

1. What strategies and approaches could HHS implement to accelerate the development and application of new medical technologies?

The need to accelerate the development and application of new medical technologies is well-known, and grows increasingly urgent. There is no magic bullet to address this need, and solutions must address the following criteria:

More appealing business models

Historically, the life science research industries have enjoyed tremendous financial success. One example of a business model that drives change is the Orphan Drug Act. Prior to the Orphan Drug Act, research companies had little financial incentive to consider developing new therapies that would benefit small patient populations. The cost of research and development was simply too great to offset any potential revenue stream from a small patient population. The Orphan Drug Act created business incentives that let commercial research companies target small patient populations with new therapies that might not otherwise prove financially viable.

While it would be difficult to financially incent companies with therapies already on the market, new therapies under development would benefit from the equivalent of the Orphan Drug Act – perhaps identified as the Personalized Drug Act. The overall message associated with this approach would be: Develop drugs for targeted patient populations and exclusivity would be provided for not only the new therapy, but also the diagnostic. Government and private reimbursements would cover the cost of the diagnostic, but would only cover the cost of the new therapy if it were confirmed by the diagnostic.

Holistic research

Speed, quantity and quality of results are necessary to address the pressing questions in medical research. Quicker application of new technologies to safety evaluation will be accomplished by defining acceptable predictive toxicological approaches and establishing guidelines for both analytical bases and criteria used in decision-making process. Work being done in the environmental safety area(EPA's Computational Toxicology program) creates valuable synergies speeding both creation of safer drugs and promoting environmental safety. Efficacy assessment will clearly benefit from the application of pharmacogenetics and guidelines are imperative. Understanding the molecular bases for dose response is an essential element for patient stratification, maximizing risk management efforts

Speeding up disease research now means taking a more holistic approach. HHS needs to promote data standards and technological resources (databases, portals, etc) that establish connectivity between genetic, metabonomic, and clinical information.

Speeding up phases I- III

Key areas for improvement include:

The overall length of the clinical trial process. Clinical research programs take years to complete. Although great strides have been made with regard to publicizing clinical trials, even websites such as www.clinicaltrials.gov fall short of actively directing patients to clinical trials. Instead, metadata-driven GUI tools should be provided to let interested parties identify relevant clinical trials by answering 'generic' inclusion/exclusion forms that are driven from the available data base information. With more patients participating in clinical trials, the primary problem of patient recruitment delays could be successfully addressed in many cases.

The design of the clinical trial: Clinical trial design should be modified wherever possible to support the concept of sequential analysis. Sequential analysis techniques, however, support the notion of frequent safety and efficacy assessments without compromising the trial's integrity. By applying sequential analysis, trial outcomes may be completed significantly earlier than the more

traditional timeline, especially in those cases where there is either clear effectiveness, or ineffectiveness. While sequential analysis and adaptive design provide supporting value when applied to non-targeted patient populations, linking these techniques to targeted therapies based on population profiles should further reduce the number of patients and the overall time with bringing new drugs through development.

2. How can HHS help its agencies (e.g., NIH (and its grantees), FDA, CDC, and CMS) to work together more effectively to eliminate obstacles to development of medical technologies?

HHS can help its agencies work together more effectively by addressing several key areas: technology, standards, interoperability, legislation/incentives and privacy management.

Technology: From a technology point of view, HHS activities – both within the government as well as throughout the affiliated commercial industries – are largely paper-based, or relying on older technology. Even after conversion to electronic form, data continues to exist in silos. The adoption of newer technology, which may include electronic data capture and management, electronic medical records, web-based systems, data warehousing and integration would all support more effective collaboration within (and external to) the HHS community.

Standards: Technology, by itself, will provide limited value to the HHS community. The implementation of standards, however, with new technology that leverages them, has the potential to create great synergies throughout HHS. A variety of research standards are in use and development – including CDISC, HL7, RCRIM and others.

The use of these standards will facilitate the transfer and use of research data throughout the HHS community. RCRIM (Regulated Clinical Research Information Management), and in particular their Protocol Representation standard, presents unique opportunities to streamline and manage the clinical research process. By building protocols through a standard representation, data capture, management and analysis activities can be substantially automated, and the research study information can be aggregated across therapeutic areas, government agencies and research programs. This aggregated warehouse provides tremendous opportunities as a single version of the truth for key research activities, including:

- Research protocol planning: Better trial planning will produce a more efficient clinical trial process in the areas of patient recruitment, quality of data, and value-documenting endpoints.
- Effectiveness assessments across research compounds: There is little incentive for commercial companies to invest in assessing their products against their competitors', unless there is the likelihood of clear marketing (and revenue) advantages. An aggregated database of clinical research results will let consumers, disease advocacy groups and independent agencies summarize the overall costs/benefits associated with related therapies. Ultimately, reimbursement agencies will have access to the same body of information in order to drive their business practices.
- Safety issues can be identified earlier in the process – especially within families of drugs that are brought to market. The larger patient populations available provide the means to better identify emerging safety concerns, whether they're related to concomitant medication use, patient profiles, or external factors. While these activities do take place today, the lack of available standards reduces their effectiveness, and delays the identification of safety trends.

Interoperability: Interoperability is a byproduct of adopting standards and implementing technology that supports them. With standardized data, ideally being managed through a single, centralized, location, government agencies will be able to more easily, and more swiftly, collaborate around clinical concerns and take appropriate action. Universal adoption of the same technology is not required, as long as the technology supports the defined standards. Instead,

researchers can identify (or build if necessary) the applications that best address their needs, and can focus on their specific system requirements.

3. How can the HHS Scientific and regulatory agencies work more effectively with CMS to eliminate obstacles to development?

The ability for health care providers to share patient information with life sciences companies (pharmaceutical and medical device manufacturers) would greatly increase the ability of all these organizations to increase levels of quality, safety and cost effectiveness. For this to be possible there must be accepted/mandated clinical data formats to allow collection of data from provider point-of-care clinical information systems and aggregate it into longitudinal, codified, comparable patient-centric records. With this data source, healthcare providers can extract valuable information related to clinical quality, service and performance. Additionally, life sciences companies, public health groups, government agencies and other participants in healthcare can extract valuable information from the data to support drug and medical device development efforts in a more timely and cost effective manner. This has the potential impact of reducing US healthcare mortality and healthcare costs in general.

Therefore HHS should actively promote:

- Common data standards for Electronic Health Records and all Federal and State mandated regulatory reporting.
- Consolidation and sharing of deidentified hospital clinical data for analysis to support outcomes improvement

4. What forums should HHS use to survey constituents about obstacles to innovation(e.g public meetings, contract research, focus groups)

While all of the options listed are useful forums, the challenge with many of these is that there is no centralized location to find these venues and they often require travel. With the plethora of organizations that leverage the internet, to truly encourage organizations and people to submit input on obstacles to innovation online options (such as webcasts, online town meetings, bulletin boards) should be leveraged more often. This removes the travel requirements and opens the forums to all interested participants. This coupled with a more centralized location for notices regarding these events, instead of having them spread throughout different locations on the HHS internet sites, will also promote interaction.

5. How can the portability of information between HHS agencies be optimized?

This has been hinted at in several of our responses and really comes down to standardization of data formats and creation of connections or centralized resources linked by common initiatives or topics/goals. As mentioned in our answer to question 1&2, the acceptance and promotion of SAS data sets and CDISC has very much simplified data sharing with the FDA and across organizations within the industry. The continuum from bench to bedside slices through many different independent realms- from scientific research through clinical development to healthcare delivery. The common element here is public health and safety, but the technologies, terminology and processes differ. Data standards (CDISC, HL7), common repositories (data registries), and standardized terminology (SNOMED, MedRA) all contribute to portability- especially in this electronic age. These in turn can support the EMR and NHI projects.

6. Which HHS policies and programs effectively spur innovation? Which policies and programs at NIH (and its grantees), CMS, FDA, and CDC should be expanded to help spur innovation? Do any policies and programs pose obstacles to innovation?"

Although there have been many initiatives that are being funded by different agencies and groups within HHS. The challenges in many of the initiatives and programs are that many of these programs have overlapping goals and/or requirements but lack requirements for connectivity

amongst programs with common goals. Connectivity between the different aspects of the scientific community is paramount to fulfilling the healthcare improvements for the next century. More direct connections driven by an unbiased champion, enabling innovations to quickly become incorporated into mainstream scientific research, clinical development, and medical practice processes.

Certainly programs like caBIG really spur innovation. caBIG is groundbreaking because it establishes a central system that is designed for groups to tap into- both internal and external- plus it starts setting up standards for ontologies and dictionaries. A prime example where the government has taken a lead as a key supporter/participant in these areas and it is reaping success, organizations are adopting caBIG terminology and standards- most commercial organizations want standardization, they are too biased towards their own technology to lead these types of movements. NECTAR, the national electronic clinical trials and research system highlighted in the NIH Roadmap, is another project that could serve as a catalyst for change in clinical data management.

However there are many smaller scope projects that require a monitor or centralized process to provide guidance and consistency on standards used and supported and other similar projects that could be leveraged. This will be especially important for the innumerable biodefense projects being created by NIAID, CDC, and other agencies. Examples of RFPs & projects with overlapping goals but minimal awareness of each other are..

- BISC- NIAID- bioinformatics system will incorporate genomic and proteomic information for study immunological diseases
- MIDAS- NIGMS- infectious disease modeling system- seen as key aspect biodefense activities, will incorporate genetic, geographic, and epidemiological information
- Biodefense(DMID-04-34)- NIAID- centralized informatics system for bioterror agents, incorporating genomics and proteomics data into microbial databases
- FoodNet- CDC- incorporating molecular information into food safety monitoring system
- PHIN- CDC- monitoring public health information for outbreaks and epidemics, building early warning system(Biowatch, BioSense, NEDSS)
- JANUS- FDA- electronic submissions clinical data warehouse

Programs that we have seen promote innovation include features that connect traditional information with cutting edge information, to allow for investigative activities and perusals while delivering monitoring data to track current status. These provide the bases for more sophisticated screening of data and establishment of early warning systems. Creating systems with ability to scale with demand that utilize industry standards, and also bring multiple disciplines together promote delivery of fresh approaches. Moving away from an agency specific approach to more of a common project/ initiative approach will drive innovation as well, along with minimizing technological hurdles bringing information together. This can be as simple as more weblinks across similar projects or as broad as common webpage/portal for overlapping projects.

7. "What role should be played by nongovernmental partners in assisting the Federal Government in this process?"

SAS has been serving customers in the life sciences, and the federal government, for more than 25 years. We have an extremely successful business in many other industries and a significant global presence. Our technologies are well-utilized across the industry and SAS data sets have been the recommended and accepted data format for clinical data submission. SAS's long history of success is due consistent delivery of quality technologies. As a leading technology organization with a strong legacy in life sciences we can be an objective industry advocate and guide for HHS in both monitoring, responding, and anticipating the public health trends and needs of companies, organizations, other governmental agencies, and other nations. This information

can be provided in both direct responses through focus groups, panels, working groups, and advisory boards as well as through indirect means as through RFPs, requests for comments, and interactions with industry groups or other collaborative projects.

As a non-governmental partner we can:

- Provide ideas on how the newest industry technologies can be applied to solve their problems- perhaps in ways they hadn't thought of.
- Provide guidance in the development and delivery of multi-agency initiatives. Often these initiatives are driven by agency representatives but have minimal involvement from external groups limiting both potential and impact because perspective is limited.
- Participate in working groups on reviewing proposals for innovation new ideas, new standards, processes, or policies presented or proposed by HHS using a more "business case" based framework. Adding a more formalized process with an economic component as well as a scientific component provides many opportunities for commercial/private collaboration. For paradigm-shifting programs like NHII and NECTAR, there is a need to marry commercial and private/governmental interests in order for these initiatives to gain acceptance and traction. This will be a key focus moving forward, HHS cannot achieve these goals without significant buy-in and support from the commercial and international sector.
- Become participants/advisors in workshops and/or working groups with industry and trade group representatives, bringing in not only our perspectives but those of our customers as well.
- Provide guidance on building data and terminology standards and provide real-world perspective on impact of standards as a neutral technological party and leading vendor. However, for universal acceptance, the federal government is the body that must take an objective view for driving towards standards and setting the rules. As the HHS is looking to promote standards, we can provide our experiences in what did/did not work in past standards initiatives and provide guidance on how to promote and facilitate wide-spread adoption and minimize uptake issues.
- Utilize our multiple touch-points within the federal government to bring cross-agency advice- what we have seen that is similar in other agencies that could be leveraged to accomplish goals, what has worked well and what has not.
- Continue to identify, support, and encourage opportunities for collaborative projects such as CRADAS
- Bring best-practices from our own experiences, not only within life sciences but from different industries (such as high tech, telco, manufacturing, finance), from outside of US, and we can bring in perspective for both scientific and business sides of the organization.