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Public Meeting on Functional Gastrointestinal (GI) Disorders Patient-Focused Drug Development

May 11, 2015

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Welcome

Sara Eggers, PhD
Office of Strategic Programs
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U.S. Food and Drug Administration

May 11, 2015

Agenda

- **Setting the context**
  - Opening Remarks
  - Overview of FDA's Patient-Focused Drug Development Initiative
  - Background on Functional GI Disorders and Therapeutic Options
  - Overview of Discussion Format

- **Discussion Topic 1**: Disease symptoms and daily impacts that matter most to patients

- **Discussion Topic 2**: Patients' perspectives on current approaches to treating functional GI disorders

- **Open Public Comment**

- **Closing Remarks**

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Opening Remarks

Donna Griebel, MD

Deputy Director, Division of Gastro-enterology and Inborn Errors (DGIEP)
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

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FDA's Patient-Focused Drug Development Initiative

Theresa Mullin, PhD
Director, Office of Strategic Program
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

May 11, 2015

Patient-Focused Drug Development under PDUFA V

- **FDA is developing a more systematic way of gathering patient perspective on their condition and available treatment options**
  - Patient perspective helps inform our understanding of the context for the assessment of benefit-risk and decision making for new drugs
  - Input can inform FDA's oversight both during drug development and during our review of a marketing application

- **Patient-Focused Drug Development is part of FDA commitments under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V)**
  - FDA will convene at least 20 meetings on specific disease areas in Fiscal Years (FY) 2013 - 2017
  - Meetings will help develop a systematic approach to gathering patient input

Identifying Disease Areas for the Patient-Focused Meetings

- **In September 2012, FDA announced a preliminary set of diseases as potential meeting candidates**
  - Public input on these nominations was collected. FDA carefully considered these public comments and the perspectives of our drug review divisions at FDA

- **FDA identified a set of 16 diseases to be the focus of meetings for fiscal years 2013-2015**
  - Another public process has been initiated to determine the disease set for fiscal years 2016-2017

Disease Areas to be the focus of meetings for FY 2013-2015

FY 2013

- Chronic fatigue syndrome
- HIV
- Lung cancer
- Narcolepsy

FY 2014

- Sickle cell disease
- Fibromyalgia
- Pulmonary arterial hypertension
- Inborn errors of metabolism
- Hemophilia A, Hemophilia B, von Willebrand disease, and other heritable bleeding disorders
- Idiopathic pulmonary fibrosis

FY 2015

- Female sexual dysfunction
- Breast cancer
- Chagas disease
- **Functional gastrointestinal disorders**
- Alpha-1 antitrypsin deficiency
- Parkinson's disease and Huntington's disease

Tailoring Each Patient-Focused Meeting

- **Each meeting focuses on a set of questions that aim to elicit patients' perspectives on their disease and on treatment approaches**
  - We start with a set of questions that could apply to any disease area; these questions are taken from FDA's benefit-risk framework and represent important considerations in our decision-making
  - We then further tailor the questions to the disease area of the meeting (e.g., current state of drug development, specific interests of the FDA review division, and the needs of the patient population)
- **Focus on relevant current topics in drug development for the disease at each meeting**
  - E.g., focus on HIV patient perspectives on potential "cure research"
- **We've learned that active patient involvement and participation is key to the success of these meetings.**

"Voice of the Patient" Reports

- Following each meeting, FDA publishes a Voice of the Patient report that summarizes the patient testimony at the meeting, perspectives shared in written docket comments, as well as any unique views provided by those who joined the meeting webcast.

- These reports serve an important function in communicating to both FDA review staff and the regulated industry what improvements patients would most like to see in their daily life.

- FDA believes that the long run impact of this program will be a better, more informed understanding of how we might find ways to develop new treatments for these diseases.

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Background on Functional Gastrointestinal Disorders and Therapeutic Options

Laurie Muldowney, MD

Medical Officer, DGIEP
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

May 11, 2015

Functional Gastrointestinal Disorders (FGID)

- Term used to describe a group of common, chronic gastrointestinal conditions
  - Can affect any part of the GI tract
  - Characterized by chronic time course and unpredictable symptom exacerbations
- Generally there are no anatomical, structural, or biochemical abnormalities
  - Signs and symptoms relate to abnormal intestinal motility, abnormal intestinal perception, and/or abnormal brain-gut communication
- Diagnosis based on signs and symptoms (Rome Criteria)

Functional Gastrointestinal Disorders

- 28 adult and 17 pediatric FGID based on the Rome III diagnostic criteria
- These include:
  - Irritable bowel syndrome (constipation predominant, diarrhea predominant, mixed/unsubtyped)
  - Chronic idiopathic constipation
  - Functional dyspepsia (non-ulcer dyspepsia)
  - Gastroparesis
  - Functional abdominal pain
- Overlap between these disorders and many patients suffer from 2 or more FGID

Highly Prevalent

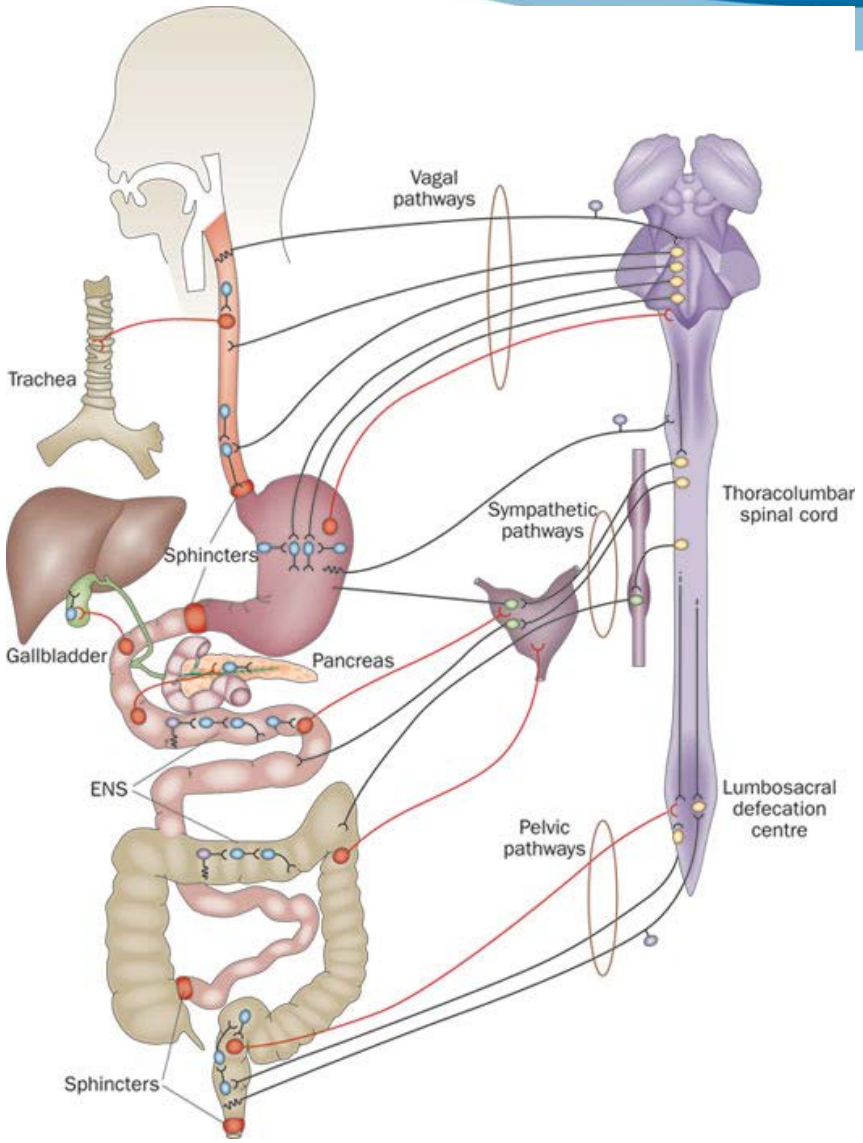
- At any one time, ~2 out of 5 people are affected by a FGID
- FGIDs impact across age, gender, race, ethnicity, and socioeconomic status

Disorder	Prevalence in General Population
Functional Dyspepsia	20% to 30%
Irritable Bowel Syndrome	10% to 20%
Functional Constipation	Up to ~25%
Gastroparesis	Up to 2%

Rome III: The Functional Gastrointestinal Disorders, Third Edition. Douglas A Drossman (senior editor) 2006.

Role of ENS

- Abnormalities in the **enteric nervous system** (“little brain in the gut”)
- Problems in communication between the enteric nervous system and the central nervous system



Signs and symptoms

- Pain
- Heartburn
- Abdominal distension
- Nausea

- Vomiting
- Bloating
- Constipation
- Diarrhea

Impact

- Individuals experience significant suffering related to their disorders
  - lower quality of life scores which assess physical, social, and emotional wellbeing
- Misunderstanding of these disorders, even in the medical community, can lead to misdiagnosis, misguided treatment, and worse outcomes
  - Can lead to unnecessary surgery

Spiegel B. IFFGD; 2007;205.
Cole JA, Yeaw JM, Cutone JA, et al. Dig Dis Sci 2005;50(12:2268-75. 5, 6

Cost of FGID

- Direct costs (i.e., medical costs) estimated at $1.5 to $10 billion
  - Close to 4 million physician visits
  - Misdiagnosis and under-recognition may lead to multiple visits, unnecessary diagnostic tests and procedures
- Indirect costs estimated at up to $20 billion
  - 4 – 13 missed work days per year (compared to 1 – 6 in patients without FGID)

Cash B, Sullivan S, Barghout V. Am J Manag Care. 2005;11:S7 – 16.
Drossman DA, Li Z, Andruzzi E, et al. Dig Dis Sci. 1993;38:1569 – 1580.

Treatment Options

- Dietary management
- Over-the-counter treatments
  - e.g., antidiarrheals, pro-motility agents, proton pump inhibitors, H2 blockers
- Prescription therapies
  - lubiprostone, linaclotide, metaclopramide, alosetron
- Off-label and investigational therapies
- Medical devices, feeding tubes

Patient-Reported Outcomes

- For conditions like functional bowel disorders, where no structural or biochemical abnormality can be seen, input from patients is especially important
- Patient-reported outcomes (PROs) can represent direct measures of treatment benefit – how a patient feels or functions
- All measurements need to be evaluated in adequate and well-controlled randomized trials
- Patient and caregiver input is essential to capture important and clinically-relevant disease symptoms in the PROs

Thank You

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Overview of Discussion Format

Sara Eggers, PhD
Office of Strategic Programs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

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Discussion Overview

Topic 1: The symptoms that matter most to you

- Which symptoms have the most significant impact on your life?
- How do these symptoms affect your ability to do specific activities?
- How have your symptoms changed?

Topic 2: Current approaches to treating functional GI disorders

- What are you doing to treat functional GI disorders?
- What are the biggest downsides to your treatments?
- What would you look for in an “ideal” treatment?

Discussion Format

- **We will first hear from a panel of patients and caregivers**
  - The purpose is to set a good foundation for our discussion
  - They reflect a range of experiences with breast cancer

- **We will then broaden the dialogue to include patients and patient representatives in the audience**
  - The purpose is to build on the experiences shared by the panel
  - We will ask questions and invite you to raise your hand to respond
  - Please state your name before answering

Discussion Format, continued

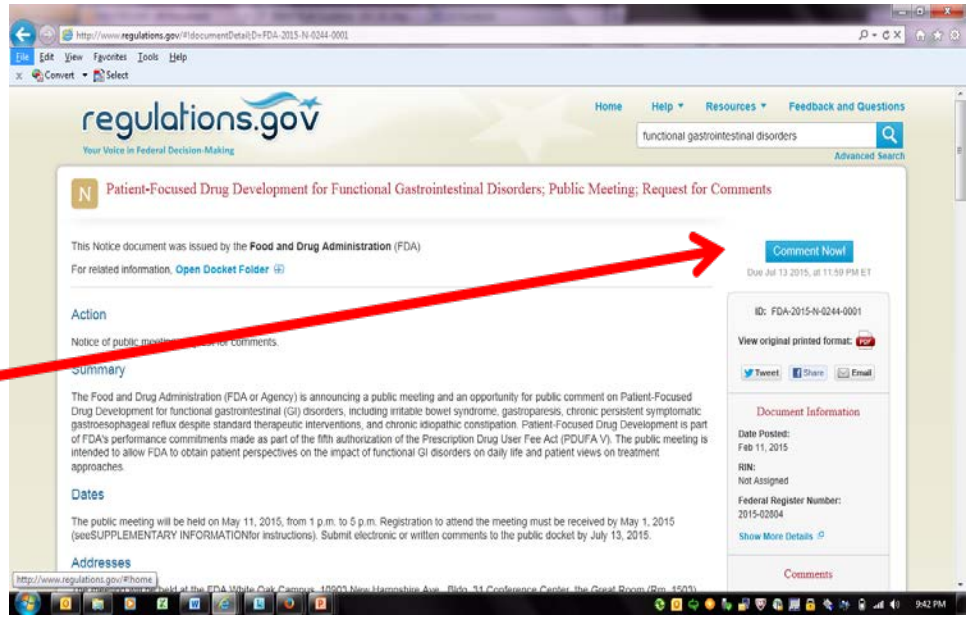
- **You'll have a chance to answer "polling" questions**
  - Their purpose is to aid our discussion
  - In-person participants, use the "clickers" to respond
  - Web participants, answer the questions through the webcast
  - Patients and patient representatives only, please

- **Web participants can add comments through the webcast**
  - Although they may not all be read or summarized today, your comments will be incorporated into our summary report
  - We'll occasionally go to the phones to give you another opportunity to contribute

Send us your comments!

- **You can send us comments through the "public docket"**
  - The docket will be open until July 13, 2015
  - Share your experience, or expand upon something discussed today
  - Comments will be incorporated into our summary report
  - Anyone is welcome to comment

Visit:
http://www.regulations.gov/#!documentDetail;D=FDA-2015-N-0244-0001
Click Comment Now!



Resources at FDA

- FDA Office of Health and Constituent Affairs
  - Contact: PatientNetwork@fda.hhs.gov, (301) 796-8460
  - Liaison between FDA and stakeholder organizations
  - Runs the Patient Representative Program
    - Patient Representatives advise FDA at Advisory Committee meetings
- CDER Office of Center Director
  - Professional Affairs and Stakeholder Engagement (PASE)
  - Contact: Christopher Melton, christopher.melton@fda.hhs.gov
  - Facilitates communication and collaboration between CDER and patient and healthcare professional stakeholders and others on issues concerning drug development, drug review and drug safety.

Discussion Ground Rules

- We encourage patients to contribute to the dialogue– caregivers and advocates are welcome too
- FDA is here to listen
- Discussion will focus on symptoms and treatments
  - Open Public Comment Period is available to comment on other topics
- The views expressed today are personal opinions
- Respect for one another is paramount
- Let us know how the meeting went today; evaluations at registration desk

Discussion Topic 1

Disease symptoms and daily impacts that matter most to patients

Sara Eggers
Facilitator

Topic 1 Panel Participants

- Bettemarie Bond
- Tanya Taylor
- Carrie Reilly
- Cynthia Bens

Topic 1 Discussion: Disease symptoms and daily impacts that matter most to patients

- Have you received a diagnosis of a functional GI disorder from a healthcare provider? If so, please state the condition.
- Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your life?
- Are there specific activities that are important to you but that you cannot do at all or as fully as you would like because of your condition?
- How has your condition and its symptoms **changed over time**?
- What **worries you most** about your condition?

BREAK

Discussion Topic 2

Patients' perspectives on current approaches to treating Functional GI Disorders

Sara Eggers
Facilitator

Topic 2 Panel Participants

- Carol Pasinkoff
- Lynn Wolfson
- Meredith Holt
- Jillian Chilson
- Anne Sirota (Phone)

Topic 2 Discussion: Patients' perspectives on current approaches to treating functional GI disorder

- **What are you currently doing** to help treat your condition or its symptoms?
- What specific symptoms do your treatments address?
- **How well** does your current treatment regimen treat the most significant symptoms of your disease?
  - How well do these treatments stop or slow the progression of your condition?
  - How well do these therapies improve your ability to do specific activities that are important to you in your daily life?
  - How well have these treatments worked for you as your condition has changed over time?
- What are the most significant **downsides to your current treatments**, and how do they affect your daily life?
- Assuming there is no complete cure for your condition, what specific things would you look for in an **ideal treatment** for your condition?

Open Public Comment Period

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Closing Remarks

Andrew Mulberg, MD FAAP

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