

## Meeting Minutes

### Department of Health and Human Services National Institutes of Health National Commission on Digestive Diseases

November 19, 2007

#### I. CALL TO ORDER

The Chairman of the National Commission on Digestive Diseases, Stephen P. James, M.D. called to order the fourth meeting of the Commission at 9:00 a.m. on Monday, November 19, 2007 at the Sofitel O'Hare in Rosemont, IL.

#### A. ATTENDANCE – COMMISSION MEMBERS PRESENT

STEPHEN P. JAMES, M.D., National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH)

BRUCE R. BACON, M.D., St. Louis University

BARBARA L. BASS, M.D., The Methodist Hospital, Houston

RICHARD S. BLUMBERG, M.D., Brigham and Women's Hospital

JOHN M. CARETHERS, M.D., University of California, San Diego

MAURICE A. CERULLI, M.D., New York Methodist Hospital

EUGENE B. CHANG, M.D. University of Chicago

MITCHELL B. COHEN, M.D., Children's Hospital Medical Center, Cincinnati

MARGARET M. HEITKEMPER, Ph.D., R.N., University of Washington

JANE M. HOLT, National Pancreas Foundation, Boston

DAVID A. LIEBERMAN, M.D., Oregon Health Sciences University

NANCY J. NORTON, B.S., International Foundation for Functional Gastrointestinal Disorders

PANKAJ J. PASRICHA, M.D., University of Texas Medical Branch

DANIEL K. PODOLSKY, M.D., Massachusetts General Hospital

KENTON M. SANDERS, Ph.D., University of Nevada School of Medicine

ROBERT S. SANDLER, M.D., M.P.H., University of North Carolina

JOANNE A.P. WILSON, M.D., Duke University Medical Center

#### EX OFFICIO MEMBERS PRESENT

LISA BEGG, Dr.P.H., R.N., Office of Research on Women's Health, Office of the Director, NIH  
GILMAN GRAVE, M.D., *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)

JAY H. HOOFNAGLE, M.D., NIDDK

YOUNG S. KIM, M.D., National Cancer Institute (NCI) [for John Milner, Ph.D.]

MARGUERITE KLEIN, M.S., R.D., National Center for Complementary and Alternative Medicine (NCCAM)

ANNETTE ROTHERMEL, Ph.D., National Institute of Allergy and Infectious Diseases (NIAID)

LAURA SEEFF, M.D., Centers for Disease Control and Prevention (CDC)

#### ADDITIONAL PRESENTERS IN ATTENDANCE

JAMES EVERHART, M.D., NIDDK

ROBERT HAMMOND, Ph.D., Executive Director, National Commission on Digestive Diseases

GRIFFIN P. RODGERS, M.D., Director, NIDDK

## **B. ATTENDANCE – NIH STAFF AND GUESTS**

In addition to Commission members, others in attendance included NIH staff representatives and interested members of the public. Attendees included the following:

Anne Bicha, American Gastroenterological Association	Megan Miller, Ph.D., NIDDK
A.J. Bownas, the Hill Group	Helyn Oscanyan, the Hill Group
Michelle Cissell, Ph.D., M.A.Cissell Consulting	Constance Ruhl, Social and Scientific Systems, Inc.
Carina May, the Hill Group	Brian Sayer, M.H.S., Social and Scientific Systems, Inc.
Marjorie Merrick, Crohn's and Colitis Foundation of America	Elizabeth Thompson, The Pancreatic Cancer Action Network
Jennifer Michelak, American Society for Gastrointestinal Endoscopy	Asad Umar, D.V.M., Ph.D., NCI

## **II. OPENING OF MEETING, WELCOME AND REMARKS**

Dr. Stephen James, the Director of the Division of Digestive Diseases and Nutrition at NIDDK and Chairman of the Commission, welcomed all participants to the fourth meeting of the Commission. He introduced Dr. Griffin Rodgers, Director of the NIDDK, who spoke briefly to the Commission.

Dr. Rodgers welcomed and acknowledged several groups of individuals whose efforts and hard work over the past 2 years have contributed to the development of the Commission's research plan. The Commission members, who represent scientists, healthcare providers, and patients committed to the advancement of digestive diseases research, have identified compelling research opportunities that will ultimately improve the lives of people living with digestive diseases. Representatives from professional and patient advocacy groups, Congressional offices, industry, Federal health agencies, and other organizations have supported the Commission's work. Dr. James and Dr. Robert Hammond, Chair and Executive Director of the Commission respectively, have done a tremendous job in keeping the Commission on schedule. Many additional experts and stakeholders participated in working groups that provided critical input to help the Commission develop its research plan. Dr. Rodgers encouraged the Commission to continue its tradition of collaboration and to involve as many stakeholders as possible as the research plan is finalized through public meetings and the planned public comment period. Finally, Dr. Rodgers reminded the Commission that, once completed, their research plan is expected to serve as a guidepost for the NIH and the larger digestive diseases research community for pursuing compelling digestive diseases research opportunities in the future.

## **III. APPROVAL OF JUNE 18-19, 2007 MINUTES, AND TODAY'S GOALS**

The minutes of the June 18-19, 2007 Commission meeting were approved unanimously.

Dr. James noted that the main focus of the meeting would be to review the Commission's proposed research goals in detail to identify potential gaps or areas of overlap and to ensure that the final report is responsive to the group's charter. In addition, other agenda items included discussion of proposed overarching goals and strategies, consideration of how the final research plan would be used, and progress on the parallel report on the burden of digestive diseases being prepared by the NIDDK.

## **IV. REPORT ON BURDEN OF DIGESTIVE DISEASES IN THE U.S.**

Dr. James Everhart updated the Commission on progress the NIDDK and its contractor, Social and Scientific Systems, Inc., have made in preparing the burden of digestive diseases report. The report will be organized according to how diseases are coded by the International Classification of Diseases. Data on

incidence and prevalence will be provided, if available, for digestive diseases. Other data elements include ambulatory care visits (i.e., visits to doctors' offices) from the National Ambulatory Medical Care Survey and a national sample of physician visits from the National Center for Health Statistics, CDC, and the number of hospitalizations from the health care utilization project and the national inpatient sample (i.e., The National Inpatient Sample of the Health Care Utilization Project [HCUP]). All data will come from 2004 as this is the most recent year for which all data sources are available. Mortality will be expressed as number of deaths and death rates, as well as years of potential life lost. The prescription database from Verispan will provide information on retail costs and the proportion of drugs for gastrointestinal infection. Data on digestive system malignancies will be taken from the SEER database of the NCI. Direct cost data will include the costs of hospitalizations, ambulatory visits, prescription drugs, over-the-counter drugs, nursing home care, and home nutrition. Indirect cost data will include productive time lost due to hospitalization or office visits, premature death, and work loss. Data on endoscopic procedures will be provided by the Clinical Outcomes Research Initiative, National Endoscopy Database.

The Commission questioned whether data on years of life lost could be categorized by race and/or ethnicity and whether survival data was available in addition to mortality for digestive cancers. A suggestion was made to include data from the CDC National Program of Cancer Registries in addition to the SEER data. The Commission discussed whether burden of disease should impact prioritization of research goals. Dr. James noted that, although it is important to report burden data as accurately as possible, many factors influence the calculation of burden. For example, a highly effective treatment might exist for a given disease, but if that treatment is expensive then the disease will appear to exact a high economic cost. Prioritization of research goals should be based primarily on research opportunities. The burden of digestive diseases report will be published separately from the Commission's research plan; however, updated statistics on the burden will be available before the research plan is finalized.

## **V. UPDATE ON NIH FY06 DIGESTIVE DISEASES PORTFOLIO**

Dr. Hammond noted that all Commission members have signed Confidentiality and Conflict of Interest statements and reminded the members not to speak individually on the Commission's behalf. He also stated that there would be time at the meeting for questions from the public and that the public was welcome to submit questions or comments to the Commission after the meeting through the Commission's website.<sup>1</sup>

The Commission's working groups were provided with lists of research grants, training grants, and other awards constituting the NIH portfolio for digestive diseases in fiscal year (FY) 2005. The working groups used these data to identify research gaps and opportunities. The Commission's research plan will include a summary of the most recently available data on the NIH digestive diseases portfolio from FY 2007. In addition, lists of grants from the FY 2005 and 2006 portfolios will be publicly available online with the electronic version of the final Commission report. Currently, data on the digestive diseases are reported by each NIH Institute, Center, and Office, which have slightly different systems for coding their grants and awards by research topic. Beginning in FY 2009, all NIH grants will be coded by the Office of Portfolio Analysis and Strategic Initiatives using sophisticated computer algorithms and common definitions to identify relevant grants and awards. Thus, significant changes in the digestive diseases research portfolio overall or for specific diseases can be expected in FY 2009.

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<sup>1</sup> The website of the National Commission on Digestive Diseases is <http://ncdd.niddk.nih.gov>.

## VI. DISCUSSION AND APPROVAL OF DRAFT CHAPTERS OF THE NCDD REPORT

For each chapter in the draft research plan, the Commission reviewed all of the proposed research goals for clarity, overlap, and gaps.<sup>2</sup> Issues that were recommended for consideration are summarized in this section. Working group chairs were asked to incorporate the Commission's suggestions into future drafts of the research plan as appropriate.

### Overarching Themes and Strategies

The Commission's current draft research plan recommends 117 goals for digestive diseases research spanning numerous important diseases and other issues of relevance to digestive diseases. Because it would be inappropriate to prioritize among goals in such diverse areas of research, four over-arching goals or "themes" were proposed that, if pursued, would help NIH achieve all of the research goals. Those themes involve broad support for: (1) fundamental research; (2) translational and clinical research; (3) research resources and infrastructure; and (4) manpower and training issues. Within each theme, specific strategies were defined.

The Commission noted that the overarching themes could apply in broad ways to many areas of biomedical research and recommended that more details be added to apply these themes specifically to digestive diseases research. Topics that could enhance the digestive diseases orientation of the themes include the enteric microbiota, the mucosal immune system, and the enteric nervous system (ENS). Other issues that could be included in this section are: behavioral research; the need for better network infrastructure and data repositories to support multi-center research studies; the healthcare provider-patient relationship as it applies to treatment outcome; support for multidisciplinary teams; and NIH partnerships with other research entities, including foundations and the pharmaceutical and biotechnology industries.

In terms of the overall research plan, the Commission suggested adding a summary paragraph at the beginning of each research chapter to highlight the major research goals. In addition, it will be important to add lay-oriented examples of advances in digestive diseases research that have had a positive impact on digestive health, as well as gaps in knowledge that require research investment. Possible success stories include advances in therapy for gastrointestinal reflux disease; the availability of vaccines and other treatments for some forms of viral hepatitis; the development of biological therapies for inflammatory bowel diseases (IBD); and the discovery of *Helicobacter pylori* as a cause of ulcer disease. Examples of important gap areas include the rising incidence of digestive cancers, other than colorectal cancer; the emergence of nonalcoholic steatohepatitis as a common liver disease; pancreatitis; foodborne illnesses; and gastroparesis.

### **Topic-Specific Chapters**

#### Research on the Basic Biology of the Digestive System

A goal on Wnt signaling could be made more relevant to signaling pathways in general, although it is still important to refer to its importance in cancer. The Commission noted an imbalance in the relative emphasis on mucosal biology compared to issues related to the ENS and motor function. Dr. Sanders will work with Dr. Blumberg to develop additional goals for research on the ENS and muscle function that are appropriate for the basic biology chapter. A recent paper in *Science* reported on a marker for a stem cell in

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<sup>2</sup> A complete set of slides listing all draft research goals and objectives discussed at the November 19, 2007 meeting is available online at:

<http://www2.niddk.nih.gov/AboutNIDDK/CommitteesAndWorkingGroups/NCDD/CommissionMeetingInformation.htm>

the intestinal crypt. An objective related to this finding could be added to one of the research goals on developmental biology of the digestive system. With respect to the research goal on obesity and satiety, it could be useful to include objectives related to the development of improved tools for measuring physical activity, nutrient intake, and energy balance, as well as the identification of genetic alleles associated with risk for obesity. Objectives related to the development of therapies, drugs, devices, and clinical trials are mostly relevant to the disease- and organ-oriented chapters. Two research goals are related to the role of the microbiome in health and disease. The objectives of these goals should be reviewed to ensure minimal overlap or to merge the goals if they are largely similar. A proposed research goal related to IBD can be deleted as the topic is covered adequately in the IBD chapter. Research goals or objectives on the stem cell niche in embryonic development and in the adult, particularly the identification of stem cell-specific markers, could be added.

#### Functional Gastrointestinal Disorders and Motility Disorders

The Commission suggested including the role of spinal neurons in inflammation to the research goal on interactions between the peripheral and central nervous systems. The term “neural integration” was defined as integration of multiple signals or stimuli into a neuron, rather than innervation of muscle. The development of new technologies could be expanded to include diagnostics. The effect of diabetes on gut motility, including gastroparesis and other complications, could be expanded into a new research goal. Neurohormonal communication that affects motility could be mentioned.

#### Infections of the Gastrointestinal Tract

The Commission recommended expanding the first proposed research goal on developing tools to identify etiologies of intestinal infections to include other issues mentioned in the objectives, such as etiology, epidemiology, pathogenesis, and diagnostics. The term “censusing” in the context of the microbiota could be confused with “quorum sensing” and could be revised. In addition, a reference to liver infections in the Introduction of this chapter could be deleted as liver infections are described within the chapter on liver disease.

#### Cancers of the Digestive System

This chapter should include an objective on the use of imaging technologies for cancer, as well as on research on chemotherapy for digestive system cancers. The Commission recommended that the research goal on identifying biomarkers for digestive system cancers be reframed to emphasize the need to improve outcomes for patients with these diseases. Also, an important objective would be to improve behavioral strategies, such as self-management, to enhance patient outcomes. Developing imaging approaches for rare gastrointestinal cancers could be included as an objective.

#### Inflammatory Bowel Diseases

The Commission recommended that the pathobiology of fistulous disease be addressed in this chapter.

#### Intestinal Failure and Regeneration, Nutritional Disorders and Support, Surgically Modified Gut, and Transplantation

The Commission noted that the success rate of intestinal transplantation is less than the 90 percent 1-year survival rate cited in the chapter text. Objectives related to necrotizing enterocolitis (NEC) will be looked at to ensure that there is no unnecessary overlap with the chapter on the stomach and small intestine, although it is appropriate to consider NEC in this chapter to some degree. Consideration was given to the

nutritional and fluid requirements of patients with ostomies, although it might not be feasible to frame a research goal on this issue.

#### Diseases of the Oropharynx and Esophagus

The Commission discussed where to mention the issue of food allergy and decided that the chapter on the stomach and small intestine would be the most appropriate context. In addition, it was recommended that an objective on developing effective screening methods for Barrett's esophagus be added.

#### Diseases of the Stomach and Small Intestine

The Commission recommended that the discussion of gastric cancer in this chapter be re-focused to concentrate mainly on Zollinger-Ellison Syndrome as gastric cancer in general is discussed in the chapter on digestive system cancers. Also, the list of potential clinical trials for eosinophilic gastrointestinal disorders (EGIDs) could be stated in more general terms to leave open the possibility of changes in the state-of-the-science; although, some likely targets based on a biological understanding of EGIDs could be mentioned. Finally, the issue of small bowel bacterial overgrowth could be added to this chapter.

#### Diseases of the Colon and Rectum

An objective on determining indications for surgery and optimal surgical approaches for diverticular disease should be modified as the question of whether a one-stage or two-stage surgical procedure is more effective has already been addressed. The Commission suggested expanding the research goal on appendicitis to include issues such as biomarkers, better diagnostics, natural history, and non-surgical therapies. An objective could be added on understanding the causes of angioectasias. In addition, objectives related to defining factors responsible for clinical manifestations of radiation proctitis and finding effective treatments for this condition based on biologic mechanisms could be included in this chapter.

#### Diseases of the Pancreas

The Commission did not recommend any changes to the research goals and objectives of this chapter.

#### Diseases of the Liver and Biliary System

The Commission suggested that objectives be added on health disparities related to the differential burden of disease and response to therapy in African Americans with hepatitis C and Asian Americans with hepatitis B. Additionally, the development of behavioral issues for nonalcoholic and alcoholic steatohepatitis could be discussed. Spontaneous bacterial peritonitis could be discussed in the context of portal hypertension.

#### Bioengineering, Biotechnology, and Imaging

An objective on the use of tissue engineering approaches could be expanded to include regeneration of any of the digestive organs. Another objective related to mechanisms of scar formation could be deleted. Finally, the issue of developing a navigation control device could be made more generic to encompass other devices and technologies.

### **VII. PUBLIC COMMENTS**

No public comments were offered at the Commission meeting.

## **VIII. COMMISSION TIMELINE AND NEXT STEPS**

Commission members who chaired working groups (see Appendix) were asked to revise their chapters based on discussion at the meeting. An updated draft of the entire research plan would be circulated for approval by the full Commission before being posted online for a public comment period. The procedure for responding to comments received from the public will be determined after the comment period depending on the number and nature of submitted comments. It is possible that some comments might be handled administratively, while others might require further input from the Commission or working group Chairs as to the best way to incorporate suggestions into the draft research plan. The Commission also discussed the issues of providing references for all statements of fact in the research plan. It was decided the research plan will include citations of epidemiological facts; in addition, lists of citations for the research advances in each chapter will be provided in the electronic version of the final research plan.

## **IX. ADJOURNMENT**

Dr. James thanked Commission members and all attendees for their time and participation. The fourth meeting of the NCDD was adjourned at 5:00 p.m., November 19, 2007.

I hereby certify that to the best of my knowledge, the foregoing summary minutes are accurate and complete.

Stephen P. James, M.D.  
Director, Division of Digestive Diseases and Nutrition, National Institute of Diabetes and Digestive and  
Kidney Diseases  
Chairman, National Commission on Digestive Diseases

APPENDIX: Working Groups of the National Commission on Digestive Diseases

1. Overview of the Digestive System (Chair: Richard Blumberg; Vice-Chair: Eugene Chang)
2. Functional Gastrointestinal Disorders and Motility Disorders (Chair: Kenton Sanders; Vice-Chair: Nancy Norton)
3. Infections of the GI Tract (Chair: Mitchell Cohen; Vice-Chair: Richard Blumberg)
4. Cancers of the Digestive System (Chair: John Carethers; Vice-Chair: Robert Sandler)
5. Inflammatory Bowel Diseases (Chair: Daniel Podolsky; Vice-Chair: Eugene Chang)
6. Intestinal Failure and Regeneration, Nutritional Disorders and Support, Surgically Modified Gut, and Transplantation (Chair: Barbara Bass; Vice-Chair: Margaret Heitkemper)
7. Diseases of the Oropharynx and Esophagus (Chair: Pankaj Pasricha; Vice-Chair: David Lieberman)
8. Diseases of the Stomach and Small Intestine (Chair: Eugene Chang; Vice-Chair: Maurice Cerulli)
9. Diseases of the Colon and Rectum (Chair: Joanne Wilson; Vice-Chair: Nancy Norton)
10. Diseases of the Pancreas (Chair: Jane Holt; Vice-Chair: Pankaj Pasricha)
11. Diseases of the Liver and Biliary Systems (Chair: Bruce Bacon; Vice-Chair: Maurice Cerulli)
12. *discontinued*
13. Bioengineering, Biotechnology, and Imaging (Chair: Barbara Bass; Vice-Chair: David Lieberman)