Legal Backgrounder

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STREAMLINING APPEALS AT FDA: A MODEST PROPOSAL

By

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The recent jury verdict finding that Merck pharmaceuticals failed to warn consumers about research indicating a small increased risk of heart attacks among individuals using Vioxx for more than 18 months has re-ignited calls for Food and Drug Administration ("FDA") reform. FDA is well aware that it is far more likely to be criticized for approving a product now believed to be harmful than for failing to approve a product believed to be beneficial. Consequently, we can expect increased conservatism from the agency, which, in turn, is likely to lead to increased conflicts and disagreements between the FDA and regulated industry. While industry has various dispute resolution options at its disposal for such disagreements, sorting through the morass of choices can be a confusing and perilous experience.

Too often, regulations and guidance meant to assist industry in its interactions with the FDA do not provide clear roadmaps for choosing the proper appeals procedure — e.g., which is the appropriate Center or Office for submitting the appeals request? Why are there some overlapping procedures? How can one be certain if the issue for appeal is purely scientific versus administrative? Fragmentation and overlap lead to indecision and delays. The ability to correct problems diminishes and the purpose for bringing an appeal in the first place becomes questionable. Drugs and devices that benefit the public health may therefore not make it to market. A comprehensive strategy to coordinate and integrate the various appeals procedures would alleviate the confusion and indecision. This LEGAL BACKGROUNDER briefly discusses the various appeal routes within the FDA and provides a modest proposal for reform.

Any appeals procedure affords the aggrieved party a rehearing of a matter believed to have unjust results or to have been decided in error. Several routes to an appeal certainly prevent a

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bottleneck in any one area. But without proper guidance, the road to alleviation may only serve to retard and erode the just result. The following non-exhaustive examples illustrate the various vehicles by which industry may seek to resolve disagreements with FDA:

1. **Federal Food, Drug and Cosmetic Act** ("FFDCA") — where scientific controversy exists between the agency and industry, § 562 to the FFDCA provides a right of a timely review of such controversy. FDA amended 21 CFR § 10.75 to comply with these statutory provisions.

2. **Internal Agency Review of Decisions per 21 CFR § 10.75** — Through this process, an aggrieved party may request that the supervisor of a Center employee review a decision or action of the employee. All requests must be in writing and should clearly identify the action for which review is being sought, as well as provide an explanation of the reason(s) for the review request. In addition, internal reviews must be based on information in the official administrative file. If new information not in the file is provided, the matter will be returned to the original decision-maker for reconsideration. In addition, the aggrieved party may request that a scientific advisory panel review a scientific controversy — if such a review is denied, the aggrieved party may then submit a request for review of denial to the FDA Ombudsman.

3. **Filing a Citizen Petition per 21 CFR §§ 10.30 and 10.20** — this process may be used by any person to appeal any FDA action or decision. These petitions must include, among other things (a) a statement of the factual and legal grounds for taking the requested action, (b) information on any environmental impact, and (c) a certification that the petition includes all information and views relied upon.

4. **Scientific/Medical Dispute Resolution during the Investigational New Drug ("IND") Phase or New Drug Application ("NDA")/Abbreviated New Drug Application ("ANDA") Phase per 21 CFR §§ 312.48, 314.103**. In addition, in the Manual of Policies and Procedures ("MaPPs"), FDA's Center for Drug Evaluation and Research ("CDER") describes the role of agency reviewers, supervisors, and management when documenting views and findings and resolving differences involving disputes regarding INDs, NDAs, and ANDAs.

5. **Guidance Documents**, such as:

    a. *CDER/CBER Formal Dispute Resolution: Appeals Above the Division Level* (2000). Scientific, medical, procedural, and administrative disputes may arise at different points, including during drug development, new drug review, generic drug review, and postmarketing oversight. The agency may send a written response to the sponsor and/or request for advisory committee review of the dispute.

    b. *Guidance for Industry: Formal Meetings with Sponsors and Applicants for PDUFA Products* (2000) — outlines procedures for requesting meetings, information to be submitted, the conduct of meetings, and dispute resolution regarding meeting minutes.

    c. *Draft Guidance for Industry: Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical cGMP* (2003) — covers all scientific/technical issues related to cGMPs that arise during (1) cGMP and preapproval inspections for manufacturers of drug products and (2) cGMP inspections for biologics.

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d. *Center for Devices and Radiological Health ("CDRH"), Guidance: Medical Device Appeals and Complaints* (1998) — outlines the appeals procedures and primary contacts regarding premarket notification, premarket approval applications, product development protocols, investigational device exemptions, humanitarian device exemptions, post market surveillance, radiological devices, and various miscellaneous issues.

6. **Good Guidance Practices** ("GGPs") — per 21 CFR § 10.115, subsection(o), if someone at FDA is not following GGPs or is treating a GGP as binding, these regulations provide that an aggrieved party may elect to do the following:

    i. Contact the supervisor in the center/office that issued the guidance document; and if not resolved, contact the next highest supervisor;

    ii. Contact the specific center/office Ombudsman; or

    iii. If cannot resolve at the center/office level or if no progress is being made, the aggrieved party may request that Agency-wide Office of Ombudsman become involved.

7. **Office of Regulatory Affairs, Regulatory Procedures Manual** — provides for the resolution of disputes regarding Warning Letters.

8. **Office of the FDA Ombudsman** — this office assists aggrieved parties when problems/concerns are not or cannot be addressed at center or district level, or when concerns exist about raising issues at those levels. Problems addressed by the FDA Ombudsman might include import/export issues, as well as responses from FDA district, center, division, or office, FDA action/inaction. The FDA Ombudsman's Office also provides guidance on the course of action to resolve problems, and how a product will be regulated.

9. **Product Jurisdiction** per 21 CFR Part 3 — This section of the CFR details the procedures for determining the Agency component with primary jurisdiction for premarket review and regulation of combination products. Where issues cannot be easily resolved at the program level, a higher level of review is available from FDA's designated product jurisdiction officer, the Chief Mediator and Ombudsman.

10. **Dispute Resolution Working Group** — Formed as part of the 2002 initiative "Pharmaceutical cGMPs for the 21st Century: A risk-based approach", FDA's Dispute Resolution Working Group includes representatives of ORA, CDER, CBER, and CVM. The goal of this working group is to promote integrity, neutrality, consistency, transparency, fairness, and scientific soundness in the dispute resolution process. While 21 CFR § 10.75 and various guidance documents exist for the same purpose, the Dispute Resolution Working Group is specifically designed to address scientific disputes arising as part of the FDA inspection process.

By choosing a particular route for an appeal, the aggrieved party may be unwittingly choosing the route for delay of the matter's resolution. Some of the procedures do not provide any or enough clarity regarding grievance content, timetable for the entire process, whether by following the chosen procedure the aggrieved party may be foregoing other resolution options, whether other deadlines need to be heeded, or when the agency will make a decision on the matter. Moreover, the

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aggrieved party may be faced with the possibility that it filed an improper appeal and may be told that it must re-start the process. Consequently, the delays and other inadequacies encourage companies to forego legitimate claims. Companies may also be apprehensive about getting on the wrong side of agency decision-makers or about appealing an outcome which almost certainly will not be overturned within the Agency. Ultimately, these issues serve to make the various mechanisms for appeal well-intentioned, but in practice not helpful. Aggrieved parties may never know which conditions serve to facilitate, delay, stay, or preclude any ongoing or future regulatory action.

There is little social utility in an aggrieved party submitting to a time-consuming procedure whose outcome is pre-ordained or perceived as such. Drug and device manufacturers have every right to expect that, when the time comes for appeal, there will be a prompt determination and fair treatment. To ensure that such is possible, it may be helpful for the agency to consider a range of solutions. The worst possible solution would be to do nothing and allow the uncertainty in the present system to impose considerable costs on aggrieved parties. A more radical solution would be to eliminate the appeals process and institute an automatic rehearing of certain decisions by the supervisor of the first agency decision-maker. A more modest and viable solution, however, would be to impose a single agency-wide standard: provide one guidance per center that clearly delineates the typical process for any particular appeal, including the scope of the process, where to send the appeal, time frames, alternative processes (if any), and the strengths and weaknesses regarding each process.

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