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The Center for Accelerating Medical Solutions

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U.S. Department of Health and Human Services
Personalized Health Care RFI
200 Independence Avenue S.W.
Room 434E
Washington, D.C. 20201

RE: Request for Information (RFI): Improving Health and Accelerating Personalized Health Care through Health Information Technology (HIT) and Genomic Information in Population- and Community-based Health Care Delivery System

Dear Madam/Sir:

FasterCures is a nonpartisan, nonprofit organization whose goal is to save lives by saving time in the discovery, development, and deployment of treatments and cures for deadly diseases. We are independent of any interest or industry groups. Our mission is to evaluate the current system of medical research; identify inefficiencies, misplaced priorities, and conflicting incentives inhibiting the pace of discovery and development; and propose and pursue improvements to the existing system. Our goal is to enhance and accelerate the efforts of those directly involved in developing and overseeing the introduction of safe and effective treatments and cures. We appreciate this opportunity to comment on improving health and accelerating personalized health care through HIT and genomic information in population- and community-based health care delivery systems.

Based on our work and input from the medical research community, we have established an Acceleration Agenda to address needs in key areas of medical research: Research Leadership and Innovation; Research Tools and Resources; and the Medical Research Environment. We are working on projects related to ensuring that clinical research is included as part of the Nationwide Health Information Network (NHIN) infrastructure so new therapies can be discovered as quickly as possible; increasing the numbers of participants in clinical trials; providing a source of timely information about why biospecimens matter to research through our web portal BioBank Central; and promoting innovation in research by bringing together the leadership of organizations known for successfully implementing innovative approaches to research initiatives.

The frontier of medical science has rarely been as exciting and as full of opportunity as it is today. From basic science through clinical research to health services research, the opportunities made available through the impressive advances of recent decades in the biomedical, physical, computational, and behavioral and social sciences have brought us to a place of unprecedented opportunity.

The successful completion of the Human Genome Project has launched scientists into the new world of genomics and proteomics, a journey that will lead to the eventual

understanding of every human protein and its role in both health and disease. The next challenge will be to identify the functions of the genes that have been mapped, the proteins for which they code, and the functions of those proteins in the body.

To understand the relationships between this molecular information and human health, population-based and clinical studies are needed, entailing the generation, storage, and analysis of enormous quantities of epidemiologic, genotypic, and phenotypic data. To understand the connections between genes, proteins, and the environment, sophisticated comparisons must be conducted. These comparisons cannot be done by hand or by eye or patient by patient. It is the collective observations of hundreds, even thousands, of patients that will shine a light on these associations.

FasterCures selected the following topics to address because they align with our mission and activities to improve the resources available to medical researchers in the form of biospecimens and electronic medical records:

- **Anticipated applications of genomic-based clinical testing in medical decision-making, safety assessment, and risk management.**

The study of genome-derived data, including human genetic variation, RNA and protein expression differences has the potential to transform our entire approach to discovering and developing new drugs and treating patients by predicting the safety and/or efficacy of drugs in individual patients or groups of patients.

Consumer oriented genetic testing is here. Individuals can provide a DNA specimen to screen for gene abnormalities. The screening will be related to genes or gene variations associated with a disease and for which there are effective preventive strategies. Screening should not be done for genes whose function has not been elucidated.

Based on the use of molecular profiling technologies, it is already clear that diseases formerly thought of and treated as one condition are actually multiple different conditions at the molecular level. It is also now well established that different individuals and groups of individuals can be identified, based on their genetic "fingerprints," as having the propensity to acquire certain conditions, respond or not respond to certain therapies and either have or not have certain adverse side effects. This genetic profiling will identify needed lifestyle and environmental changes that, if implemented, will delay or prevent the development of certain diseases.

Molecular medicine has the potential to bring multiple benefits to patients, including the ability to predict and potentially change the course of their disease, the ability to avoid adverse effects from drugs certain individuals will not tolerate well, and the ability to gain access to drugs likely to cure or improve their condition. But the rate at which molecular medicine can come to fruition is still a question, based on the technical, ethical, educational, and economic issues confronting the field.

By focusing now on the various challenges molecular medicine raises, regulators can prevent a divergence between the course of scientific developments and the development of appropriate regulatory review processes for these new therapies.

Some of the key questions that need to be addressed are:

- What information technology infrastructure is needed to manage and benefit from the tidal wave of emerging genomics-based information?
- How can repositories of human tissue and associated clinical information be expanded and handled on a national basis to accelerate statistically robust and disease-based research?
- Who is responsible for educating patients about such new diagnostics and therapeutics?
- Is it acceptable to stratify patients entering into a clinical trial a priori based on a pharmacogenetic test?
- What incentive is there for large pharmaceutical companies to develop drugs for sub-groups, when they rely heavily on blockbuster drugs for the return on their investment?

➢ **Concepts or models on the potential use of clinical data and related resources for research applications**

This has been a central area of study and action for *FasterCures*. We believe that the study of large samples of medical records or clinical datasets could be an essential step toward understanding the etiology and progression of disease, treatment methods, and outcomes across varied populations and disease groups. In the *FasterCures* report "Think Research: Using Electronic Medical Records to Bridge Patient Care and Research," (available on the Web at www.fastercures.org/pdf/emr_whitepaper.pdf) we present several models of how groups are using electronic medical records (EMRs) and clinical data *today* in the provision of health care and, to a lesser degree clinical research.

The trend toward the capture and storage of patient information in digital form provides researchers with a potentially more efficient and effective means of accessing this data to:

- form hypotheses about disease initiation and progression;
- look for patterns of health and illness in a given population;
- conduct post-marketing surveillance studies of new drugs to identify adverse events or improve prescribing and labeling practices; and
- most importantly, identify potential study participants for clinical research.

There are practical benefits to the research use of EMRs as well.

- Much of the patient information collected for clinical trials already exists in the patient record. If clinical researchers could quickly import such information (especially if it is standardized) from the existing practice record into the research record, both time and money could be saved.

- EMR systems could speed data acquisition and searching, allow mass computing and sampling, and provide the research community access to a broader and more diverse patient population.

We propose two courses of action to maximize the potential of using the records in research. First is to link these records through a Global Research Network to make metadata available to bona fide researchers over the Internet. This network can then serve to link researchers to more specific records through an agreed upon system of access that is uniform across institutions. Second, in our subsequent report on clinical research and the NHIN "Ensuring the Inclusion of Clinical Research in the Nationwide Health Information Network," we discuss how these existing records can be used today for clinical trial recruitment and for post-marketing surveillance of adverse events of newly approved drugs.

- **Organizational or institutional practices to address ethical, legal, and social implications regarding the use of patient information, including genetic data, to support personalized medicine**

The human research enterprise is highly regulated and medical records research using patient information including genetic data is no exception. The major ethical concerns in research with human subjects focus on the protection of privacy and confidentiality and the minimization of risk. In the case of EMRs, fears of unauthorized access to and use of EMR systems continue to be a significant barrier to their adoption. Ensuring the security and privacy of EMR systems that contain very personal patient information remains a substantial challenge.

In the *FasterCures* white paper "Think Research" we note that experience has shown that security is easier to manage in a centralized database, where only one copy of a specific person's record is kept. However, if patients and/or providers are keeping copies of their records on some kind of portable media, access and security issues multiply.

As a specific response to the possibility of genetic discrimination, *FasterCures* supports the Genetic Information Nondiscrimination Act because the fear of misuse of genetic information limits the use of genetic tests. This lack of participation in research has a negative impact on researchers, clinicians, and industry, slowing the research and development process for targeted drugs and treatments. In order to fully promote personalized medicine and the use of genetic information in healthcare, we must pass the GINA legislation.

- **Establishment of biospecimen resources obtained from clinical medical services for application in research, clinical trials, health services planning, clinical effectiveness, and health outcomes evaluations**

Biospecimens are often cited by the research community as the most critical of all issues. With rapid and unfettered access to large quantities of high quality, clinically annotated biospecimens, researchers can conduct the genomics-based experiments that lead to

discovery of biomarkers and new approaches to disease diagnosis and treatment. Without such access, research is slow or disrupted.

Biobanks – when implemented effectively – can harness the power of both genomic and clinical data and serve as a critical bridge between basic and applied research, linking laboratory to patient and getting to cures faster.

In April 2006, *FasterCures* launched BioBank Central, a health information system that serves as an accurate and timely source of news and knowledge about biorepositories and their role in research and drug development. *FasterCures* believes that biobanks are the meeting point of two major information trends in biomedical research: the generation of huge amounts of genomic and other laboratory data, and the electronic capture and integration of patient clinical records. BioBank Central aims to:

- serve as the most accurate and timely source of knowledge and news about biorepositories and their role in research and drug development;
- enable many different stakeholders to share best practices and contribute to the development of standard biorepository policies and operations;
- facilitate collaboration and cooperation within the biorepository community;
- educate the general public about the potential for biomedical advancements from the information captured in biorepositories and the need for contributions to such repositories if the potential is to be achieved; and
- facilitate the linkage between researchers and the specimen inventory and databases that comprise a national biorepository network.

FasterCures believes it is important that patients understand the key role that biospecimens play in translational research, and how critical they are to future research discoveries. As with clinical trials, the time to educate patients about tissue donations is not at the moment a consent form is being signed for a donation. Patient groups must be brought into the process as partners in helping to ensure that the patient community understands how biobanks work, and the role they plan in the clinical research infrastructure.

- **Need for community-wide standards or best practices that will facilitate large-scale data integration and exchange to benefit personalized health care**

To achieve the promise of better health and a better healthcare system, the NHIN must address the needs of the entire system and enhance the exchange of information among the domains of personal health management, healthcare delivery, public health, and health research. By enabling research use of information collected in the patient care process, the NHIN will significantly accelerate the search for cures.

The proprietary basis of many EMR products raises key issues regarding the interoperability of systems, including the need for standard underlying reference vocabularies and presentation formats for clinical data. And EMR adoption must be able to grow with the information technology and healthcare environment, including new

technologies such as handheld devices, wireless communications, biometrics, continuous speech recognition, new imaging techniques, Web access, and personal health record support via the Internet.

Many of these barriers are being tackled through collaborative efforts. For example:

- The federal **Consolidated Health Informatics** initiative seeks to adopt uniform standards for electronic exchange of clinical information across the federal health enterprise.
- Eight large technology companies have formed the **Interoperability Consortium** to aid the federal government's development of a digital health network.
- The private-sector **Certification Commission for Healthcare Information technology** was created last year with the goal of creating a mechanism for certifying health information technology products.
- The Markle Foundation established the public-private collaborative **Connecting for Health**, which has worked to build consensus on the adoption of an initial set of data standards, develop case studies on privacy and security, and define the electronic personal health record.

Clearly standards and best practices to facilitate large-scale data integration need to be collected and disseminated. We suggest turning to the early adopters of EMRs as one starting point for this effort.

➢ **Examples of utilizing large clinical data repositories for practical clinical research to discover effective technologies, therapeutics, diagnostics, and prevention strategies for different populations**

FasterCures' white paper "Think Research" contains many examples of the institutions that have overcome enormous obstacles and forged ahead to find ways to meld clinical practice data with research goals. This is not easily accomplished, because most clinical EMR systems are designed to support clinical workflow, not research. Numerous academic medical centers are in the early stages of EMR adoption generally, and many are contemplating the value of EMRs as a research resource.

EMR systems could speed data acquisition and searching, allow mass computing and sampling, and provide the research community access to a broader and more diverse patient population. Here are just a few examples of what the pioneers and innovators are doing:

- **Pointing the way to new treatments.** Researchers from IBM and the Mayo Clinic are using Blue Gene supercomputing technology and applying customized algorithms, data mining, and pattern recognition to uncover correlations between particular proteins, genetic markers, patient outcomes, and other factors that could lead to new diagnostics and treatments. Experts envision a time when computer

programs will be developed to note patterns and trends of interest on their own, without humans having to create a query.

- **Conducting post-marketing research.** With an EMR system, one could look at entire populations and know the impact of a new drug or device on, for example, diabetics, asthmatics, African American women over 65, or whatever population subset was chosen. Impact could be ascertained on a weekly, monthly or yearly basis. A recent study conducted with Kaiser Permanente records of almost 1.4 million patients into the effects of COX-2 selective agents on heart disease resulted in the manufacturers of these agents voluntarily withdrawing their products from the market pending further safety studies.

- **Making clinical trials cheaper and easier.** The Mayo Clinic conducts more than 4,000 clinical trials each year, and many trials rely on information from medical records, primarily to identify potential research subjects. Mayo has 6.5 million patient records collected systematically and electronically indexed. More than 95% of its patients allow their records and samples to be used for research.

FasterCures believes that an ultimate goal is to allow researchers entry (with permission) into these various databases. This type of system will enable users to rapidly find out if a desired database exists and to discover what types of patients and data are included. It will also provide step-by-step instructions for contacting the owner of the database and gaining access.

Such a Global Research Network will not provide the actual data contained within the database, however, it will allow individuals to conduct a sophisticated query of existing databases in order to determine their usefulness. Each database would be subject to its own procedures, rules and regulations for use. In our "Ensuring the Inclusion of Clinical Research" report we asked, "To what extent are people seeing their data as being a strategic asset that they aren't interested in sharing?" This is the question that will need to be pursued as more and more EMR databases are created and the value proposition for clinical research becomes clearer.

- **Feasibility and potential benefits for establishing linkages of institutional or organizational data resources with private and publicly available health databases.**
- **Development of ontologies across different clinical data repositories or organizational data resources with private and publicly available databases.**
- **Opportunities and challenges for the development of electronic tools to aid in the integration and analysis or large datasets of clinical parameters to assist in outcomes evaluations.**

We have chosen to address all three of these issues together.

Impressive examples of EMR systems are in place both in U.S. hospitals and in some ambulatory practices. But will all of these efforts be creating new silos of information

that will mount technical and cultural barriers to mining data across institutions?

To facilitate data mining of EMR databases by investigators:

- all the systems to be searched need to be accessible somehow by the researcher (or, more specifically by the software the researcher is using) using HTTP connections, database connection tools, or a yet-to-be-developed standard;
- all of the translation issues between different systems and formats need to be addressed;
- the issue of patient consent to have their medical data used for research would need to be addressed;
- some mechanism would need to be developed and enforced that would appropriately anonymize the data to be searched.

These goals will be difficult to achieve unless there is a central authority providing guidance and a clear, detailed set of standards and instructions for the designers and users of EMRs, as well as for the developers and users of searching and interconnecting tools.

Still, there are instances of institutions working successfully to overcome interoperability challenges. For example, a critical mass of multispecialty group practice users are choosing the same software vendor, including Kaiser Permanente, Cleveland Clinic, University of California at Davis, and Palo Alto Medical Foundation (Sutter Health), a development that may lead to increased opportunities for interoperability among care systems. Under the auspices of the Council on Accountable Physician Practices, some of these group practices are beginning to meet with each other to standardize data flow and share learning. And several large research institutions – for example, Stanford University and the Dana Farber Cancer Institute – are developing systems to move data from real-time clinical records to research repositories.

Conclusion

The application of information technology to patient records offers the promise of new knowledge that can be obtained only by integrating and analyzing data extracted from hundreds if not thousands of patient records, including clinical information, medical images, environmental profiles, and genetic analyses, combined with new findings from molecular and genomics research.

The promise for personalized medicine offered by these integrated records is immense. Investigators at institutions that have developed the capability and permission to search the databases for information will ultimately be positioned to use the knowledge arising from genomics and proteomics research. We believe EMRs and clinical databases and warehouses can make the work of specialists in one discipline widely accessible to specialists in many disciplines.

Importantly, improvements made in EMR systems in response to research needs will

ultimately serve clinical care needs as well. For example, in trying to achieve consistency and standardization, patient record systems will not only become more useful for research but will also contribute to improved quality of patient care. Likewise, the development of customized algorithms and pattern recognition systems will aid researchers while simultaneously providing physicians with smart clinical decision support tools.

The clinical research community sees enormous potential in the ability of researchers to access and analyze the clinical information contained in millions of medical and personal health records. With appropriate privacy and human subjects protection safeguards in place, this capability could speed the discovery of new therapies beyond anything imaginable today.

We thank the Department of Health and Human Services for this opportunity to provide comment and look forward to further discussion on these important topics.

Sincerely,

Gregory C. Simon
President
FasterCures / The Center for Accelerating Medical Solutions