Meeting Minutes

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

June 18-19, 2007

I. CALL TO ORDER

The Chairman of the National Commission on Digestive Diseases (NCDD), Stephen P. James, M.D. called to order the second meeting of the Commission at 9:00 a.m. on Monday, June 18, 2007 in Ballroom C of the Sheraton Crystal City Arlington, Virginia.

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, Texas
RICHARD S. BLUMBERG, M.D., Brigham & Women's Hospital
JOHN M. CARETHERS, M.D., University of California, San Diego
MAURICE A. CERULLI, M.D., New York Methodist Hospital
MITCHELL B. COHEN, M.D., Children's Hospital Medical Center, Cincinnati, Ohio
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

COMMISSION MEMBER ABSENT

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

***EX OFFICIO* MEMBERS PRESENT**

LISA BEGG, Dr.P.H., R.N., Office of Research on Women's Health, Office of the Director, NIH
BROOKS D. CASH, M.D., MC, USN, National Naval Medical Center
SARAH DUNSMORE, Ph.D., National Institute of General Medical Sciences (NIGMS) [for Michael Rogers, Ph.D.]
DAVID P. GOLDMAN, M.D., M.P.H., United States Department of Agriculture (USDA)
RAJ K. GOYAL, M.D., VA Boston Healthcare System
GILMAN GRAVE, M.D., National Institute of Child Health and Human Development (NICHD)
JAY H. HOOFNAGLE, M.D., NIDDK
CHRISTINE A. KELLEY, Ph.D., National Institute of Biomedical Imaging and Bioengineering (NIBIB)
JAG H. KHALSA, Ph.D., National Institute on Drug Abuse (NIDA)
MARGUERITE KLEIN, M.S., R.D., National Center for Complementary and Alternative Medicine (NCCAM)
DENNIS LANG, Ph.D., National Institute of Environmental Health Sciences (NIEHS)
SUSAN F. MARDEN, Ph.D., R.N., National Institute of Nursing Research (NINR)

JOHN MILNER, Ph.D., National Cancer Institute (NCI)
ANNETTE ROTHERMEL, Ph.D., National Institute of Allergy and Infectious Diseases (NIAID)
FRANCISCO SY, M.D., Dr.P.H., National Center on Minority Health and Health Disparities (NCHMD)
SAM ZAKHARI, Ph.D., National Institute on Alcohol Abuse and Alcoholism (NIAAA)

ADDITIONAL PRESENTERS IN ATTENDANCE
ELIZABETH L. WILDER, Ph.D., Acting Associate Director, Office of Portfolio Analysis and Strategic Initiatives, Office of the Director, NIH
ROBERT HAMMOND, Ph.D., Executive Director, NCDD

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
A.J. Bownas, the Hill Group
Jill Carrington, Ph.D., NIDDK
Michelle Cissell, Ph.D., M.A.Cissell Consulting
Leslie Curtis, NIDDK
Erika Elvander, Office of Research on Women's Health, NIH
Carol Feld, NIDDK
J. Michael Hall, American Liver Foundation
Brian Harvey, M.D., Ph.D., Sanofi-Aventis
Eleanor Hoff, Ph.D., NIDDK
Joyce Korvick, M.D., M.P.H., Food and Drug Administration
Carina May, the Hill Group
Megan Miller, Ph.D., NIDDK
Helyn Oscanyan, the Hill Group
Stacey Poole, TAP Pharmaceuticals
Sharon Pope, NIDDK
Anne Wright, Circle Solutions, Inc.

II. WELCOME, APPROVAL OF NOVEMBER 6, 2006 MINUTES, AND TODAY'S GOALS

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 third meeting of the NCDD. Commission members have all signed conflict of interest statements as a requirement for membership on a federal advisory committee and were reminded not to speak individually on behalf of the Commission. The minutes of the November 6, 2006 meeting were approved unanimously.

Dr. Robert Hammond, Executive Director of the NCDD, informed meeting attendees that limited time was available at the meeting for comments from the members of the public. However, the public was invited to submit written comments after the meeting through the Commission's website. The main goal of the meeting was to review proposed goals and challenges from each working group to identify gaps and overlapping issues. This will focus the Commission's preparation of a draft report on the highest priorities in digestive diseases research.

III. OFFICE OF PORTFOLIO ANALYSIS AND STRATEGIC INITIATIVES (OPASI), NIH

Dr. Elizabeth Wilder, Acting Associate Director of OPASI, spoke to the Commission with respect to central NIH planning efforts and large-scale research projects that have been undertaken in the context of the NIH Roadmap for Medical Research. The Roadmap process was initiated in response to a report released by the Institute of Medicine in 2003 that discussed research planning at NIH. Major recommendations from that report were: 1) NIH should conduct strategic planning as a whole and consider trans-agency issues; 2) NIH should consider new ways to stimulate innovative research; and 3) NIH should develop means to facilitate clinical research. The first cohort of grants funded from the Roadmap that was developed in response to those recommendations was funded in 2004. The Roadmap

has recently undertaken a new planning effort to develop a second cohort of initiatives that will begin to be rolled out in 2007; Dr. Wilder's presentation focused on planning and implementation of these new initiatives.

The Roadmap operates as an "incubator space" to foster research in broad, cross-cutting areas that are critically important for NIH as a whole. Roadmap support is intended to jump-start research programs that then either complete their objectives or transfer to ongoing support by one or more Institutes or Centers (ICs). Thus, as initiatives from the first funding cohort approached a transition point, NIH began a process to solicit ideas for new initiatives. Criteria established for projects that could be considered for Roadmap support included: initiatives are expected to transform the way biomedical and behavioral research is conducted; although Roadmap initiatives are not disease-oriented, anticipated outcomes should synergize with disease-oriented research supported by individual ICs; programs should require the participation from NIH as a whole or address areas that do not fall within the scope of any one IC or program office; and initiatives should be something that no other entity (e.g., pharma, NSF) is likely to do.

The identification of new Roadmap initiatives began in the summer of 2006 with a solicitation of ideas from panels of scientific experts, NIH staff, and the general community. Ideas were vetted for response to the criteria for Roadmap initiatives, evaluated through a portfolio analysis of current funding in proposed areas, and prioritized by the IC directors. One group of initiatives that were identified through this process includes topics that require on-going trans-NIH coordination, but not necessarily support from the Common Fund (the funding mechanism for the Roadmap). Topics for trans-NIH coordination to eliminate redundancies and foster communication are regenerative medicine, pharmacogenetics, and bioinformatics. Two additional areas—a connectivity map and transient molecular complexes—were selected as potential pilot topics that are highly innovative, but perhaps not ready for the development of major initiatives. The issue of training and careers will be the focus of an NIH working group to determine workforce needs and design better training programs. The Roadmap will also coordinate with the NCMHD to look for ways to enhance research in health disparities. Finally, a task force has been appointed to consider issues related to the science of science administration and review processes.

Two major topics have been approved for immediate implementation in the Roadmap. The Human Microbiome Project will support several initiatives related to the importance of the microbiome to human health. The Project will start with efforts to sequence the microbiome at several sites in the body in healthy individuals and to develop new technologies for research on the microbiome. The Epigenomics program will investigate the correlation between epigenetic changes and human health and will include an international consortium to sequence reference epigenomes. Two other proposals were approved for continuing development for potential implementation in future years. The phenotyping initiative would encourage the development of resources to catalogue human phenotypes for characterization of human diseases. The protein capture and proteome tools project would develop tools to identify, isolate, and probe human proteins.

In response to questions from the Commission, Dr. Wilder provided additional information:

- The trans-NIH working group for training and career issues is led by Dr. Story Landis, NINDS Director, and Dr. Norka Ruiz-Bravo, Deputy Director for Extramural Research. The group plans to conduct a series of workshops to define the workforce and needs in this area.
- Inflammation, which had been suggested as a topic for the Roadmap, was determined to be an area that already received robust support at NIH, but that could benefit from improved coordination. Future plans in this area are under discussion by the IC directors.
- In FY 2007, and possibly FY 2008, the budget for the Roadmap was not collected from the ICs, but was a separate line item in the NIH appropriation. Currently, the Roadmap represents 1.7 percent of the NIH budget. Various funding mechanisms are used to implement Roadmap initiatives.

- The Microbiome Project does not include a training component. The first initiative related to this Project will be a sequencing initiative that will likely involve a network of researchers.
- The development of clinical databases is included as a component of the Clinical and Translational Science Awards (CTSAs), which may be further supplemented with support to allow better communication and sharing of information among the CTSAs.
- The intent of the phenotyping initiative is to develop consensus of how clinical data are gathered so that data can be directly compared across institutions, laboratories, and studies.

IV. WORKING GROUP UPDATES

Each working group chair presented a draft of the major research goals and challenges/steps to achieve the goals that had been identified by their working group. (A list of the working groups, chairs, and vice-chairs can be found in the appendix to these minutes). The Commission discussed the prioritization of the goals, and potential gaps or overlapping issues between chapters. A summary of the discussion and suggestions for each working group report follows in the order of presentation. This discussion was taken into consideration by the chairs as they finalized the research goals for each group and drafted a chapter for the Commission report. These minutes represent only highlights of the discussion after the chairs' presentations and do not cover the entire content of each working group report.

Inflammatory Bowel Diseases (WG 5)

The microbiome is a relevant theme in many chapters. Research related to the microbiome could be split to put a focus on generating new tools and databases in the Overview chapter (WG1) and leaving disease-oriented aspects of microbiome research in this and other disease-related chapters. The topic of mucosal immunity could be handled in a similar way. Reciprocity between the microbiome and the mucosa is addressed in relation to the immune system and its interactions. Psychosocial issues could be expanded from a focus on children to include adults, coping, behavioral intervention, and other aspects of total care. The group discussed the level of detail that would be appropriate in the final report and noted the importance of focusing the report on fewer, high-priority goals. However, the report overall should indicate the importance of behavioral and social sciences research as an overarching issue in digestive diseases. The challenge of methodologic development includes the need to develop computational tools to analyze the microbiome, *in vitro* models, and *in vivo* animal models. Issues that will require non-traditional funding mechanisms could be mentioned. The development and use of drugs for prevention of disease and the development of naturally occurring chemicals as drugs are relevant to this chapter.

Infections of the GI Tract (WG 3)

Chronic manifestations or long-term residual effects of infections in terms of both non-GI and GI diseases, such as IBD and IBS, are an important topic and will overlap with some other chapters. The Commission discussed the need to promote the clinical and translational applications of basic research and the importance of developing therapeutics for infections in addition to vaccines which are a significant research goal. There may be opportunities in the report to point out areas in which NIH could collaborate with partners in industry or the private sector for translational goals. Proposals related to international issues such as the Fogarty International Center global initiatives to treat parasitic and other infections in developing countries would need to be expressed in terms of research-oriented goals rather than health delivery. Research to better define the hygiene hypothesis and its role in developing a balanced immune response could include, among other issues, the use of probiotics to help stimulate an immune response in early childhood. Some goals developed by this working group, such as the creation of repositories, are process-oriented and will be reframed as challenges and steps to achieving the research-oriented goals.

Cancers of the Digestive System (WG 4)

New markers of risk for colorectal cancer should include the use of genomics, proteomics, and related technologies. It was noted that colon cancer in IBD and ulcerative colitis patients may have different mechanism than in sporadic cases. Research is need both to improve the effectiveness of colorectal cancer screening through colonoscopy as well as to validate alternate forms of screening like CT colonography. Nutripreventive or nutriceutical approaches could be mentioned in terms of prebiotic approaches that may alter the microbiota and impact the interaction between the intestinal microbiome and the predisposition to colorectal neoplasia or epithelial health. The issue of inflammation as a mechanism for cancer should be considered. The Commission noted the high priority of determining the natural history of premalignant conditions like colon polyps and Barrett's esophagus. This issue is related to determining the clinical value of screening methods. The development of targeted, molecularly-guided approaches to cancer diagnosis and treatment in addition to broader strategies such as epigenetics are critical research goals. Identifying biomarkers encompasses chromosomal instability among other genomic markers. Deaths from pancreatic cancer and the incidence of adenocarcinoma of the esophagus have both increased in recent decades; epidemiological research to understand these trends is important. Psychosocial issues, including ways to enhance quality of life before, during, and after treatment and end of life care, are relevant to cancer but also have a broader, cross-cutting importance. Standard of care for patients requires multidisciplinary management; research aimed at evaluating different strategies for health care delivery could be included in the report.

Diseases of the Pancreas (WG 10)

An important focus is to conduct comprehensive epidemiological studies to map the natural history or clinical course of pancreatic diseases, including autoimmune pancreatitis among other diseases. Similarly, understanding the natural history of fibrosis and pathological tissue response to injury is an issue that impacts not only the pancreas, but other organs as well. Research is needed on precursor lesions—for example, pancreatic intraepithelial neoplasias—to determine the likelihood of regression or of progression to cancer. Major challenges in this field include the need for better *in vitro* and animal models, especially ones that are not ethanol-based, and the urgent need to attract new investigators to research on pancreatic diseases.

Functional GI Disorders and Motility Disorders (WG 2)

Defining the natural history of disease is an issue for functional GI and motility disorders as in other disease areas. A clinical limitation has been the ability to access tissue from human patients; the development of endoscopic approaches to access muscle and enteric nervous system tissue is important. Neurogenic inflammation should be considered. Research is needed to validate targets for the development of new treatments. The potential role of infections in inducing IBS could be considered. Research on behavioral therapies should be expanded beyond physician-patient relationships to encompass interdisciplinary studies on patients' interactions with all healthcare providers. Novel behavioral treatments are needed utilizing new technologies to examine the relationship between stress and symptoms in patients with these conditions. A major challenge is the need for consistent phenotyping of patients, in ways that could include the biology of individual cells, brain-gut imaging, physiology, genetics, and other parameters. Several research goals on fundamental mechanisms related to these diseases might overlap with goals in the overview chapter and will need to be resolved as the chapters are developed.

Diseases of the Oropharynx and Esophagus (WG 7)

More research is needed on the natural history and epidemiology of Barrett's esophagus in a population based group that has not been selected for a history of GERD. A common diagnostic definition of dysplasia and its grade, including a more comprehensive molecular definition, would be useful for studying the natural history of Barrett's. The NIH could consider partnering with other organizations to

set up and share the costs of multicenter consortia. A challenge in this area is to develop a good animal model with an esophagus that more closely resembles the human structure.

Diseases of the Liver and Biliary System (WG 11)

The development of non-invasive tools for diagnosis and prognosis of liver disease (e.g., sensitive measures of fibrosis or inflammation) is an important topic for consideration. A major cause of death for people waiting for a liver transplant is hepatorenal syndrome; new therapies are needed to treat this condition. Chronic alcohol consumption affects many conditions related to the liver and other digestive organs including: cancer (colorectal, liver, esophagus), intestinal permeability, intestinal flora, and nutrition; moreover, the interaction between alcohol and some medications (e.g., acetaminophen) can impact the development of cancer. Regenerative tissue engineering or other approaches to develop biosupport devices for patients waiting for a liver transplant could be considered. The issues of regenerative medicine and stem cells were broadly addressed by the biotechnology (WG 13) and the overview (WG1) groups. Overcoming barriers to xenotransplantation could allow many more patients to receive liver transplants. Metastatic liver cancer will be considered by the cancer group (WG 4).

Diseases of the Stomach and Small Bowel (WG 8)

Non-ulcer clinical dyspepsia is a common clinical problem and would benefit from better phenotyping of the condition, although this overlaps to some degree with the functional GI disorders group (WG 2). Gastroparesis as well as electrical pacing and related technologies were also addressed by WG 2. The proposed goals from this group could be grouped into common thematic areas. The goal of developing a standard of care for probiotics to prevent NEC should be stated more broadly to cover the development of other preventive or therapeutic strategies. A database of information on patients with rarer diseases (e.g. Crohn's disease) would facilitate epidemiologic studies that would have some advantages in terms of time and funding over prospective trials. Research goals related to epidemiology have cross-cutting importance.

Diseases of the Colon and Rectum (WG 9)

Diverticular disease is a major burden for the healthcare system due to the large number of people who are affected, but very little research has been done in this area. A surgery-based trial might not be the highest priority because surgical decisions are usually dictated by other co-morbidities. Progress could be made through a long-term observational study rather than a randomized, controlled trial for diverticular disease. Development of an animal model for this disease would also accelerate research. Understanding the microenvironment within diverticuli compared to the general gut microflora and nutritional research are additional issues related to diverticular disease. Appendicitis is another under-studied area. Characterizing patients with appendicitis who experience aggressive, progressive disease that leads to perforation compared to those that could possibly be treated with medical management would be an important study. Colonic AVMs (arteriovenous malformations) also cause significant morbidities and little is known about the development of this condition. Radiation proctitis is becoming a more common problem due to prostate cancer therapy. Ano-rectal complications overlap with the chapter on IBD (WG 5), but will remain with the colon and rectum group for discussion in the report.

Intestinal Failure and Regeneration, Nutritional Disorders and Support, Surgically Modified Gut, and Transplantation (WG 6)

Longitudinal follow-up of patients who have undergone bariatric surgery for weight loss should include assessments of non-weight related issues such as neuroendocrine and hormonal status or bone density. Non-surgical approaches to obesity treatment could also be considered; this issue overlaps with the bioengineering group (WG 13). Many patients with type 2 diabetes who undergo surgery experience a rapid and dramatic resolution of the diabetes; research to replicate this effect without surgery would be important. Goals related to gastric pacing and stimulation will be moved from WG 2 to the technology

chapter (WG 13). Enterodistraction—mechanical stretching of the intestine—has been shown in animal models to augment the intestinal mucosa; more research on this technique is needed.

Bioengineering, Biotechnology, and Imaging (WG 13)
The NCI has an image-guided intervention initiative through which the institute holds INDs and assists in the development and production of GMP-grade small molecules for use in clinical trials. A rigorous research agenda is needed to validate new technologies that are being developed in other settings. Understanding the long-term sequelae and morbidities associated with new technologies is an important research area. Health disparities with respect to access to appropriate care is a national issue and would benefit from the establishment of simulation centers across the country for practitioners and researchers in multiple disciplines to learn new technologies.

Overview of the Digestive System (WG 1)
The topic of mucosal immunity could be expanded to include inflammation, which will overlap with WG 5 and others. Genetic manipulation of the microbiome could have therapeutic applications. Diabetes will not be explicitly addressed in the report, although the disease has multiple effects on the GI tract including motility issues, bariatric surgery, the link with obesity, feeding behavior, and GI hormones, and the role of nerves in the pancreas. The relationship of visceral fat to GI organs is an important issue, but one that is already addressed by the trans-NIH Obesity Task Force. Viruses in the gut are included in research on the intestinal microbiome. Primary diseases of the smooth muscle in the gut should be added, including differences between tonic muscles and phasic muscles as well as calcium-handling by smooth muscles.

The Chairs were asked to revise their presentations to reflect the discussion, to reframe their goals into thematic areas rather than a timeline format, and to reduce their list to approximately 6-10 research goals. In addition, they were asked to identify two to three goals that they felt would be the highest priority.

The meeting adjourned for the day at 7:04 p.m. and resumed on Tuesday, June 19, 2007 at 8:00 a.m.

V. TODAY'S GOALS, TIMELINE AND NEXT STEPS, STRATEGIES TO ADDRESS CROSS-CUTTING ISSUES

The NCDD charter directs the Commission to consider training, education, and career development in digestive diseases research. Several members volunteered to serve on a working group that would identify major objectives in this area. Ideally, a chapter developed on this theme would have suggestions that go beyond generic training and career development issues and propose solutions that are tailored to digestive diseases research. Retention of MD investigators in biomedical research careers appears to lag behind that of MD, PhD researchers, possibly due to insufficient mentoring among other factors. Efforts are needed to help PhD trained investigators enter into a translational research environment. More behavioral scientists with a focus on digestive diseases are needed. It would also be timely to examine barriers to women's careers in science. Quantitative evaluation of the success of training mechanisms is important. The conflict between the length of clinical training and that of T32 training periods makes it difficult for some MDs to choose a research career path. These and other issues will be considered by the training working group, which will develop a draft chapter for review at the November NCDD meeting.

Another issue in the charter is a focus on programs for the collection, dissemination, and exchange of information and resources in health and disease relevant to digestive diseases research. This could include items that were raised by several working groups such as databases and repositories. However, the intent of the charter language could be broader in terms of making information available to healthcare providers and the public. Again, several groups did propose goals and steps related to patient and provider education and public awareness about specific disease topics and research advances. A key component of

translational research is implementation of findings into practice; this issue should be addressed as part of the response to the charter mandate. Information about currently funded projects could be disseminated and a portfolio analysis of digestive diseases research NIH will be included in the Commission's report. Another aspect is to better communicate resources, such as transgenic mice or cell lines, that have been developed through NIH-sponsored research and are available to the community.

A number of overarching themes emerged from the working group presentations, including: animal models, genetics, microbiology, biomarkers, regenerative medicine, epidemiology, imaging, innovative technologies, phenotyping, immunology and inflammation, and translation to clinical practice. Common resource themes include career development, team research, clinical training, financial issues, barriers to clinical research, clinical trials, and special populations. These themes will be developed into a separate chapter that synthesizes these cross-cutting items.

The Commission expects to have a draft of the complete report by the time of its next meeting in November 2007. An opportunity for the public to address the Commission will be available at that meeting. In addition, a period of time will be set aside for public comment on the draft report. A final report should be approved by the Commission and ready for release around June, 2008.

VI. RECAP OF HIGHEST PRIORITY GOALS AND IDENTIFICATION OF CROSS-CUTTING ISSUES

The chairs of each working group summarized the changes made to their list of research goals and identified the highest priority goals for their area. A summary of each group is provided in the order of presentation. These goals will continue to be refined as the chairs draft a chapter based on the research goals and other materials; thus, the highest priority goals identified in this session might not appear verbatim in the final report.

Overview of the Digestive System (WG 1)
The highest priority goals were identified as: identify the intestinal stem cell and use it to develop regenerative approaches to therapy and understand development of the GI tract; develop methods to define the intestinal microbiome; and understand the biology of mucosal inflammation.

Functional GI Disorders and Motility Disorders (WG 2)
Important goals were suggested to be: understand peripheral and central pain in sensory pathways and how these pathways are affected in functional GI motility disorders; and understand the integrated function of the tunica muscularis and the intrinsic and extrinsic nervous systems. Research goals on stem cell research and transplantation will be removed from this chapter and handled elsewhere in the report. A goal related to improving quality of life will be retained in this chapter as it is extremely important issue for patients. Research that combines quality of life and patient satisfaction with biological or biobehavioral markers would fill a gap. Phenotyping patients is of particular importance for this category of diseases and the need to understand the biological basis for why women are disproportionately affected should be emphasized.

Inflammatory Bowel Diseases (WG 5)
Major priorities for research in this area include: determine how the microbiome is altered in the context of IBD; characterize the role of genes that have been validated through genome-wide screens; and identify biomarkers as a means to accelerate clinical translational and development. Some mention of atypical inflammatory disease, such as microscopic colitis, would be useful in the report.

Intestinal Failure and Regeneration, Nutritional Disorders and Support, Surgically Modified Gut, and Transplantation (WG 6)
High priority goals include: define the stem cell niche and differentiation and growth pathways, and enhance those paths to treat short gut and intestinal failure; develop regenerative medicine approaches such as scaffolds or a bioartificial gut; validate non-invasive markers of intestinal growth and adaptation; and identify a non-invasive marker for rejection of intestinal transplant and develop methods to better preserve organs for transplantation.

Bioengineering, Biotechnology, and Imaging (WG 13)
In order to develop and evaluate new technologies, it will be important to develop interdisciplinary collaborations with investigators who do not traditionally work together—for example, engineers and computer scientists. A high priority research goal is to develop methods for real time biopsy of luminal abnormalities. Simulation and workforce preparation is another critical issue. Improvements in endoscopy instrumentation for both diagnosis and therapy should be included in this chapter and also mentioned in other relevant chapters, for example on the colon or the esophagus.

Infections of the GI Tract (WG 3)
The list of research goals was condensed to four over-arching priority areas: identify the etiologies of intestinal infections; improve the prevention and treatment of intestinal infections; understand and modulate the long-term intestinal and non-intestinal consequences of intestinal infections; and understand and modulate the human microbiome to promote health and diminish disease.

Cancers of the Digestive System (WG 4)
This chapter will include both overarching goals and basic mechanisms that are relevant to all GI cancers, as well as goals that are specific to different types of cancer.

Diseases of the Oropharynx and Esophagus (WG 7)
High priority research goals would include: understand neural injury, plasticity and repair in the central nervous system and the enteric nervous system; prevent and reverse Barrett's esophagus; and understand the neuroanatomical derangement in GERD and associated dysmotility.

Diseases of the Pancreas (WG 10)
The priority research goals were identified as: understand the biology of the earliest events in pancreatitis; predict and prevent acute pancreatic necrosis by understanding the pathways to necrosis and recovery; and effectively treat pain with modern pharmacological and non-pharmacological approaches.

Diseases of the Stomach and Small Bowel (WG 8)
Research goals were re-organized into general themes related to: the microbiome; *H. pylori* and ulcer disease; NSAID-induced complications; absorption, secretion and diarrhea; and celiac disease and autoimmunity. The development of tight junctions in relation to NEC could be considered.

Diseases of the Colon and Rectum (WG 9)
Vascular biology of the intestine, including radiation proctitis, along with colonic ischemia and angioectasias could be included as a priority theme. The topic of radiation or chemical injury as related to biodefense could be considered either in this section or with respect to the small bowel. Treatment approaches for fecal incontinence are a major issue.

Diseases of the Liver and Biliary System (WG 11)
High priority research goals include: develop antifibrotic therapies; develop a vaccine for hepatitis C; and develop targets for therapeutic development for hepatocellular cancer, cholangiocarcinoma, and gall

bladder cancer. Given the burden of disease and the impact, prevention of gall stones could be another important goal.

VII. ADJOURNMENT

Dr. James thanked Commission members and all attendees for their time and participation. The third meeting of the NCDD was adjourned at 11:57 a.m., June 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: NCDD Working Groups

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)