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MEMORANDUM

FDA GUIDANCE ON GOOD REVIEW MANAGEMENT PRINCIPLES AND PRACTICES

On March 31, 2005, the Food and Drug Administration ("FDA") issued its "Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products" ("GRMP Guidance" or "Guidance").[1] The Guidance discusses the agency's GRMPs for New Drug Application ("NDA") and Biologics License Application ("BLA") first cycle reviews. The GRMP Guidance was issued as a draft in July 2003[2] pursuant to the June 2002 Prescription Drug User Fee Act ("PDUFA")

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1 A copy of the guidance document is available at <http://www.fda.gov/cder/guidance/5812fnl.pdf>; see also FDA, Notice, Guidance for Review Staff and Industry on Good Review Management Principles and Practices for Prescription Drug User Fee Act Products; Availability, 70 Fed. Reg. 16,507 (Mar. 31, 2005) (available at <http://www.fda.gov/OHRMS/DOCKETS/98fr/05-6404.pdf>).

2 See FDA, Notice, Draft Guidance for Reviewers and Industry on Good Review Management Principles for Prescription Drug User Fee Act Products; Availability, 68 Fed. Reg. 44,345 (July 28, 2003) (available at <http://www.fda.gov/ohrms/dockets/98fr/03-19026.pdf>).

reauthorization performance goals agreed to by the agency.[3] These performance goals require FDA to provide guidance to industry and agency review staff on the following GRMP issues in order to promote quality, efficient, clear, transparent, and consistent management of marketing application reviews:

1. The filing review process, including communication of issues identified during the filing review that may affect approval of the application.

2. Ongoing communication with the sponsor during the review process (in accordance with 21 CFR 314.102(a)), including emphasis on early communication of easily correctable deficiencies (21 CFR 314.102(b)).

3. Appropriate use of Information Request and Discipline Review letters, as well as other informal methods of communication (phone, fax, e-mail).

4. Anticipating/planning for a potential Advisory Committee meeting.

5. Completing the primary reviews – allowing time for secondary and tertiary reviews prior to the action goal date.

6. Labeling feedback – planning to provide labeling comments and scheduling time for teleconferences with the sponsor in advance of the action goal date.

Id.[4]

The GRMP Guidance explains FDA's current best practices concerning marketing application review and management. It is the first time the agency has consolidated and

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[3] See PDUFA Reauthorization Performance Goals and Procedures, § X.B, June 4, 2002 (available at <http://www.fda.gov/oc/pdufa/PDUFAIIIGoals.html>).

[4] FDA has addressed some of these issues, such as Information Request and Discipline Review letters, more fully in separate guidance documents. See FDA, "Guidance for Industry: Information Request and Discipline Review Letters Under the Prescription Drug User Fee Act," (Nov. 2001) (available at <http://www.fda.gov/cber/gdlns/pdufa-irdr.pdf>).

fully discussed these practices in a single document. Therefore, applicants are strongly encouraged to become familiar with and fully knowledgeable about the GRMPs.

The GRMP Guidance first explains the fundamentals and operational principles of good review management, such as active applicant involvement and effective timely communication between FDA and applicants during the review process. Applicants are urged to work with their assigned Regulatory Project Manager ("RPM") to create a clear communication strategy for issues that might arise during the review process. RPMs are advised to promptly communicate those issues to FDA review staff, and to timely notify applicants of correctable deficiencies identified by FDA review staff. The GRMP Guidance also discourages applicants from requesting FDA review staff to speculate about regulatory actions.

After explaining good review management fundamentals and operational principles, the GRMP Guidance focuses on the goals, milestones, and timelines for each of the five phases of a typical NDA/BLA first cycle review:[5] (1) Filing Determination and Review Planning Phase; (2) Review Phase; (3) Advisory Committee Meeting Phase; (4) Action Phase; and (5) Post-action Phase. Accompanying the discussion of each review phase are detailed tables that outline the phase and responsibility assignments, and refer to applicable regulations, guidance documents, and policies and practices.

The major application review milestones identified in the GRMP Guidance for each first cycle review phase of a "standard" and "priority" review are discussed briefly below.[6]

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[5] A first cycle review is the "standard" (ten month) or "priority" (six month) review period for a particular original NDA, BLA, or efficacy supplement (excluding labeling supplements that contain clinical data), which may be extended for an additional three months if a major amendment is submitted during the last three months of a review. A second cycle review begins when FDA receives a complete response to all deficiencies listed in an "approvable" or "not approvable" action letter (i.e., an application resubmission). See FDA, "Guidance for Industry: Classifying Resubmissions in Response to Action Letters," (Apr. 1998) (available at <http://www.fda.gov/cder/guidance/2360fnl.pdf>).

[6] The timelines identify the periods of time for a "standard" review. The number in parentheses indicates the timeline for a "priority" review.

Filing Determination and Review Planning Phase. Within 14 days of receiving an application, FDA assigns a review team from the applicable Center for Drug Evaluation and Research ("CDER") or Center for Biologics Evaluation and Research ("CBER") review division, and schedules a filing review meeting. Potential issues that could cause the agency to refuse to file an application should be communicated to an applicant as early in the review cycle as possible. The decision to file an application and to classify it for "standard" or "priority" review is typically made within 45 days of application receipt. In addition, the CDER/CBER review division conducts a planning meeting to develop a timeline for application review. Major review milestone timelines should be communicated to applicants. By day 60, the review division communicates a filing decision, and filing status (i.e., "standard" or "priority") if the application is filed. By day 74, the CDER/CBER review division sends a letter to the applicant identifying potential review issues (or the lack thereof).

Review Phase. The review of an application begins at the time it is assigned to a review division. Within 5 months (3 months for "priority" review) of receiving an application, the review division holds an internal mid-cycle meeting to discuss review status, revise the application review plan if necessary, and evaluate the need for additional interaction with the applicant concerning labeling, risk management, and potential postmarketing commitments. The review division should complete its review of an application by the end of month 8 (5 for a "priority" review).

Advisory Committee Meeting Phase. If FDA decides, during its review of an application, to convene an advisory committee meeting (e.g., because the drug is a new chemical entity, or raises significant safety or efficacy issues), the meeting should take place by the end of month 8 (5 for a "priority" review). The review division will follow-up with the applicant as necessary to address issues raised during an advisory committee meeting.

Action Phase. By the end of month 8 (5 for a "priority" review), the review division holds an internal wrap-up meeting to integrate the outcomes of reviews, consults, inspection reports, and advisory committee meeting follow-up. Labeling discussions with the applicant are scheduled to occur approximately 3 weeks prior to the PDUFA action date. If necessary, the review division and applicant will also discuss appropriate postmarketing commitments and risk management programs.

Post-action Phase. The postaction phase does not include specific timelines. The review division and applicant may meet to discuss lessons learned during the review process. In cases where an application was not approved, deficiencies may be clarified and expected responses (including resubmission) discussed.

Pursuant to the PDUFA reauthorization performance goals agreed to by the agency in June 2004, FDA has contracted with an independent consultant to undertake a study to evaluate issues associated with the conduct of first cycle reviews, including FDA's implementation of GRMPs. The study is ongoing, but should be issued by the end of Fiscal Year 2005.

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If you have any questions about this memorandum or would like additional information on GRMPs or drug development issues, please contact Kurt Karst (202.737.7544; krk@hpm.com).