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May 6, 2010

Food and Drug Administration

Division of Dockets Management (HFA-305)

5630 Fishers Lane, rm. 1061.

Rockville, MD 20852

## **Re: Docket No. FDA-2010-N-0128 (Prescription Drug User Fee Act Reauthorization)**

Dear Sir or Madam:

On behalf of the patients we represent, National Patient Advocate Foundation (NPAF) is pleased to submit comments to the Food and Drug Administration regarding the reauthorization of the Prescription Drug User Fee Act (PDUFA). The comments submitted are a collaboration of National Patient Advocate Foundation's regulatory staff, the Scientific Advisory Committee of the Board of Directors chaired by Robert Rifkin, MD, FACP, Director of NMDP Collections at Rocky Mountain Cancer Centers, and the Scientific Advisor to the Executive Board of Directors, Dennis Gastineau, MD, Chair, Division of Hematology at the Mayo Clinic.

NPAF is a national non-profit organization which provides the patient voice on issues relating to improving access to, and reimbursement for, high-quality, affordable healthcare. The advocacy activities of NPAF are informed and influenced by the experience of patients who receive case management services from our companion organization, Patient Advocate Foundation (PAF), which provides professional case management services to patients with chronic, debilitating or life-threatening conditions. In 2009, the PAF Patient Services Division provided direct assistance to 55,384 new patients, which constitutes a 15% increase from 2008 and a 102% increase from 2005. [1]

NPAF has assessed the overall performance of PDUFA IV in preparation for the scheduled reauthorization and with this letter is commenting on particular aspects of the law that we believe should be retained, changed or discontinued. NPAF acknowledges that PDUFA has contributed to a more streamlined, safe and efficient drug development and review process. Since PDUFA was enacted, the review and approval time for drugs has dropped nearly 60% which has facilitated increased patient access to new drugs and biologics. Specifically, from FY1993-2009, FDA approved over 1,000 New Drug Applications (NDA) and 100 Biologic License Applications (BLA). [2] Since some patients diagnosed with chronic, debilitating or life-threatening diseases are willing to accept a higher risk level for the possibility of alleviation or eradication of their disease, they stand to benefit the most from decreased drug approval times.

While PDUFA has decreased drug approval times, NPAF believes there are significant issues that need to be addressed with the implementation of PDUFA V. Further discussion between stakeholders and the FDA is imperative in certain areas, including the balance between safe and effective drugs and the need for faster drug development, the importance of increased PDUFA funding from both user fees and federal appropriations and the need for increased transparency as the PDUFA reauthorization process moves forward.

Patient safety is of the utmost importance to NPAF. We are pleased that PDUFA IV incorporates efforts to enhance patient safety by improving drug safety and reviewing serious adverse event data. However, we are concerned that PDUFA IV provisions repeatedly require the FDA to perform multiple functions for which they are inadequately funded. Areas of concern that we would like to address are noted below.

### **Postmarket Studies and Surveillance**

NPAF acknowledges that PDUFA IV allows consumers and medical professionals to access drug information in a more transparent way through an accessible, consolidated website which includes information found on the United States Library of Medicine's Daily Med and Medicine Plus websites. These sites include patient labeling and packaging inserts, as well as links to medication guides and clinical trial registries. [3]

Medication guides can be extremely helpful to patients. However, NPAF is concerned that the language included in the guides is often not easily understood by patients as it is complex and cites unfamiliar scientific terms. These guides are supposed to be written in language that the patient can understand but currently, the acceptable level of language is not being met. As a result, we believe that adherence to drug protocols will suffer since many patients will not read the guides, either because they are difficult to understand or because the message is stark and direct. NPAF recognizes that FDA appreciates the importance of developing easily understandable medication guides in order to maximize effectiveness and patient safety. As a result, we expect that the current guides can be improved by writing them at a sixth grade reading level, as well as in a clear, concise format that is appropriate for patients.

### **Risk Evaluation and Mitigation Strategy**

NPAF is concerned that the increasing number of administrative requirements placed on physicians may be overly burdensome. Since not all REMS reports are structured similarly, and the number of products requiring REMS is increasing, NPAF believes that developing a more universal, formal REMS structure can allay some of this burden. A more standardized REMS format would enhance clarity and allow critically important information to be succinctly summarized so that doctors and patients can better understand the risks and benefits of a given therapy. NPAF believes that patients, as well as patient advocates, should be aware of the REMS process and be given an opportunity to participate in a reasonable manner.

NPAF also believes that constant REMS evaluations may in fact be unnecessary. It is the conclusion of our collaborators that at the end of three years, adequate conclusions regarding a specific REMS should have been reached. NPAF supports the elimination of the seven year assessment after an adequate review of the three year assessment.

While NPAF agrees that it is necessary for patients to fully understand the risks and benefits of a given treatment, we would like to stress that the REMS process is emotionally difficult for doctors and patients alike, given that the discussion of "possible death" appears in the first line of certain REMS. Risk statements should be proportionate to the actual risk, and "possible death" in the first line may be an overemphasis that causes disproportionate distress among patients and providers alike. This further illustrates the need to draft language that is easily comprehended by the patient with as much sensitivity to human fear and emotion as possible.

### **Assuring Access and Minimizing Burden**

Patient registries are an invaluable mechanism used to collect patient data and evaluate crucial outcomes for a particular patient population, especially with regard to safety. NPAF urges the development of standardized, structured patient registries that apply to both brand name and generic drugs in order to simplify the process for physicians. NPAF recognizes that numerous patient registries add significantly to physician workloads, not only in terms of updating, but also reviewing registry information. Moreover, the abundance of patient registries place doctors in the unfortunate position

of trying to determine whether or not they have time to sign up for a particular registry and which ones are the best to use, potentially affecting the choice of drug recommended. We believe that standardization could ease physician workload and would provide a consistent mechanism to assess patient outcomes.

### **Active Postmarket Risk Identification and Analysis**

The PostMarket Risk Identification and Analysis provision of PDUFA IV states “ not later than 180 days after the date of the establishment of the active postmarket risk identification and analysis system under this subsection, the Secretary shall establish and implement procedures under which the Secretary may routinely contract with one or more qualified entities to classify, analyze, or aggregate data described in paragraph (3)(C) and information that is publicly available or is provided by the Secretary.” [3]

NPAF believes that the methodology implemented in this analysis system is imperative to assure the quality of the data, which can be further enhanced by limiting its scope. Thus, we commend the legislation for the inclusion of the following provision in PDUFA IV:

“(ii) REQUEST FOR SPECIFIC METHODOLOGY.—The procedures described in clause (i) shall permit the Secretary to request that a specific methodology be used by the qualified entity. The qualified entity shall work with the Secretary to finalize the methodology to be used.

NPAF also believes that qualified entities must meet clearly defined requirements in order to accurately analyze aggregate data. We further commend the legislation for the including the following provision in PDUFA IV:

“(ii) QUALIFICATION.—The Secretary shall enter into a contract with an entity under clause (i) only if the Secretary determines that the entity has a significant presence in the United States and has one or more of the following qualifications:

“(I) The research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the activities under this paragraph, including the capability and expertise to provide the Secretary de-identified data consistent with the requirements of this subsection.

“(II) An information technology infrastructure in place to support electronic data and operational standards to provide security for such data.

“(III) Experience with, and expertise on, the development of drug safety and effectiveness research using electronic population data.

“(IV) An understanding of drug development or risk/benefit balancing in a clinical setting.

“(V) Other expertise which the Secretary deems necessary to fulfill the activities under this paragraph.

### **User Fees / Adequate Funding**

NPAF believes that FDA needs additional funding and should not rely so heavily on user fees. User fees fund a major share of human drug review program costs. In FY2008, 65% of human drug reviews were funded with user fees. [2] NPAF believes that a 65% user fee proportion weakens public confidence in PDUFA and does not serve the best interest of patients. NPAF supports increased federal appropriations to better equalize PDUFA funding. The Alliance for a Stronger FDA, to which we belong, sought a \$500 million increase (21.2%) in FDA’s appropriation for FY 2011. [4] NPAF supports this appropriation request. In addition, FDA needs a \$120 to \$140 million increase just to sustain current program levels and about a \$250 million increase to fund both current program levels at FDA and the program growth recommended by the President. President Obama’s budget request was for a \$154 million increase for FDA, a little over 6%. [4] It is a good start compared to the President’s recommendation for other agencies, but not nearly enough to fund both current program levels and the newly mandated growth at FDA.

An increasing number of NDAs and BLAs are now being discussed at Advisory Committee meetings. In 2009, nearly 60 NDAs/BLAs required an Advisory Committee meeting. [5] The Center for Drug

Evaluation and Research (CDER) recent hiring surge resulted in a decline in the average level of on-board review expertise in PDUFA IV [5], which NPAF anticipates will reduce the number of approvals in 2010. The Food and Drug Administration Amendments Act of 2007 (FDAAA) added additional requirements to the FDA which were not accounted for in FDA-industry fee negotiations and goals that FDA committed to in PDUFA IV [5]. For example, under Title IX in FDAAA, over 200 post-marketing studies and clinical trials, as well as 32 safety label changes were required by March 1, 2010. [5]

NPAF would like to emphasize that an underfunded FDA faced with expanding responsibilities may adversely affect the drug development and review process, which will ultimately impact patient access to life-saving therapies and is a disincentive to sustained research and development in the United States.

### **PDUFA IV Drug Safety Enhancement Resources**

Current funding for Postmarket Safety Activities is \$13 Million FY 2008 - \$16 million FY 2012, and funding for Epidemiology Best Practices and Expanded Health Data is \$7 million FY 2008 – \$9.5 million FY 2012. [6] NPAF questions whether the respective funding levels are adequate to support the scope of these initiatives. Will FDA need to hire additional staff to implement Postmarket Safety and Epidemiology Initiatives? NPAF seeks further information regarding the labor pool required to fill these positions, including job descriptions and credentials, as well the sources of the new hires. Due to sustained and accelerated health care related workforce issues, NPAF urges FDA to establish a formal workforce committee to address these questions and to report their findings to Congress. NPAF is hopeful that FDA can complete a study of its resource needs and make the findings available.

NPAF supports an open, transparent PDUFA reauthorization process that includes perspectives from consumer groups, health care professionals, representatives from regulated industry and patients, and thanks FDA for the opportunity to share our perspectives. Patients, especially those diagnosed with chronic, debilitating or life-threatening diseases rely on the health care system for their very lives and thus, have a unique and valuable perspective that provides clarity and credibility to the PDUFA reauthorization process.

Thank you for the opportunity to submit comments on PDUFA reauthorization. When we can be of assistance, please do not hesitate to contact us.

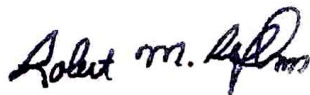
Sincerely,



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## Endnotes

- [1] Patient Advocate Foundation, “Patient Data Analysis Report: 2009”, pg. 7-8. April, 2010.
- [2] Mullen, Theresa M. “PDUFA Program Overview”, U.S. Food and Drug Administration, pg. 7, 10, 2010.
- [3] Public Law 110-85, 110th Congress.
- [4] Alliance for a Stronger FDA. “President Obama’s FY2011 Request for the FDA Compared to the Alliance for a Stronger FDA’s FY 2011 Request.”  
[http://fdaalliance.files.wordpress.com/2009/11/fda\\_alliance\\_administration-appropriation-request-fy11-vs-alliance-request-\\_02-02-10\\_-latest.pdf](http://fdaalliance.files.wordpress.com/2009/11/fda_alliance_administration-appropriation-request-fy11-vs-alliance-request-_02-02-10_-latest.pdf)
- [5] Jenkins, John K. “FDA Drug Review in PDUFA IV”, U.S. Food and Drug Administration, pg. 10-12, 2010.
- [6] U.S. Food and Drug Administration, “Prescription Drug User Fee Act (PDUFA) IV Drug Safety Five-Year Plan” pg 14, December, 2008.