



**Breakthroughs that
change patients' lives**

FDA Public Meeting on *Promoting Effective Drug Development Programs: Opportunities and Priorities for the FDA's Office of New Drugs*

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Presentation Topics

- Development of new medicines for severely debilitating or life-threatening disorders (SDLTs) beyond oncology and hematology
- Post-market requirement (PMR) and commitment (PMC) process
- Adoption of novel regulatory science tools and methods



Severely Debilitating or Life-Threatening Diseases (SDLT)

- Examples of potential SDLTs with short-term survival rates and rapidly progressing disease span across divisions¹

Office of Infectious Disease	Office of Cardio, Hematology, Endo, & Nephrology	Office of Neuroscience	Office of Immunology and Inflammation
Ebola	Severe congestive heart failure	Advanced Parkinson’s disease	Lupus Nephritis
Congenital CMV	Late stage diabetic nephropathy	Progressive Supranuclear palsy	Diffuse systemic sclerosis
		Advanced multiple sclerosis	Advanced COPD

- FDA recently issued ICH s9-like *Guidance for Severely Debilitating or Life-Threatening Hematologic Disorders: Nonclinical Development of Pharmaceuticals* to facilitate streamlined nonclinical studies for SDLTHD
- The current definition of SDLTHD is applicable to SDLT diseases **across therapeutic areas** (outside of oncology or hematology) for which there is a high unmet need due to an inadequate standard of care.
- Benefits of enabling efficient development of SDLT therapeutics across therapeutic areas include:
 1. Earlier patient access to new therapies for SDLT diseases
 2. Avoidance of unnecessary use of animals and other drug development resources, and
 3. Reduction in the economic burden and societal costs associated with late-stage and end-of-life conditions.



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¹ JS Prescott, PA Andrews, RW Baker, et al. Evaluation of Therapeutics for Advanced-Stage Heart Failure and Other Severely-Debilitating or Life-Threatening Diseases. *Clinical Pharmacology & Therapeutics* 102(2), 219-227 (August 2017).

Defining scope and requirements is critical to ensure patient safety and consistent application of SDLT designation

Recommendations

1. A **SDLT workshop** focused on objective criteria to define SDLTs across therapeutic areas, considerations for nonclinical and clinical development expectations of SDLTs, and post-marketing expectations.
2. New, Cross-Therapeutic **Guidance** to:
 - Broaden Definitions to Include SDLT Across Therapeutic Areas
 - Establish Objective Scope and Criteria for Consistent Application of SDLT Designation
 - Clarify Nonclinical and Clinical Development Expectations

Scope/Requirements

- Objective and quantifiable medical, clinical, or scientific data which support:
 1. A defined patient population including objective criteria that distinguishes between SDLT and non-SDLT patients
 2. Evidence that the selected patient population is either severely debilitated or has a shortened life expectancy due to the disease, and that adequate therapy is unavailable resulting in a high unmet medical need
 3. Safety and response to the investigative drug can be appropriately monitored in the clinic



PMC / PMR Process Reforms

- Pfizer recommends the acceptance of novel trial designs to satisfy post-marketing commitments (PMCs) and requirements (PMRs).
- Variation exists in how review divisions approach the selection of PMC/PMRs, both with respect to the types of studies required and the timing of these discussions which can occur quite late in the review period or in the post-market.
- This can result in insufficient opportunity for scientific dialogue around study objectives and feasibility.

Recommendations:

1. Adequate Time for Scientific Discussion of PMR Objectives and Feasibility
2. Post-Market Dialogue around PMC/PMR Study Progress
3. Novel Approaches to Satisfying PMC/PMRs



Regulatory Science Adoption and Change Management

- FDA regulatory science initiatives and pilots would benefit from a structured change management and implementation process across the project lifecycle - from ideation to initiation of new initiatives to full-scale adoption (or non-adoption) of the regulatory science approach across review divisions.
- A more structured regulatory science implementation process should be based upon the principles of change management to build quality into regulatory science programs from the outset and ensure clarity in the process.
 1. Identification of what regulatory practice or tool will be changed
 2. Evaluation of the impact of the change on drug development, review, and regulation
 3. Planning and implementation of the change across all relevant offices and functions
 4. Validation and monitoring of the change to ensure consistent and effective implementation
- A public communication plan would be valuable for transparency and to improve predictability in regulatory science decision-making

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Thank You