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From Bench to Bedside: The Role of Health and Human Services (HHS) Agencies in the Evaluation of New Medical Products

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From Bench to Bedside: The Role of Health and Human Services (HHS) Agencies in the Evaluation of New Medical Products

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Summary

Within the Department of Health and Human Services (HHS), a network of agencies conducts and funds basic research and clinical evaluation of new medical technologies. Critics say the system is not well coordinated among HHS agencies. Ultimately, data on how a new medical product impacts health outcomes are necessary to make judgments on the effectiveness and value of that product to patients. Little of these data are collected in a systematic way. HHS is interested in identifying barriers and implementing strategies to make data collection easier, more coordinated, and consistent among the agencies. This report discusses the types of medical research supported by HHS and gives an overview of the agencies' missions. The report, which will be updated, also lists options for making the process of bringing medical innovation from the laboratory bench to the patient's bedside more efficient and predictable.

Types of Research on Medical Technology

Basic research is conducted for the advancement of knowledge. In medicine, research questions focus on the cause and effects of health and disease. There is no obvious application of basic research, other than laying a foundation of knowledge for other scientific endeavors. Findings are often published in peer-reviewed journals. *Applied research* builds on the foundation to ask specific questions for a specific purpose. Increasingly, the line between basic and applied research is blurred, as some would argue that the overarching goal of basic research is to uncover information about targets and processes to ultimately improve health and ameliorate disease.

Clinical trials are studies that investigate the safety and effectiveness of new drugs or medical devices compared to a placebo or current alternatives. Clinical trials are designated as phase I, II, III, or IV, based on the questions that the study is designed to answer. Phase I trials initially study a new drug or device in a small group of people (e.g., 20-80) to evaluate its safety, determine a safe dosage range for drugs, and identify side effects. Phase II trials study the product in a larger group of people (e.g., 100-300) to see

whether it is effective and to further evaluate its safety. Phase III trials investigate the drug or treatment in large groups of people (e.g., 1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments or devices, and collect information that will allow the drug, treatment, or device to be used safely. Phase IV trials are usually large-scale, multicenter *post-marketing studies*, which are conducted after the Food and Drug Administration (FDA) approves a new drug or device for marketing, in order to demonstrate further evidence of effectiveness in a broader clinical context.¹

Health services research (HSR) investigates the relationship between medical services and health outcomes experienced by a patient, and strategies to understand how a health care delivery system can provide access to high-quality, high-value care for various patient populations. The results of HSR studies can provide policymakers with information to assess the impact of system changes on outcomes, quality, access to, cost, and use of health care services across different populations.

HHS Agencies That Evaluate New Medical Products

Within the Department of Health and Human Services (HHS), a network of agencies conducts and funds basic research² and clinical evaluation of new medical technologies. Critics say the system is not well coordinated along the continuum of technology transfer from benchtop research to patient care. Current estimates suggest that it takes 10 to 15 years, and \$800 million to \$1.7 billion in public and private investment, for a new drug to go from the laboratory to patient care.³ HHS invests heavily in medical innovation⁴ all along the continuum, including (1) grants for basic research; (2) funding for clinical trials; (3) technology assessment to support decision-making; (4) health outcome studies; (5) programs or demonstration grants administered by states; or (6) coverage in public insurance systems (e.g., Medicare and Medicaid). In supporting these efforts, Congress may wish to consider the data needs of each agency that ultimately impact when and how a medical product will become available for patient care.

National Institutes of Health (NIH). The goal of NIH research is to acquire new knowledge to help prevent, detect, diagnose, and treat disease and disability, from the rarest genetic disorder to common conditions. NIH conducts research in its own laboratories, supports the research of nonfederal scientists in universities, medical schools, hospitals, and research institutions throughout the country and abroad, helps to train research investigators, and fosters communication of medical and health sciences

¹ See 21 C.F.R. § 312.21.

² See CRS Report RL31940, *Public Health Service Operating Agencies*, by Sharon Coleman.

³ Tufts Center for the Study of Drug Development, “Backgrounder: How New Drugs Move through the Development and Approval Process” (Boston, Nov. 2001). J. Gilbert, P. Henske, and A. Sing, “Rebuilding Big Pharma’s Business Model,” *In Vivo: The Business and Medicine Report* (Windhover Information), vol. 21, no. 10 (Nov. 2003) as cited in the FDA report, “Challenge and Opportunity on the Critical Path to New Medical Products,” Mar. 2004.

⁴ Other federal agencies (e.g., the Department of Defense, the Department of Energy, and Department of Veterans Affairs) also support some medical research and/or medical benefits.

information.⁵ The NIH budget has doubled in the past five years to \$27 billion. The NIH Roadmap Initiative, put forth by Director Elias A. Zerhouni, and developed with input from more than 300 nationally recognized leaders in academia, industry, government, and the public, is a plan to prioritize and speed the transfer of research into clinical practice.⁶

Food and Drug Administration (FDA). The FDA is responsible for protecting the public health by assuring the safety and efficacy of drugs, biological products, and medical devices. The agency helps to ensure that the public gets accurate, science-based information needed to use medicines and diagnostics effectively.⁷ FDA reviews drugs and devices, but it does not review entire treatments or procedures. In the face of declining numbers of product submissions, the agency recently published its Critical Path Initiative, which aims to identify and prioritize the most pressing problems in product development and areas and calls for a collaboration of stakeholders to develop targeted solutions.⁸ FDA recently sought comment on scientific and technical hurdles that cause delays in the product development process (69 *Federal Register* 21839 [April 22, 2004]).

Centers for Medicare and Medicaid Services (CMS). CMS's mission is to ensure health care for beneficiaries, with the goals of protecting and improving beneficiary health and satisfaction, fostering appropriate and predictable payments and high-quality care, promoting understanding of CMS programs among beneficiaries, the health care community, and the public, and promoting the fiscal integrity of CMS programs.⁹ Medical innovation does not reach patients unless someone pays for it. For persons covered by the program (the elderly and certain disabled individuals), Medicare plays a large role in determining what services will be covered for beneficiaries.¹⁰ In 2002, Medicare expenditures for new drugs and devices were approximately \$4 billion to \$6 billion (69 *Federal Register* 29544 [May 24, 2004]). Despite efforts beginning in 1989, Medicare has not been able to promulgate criteria by which coverage decisions are made.¹¹ CMS policy, however, has been working toward making the process more open to the public, so that coverage decisions about new technologies can be vetted.

Agency for Healthcare Research and Quality (AHRQ). AHRQ is the health services research arm of HHS, complementing the biomedical research mission of its sister agency, the NIH. Research at AHRQ specializes in major areas of health care, such as quality improvement and patient safety, outcomes and effectiveness of care, clinical practice and technology assessment, health care organization and delivery systems, primary care (including preventive services), health care costs and sources of payment.

⁵ The NIH Mission Statement, at [<http://www.nih.gov/about/Faqs.htm#NIH>].

⁶ See [<http://nihroadmap.nih.gov>].

⁷ The FDA Mission Statement, at [<http://www.fda.gov/opacom/morechoices/mission.html>].

⁸ See [<http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.html>].

⁹ The CMS Mission Statement, at [<http://www.cms.hhs.gov/about/mission.asp>].

¹⁰ See also CRS Report RL31711, *Medicare: Coverage Process*, by Jennifer O'Sullivan.

¹¹ S.R. Tunis "Why Medicare Has Not Established Criteria for Coverage Decisions," *New England Journal of Medicine*, vol. 350, no. 21 (May 20, 2004), pp. 2196 ff.

ARHQ is a major source of funding and technical assistance for health services research and training at leading U.S. universities and other institutions.¹²

Centers for Disease Control and Prevention (CDC). The goal of CDC is to promote health and quality of life by preventing and controlling disease, injury, and disability. The CDC seeks to accomplish its mission by working with partners to monitor health, to detect and investigate health problems, to conduct research to enhance prevention, to develop and advocate sound public health policies, to implement prevention strategies, to promote healthy behaviors, to foster safe and healthful environments, and to provide leadership and training.¹³ This role supports new technology development by tracking disease and statistics, and monitoring the health of the population.

Health Resources and Services Administration (HRSA). HRSA's mission is to improve and expand access to quality health care for all Americans, and to ensure the availability of quality health care to low-income, uninsured, isolated, vulnerable and special-needs populations.¹⁴ HRSA helps to support technology development by ensuring that medical innovation addresses the health needs of vulnerable populations, and that appropriate populations are included in clinical research.

Strategies for Evaluating Medical Innovation

Ultimately, data on how a new medical product impacts health outcomes are necessary to make judgments on the effectiveness and value of that product for patients. In times of constrained resources for healthcare, some assert that HHS needs to assess the effectiveness and value of new technologies at each stage of research activity through more effective collaboration of federal assessment efforts and integration with private efforts. HHS agencies, they say, will need a better means of “handing the baton” among agencies to evaluate different snapshots of the process to create a panoramic view of effectiveness and value, and to put the nation's investment in research into practice without stifling innovation. Advocates urge that funding initiatives include downstream investments in health services research as a natural outgrowth of the substantial investment in basic research.

Legislation may have impact across the spectrum of medical technology transfer, rather than just on isolated elements. For example, the Food and Drug Administration Modernization Act of 1997 (FDAMA) made it easier and quicker for medical products to get FDA approval. The Act included language in section 505(d) to clarify that “data from one adequate and well-controlled clinical investigation¹⁵ and confirmatory evidence” could constitute substantial evidence of effectiveness if FDA so found, where previously

¹² AHRQ Mission statement, at [<http://www.ahrq.gov/about/whatis.htm>].

¹³ The CDC Mission statement, at [<http://www.cdc.gov/aboutcdc.htm#mission>].

¹⁴ HRSA Mission statement, at [<http://www.hrsa.gov/about.htm>].

¹⁵ The requirements for clinical studies can be found in 21 C.F.R. § 314.126.

evidence from several trials were typically required. In addition, the Act encouraged the agency to develop surrogate endpoints as predictors of a drug's therapeutic effect.¹⁶

These actions to bring medical products to market quicker seem at odds with requirements of Medicare, where FDA approval is often necessary, but not always sufficient, for the program to pay for a service. In contrast to FDA's regulations, the statutory standard for a covered item under Medicare as defined in Title XVIII of the Social Security Act, Section 1862(a)(1)(A) is that the item be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.¹⁷ Medicare has interpreted the statute by looking for evidence that the service is medically necessary and effective, and that the service is not experimental. Medicare's guidelines for assessing effectiveness¹⁸ rely on outcomes data.

In the past, FDA and CMS have been interested in coordinating their assessments, but cultural, political, regulatory, and/or statutory differences in their authorities may prevent them from sharing data. Characterization of the barriers and the extent to which they may impede more efficient technology assessment was considered in a 2004 HHS meeting on medical innovation.¹⁹ In January 2005, HHS released a report detailing five recommendations: (1) enter into new or expanded Memoranda of Understanding with appropriate non-HHS federal agencies to promote more rapid and efficient technology transfer; (2) streamline HHS involvement in medical technology transfer; (3) improve collaborations between FDA and CMS; (4) support standardized formats for electronic clinical trials data; and (5) initiate a training program in technology development and transfer for HHS personnel, scientists, and engineers.²⁰

Several additional ideas have been suggested for improving coordination between agencies. Proponents envision these ideas as complementing each other without being redundant, and facilitating interagency coordination rather than stifling innovation.

- The NIH, FDA, and HRSA could work together to include vulnerable populations (e.g., children, the elderly, minorities, or patients with cognitive impairment) in clinical trials. This action would help to assure

¹⁶ Surrogate endpoints are typically laboratory signs or physical findings that are plausibly correlated with a health outcome. See *57 Federal Register* 58942 (Dec. 11, 1992). Use of surrogate endpoints reduce the time a drug needs to be studied. The problem with surrogate endpoints is that often they are found not to be highly predictive of a health benefit. As a result, other programs — such as Medicare — still rely on actual health outcomes as measured endpoints before “approving” an intervention under their program.

¹⁷ Medicare does cover certain preventive services as a matter of exception under Section 1861(s)(10) (i.e., for pneumonia, influenza, and hepatitis B vaccines), and certain screening services that are defined in the statute.

¹⁸ CMS, Medicare Coverage Advisory Committee (MCAC), “Recommendations for Evaluating Effectiveness,” available at [<http://www.cms.hhs.gov/mcac/recommendations.asp>].

¹⁹ DHHS, “Stimulating Innovation in Medical Technologies,” *69 Federal Register* 61018 (Oct. 13, 2004).

²⁰ DHHS, “Moving Medical Innovations Forward — New Initiatives from HHS,” Jan. 2005, at [<http://www.hhs.gov/reference/medicalinnovations.shtml>], accessed Jan. 3, 2005.

safety and effectiveness in the same populations that CMS and/or AHRQ will need to evaluate for determining coverage or social value of service.

- The NIH, CDC, FDA, and CMS could establish a working group to determine relevant data elements for measuring, evaluating and tracking the course of disease (or health) and the effectiveness of intervention. Following approval of a product for marketing and/or coverage, FDA and CMS could make, as a condition of approval or payment, requirements for reporting information to CDC and/or FDA for post-market surveillance.
- The FDA and CMS could work together with researchers, manufacturers, and sponsors who are planning clinical studies to develop protocols that would provide for the collection of the relevant outcomes measures the agencies would need to demonstrate safety and effectiveness for FDA, and medical necessity for CMS.²¹ After the study was completed, the agencies would separately evaluate if the sponsor met the respective standards and would define the circumstances of product approval and/or coverage applications.
- If CMS requires data beyond those that are necessary for FDA approval, FDA and CMS could work to determine appropriate post-market requirements. These requirements could consider data that AHRQ may use to support an evidence report or technology assessment.²² Under a discretionary provision, FDA may require post-market surveillance for products if deemed necessary to protect the public health.²³ CMS expressed recent interest in working with NIH to develop a registry for post-market surveillance for implantable cardioverter defibrillators.²⁴
- CMS and AHRQ could work with the sponsor of the technology to define flexible criteria or thresholds for establishing acceptable effectiveness or value of a new medical product. These can be technology-, service-, or disease-specific. Once the threshold of the medically reasonable and necessary standard is met, further studies could address value.

²¹ M. M. Schoonmaker, G. P. Bagley, and M. K. Scanlan, "Coordination of Federal Regulation and Payment for New Diagnostic Tests: A Proposed New Approach," *Food and Drug Law Journal*, vol. 57, no. 2 (2002), pp. 195-204.

²² Evidence-based practice centers review literature on clinical, behavioral, and organization and financing topics to produce evidence reports and technology assessments. They provide technical assistance in helping to inform coverage policies. See [<http://www.ahrq.gov/clinic/epc>].

²³ See FDA, "Post Market Surveillance Studies," available at [<http://www.fda.gov/cdrh/devadvice/352.html>].

²⁴ "Medicare Draft National Coverage for Implantable Cardioverter Defibrillators includes Registry of Recipients to Track Progress," Sept. 28, 2004, available at [<http://www.cms.hhs.gov/media/press/release.asp?Counter=1212>].