FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)
Meeting of the Peripheral and Central Nervous System Drugs Advisory Committee

December 6, 2007
Questions

1) Do the findings on the secondary efficacy outcomes (lack of a beneficial effect of tetrabenazine on numerous measures of function and cognition and/or numerical superiority of placebo on some measures) by themselves raise sufficient concerns about the utility of tetrabenazine's effect on chorea to justify not approving the application?

2) If not, is the panoply of adverse effects associated with tetrabenazine use sufficient to justify not approving the application? When considering this question, we are particularly interested in hearing the committee's views about whether or not a dosing regimen can be identified that would provide a benefit on chorea without an unacceptable risk of adverse events. Failing this, we would be interested in hearing the committee's views about any maneuvers that might mitigate these risks sufficiently to justify approval (e.g., reducing the dose, discontinuing the drug, instituting concomitant treatments [e.g., antidepressant therapy]). Further, we are also interested in the committee's views of the aforementioned Agency concerns that it might be difficult for the practitioner to discern if clinical worsening in various areas (e.g., cognition, depression, etc.) is drug related or not, with the possibility that, if drug related, the adverse events could become severe and/or irreversible.

3) If the committee determines that, for any reason, the application should not be approved, what studies (if any) could the sponsor perform to establish the necessary substantial evidence of effectiveness and/or safety in use?

4) If the committee determines that the application should be approved, are there any studies that the Sponsor should perform post-approval?