Workgroup Instructions and Report Out Slide
22-23 April 2013

Breakout 1: Patient Enrollment

* Disease severity criteria for inclusion
* Standardizing the definition for HABP/VABP
* Pre-study AB drug and time period (as related to mortality EP)
* Informed consent issues

Breakout 2: Efficacy and Safety Outcomes

* Considerations for a hierarchical endpoint with clinical criteria
* NI margin, sample size and mortality rate
* Criteria for comparator drug
* Target severity/ comorbidity criteria for mortality rate, and stratification to balance arms
* Safety outcomes (and safety reporting)

Breakout 3: Evaluable Population

* Method of microbiology confirmation
* Microbiological criteria for inclusion in evaluable population (% micro confirmed for micro-ITT and analysis)
* Allowed concomitant AB drugs
* Pre-study micro evaluation

DAY 1: Breakout Exercise to apply to each issue

1. List the problems that arise from the issue that hinder the successful and efficiently completion of the trial. Phrased differently, when, where, and how are "errors that matter" occurring?
2. List alternate solutions to mitigate the issue
3. Rate this alternate approach in terms of feasibility and successful outcome for the study

0 ——————————————————————— 100

where 0=poor quality, unusable data, and 100 = best quality

5. Select top two alternates and provide rational for why the group picked them

Report out for Session 3 Day 1

ISSUE:

* Alt1:
* Alt2:
* If all did not agree provide the Majority/Minority opinion

Day 2: Breakout Exercise

You will now operationalize your alternative proposed solutions from Day 1

* Does the proposed solution require changes to other aspects of trial design, implementation, oversight, or reporting?

* Explore any downside of operationalizing the alternate solution
    * Do any of the original operational issues still remain?
    * Does this solution raise significant new issues (i.e. that materially impact subject safety or that impact trial analysis)?

* What proactive steps can be taken to avoid or minimize the operational challenge identified? (That is, what would remove the problem or decrease its likelihood of occurring?)

* Will the propose solution also be feasible globally? What considerations are needed to support a multiregional trial?

Report out for Session 1 Day 2

Operational considerations and recommendation

DAY 1: Issues Polling Instructions

Please provide your comments in the polling station set up:

1. Please reflect on the discussion and provide any additional barriers to study feasibility that did not make it into the pre-solicited top challenges.
2. Please place the 3 stickers provided on the CTQ chart categories that you perceive make the trials complex and difficult to overcome
3. Provide comments related to these concerns on the CTQ chart or flip chart