

Pfizer Inc
235 East 42nd Street
New York, NY 10017
Tel 212 573 1134 Cell 917 744 4149
Email joseph.feczko@pfizer.com

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Joseph M. Feczko, M.D.
Senior Vice President
Chief Medical Officer

January 29, 2007

The Honorable Michael O. Leavitt
Secretary
U.S. Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Secretary Leavitt:

Pfizer Inc. appreciates the opportunity to submit comments to you and the U.S. Department of Health and Human Services (HHS) on the Request for Information on Improving Health and Accelerating personalized Healthcare Through Health Information Technology and Genomic Information in Population and Community-based Healthcare Delivery Systems.

Pfizer is the world's largest private research-based pharmaceutical company dedicated to the discovery and development of novel medicines and treatments to improve the quality of life of people around the world. Our mission is to meet patients' needs by providing innovative medicines and health management services which are enabled by advancing the quality and safety of healthcare through research.

Pfizer strongly supports accelerating personalized healthcare through use of genomic information and health information technology (HIT). Pfizer supports widespread adoption of HIT and personalized medicine practices and sees the unique promise this technology holds to fundamentally improve healthcare by transforming clinical practice and reducing health disparities. We also see vast potential for HIT and genomic information to aid clinical research organizations in improving the way diseases are diagnosed and treated by advancing research and development of innovative therapeutics. Clinical data collected from electronic health records (EHRs) can help speed delivery of novel pharmaceuticals to market and monitor their efficacy and continual safety. Through good data stewardship and the appropriate use of science and technology health information technology can accelerate the delivery of personalized healthcare.

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Pfizer's fundamental goal in the effort to advance personalized medicine and HIT is to bring clinical research to the point of care and the point of care to clinical research. This inclusive approach to specialized healthcare and clinical research will help speed the delivery of innovative therapies for the prevention and treatment of disease.

Pfizer's approach to HIT is guided by the following key principles:

- **Patient First:** Patients' rights and needs must drive the evolution of HIT. Essential patient interests include safety, quality, individualized care, privacy, public health, and access to care.
- **Primacy of Clinical Judgment:** HIT should provide greater access to data and support to enable the provider to make better healthcare decisions in collaboration with the patient.
- **Healthcare Cost Awareness:** New technologies should be used to reduce total cost in healthcare by improving the understanding of long-term costs and outcomes, reducing errors and redundancies, and increasing efficiencies.
- **Rigorous Standards for Healthcare Information:** All parties disseminating information that influences patient outcomes should be subject to equivalent standards of research, presentation, and communication.
- **Shared Responsibility:**
 - ◆ **Shared Governance:** All healthcare stakeholders must share the responsibility of creating and enforcing efficient processes and robust safeguards within HIT to assure the adoption of systems aligned with the provision of quality care.
 - ◆ **Systems Affordability:** HIT must advance in such a way that no stakeholder is unduly burdened by the cost of purchasing technology and constructing infrastructures.
- **Integrity in Technology:**
 - ◆ **Neutral Platform:** HIT should be provided through neutral platforms that support honest brokers. HIT should not advance the commercial interests of any party to the potential detriment of patients.
 - ◆ **Interoperability:** HIT must conform to prevailing quality and technical standards to facilitate adoption and control costs, but also be flexible to support innovation and improvements.

SPECIFIC COMMENTS

- I. **Concepts on anticipated approaches for the use of EHR and population- and community-based health care system databases for longitudinal data collection in addressing: disease susceptibility, clinical course and outcomes, treatment response, evidenced-based clinical decision support, optimal healthcare delivery systems.**

Establishment of EHR and Clinical Trial data standards would provide an unprecedented wealth of information to healthcare and medical research professionals. These collective data have the potential to vastly improve our ability to diagnose and treat disease while

large longitudinal data would advance medical and pharmaceutical research. Data collected through the EHR will assist researchers and providers to better understand the prevalence of medical conditions, monitor the safety and usage of existing treatments, and conduct clinical research in a more timely and efficient manner. This will help speed the delivery of future promising pharmaceuticals to market and enhance the ability to monitor their safety and efficacy.

With the increasing availability of EHR data, it becomes possible to examine large population-based information in ways not previously possible. Large data sets describing a patient's course of treatment, medication, or hospitalization can be matched to data from comparable patients with similar clinical experiences and analyzed to identify trends and best practices in care, outcomes and efficacy. For example, analyses based on sound scientific criteria could provide large scale safety and efficacy data for different drugs within the same therapeutic class for the purpose of evidence-based clinical decision-making. This can be extrapolated into various areas in healthcare such as medication safety and efficacy, surgical therapy versus medical therapy, and nursing strategies.

Additionally, data from EHRs can be used to measure whether the latest therapeutic guidelines are in practice in the community. This allows healthcare providers or organizations an opportunity to improve their healthcare practices and delivery based on current clinical guidelines. For example, identifying whether patients receive the appropriate therapies within a specific timeframe following myocardial infarction can be measured at the practice, community or regional level. The outcome of these efforts should be used to drive continuous quality improvement.

Population-based healthcare data can be used to identify disease trends at the population level, provide a medium for bioterrorism surveillance, help to measure quality, and facilitate research. Specifically, computer assisted analysis tools could rapidly analyze patient data housed in a system that can aggregate the data. Because these data analysis tools are most effective with a large sample size, EHR data should be stored in a manner such that it can aggregate data from local repositories. A distributed or decentralized model of data storage adds excess organizational layers and could lead to the inability to aggregate the data and consequently less reliable detection of events or signals. Optimal use of algorithms depend on many variables, including sample size, completeness of recorded information, and use of embedded data standards to allow appropriate matched comparisons of information. Signal detection in this manner, could help to identify adverse events for pharmacovigilance, pandemics as population outbreaks occur, bioterrorism detection, or other independent events that precede larger population impact.

At the same time, centralized data repositories can create challenges around data ownership, conditions under which the data may be used, and privacy concerns. There are other potential models for supporting the use of distributed or federated data for research purposes using common query languages and methodologies (discussed below). Pfizer recommends that the Secretary support the continuing exploration of multiple methodologies for supporting clinical research using external data sources.

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

A key application of genomic-based clinical decision-making is the ability to predict disease risk, make early diagnosis, and determine which therapies and course of treatment will deliver the most optimal outcome for each individual patient. Many studies have shown marked variability in response to treatment and existing data indicates part of the nature of variable response to treatment is genetic. Research using new molecular biology technologies; genomics (including RNA-based technologies), genetics, proteomics, and metabonomics, are being applied in the discovery and development of novel therapeutics. Examples of molecules being developed from an understanding of genetics suggest these new drugs can be more specifically targeted to specific treatment populations. In addition, as drugs move through the development process and into the market, correlations of molecular knowledge combined with drug response (both efficacy and safety) will enable more accurate determinations of patients most likely to have the greatest benefit-risk balance when taking the new therapeutics. This approach will be enabled by the co-development of diagnostics which will allow rapid identification of specific individuals with characteristics most likely to respond to particular therapies.

The development of biomarkers (protein, genomic, etc.) of disease, prognosis, drug action and drug response can accelerate the translation of basic biological information into useable strategies for drug development. In concert with efforts around translational research (including those advocated and/or sponsored by Food and Drug Administration (FDA), the National Institutes of Health (NIH), and pharmaceutical companies, for example the Biomarker Consortium), the collection and use of samples and data for research purposes can support personalized healthcare by optimizing biomarker qualification (biological and clinical validation), by encouraging appropriate acceptance of validated safety and efficacy biomarkers, and preventing premature acceptance of inadequately validated safety and efficacy biomarkers.

The ability to predict disease risk and make early diagnosis could enable early patient-specific interventions and ameliorate disease progression. This novel approach to individualized risk assessment, disease prevention, and early treatment will serve to accelerate the research and development of highly effective and targeted therapies. As pharmaceuticals with associated clinical diagnostics are introduced, the likely impact will improve risk-benefit ratios for patients through safer, more effective, and targeted therapies. These approaches, commonly called pharmacogenomics, will help target patients more specifically for delivery of personalized healthcare.

On a population level, the emerging practice of personalized medicine has substantial public health implications. By better understanding the distribution of various genetic markers within a population, public health organizations can customize their efforts to target specific diseases more prevalent from one population to another. For example, certain tribes of Native Americans have a higher rate of diabetes than the general population. If it were possible to understand the genomics of this population, it might be

possible to target more specific therapies to this cohort. Similarly, there are certain populations of African Americans who are known to respond better to one anti-hypertension medication than another. With a genetic profile, clinicians could better treat these people earlier and with more directed therapies resulting in improved health outcomes.

Modernization of clinical practice and healthcare delivery by utilizing genomic information will not be achievable without development of HIT standards and infrastructure. These standards must ensure the security and privacy of patient clinical information while maintaining data quality for application of clinical decision-making and personalized healthcare.

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

Pfizer is actively exploring ways to manage research and clinical data within conformant data warehouses (i.e., information factories) to better understand the impact our products have on disease, to improve safety, and to deliver innovative and advanced healthcare solutions to patients. We continue to experience marked progress by leveraging healthcare industry standards and shared infrastructures (e.g., CDISC, Janus, CRIX) for the exchange and management of research, clinical, and genomic data. To facilitate genomic research, samples are collected from patients in Phase I through IV clinical trials, with broad-based informed consent from trial subjects. This facilitates hypothesis-driven and exploratory research which forms the basis for the development of personalized medicines.

Pfizer has developed secure systems for anonymization and/or de-identification of data that will be ultimately used for research purposes. In concert with rigorous adherence to sound processes, we can prevent the linking of research data back to identifiable research participants. A critical factor in this process is the nature of the written informed consent and the level of transparency provided to the patient when he or she is asked to donate samples and data for research purposes. It is important to note that our protocols always receive approval and are overseen by Institutional Review Boards (IRB) or Institutional Ethics Committees (IEC).

Notably, Pfizer has developed a state-of-art BioBank that manages samples and associated information (e.g., DNA, biofluids, tissues) collected from clinical trials and research collaborations. The vast amount of research we conduct and our efforts in translational medicine generates essential genomic, biomarker, proteomic, and metabonomic samples that will drive a much greater understanding of the molecular basis of drug response and subsequently diagnostic and personalized medicine.

In concert with BioBank we have developed a system that allows scientists to generate and test their hypotheses against anonymized or de-identified clinical and genomic data. The facility utilizes robotics to maximize consistency and reliability of sample ordering,

has a capacity to store and retrieve up to 6 million samples, and adheres to strict international data privacy and consent guidelines. The system includes a sophisticated one-way de-identification engine and uses detailed rigorous processes to ensure security and privacy of sample data. Pfizer would be happy to share our knowledge and methodologies used to collect, store, analyze, and protect data.

Importantly, we must develop a consensus among healthcare providers, the pharmaceutical industry, IRBs/IECs and government agencies on the mechanism whereby such samples can be collected, stored and analyzed. For example, many IRBs/IECs routinely request that samples are anonymized or de-identified; however, it is not clear whether the FDA will accept data submissions containing de-identified and anonymized data. We must also find consensus concerning the terms of use of data generated from disparate specimens. Often genetic material is deemed special due to its pertinence (e.g., importance to relatives of the donor) and its persistence (e.g., status for the life of the individual). However, there are many examples of clinical trial and healthcare data for which the same can apply or which have extra sensitivity (e.g., HIV status). It may be more appropriate to capture and use specimens/data according to terms of use of the data (e.g., unspecified future research, hypothesis generation, and specific trial hypothesis) and the level of consent obtained rather than arbitrary levels of data sensitivity (e.g., genetic versus metabonomic versus expression samples, etc.).

IV. Organizational or institutional practices to address ethical, legal, and social implications regarding the use of patient information, including genetic data, to support personalized health care

To facilitate adoption of HIT and personalized healthcare, technical and administrative standards and safeguards must be established to ensure the confidentiality, security, integrity, and availability of patient data. Pfizer believes a robust HIT system can be developed that adequately guards the confidentiality of health records while still allowing access to patient de-identified data for clinical research and therapeutic and safety surveillance purposes. Any HIT system must have the full confidence of patients, users, and the public at large; this is particularly important when considering genomic data. Building both patient and physician trust from the onset is critical to adoption and utilization.

Individual patient confidentiality and privacy is essential and must be balanced with the needs and potential benefits for population health. Patient data can be anonymized or de-identified without removing necessary data elements for clinical research. A patient identifier key may be held separately so that patient data and patient identity can not be reconciled. Additionally, newer more sophisticated methods of de-identification, such as one way de-identification mentioned above, have been developed, which together with improved processes, allow for greater confidentiality assurance and privacy protection while allowing for the possibility of audit where required.

Pfizer abides by strict guidelines in its clinical research practices and works closely with IRBs, IECs, and other agencies to maintain and ensure patient safety and confidentiality.

Although genomic data encompasses an enormous amount of information, genomic data can be de-identified and safely used in aggregate to further the mission of clinical research. Technology exists today that can de-identify and anonymize patient information and ensure confidentiality and privacy while still allowing access to data for clinical research.

Genomic data is not inherently more or less sensitive than other types of clinical data. It is important that all health data be provided a level of security that ensures privacy and confidentiality of the patient. All forms of clinical data should be protected while still allowing for data sharing where appropriate patient consent has been given and IRB/IEC oversight is maintained.

The following are examples of multi-organization partnerships engaged in efforts to bring personalized medicine to clinical practice through advancement of HIT.

Cancer Biomedical Informatics Grid (caBIG). The Cancer Biomedical Informatics Grid, or caBIG, is a voluntary network or grid connecting individuals and institutions to enable the sharing of data and tools, creating a World Wide Web of cancer research. caBIG is a partnership between the National Cancer Institute (NCI) and the private sector to facilitate integration of clinical information and the growing volume of genomic and proteomic data for the purpose of advancing development of new therapies. In conjunction with 80 companies, as well as NCI, NIH, and FDA, Pfizer is working on the CRIX (Clinical Research Information eXchange) initiative to expand the caBIG vision from cancer to other therapeutic areas. caBIG is being built on open source, open access, open development, and federation principles. Sharing and integrating functional genomics and clinical trial data can improve cancer prevention, cancer treatment, and clinical research.

Clinical Research Information Exchange (CRIX). CRIX is a collaboration of representatives from the bio-pharmaceutical industry and academia to implement a common, secure standards-based electronic infrastructure to support the sharing of clinical research data for faster more efficient development of new drugs. The objective is to provide a shared utility infrastructure that facilitates and enables automated and paperless regulatory submission, where information is efficiently shared across the clinical research community and where security and intellectual property protection are guaranteed. Development of industry-wide standards will enhance the precision of acquiring biomarker information or samples, the methods of processing and analyzing signals, and the data transfer, archiving and management of such data. Establishing these standards will allow de-identified aggregate data to be used as a platform for development of more comprehensive definitions of disease by improving biochemical, genomic, and imaging measurements.

In addition to current data analysis, secondary data use should be allowed for 'legacy' clinical data for identification of new therapeutic opportunities. These legacy data can be analyzed with current genetic knowledge and lead to a better understanding of disease,

drug safety, and pharmacology, and to the validation of new types of biomarkers and analyses.

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

While all clinical research organizations need complex, consistently defined data, HIT needs vary widely across specific disciplines. For example, the needs of biosurveillance will be different than organizations seeking to measure quality. In spite of these differences in uses, the baseline data will come from a similar source, the electronic health record and personal health record. The better the validity of data in EHRs and PHRs, the easier and more reliable subsequent studies can be. Pfizer believes that to have long term, high quality data, frontline efforts must be made to educate clinicians starting in medical school as to appropriate data entry methods. An example of such an effort is PRIMIS+ in the UK, a group working closely with the Connecting for Health project of the National Health Service. PRIMIS+ employs over 400 facilitators who travel around the country to meet with general practitioners for purposes of training physicians to enter data in a consistent fashion.

In the US, the American Medical Informatics Association (AMIA) 10x10 program has a goal of training 10,000 clinicians to understand and properly utilize HIT by 2010. The AMIA 10x10 program seeks to train and educate clinicians, and other key strategic partners, to create a new generation of clinical informaticians to lead the transformation of the American health care system through the deployment and use of advanced clinical computing systems of care. Organizations in the UK and the US recognize that proper training is necessary to ensure complete and high-quality data and to ensure usage. As efforts like PRIMIS+ and AMIA 10x10 continue, the quality of the data produced would improve as would the return on the investment in both EHRs and facilitators.

Genomic research has markedly advanced in the last decade and has enormous potential for furthering personalized medicine and development of individualized patient-specific treatment plans, drug therapies and procedures. This type of research is largely dependent upon HIT relating to bio-marker capabilities and repositories and the ability to link genetic information to clinically derived phenotypes, environmental exposures, and differential outcomes in clinical trials. By aggregating clinical data, outcomes data, and genetic data, it becomes possible to identify and link exact biomarkers to specific diseases and link specific treatments to specific outcomes.

As the costs and time for clinical trials continue to grow, it becomes important to develop more efficient methods for conducting clinical research. Large clinical data repositories can be used to create more realistic pharmaco-statistical models and/or in developing bottom-up predictive models to determine drug safety and efficacy, or to test the feasibility of conducting a clinical trial before committing significant resources. An example is Immunetrics (www.immunetrics.com), a company that currently offers predictive models based on known biological pathways. With the appropriate genetic

information, more clinical research could be performed *in silico* as compared to the higher risk and costly *in vivo* methodology.

A current effort to develop clinical and genomic data repositories is the Genetic Association Information Network (GAIN), a public-private partnership of the Foundation for the National Institutes of Health, Inc. and the NIH with Pfizer and other corporate partners. This initiative is taking the next step in the search to understand the genetic factors influencing risk for complex diseases. In the first stage of this project, six whole genome association studies have been selected using a rigorous peer- and technical-review process. Samples from existing case-control and family studies of patients with common diseases will be analyzed to identify genetic pathways that make an individual more susceptible to these diseases. Information gained from these genomic studies will facilitate discovery of new molecular targets for prevention, diagnosis, and treatment. Further, the GAIN database, dbGaP, will be expanded to include many other NIH sponsored studies including the Framingham studies, setting a new innovative standard for data availability and access.

To encourage the advancement of analysis tools and the understanding of disease, GAIN data will be released as broadly and rapidly as possible, with equal opportunity for access for all potential users. To promote the responsible use of GAIN Project Datasets, investigators and their institutions seeking access to genotypic or phenotypic data will submit a Data Use Certification specifying their intended use of the data and acknowledgement of their agreement with GAIN policies and procedures. All investigators, including Contributing Study Investigators, GAIN Partners, and others, will access the GAIN Project Datasets through the same mechanism.

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

Pfizer strongly supports the efforts of the American Health Information Community (AHIC) to establish the National Health Information Network (NHIN) and the growing discussion around clinical research. As AHIC evaluates the demonstration projects currently underway, it is important that whatever model or models are adopted, that there is a means by which community wide data aggregation can occur for secondary analysis. Data standards, interoperability, integrity of data are all key elements which are critical to the success of achieving data integration and exchange between healthcare providers and researchers to support personalized health care.

We believe creation of a NHIN has the unique potential to fundamentally improve healthcare by transforming clinical practice and reducing healthcare disparities that exist today. Data collected through the NHIN could be used to help Pfizer and other organizations better understand the prevalence of disease, monitor the safety and usage of existing therapeutics, and to conduct clinical research in a more timely and efficient manner. At this time, however, Pfizer believes further direction is needed to ensure that the NHIN will have the ability to serve important public health and research purposes. Part of the promise of the NHIN is that healthcare data be aggregated and analyzed to

better understand the prevalence and development of disease and the outcomes associated with interventions. An essential part of this is appropriate access to data for clinical research purposes.

An example of systems under development that could facilitate large-scale data integration and exchange is the CRIX infrastructure that provides the framework for Janus which could serve as a clinical data repository of structured clinical data for the research community. Importantly, data should be in compliance with the Clinical Data Interchange Standards Consortium (CDISC) standards, as well as BRIDG to ensure interoperability between EHR systems and clinical data systems. As the exchange and aggregation of health data occurs, research organizations can identify valid biomarkers to deliver personalized health care for specific communities and/or populations.

VII. Feasibility and potential benefits for establishing linkages of institutional or organizational data resources with private and publicly available health databases

Pfizer is building a Clinical Data Warehouse developed and designed according to the CDISC/BRIDG and Janus principles and the model will be aligned with the Janus reference model. The Data Warehouse has been designed to enable linkage of records from regulated clinical trials and non-regulated health care records collection (e.g., data purchased from a vendor or directly captured from an EHR or local RHIO). Additionally, Pfizer is defining dimensional data marts to support speedy access and hypothesis generation across a vast collection of health data. The dimensional data model will be submitted to CDISC as an extension. Initially, the data will be accessed by a specific application that enables a case-by-case, patient-by-patient viewing or for hypothesis generation across an entire set of data. This application will be published in the CRIX environment for sharing among the research community.

CDISC/HL7/BRIDG, CRIX, semantic web HCLSIG, HCLSIGDSE and the FDA critical path initiative all have components that facilitate the standardization, semantic interoperability and streamlining of clinical data that will help integration of many forms of clinical and pre-clinical information across organizations. In addition, semantic technologies will help to encode meaning into the data (i.e., incorporation of contextual information) and re-use/sharing of knowledge gained from interpretations. Of particular interest to Pfizer is the Janus initiative, which will provide an open source standards-based clinical data repository capable of capturing the entire life cycle of clinical research data which will provide a collaborative environment for sharing amongst many partners. CRIX may be an especially important forum for development of the Janus model. Together with techniques such as dimensional data models and the proliferation of software that works with Janus (e.g., iReview, Arraytrack, Websdm), an important research and development system will be created.

This new healthcare information environment can facilitate the introduction of evidence-based medicine. For example, data collected in a regulated clinical trial context could be combined with other data sources which could greatly reduce the resource requirements for phase IV (post-marketing) trials. This could generate a more comprehensive

evidence-base for new drugs by integrating company repository data along with healthcare data and more effectively enable the conduct of clinical trials. As clinical research data is shared among academic research centers and bio-pharmaceutical companies, clinical trials could be run more efficiently as they leverage prior studies and analyses of data.

Challenges exist in finding the optimal business and governance models which will sustain the effort of creating shared resources. We note that open standards processes and open source software development methodologies appear to be strong trends which are promoting cooperation among stakeholders without unduly burdening any individual stakeholder.

VIII. Development of ontologies across different clinical data repositories that will facilitate the utility of the data for answering clinical research questions

There are many different HIT-related use cases, such as clinical decision support, clinical research, reporting on clinical benchmarks, and electronic prior authorization of drugs and procedures, that share a common need to ask questions of clinical data. While technical characteristics of quantitative biological data (including genomic data) may differ in terms of scale and representation (e.g., time, techniques, and location of collection parameters) from other types of clinical data, the need to query data across different repositories is shared by all use cases independent of data type. Additionally, those who author the question, those who seek the answer to the question, and those who directly query the data to answer the question often reside in entirely different systems. Therefore, rather than establishing genomics or clinical research as a specialized use case, there should be establishment of a single common, standardized computable query language as the lingua franca, or language of exchange, to answer clinical questions for all use cases, including clinical research.

One potential candidate for serving as the lingua franca for clinical queries is the ANSI-accredited HL7 Guideline Expression Language standard known as GELLO. Pfizer has been leading a multi-stakeholder effort to establish the framework and tools required for building standards-based, computable clinical queries that can be used to support the many use cases. These tools are being developed as Open Source Software to encourage widespread participation in GELLO's development and reduce barriers to adoption. In 2007, Pfizer will specifically apply our efforts to clinical research questions to determine the appropriateness and potential gaps of using GELLO for this purpose.

In the absence of any such common language, it can be time consuming⁶ and expensive to map specific fields. An example is seen in the pharmaceutical industry. A subset of SNOMED CT is currently being used to code sections of the US Package Insert label to provide an accurate but not necessarily complete representation of important adverse events related to a specific product, and MedDRA terminology is being used for reporting of specific adverse events related to a specific product to the FDA. These two systems of nomenclature do not directly map to each other which creates numerous challenges for the industry. In addition, the meaning of a specific term in one nomenclature is not

necessarily a synonym for a term in the other. In planning activities related to health care systems for moving towards personalized healthcare, it is extremely important that various terminologies in use in the pharmaceutical industry and in clinical practice either be mapped or an interface be developed which supports both nomenclatures and provides a common denominator (such as GELLO described above). Without this provision, there is a risk that entire systems and repositories of data will be generated that will not be easily accessed or linked due to the selected terminology and the method in which the nomenclature was implemented. Another risk is there will not be clear understanding of available information because of different meanings or definitions behind similar terms.

Whether GELLO or another standardized expression language emerges as the best candidate for a common means for stating questions about clinical data, Pfizer encourages the development of a common approach as this will provide the best possibility of being widely adopted by vendors who could then map their own proprietary or divergent means for maintaining clinical data to that common expression language.

IX. Models for linking clinical data repositories across disparate care providers

CDISC/HL7/Bridg, CRIX, semantic web HCLSIG, HCLSIGDSE and the FDA critical path initiative all have components that facilitate the standardization, semantic interoperability and streamlining of clinical data that will facilitate the integration of many forms of clinical and pre-clinical information across organizations. In addition, semantic technologies will help encode meaning into the data (i.e., incorporation of contextual information) and re-use/sharing of knowledge gained from interpretations. Of particular interest to the research community is the Janus initiative, mentioned above, which will provide an open source, standards-based clinical data repository capable of capturing the entire life cycle of clinical research data and providing a collaborative environment for sharing amongst many partners. Janus will contain all clinical trial data, including the data, protocol, and analysis plan and results to be shared for further analysis and research. The Janus initiative leverages the BRIDG model which is currently under development by CDISC, HL7, NCICB, and caBIG, and will be 21CFR11 compliant.

The Janus program is provided through the CRIX infrastructure, and will be one of many services to facilitate the sharing of non-competitive research data. CRIX is a private-public partnership between industry, academia, and government agencies with its own board of directors. The CRIX partnership seeks to create a collaborative environment for the advancement of clinical research. Together with techniques, such as dimensional data models and the proliferation of software that works with Janus (e.g., iReview, Arraytrack, Websdm), an important research and development system will be created with the goal of benefiting population health.

Another example in which the pharmaceutical industry is partnering with other research organizations is the NHIN Slipstream project. Multiple pharmaceutical companies have partnered with other research organizations to promote clinical research use cases into the NHIN discussions. The NHIN Slipstream project has identified two high level use cases on clinical trial execution and post-marketing surveillance. Under the clinical trial

execution, the initiative has further identified and documented use cases for 'connecting patients to trials' and 'safety & surveillance'. Representatives from the NHIN Slipstream project testified before the National Committee on Vital Health Statistics (NCVHS) in July 2006 on the need for clinical research to be considered as the US develops a Nationwide Health Information Network.

Models of collaboration, such as CRIX, JANUS, and NHIN Slipstream, demonstrate the feasibility of establishing partnering organizations with the joint purpose of sharing clinical information between disparate sources while supporting healthy competition and innovation. As critical as standards and technology are for the sharing of clinical information, it is equally important that there be a formal governance model to oversee the organization and the use of the data.

X. Examples of the use of disease registries to track specific diseases and response to drug therapies across different subpopulations

In 2001, Pfizer partnered with the state of Florida to establish a state-wide program designed to improve the health of chronically ill Medicaid beneficiaries while reducing state Medicaid costs. The program targets Medicaid beneficiaries in four high cost disease states; asthma, diabetes, heart failure, and hypertension. Community-based multidisciplinary care teams of registered nurses, health educators, and medical directors educate participants about their disease to help improve beneficiaries' ability to adopt behaviors that can stabilize and improve their condition. The program reinforces behavior and lifestyle changes through individualized care plans and the provision of home health monitoring devices. As of July 2006 the Florida: A Healthy State Program has served over 180,000 Medicaid beneficiaries.

Clinical outcomes and utilization data from the program showed that better control of chronic conditions led to more efficient utilization of healthcare resources, such as emergency department visits and hospital admissions:

- ◆ People with heart failure reduced their ED visits by 18 percent and their costly hospitalizations by 22 percent.
- ◆ Asthmatics reduced their ED visits by 12 percent and hospitalizations by 23 percent.
- ◆ Participants with high blood pressure reduced ED visits by 11 percent and reduced hospitalizations by 31 percent.
- ◆ Overall, ED utilization was reduced by 12 percent and hospitalizations fell by 28 percent.

Financial analysis reported by Medical Scientists Inc., an independent organization, showed that in year three alone, Florida: A Healthy State reduced Florida's healthcare costs by \$30.7 million. Over the span of the first three years the program generated \$70 million in healthcare cost savings.

XI. Strategies for accumulating patient data necessary for research that may not be available through EHRs

The definition of patient data is expanding beyond the information that has been traditionally captured in an Electronic Health Record (EHR). These additional data include:

- ◆ Information from vital signs monitoring devices kept in the patient's home or worn by the patient.
- ◆ Information from passive sensors in the home which can provide surrogate markers of a patient's health.
- ◆ Date/time information from medication adherence devices.
- ◆ Audio/video information from AV capture devices, which can provide additional perspective on a patient's well-being.
- ◆ Information from fitness devices, such as treadmills and pedometers.
- ◆ Information captured from gaming devices designed for physical or mental assessment/rehabilitation.
- ◆ Information on a patient's daily nutritional intake.
- ◆ Genomic information on the patient, and the patient's family members and ancestors.

Strategies for accumulating this type of information involve more than just acquiring devices capable of capturing the data. Traditional EHRs do not have the ability to store most of the above information, nor do they have standards for the definitions and attributes of these data. The EHR, as well as the relatively new Personal Health Record (PHR), must have the capacity to evolve into a comprehensive Lifespan Planning Record. This record would be capable of storing, organizing, and making available for analysis all the patient data types mentioned above.

In order to create this type of record, device manufacturers will need to converge on a set of standards supporting the transfer of information from devices to the Lifespan Planning Record. This will also require that standards developed in the patient data arena include standards and guidelines for this expanded set of patient data. Databases containing patient data will need the capacity to evolve to accommodate this new information. Similarly, traditional analytic tools will need to evolve as will new algorithms which can account for relationships between traditional and novel types of patient information.

The Continua Healthcare Alliance, formed in 2006, has as its goal to accelerate the penetration of home healthcare technology, by selecting and promoting standards that will foster interoperability among home healthcare components. Continua plans to publish Version 1 of the selected standards in 2007 and anticipates that devices receiving Continua certification will begin appearing in 2008. Pfizer is a member of Continua and has provided thought leadership in the interoperability of EHRs and medical devices for chronic care monitoring and elder care monitoring.

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

Standards that govern how research is conducted must be developed and implemented to ensure that conclusions reached are widely accepted. Similarly, there is a need for a national census concerning performance and accountability measures which will be applied to all clinical researchers and healthcare providers. Metrics should focus on healthcare access, delivery and quality, and must evolve to include healthcare outcomes, reductions in total cost of care, changes in utilization and practice patterns, and changes in key clinical indicators. It is essential that these metrics are adequately measured and benchmarked.

Data created as a by-product from the use of EHR systems is growing in its availability. With the advent of Certification Commission for Health Information Technology (CCHIT) certification, these data will allow for a greater degree of interoperability and will further support a wide array of applications in the research space. Certification will help accelerate the adoption of HIT by creating efficient, standardized, and valid data collection and storage systems.

One major application for EHRs and their related data is the use of specific computerized algorithms to constantly scan the data to find patients who fit criteria for inclusion in clinical trials. At present, a patient diagnosed with a specific type of cancer seeking to participate in a clinical trial has limited means to identify and receive acceptance in a trial. Clinicians encounter similar obstacles in identifying open clinical trials, determining whether a patient is an appropriate candidate for a trial, and subsequently connecting the patient to the trial. EHR systems and their data can facilitate identification of appropriate patients for inclusion into clinical trials to the advantage of the patient and their clinician. The time to recruit a patient into a trial can be reduced dramatically.

Another use of these data is to evaluate therapeutic efficacy. Researchers, empowered by the appropriate tools and access, will have the ability to analyze and correlate population level data to identify trends in medication use and patient outcomes. These analyses have the potential to serve as a powerful tool for measuring both appropriate and inappropriate uses of drugs, procedures and other therapies. These analyses will be able to spur Phase IV clinical trials while compressing the time required for performing such trials. Clinical researchers will have a greatly enhanced ability to detect new trends, safety issues, and possible new indications when they can access anonymized or de-identified data for this purpose. Epidemiologists will be able to use these data to detect safety issues much sooner than they can in the current day environment. The ability to detect adverse events in a structured manner will allow for earlier detection of these events, leading to safer outcomes for patients.

Pfizer plans to conduct research in 2007 on the potential for EHRs to facilitate linking patients to clinical trials. In this project, we will assess the requirements for a clinical trial "enabled" EHR as well as the requirements for clinical research units conducting Phase I trials to link to EHRs.

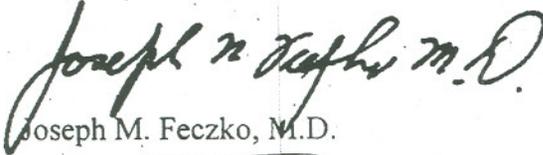
XIII. Conclusion

As a global organization that is subject to laws and regulations around the world, Pfizer strongly encourages the Secretary and members of the health information community to maintain a global view as they consider issues related to secondary data access and usage, and messaging and terminology standards, especially those related to genomic data. United States healthcare stakeholders have an opportunity to join other regions around the world in establishing common, global standards for clinical data sharing and regulatory data submission *before* their use becomes widespread and methodologies diverge.

Pfizer encourages the development of methods for improving the bi-directional flow of information between and among healthcare providers and clinical researchers. The overarching goal for all stakeholders interested in personalized healthcare should be to bring clinical research to the point of care and the point of care to clinical research.

Pfizer is grateful for the opportunity to participate in the dialogue to accelerate adoption of HIT and personalized medicine and we look forward to collaborating with the Administration on the various issues raised in this request. I would welcome an opportunity to meet with you and others at HHS to discuss these issues in further detail.

Sincerely,



Joseph M. Feczko, M.D.

JMF/mf