



November 28, 2016

Division of Dockets Management (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2016-N-2872: Medical Device User Fee Amendments; Public Meeting; Request for Comments; Extension of Comment Period

Dear Sir or Madam:

On behalf of the 30 million Americans with one of the nearly 7,000 known rare diseases, NORD thanks the Food and Drug Administration (FDA) for the opportunity to provide comments on the Agency's "Medical Device User Fee Amendments; Public Meeting; Request for Comments; Extension of Comment Period".

NORD is a unique federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

The reauthorization of the Medical Device User Fee Act (MDUFA) every five years gives the FDA, the regulated device industry, and patient stakeholders the opportunity to reexamine the medical device review process to make devices safer, more effective, and more patient-focused.

The MDUFA IV Commitment Goals Letter outlined within this Request for Comments includes several important provisions for the rare disease patient community. Below are our comments on two specific sections of the Goals Letter followed by several additional policy areas to consider.

III. Proposed MDUFA IV Recommendations:

L. Patient Engagement:

NORD is thankful for the inclusion of this proposal to facilitate greater Agency actions to "advance patient input and involvement in the regulatory process".

Greater patient involvement in the medical device development and review process is one of NORD's main priorities for the MDUFA reauthorization as discussed in our July 2015 public statement, and reiterated throughout the monthly stakeholder meetings. We believe that patients and patient organizations need to be fully integrated into the device development and review process in order for more patient-centric devices to reach rare disease patients.

We believe this provision will successfully move us forward in this direction. FDA will build its staff capacity and expertise to incorporate and review patient perspective information (PPI) and patient reported outcomes (PROs) through additional MDUFA-supplied resources. The FDA will also hold one or more public meetings to facilitate public discussion and feedback on the generation and integration of PPI and PROs.

In order to focus the FDA efforts within this initiative, FDA proposes to “identify priority areas where decisions are preference-sensitive and PPI data can inform regulatory decision-making, in order to advance design and conduct of patient preference studies in high impact areas”. While we understand the need to focus efforts to the areas of greatest potential benefit, we request that FDA do so incredibly carefully. Too often rare diseases have been forgotten due to the small patient populations and limited advocacy resources.

If the FDA moves forward with identifying priority areas for PPI development, we request that the FDA put forward extensive and easily digestible information and instructions for disease areas or patient populations that may not have been identified as a priority. Potentially analogous is the Patient-Focused Drug Development (PFDD) Initiative administered by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). The PFDD Initiative will hold twenty four public meetings on specific diseases or disease areas, and has also put forward instructions for patient organizations to move forward with their own meetings.

We hope FDA will similarly ensure that patient organizations can fully take advantage of the new FDA offerings and information on PPIs and PROs even if their disease area is not identified as a priority.

Similarly, we request that FDA ensure that all information put forward on how patients and patient organizations can participate within this initiative is accessible and digestible to the full spectrum of regulatory sophistication within the patient organization community. Approximately seventy percent of NORD’s over 250 member rare disease patient organizations have fewer than five full-time employees, and they likely have very limited resources to dedicate to regulatory engagement and expertise development or investment.

For this reason, we request that FDA put forward resources with patient organizations of all sizes and regulatory capabilities in mind in order to ensure that all rare disease patients and their organizations have an opportunity to benefit from this exciting initiative.

Finally, with similar initiatives on patient preference information proposed as part of the Prescription Drug User Fee Act (PDUFA) reauthorization, we hope these initiatives will develop consultatively and collaboratively to ensure they work in harmony, and patients and patient organizations are not presented with confusingly disparate opportunities.

M. Real World Evidence (RWE)

We thank FDA and the regulated industry for the inclusion of this provision on real world evidence. Rare diseases are nearly uniformly under studied and investigated resulting in a dearth of data on the

treatment of rare diseases. Through the MDUFA investment in the National Evaluation System for health Technology (NEST), additional data on the use of devices in rare diseases can be collected.

This data could prove incredibly valuable. Many rare disease patients use a device off-label because that particular device was never studied in the rare disease population prior to marketing approval. Through the collection of real world data in these populations, indications could be expanded, and rare disease indications could be added using real world evidence.

Finally, we request patients and patient organizations to be formally included within the infrastructure of the NEST. We understand it is the intention for patients to be well represented on the board of the NEST, but we request formal assurance that patients and their organizations will be represented.

Additional Areas to Consider:

As the MDUFA agreement progresses towards final enactment, NORD would like to propose additional areas to consider policy changes.

Regulatory Review of Certain Device-led Humanitarian Use Device and Drug Combination Products:

Drugs are approved based upon their safety and effectiveness (FD&C §505). Humanitarian Use Devices (HUDs) are devices that treat fewer than 4,000 individuals per year. HUDs are given a Humanitarian Device Exemption (HDE) from showing efficacy, and are instead approved based upon safety and probable benefit (FD&C §520). This is because the small patient populations make showing efficacy incredibly difficult.

In combination products, all components of the product must be approved using the same standard. Under statute, drugs may only be approved based upon safety and effectiveness. In a combination product that combines a drug and a humanitarian use device, the combination product must be approved based upon safety and effectiveness because the drug cannot be approved on any other standard.

If a HUD is a component of a combination product, it is required to meet the drug component's required safety and effectiveness standard. Effectiveness is very difficult for HUDs to demonstrate due to the economic and logistical barriers of studying small patient populations.

It is therefore very difficult for sponsors to show effectiveness in a HUD. Alternatively, a sponsor of a drug/HUD combination product could get each of the components approved individually, but this is economically and regulatorily infeasible.

This results in combination products with a HUD as a component simply not being developed due to the often unachievable effectiveness standard.

We believe there may be a simple solution. For drug/HUD combination products in which the drug component has already been approved by CDER or CBER on safety and effectiveness, the drug/HUD combination product will be approved based upon safety and probable benefit.

This targeted approach will allow drug/HUD combination products to reach patients without compromising their safety. Only drug/HUD combination products in which the drug has previously been approved in other routes of administration will qualify. Thus, there should be no concern regarding exposing patients to potentially unsafe or ineffective treatments.

NORD intends on continuing our advocacy for this targeted change as part of the MDUFA reauthorization process.

Office of Patient Affairs:

While NORD is certainly supportive of the growing number of opportunities for patients to participate within FDA processes, we are growing concerned about the lack of coordination amongst such opportunities and are worried patients may be confused on how best to participate.

For this reason, we have proposed that the current Patient Liaison Program (PLP) housed within the Office of Health and Constituent Affairs be elevated to become the Office of Patient Affairs directly beneath the Commissioner (the same level as the Office of Women's Health and Office of Minority Health).

This location will allow the Office of Patient Affairs to more visibly publicize patient involvement opportunities, and assist in the coordination of CDER's PFDD initiative and Professional Affairs and Stakeholder Engagement (PASE) office, CBER's patient involvement opportunities, CDRH's efforts on patient perspective data and the Patient Engagement Advisory Committee, and the various opportunities the PLP already oversees, among others.

This office will be better equipped to handle patient inquiries on expanded access and can better assess patient's conflict-of-interest determinations. All in all, we believe this office could greatly improve rare and common disease patient's involvement with the FDA, and we are hopeful for its enactment. For more information on this proposal, please visit our website at rarediseases.org.

We thank FDA for the opportunity to comment, and we look forward to working with FDA to ensure the continued growth in therapeutic development for rare diseases, and the continued involvement of patients in the development and review process. For questions regarding NORD or the above comments, please contact me at mrinker@rarediseases.org or (202) 588-5700, ext. 102.

Thank you in advance for your consideration.

Sincerely,

A handwritten signature in blue ink, appearing to read "Martha Rinker".

Martha Rinker, J.D.
Vice President, Public Policy