Biotechnology Industry Organization
1225 Eye Street NW, Suite 400
Washington, DC 20006

November 17, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, Maryland 20852

Re: Docket No. 2003N-0472, Federal Register: October 21, 2003 (Volume 68, Number 203, pp. 60108-60109)

Dear Sir/Madam:

The following comments are provided by the Biotechnology Industry Organization (BIO). BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in all 50 U.S. states and 33 other nations. BIO members are involved in the research and development of health-care, agricultural, industrial and environmental biotechnology products. BIO appreciates the opportunity to comment on the Food and Drug Administration's sample *Statement of Work for the Evaluation of First Cycle Review Performance.*

BIO supports the proposed statement of work and believes that the planned evaluation of first cycle review performance is generally consistent with the PDUFA III performance goals. We do, however, have some comments and recommendations regarding specific details of the statement of work, as outlined below.

Section A – Background: The first paragraph in this section, third sentence, reads "These GRMPs clarify the roles and responsibilities of review staff in managing the review process. . . ." BIO believes that this sentence does not provide a complete description of what the Good Review Management Principles (GRMPs) are intended to be under the PDUFA III performance goals. We believe it fails to indicate the major underpinning of the GRMP commitment of identifying "best practices" to enhance communication, consistency between review divisions, proactive review planning and efficient time management to improve the overall review process. BIO recommends that this sentence be revised to read, *"These GRMPs clarify the roles and responsibilities of*

review staff and identify best practices intended to enhance the efficiency of first cycle reviews and improve the consistency of FDA's processes for overall management of the review process. The GRMPs also identify ways in which NDA and BLA applicants may enhance the effectiveness and efficiency of the review process."

Section B – Key Objectives of the PDUFA III Evaluation of First Cycle Review Performance: The first objective calls for a determination of current performance including a retrospective analysis of the cycles necessary for approval and the reasons for multiple cycle reviews of NDAs for NMEs and BLAs submitted in FY 2002. We believe that relying upon data from only a single year for the retrospective analysis would involve a rather limited sample of applications, and thus may not be fully representative since the percentage of first cycle approvals has fluctuated from year to year. BIO therefore recommends that the agency consider including applications from at least three fiscal years in the analysis to provide a broader perspective on the baseline.
In addition, the study that FDA agreed to undertake (as described in the PDUFA performance goals) to evaluate issues associated with the conduct of first cycle reviews is not limited to only NDAs for NMEs and original BLAs. The GRMPs are intended to apply to all applications. Therefore, while evaluating the first cycle review history of NDAs for NMEs and BLAs is certainly a critical component of the study, BIO believes it would be important to also include NDAs for non-NMEs and efficacy supplements in the study to obtain a more complete evaluation. Accordingly, we recommend that the objectives described in items 1, 2 and 3 of section B be revised to include NDAs for non-NMEs and efficacy supplements.

Section C – Scope of Work: The second paragraph of this section indicates that the evaluation will include all original NDAs for NMEs submitted to CDER and all original BLAs submitted to CBER in FY 2003 through FY 2007. As noted above, BIO believes the scope of the study should include all NDAs, BLAs and efficacy supplements. In addition, following the recent organizational changes effected within FDA in mid-2003, it is likely that original BLAs will also be submitted to CDER in the future. Therefore, BIO recommends that the first sentence in the second paragraph be revised to read, "*The evaluation of first cycle review programs will include all NDAs, BLAs and efficacy supplements submitted in FY 2003 through FY 2007. . . .*"

Section D – Key Tasks: Task No. 1 in this section calls for assessing baseline review performance of NDAs for NMEs and BLAs submitted to FDA in FY 2002. As noted above, BIO recommends including applications from at least three fiscal years in the evaluation to provide a broader and more representative sample for determining baseline review performance. We also recommend that NDAs for non-NMEs and efficacy supplements be included in the retrospective analysis.

Task No. 2 calls for identifying the best practices of FDA and industry that increased the effectiveness and efficiency of the review process, and identifying the causes of multiple review cycles. Two examples of sample evaluations are included in the work statement: a) quality and effectiveness of FDA-applicant interactions, including use of information request and discipline review letters, and b) characteristics of the product, application, applicant and review team. BIO believes this task is an extremely important component of the work statement, but we are concerned that some critical factors could be

overlooked unless they are included in the list of examples. Accordingly, BIO recommends that the list be expanded to include the following additional examples:

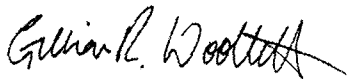
c. Application of review management planning by the responsible review division, and assessment of the degree of adherence to the established plan.
d. Frequency and type of communication with the applicant.
e. Timeliness of communication of deficiencies to the applicant and timeliness of applicant responses.
f. Timeliness of communication of FDA's comments on the draft labeling to the applicant, and whether the timing of such communications provided for a reasonable period of time for negotiation to reach agreement on the final wording before the PDUFA goal date.
g. Timing for FDA's communication to the applicant of any proposed post-approval commitments, including, when relevant, proposals for risk-management plans, and whether the communication process included a reasonable period of time for FDA-applicant negotiations regarding the necessity, objectives, and feasibility of the proposals.

Consistent with our recommendations under Key Objectives and Scope of Work, BIO recommends that the task to identify best practices of FDA and industry and causes of multiple review cycles should be extended to cover all NDAs, BLAs and efficacy supplements submitted during FY 2003 through FY 2007.

Task no. 4 calls for investigation of correlations between review actions and outcomes of the first review cycle, and for a sample of applications, evaluation of the impact of the use of GRMPs in product review. We believe the reference to a "sample" of applications is vague. It is not clear how many applications are to be included in the sample, and what the selection criteria would be. Accordingly, BIO recommends that the evaluation of the impact of the use of GRMPs should be applied to all applications submitted during FY 2003 through FY 2007 that will be included in the evaluation.

Thank you for your consideration of these comments. Please do not hesitate to contact me should you have any questions.

Sincerely,



Gillian R. Woollett, MA, DPhil
Vice President
Science and Regulatory Affairs