issues (not product-related)

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