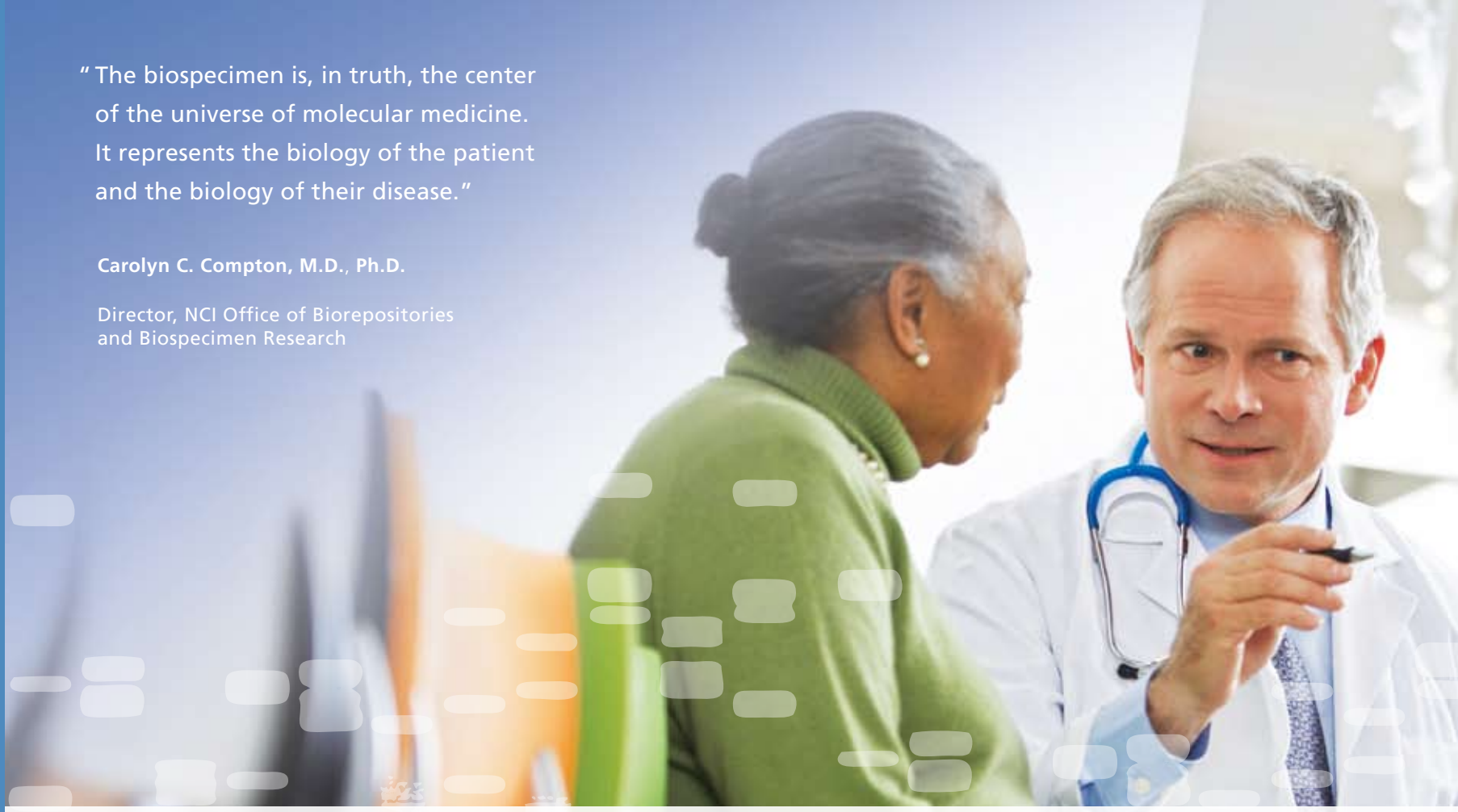
National Cancer Institute



"The biospecimen is, in truth, the center of the universe of molecular medicine. It represents the biology of the patient and the biology of their disease."

Carolyn C. Compton, M.D., Ph.D.

Director, NCI Office of Biorepositories and Biospecimen Research

OFFICE OF BIOREPOSITORIES AND BIOSPECIMEN RESEARCH:

Setting the Standards and Creating the Infrastructure for High Quality Biospecimens

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

THE **IMPACT** OF BIOSPECIMENS

Biospecimens are tissues and fluids taken from the human body that can be used for cancer diagnosis, analysis and research. Biospecimens are critical to cancer research because they contain an extraordinary amount of biological information, written in the language of cells, genes and proteins, that define a patient's disease. Biospecimens are stored in biobanks or biorepositories, which are an essential resource for cancer research.

Biospecimens are vulnerable to environmental and biological stresses introduced by routine handling during collection, processing, storage and transport. These handling variables may change the molecular properties of the biospecimen before it ever reaches the doctor or researcher for analysis. The molecular changes may be misread as representative of the patient's disease rather than an artifact of the handling process.

The availability of high-quality biospecimens is dependent upon:

- standardized, evidence-based collection, processing, annotation, storage and transport procedures to ensure the biospecimen's molecular properties and usefulness are kept intact
- stringent ethical, legal and policy practices that ensure the highest standards are attained in the protection of patient rights and privacy
- removal of competitive barriers to biospecimen access

The lack of standard and uniform operating procedures for collection, processing, annotation, storage and transport of biospecimens has resulted in a critical shortage of these important resources. Many potentially high-impact research initiatives and cancer diagnostic and therapeutic development efforts are being significantly hindered by the limited quantity and quality of biospecimens. In fact, studies have shown that cancer researchers restrict the scope and question the validity of their work because of the uncertain quality of the biospecimens available to them.

"Patients who donate their tissue or their biospecimen do so to help scientists learn as much as possible about cancer so that they can do something about it."

Deborah E. Collyar

President, Patient Advocates in Research (PAIR)

"We envision an era where every patient will have the ability to have their specific tumor type subclassified based on its molecular profile, then treated with a combination of targeted therapies aimed at its specific molecular complexities."

Carolyn C. Compton, M.D., Ph.D.

Director, NCI Office of Biorepositories and Biospecimen Research

THE **LINK** BETWEEN BIOSPECIMENS AND PERSONALIZED MEDICINE

Advances in biomedical science offer the opportunity to understand cancer at the molecular level, raising hopes for more specific and targeted approaches to detecting, treating and preventing the disease. Biospecimens support many aspects of patient management including diagnosis, staging and prognosis of cancer. In addition, biospecimens provide a critical link between molecular and clinical information that will ultimately allow doctors to tailor treatments based on the genetic profile of a patient's disease. This is often referred to as personalized medicine. It includes:

- treatments that target the specific molecular changes that allow a person's cancer cells to grow and survive
- molecular screening methods that allow a person's cancer to be detected and treated before the onset of symptoms
- individualized cancer prevention strategies that are based on a person's genetic makeup

Preserving biospecimens in the correct manner will be essential for the development and use of molecular tests that diagnose disease, as well as therapies that target the molecular changes of the patient's cancer. High-quality biospecimens give researchers and doctors the confidence that the molecular changes seen in the biospecimen are a result of the patient's disease and not an artifact of the biospecimen handling process. The National Cancer Institute (NCI) is committed to improving biospecimen quality to speed progress in cancer research and, ultimately, patient care and treatment.

SETTING BIOSPECIMEN **PRIORITIES**

Over the past several years, NCI has undertaken an intensive review process to understand the state of its funded biospecimen resources and the quality of biospecimens used in cancer research. In recognition of the critical role of biospecimens in cancer research, NCI established the Office of Biorepositories and Biospecimen Research (OBBR) in 2005.

OBBR **MISSION**

To ensure that the human biospecimens available for cancer research are of the highest quality, OBBR is focused on the following strategic priorities:

- develop and disseminate state-of-the-science methods to assess, improve and ensure the quality of NCI-supported biospecimen resources
- sponsor and collaborate on large-scale NCI and NIH projects in which the principles of high-quality biospecimen resources are critical for achieving research goals
- collaborate with other major initiatives outside NCI to achieve global improvement in processes for patient consent and biospecimen handling, annotation, storage, information management and transport
- develop educational tools and resources for all potential stakeholders that address the range of issues related to human biospecimens
- establish a national cancer Human Biobank (caHUB) for human biospecimen collection, processing, storage and distribution

OBBR'S STEPWISE APPROACH

Since its inception, OBBR has achieved several milestones, including:

- developing the *NCI Best Practices for Biospecimen Resources*
- enhancing biospecimen science and technology through the Biospecimen Research Network and the Innovative Molecular Analysis Technologies program
- leading the development of a national biospecimen resource: the Cancer Human Biobank (caHUB)
- raising awareness and support of biospecimen issues within the cancer research community

Providing Guidance: NCI Best Practices for Biospecimen Resources

OBBR published the *NCI Best Practices for Biospecimen Resources* to:

- define state-of-the-science biospecimen resource practices
- promote biospecimen and data quality
- support adherence to ethical and legal requirements
- promote harmonized approaches to ethical, legal and social issues surrounding the use of human biospecimens in biomedical research

These practices are the initial step toward harmonizing biospecimen resource practices to ensure a level of consistency and standardization across all biospecimen resources.

Improving Science & Technology: The Biospecimen Research Network

There are limited scientific data on the effects of biospecimen handling variables on the molecular integrity of human biospecimens. In response, OBBR established the Biospecimen Research Network (BRN) program to systematically assess the effects of handling variables on different human biospecimen types (e.g., blood, urine, tumor tissue), molecular measures (e.g., DNA, RNA, protein) and outcomes of genomic and proteomic studies conducted for clinical diagnosis and cancer research. Results of BRN research will contribute to the development of evidence-based standard operating procedures (SOPs) for biospecimen handling, building on the *NCI Best Practices for Biospecimen Resources*.

Specifically, the BRN is designed to:

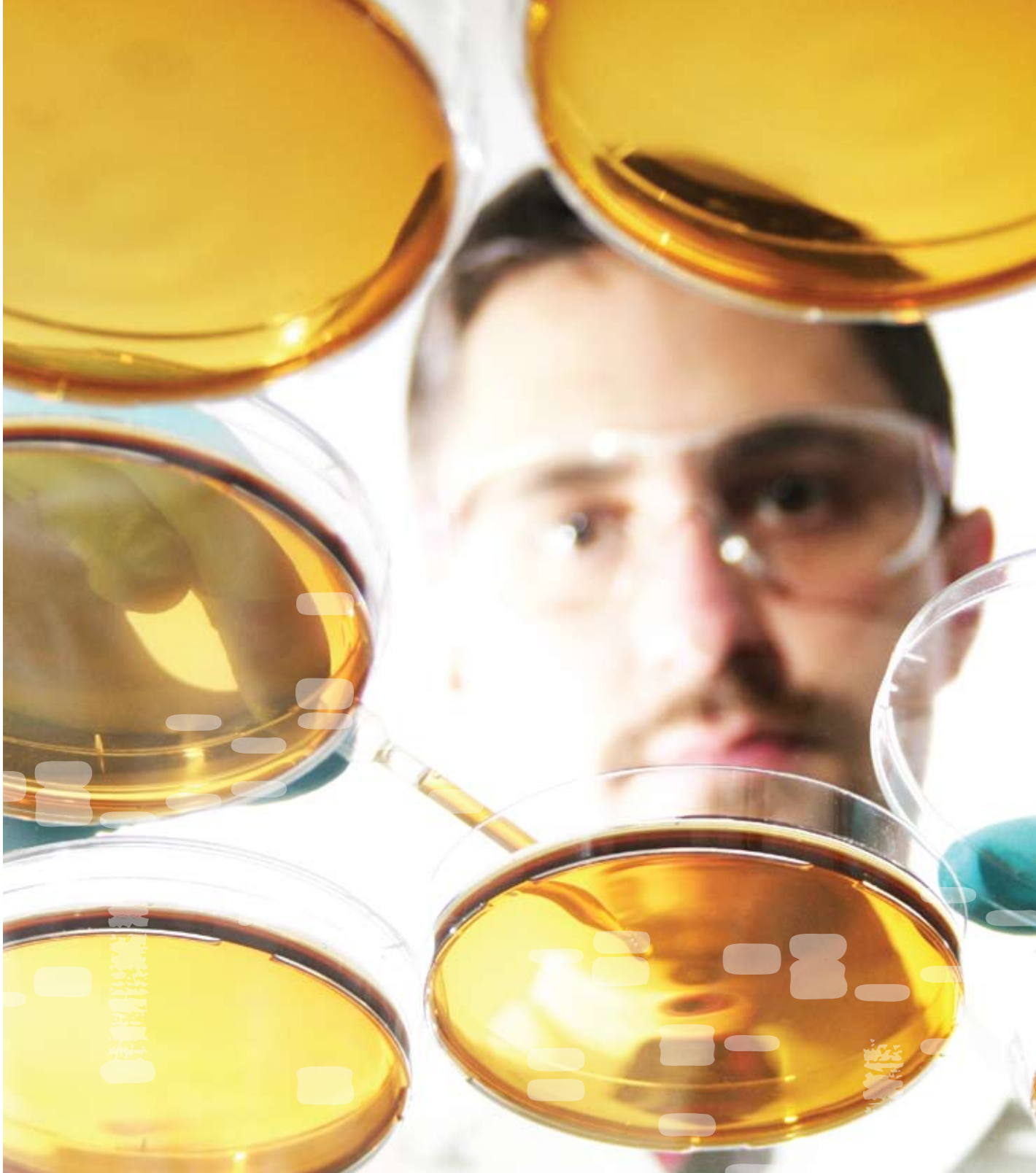
- bridge the gap between existing clinical practice for biospecimens and emerging technologies for personalized diagnostics and therapies
- define the most significant variables for future collection of tissues, blood and bodily fluids
- develop evidence-based biospecimen quality indicators for specific analysis technologies

Each year the BRN sponsors a research symposium to convene the cancer research community around biospecimen science. The BRN symposia define the current scientific understanding of the biology of the biospecimen, and the challenges that must be met and solutions that must be identified to create evidence-based standards for human biospecimens used in research.

"Think about the target discovery or development process. If the sample collection quality has been variable, inaccurate data derived from those samples could certainly lead you down a wrong path. We need good quality samples so that we can understand both the expression of our drug targets, and in analysis of samples collected from clinical trials, identify whether or not the drug is working in the manner we expect it to."

Scott D. Patterson, Ph.D.

Executive Director, Medical Sciences,
Amgen, Inc.



"I'm a cancer doc in the trenches, so I want and need these technologies and the results from the biospecimens available tomorrow. I had two patients already today that have passed away from cancer, so I'm not in a position of waiting. I'm not in a position of planning for the next decade or two. It's tremendously important, but I care about things today, and I want answers that I can use in the near term."

David B. Agus, M.D.

Professor, Keck School of Medicine USC
Director, USC Center for Applied Molecular Medicine

Improving Science & Technology: Innovative Molecular Analysis Technologies

Innovative methods and technologies are essential for translating today's basic research discoveries into tomorrow's patient care. With the goal of strengthening this stream of innovation, the Innovative Molecular Analysis Technologies (IMAT) program was created to support the development of next-generation analytical methods and tools that have the potential to revolutionize the way research can be pursued.

The IMAT program accomplishes these goals by:

- pursuing and supporting highly innovative technologies from the scientific and clinical communities
- fostering collaboration between the life sciences and non-life science disciplines by overcoming technical barriers to cancer research
- focusing solely on the development of a technology to demonstrate technical feasibility

IMAT's focus is on the early stage technical development of tools that have the potential to revolutionize state-of-the-art science in cancer care and research. Through a range of funding opportunities, innovators are provided the infrastructure to support the development of their technologies from beginning to technical validation.

Building Tools to Share Knowledge

Through its cancer Biomedical Informatics Grid (caBIG®) initiative, NCI supports the development of information technology tools and infrastructure to facilitate the appropriate collection, processing, storage and distribution of biospecimens. Such tools include:

- caTISSUE—addresses all aspects of donor enrollment and informed consent, collection and tracking of samples
- Clinical Annotation Engine—addresses annotation of biospecimens with molecular and clinical data
- caTIES—extracts structured data from free-text pathology reports
- Specimen Resource Locator—pools summary level information on biospecimen collections from approximately 30 biobanks and biorepositories

In addition to encouraging sharing of relevant biospecimens-related data, OBBR seeks to collate the data in a meaningful way. The Biospecimen Research Database (BRD) is a joint effort of the BRN, the RAND Corporation and the NCI Center for Bioinformatics to survey and collate existing scientific literature that defines the precise relationships between biospecimen handling and the quality and reproducibility of data for cancer research. The BRD allows users to search for information about how specific biospecimen procedural variables can produce variation in gene expression patterns and protein biomarker detection. Examples of biospecimen procedural variables include length of time between surgical removal and biospecimen freezing, conditions of tissue fixation, blood collection and separation procedures, and sample storage conditions. Researchers can use the BRD to optimize their experimental conditions based on prior research findings.

Providing a Solution through a National, Centralized Resource

Another NCI solution to address the current shortage of high-quality biospecimens is the development of a national cancer Human Biobank (caHUB). No centralized resource of this type currently exists in the United States.

caHUB aims to modernize the field of biobanking and contribute to medical advances by providing high-quality human biospecimens and data as well as analysis, scientific tools and services to the cancer research and product-development communities by:

- designing, developing, managing and providing access to a national cancer biospecimen resource
- adhering to the highest ethical and technical standards for biospecimen collection and storage
- developing and managing a network of institutions that will contribute biospecimens to caHUB
- standardizing and developing improvements to biospecimen science and best practices
- developing enabling technologies
- providing laboratory services and online access to resources
- fostering communication, collaboration, partnerships and education and earning the public's trust

Fostering Collaboration, Creating Partnerships

Biospecimens are used throughout the entire research continuum, from basic research to clinical care. The collection of high-quality biospecimens that are properly consented and thoroughly annotated requires the cooperation of surgeons, pathologists, nursing staff, researchers and patients. NCI is actively engaged in constructing the partnerships necessary to improve biospecimen quality and patient care.

Partnerships:

- *College of American Pathologists (CAP)*
  Members of CAP, the leading organization of board-certified pathologists, use their years of experience in laboratory accreditation and extensive knowledge of biospecimens to develop evidence-based SOPs for biospecimens. The importance of SOPs will increase in the era of personalized medicine as biospecimens are used in molecular tests to determine diagnosis, prognosis and treatment.
- *Cancer Biomarkers Collaborative (CBC)*
  CBC includes representatives from the Food and Drug Administration (FDA), the American Association for Cancer Research, the pharmaceutical industry, academia and patient groups to address efforts to advance the Critical Path Initiative (CPI). The CPI is a high-priority FDA program intended to change the way clinical research is being conducted, from early discovery through translational research and marketing. The CBC identified biospecimen standardization as one of four critical areas in the preclinical development of biomarkers and created a biospecimen subcommittee to address the significant biospecimen issues in biomarker development.

"As with treatment and care of the cancer patient, it takes an entire community to ensure the integrity of the biospecimen: from surgeon and operating room staff to pathologist to biobanking staff to researchers. Biospecimen integrity cannot be resolved by any single expert—it will take the entire community to converge on this issue."

Carolyn C. Compton, M.D., Ph.D.

Director, NCI Office of Biorepositories and Biospecimen Research

To learn more about OBBR and its initiatives, visit **http://biospecimens.cancer.gov**.

Sign up to receive email updates at **http://biospecimens.cancer.gov/email_signup.asp**.

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NIH Publication No. 10-7684
Printed October 2010