



PARTNERSHIP TO ADVANCE
CLINICAL ELECTRONIC RESEARCH

MAY 2011

*Transforming and
Improving Clinical Research
Capabilities in New York
State to Benefit Patients*

PHASE 1 WHITE PAPER
FEASIBILITY ASSESSMENT AND PHASE 2 PLAN

3	I. EXECUTIVE SUMMARY
6	II. PACeR PHASE 1 PARTICIPANTS, OBJECTIVES, AND GUIDING PRINCIPLES
12	III. PACeR PHASE 1 FINDINGS AND CONCLUSIONS
	<i>A. Data Availability</i>
	<i>B. Legal and Regulatory Constraints</i>
	<i>C. Economic Sustainability Considerations</i>
28	IV. PACeR RECOMMENDATIONS AND PHASE 2 PLAN
30	APPENDIX A: <i>Process for Capturing Additional Clinical Data</i>
33	APPENDIX B: <i>Business Model Work Group Supporting Analysis</i>
37	PACeR KEY PARTICIPANTS

I. EXECUTIVE SUMMARY

The goal of the Partnership to Advance Clinical electronic Research (PACeR) is to increase the speed, quality, and efficacy of clinical studies, helping to provide patients with quicker access to new treatments and life-saving medicines.

PACeR aims to achieve this goal by designing and launching an economically sustainable, electronic clinical research data network in New York State to more efficiently identify potential candidates for clinical research trials and manage their care.

In creating this data network, PACeR endeavors to:

- » support improvement in patient care and the research missions of participating institutions;
- » improve the operational efficiency and scientific integrity of clinical research;
- » advance the objectives of medical institutions regarding the primary and secondary use of clinical data; and
- » serve as a viable, practical model for other states, regions, and the nation, that recommends solutions to relevant technical, legal, regulatory, economic, and operational issues.

PACeR stands apart from other attempts to improve the clinical research process because of its inclusiveness and responsiveness to the needs of multiple stakeholders. The Healthcare Association of New York State (HANYS) serves as a neutral partner and coordinator, bringing together multiple medical centers, health systems, community hospitals, patient representatives, pharmaceutical companies, health information technology companies, and others to engage in a multi-year collaborative. The guiding principle behind this endeavor is the benefit to patients, and ensuring robust patient privacy and consent protections is paramount.

Key highlights in PACeR's development:

- » Phase 1 of PACeR identified barriers to the secondary use of electronic health data for evidence-based research, and developed recommendations to address those barriers.
- » Phase 2 of PACeR will consist of demonstration projects to address these barriers and develop an infrastructure for an efficient clinical research data network in New York State.
- » As PACeR embarks on Phase 2, additional participants are welcome.

PACeR's objectives are aligned with those of other important public and private sector health care initiatives. For example, investments and programs developed by the Health Information Technology for Economic and Clinical Health (HITECH) Act as part of the American Recovery and Reinvestment Act (ARRA), Food and Drug Administration (FDA), and state and regional organizations focus on collecting high-quality, standardized electronic health data and rigorous research methodologies.¹

In developing an institutional infrastructure supporting the delivery of high-quality, evidence-based research, PACeR envisions a "federated" database approach where participating institutions continue to own and control access to their data – PACeR will enable database queries across the federation to conduct specific analyses.

In addition, PACeR offers a comprehensive, long-term roadmap for improving clinical data and facilitating relationships among multiple participants for the full range of scientific evidence-based research, such as outcomes, epidemiology, comparative effectiveness, and safety surveillance research, within and beyond the borders of New York State to the rest of the country.

PACeR's Phase 1 findings provide, in addition to a short-term way forward, a long-term perspective on how to address the current challenges and improvement opportunities associated with the design of existing electronic medical records (EMRs) and the confidentiality and ownership of patient health data. The chart below illustrates the hurdles identified by PACeR Phase 1 and proposed solutions that will be tested in subsequent phases. This white paper describes each of these barriers and solutions in detail.

¹ <http://www.ahima.org/advocacy/arraHITECH.aspx>
<http://www.fda.gov/Safety/FDAsSentinelInitiative/ucm2007250.htm>
<http://www.healthcareitnews.com/news/new-york-rhio-deploys-new-data-software-platform>

ADDRESSING BARRIERS TO SECONDARY USE OF DATA FOR CLINICAL RESEARCH

<i>Barriers Identified</i>	<i>Solutions</i>
<p>Insufficient Clinical Data. Existing EMR systems are unable to capture all of the patient-specific clinical data required to conduct high-quality, evidence-based research.</p>	<p>PACeR has a short-term approach to capturing the additional clinical data needed to support scientific, evidence-based clinical research, over and above data currently available in EMRs and other electronic repositories.</p>
<p>Inconsistent Systems. There is a lack of standard terminology and nomenclature within installed clinical software applications across providers of health care.</p>	<p>PACeR has a plan to develop a standard method to map institutional data to a common terminology across multiple hospitals and medical centers in New York State.</p>
<p>Legal, Regulatory, and Structural Constraints. These constraints on the secondary use of patient health data, and concerns about patient privacy and confidentiality must be reconciled if patient data are to be used for research purposes.</p>	<p>The PACeR clinical data network will be designed to address technical, legal, regulatory, and economic challenges inherent in the use of patient-specific data, and to protect patient privacy.</p>
<p>Economic Sustainability. Financial considerations must be addressed to foster the routine collection of the full set of electronic health data required for high-quality, evidence-based research.</p>	<p>PACeR offers an economically viable, sustainable approach that captures the value of accessing a high quantity of multi-institution data analyses through a single point of use for researchers, and benefits all participants in the use of clinical data for evidence-based research. A “ballpark” top-down analysis suggests that PACeR’s revenue potential for protocol modeling alone is more than \$50 million annually.</p>

PACeR’s Phase 1 results confirm that significant benefits are achievable for all health care stakeholders, including:

- » **Patients:** PACeR will improve identification and matching of patients for clinical trials and accelerate the process of getting innovative medicines to the public.
- » **Academic Medical Centers, Community Hospitals, Principal Investigators, and Other Scientists:** PACeR identified opportunities to improve the underlying data and processes for conducting medical research and improving patient care.
- » **The Research Community:** Timely analysis of large amounts of high-quality clinical care data will streamline the clinical trial protocol development process.
- » **Health Information Technology Companies:** PACeR will provide input to functional specifications for health IT systems to capture and organize the data necessary to meet the needs of scientific, evidence-based research, observational research, and cost effectiveness analysis.
- » **Regulators:** Access to improved data and analysis will support safety surveillance initiatives and causal analysis of adverse events.
- » **Public/Private Initiatives Such as Regional Health Information Organizations (RHIOs):** PACeR offers a mechanism for clinical data nomenclature standardization and interoperability across hospitals and physician networks.

- » **New York State:** PACeR will enhance the state’s position as a center for medical research and home to some of the world’s most prominent academic medical centers, and attract a greater share of strategic investment in clinical research.

Phase 1 was designed to confirm the feasibility of developing a sophisticated clinical data network across New York State that can be used for evidence-based research, with the long-term aim of extending the network across the country. Component pieces to develop this system exist within each of the participating medical networks, but much work needs to be done to build a statewide, standardized, consistent, and complete platform. That is PACeR’s future work plan and goal.

PACeR Phase 2 will demonstrate the practical feasibility of the secondary use of electronic clinical data, such as clinical trial protocol modeling and patient recruitment, through a series of demonstration projects in 2011 involving participating community hospitals, academic medical centers, technology companies, and the pharmaceutical industry. Specific PACeR Phase 1 recommendations and next steps for Phase 2 implementation pending funding include:

- » **New York State Center for Support of Clinical Terminology and Ontology Mapping.** This entity would standardize data nomenclature.

- » **Market Making.** This capability would streamline and deliver protocol modeling and patient selection services using data from multiple institutions, thereby enabling one-stop access to a large quantity of high-quality clinical data analyses.
- » **PACeR Privacy Board.** Further explore hospital and medical center interest in this concept to create a better, faster, and more flexible approach to using de-identified data for trial modeling purposes.
- » **Capture More Data.** Develop and implement clinical software solutions and related processes and compensation approaches that “wrap around” currently deployed EMR systems to capture additional clinical data, using standardized clinical nomenclature. These solutions will demonstrate the economic value of investment in clinical software systems for scientific quality and outcomes research.
- » **Empower Patients.** Create technology, methods, policies, and procedures that will enable individual patients to determine when and how their data are used for research through improved education and informed consent.
- » **Use Data to Advance Health Care Priorities.** Ensure that approaches developed not only improve the efficiency of clinical trial research, but also enable improvements in other secondary data uses and types of research that are top priorities for PACeR participants, such as disease outcomes, epidemiology, comparative effectiveness, and safety surveillance research.

PACeR draws strength from the broad diversity of its participants. Through the cooperation and collaboration of the providers of clinical data such as clinicians, hospitals, and patients; the users of data such as principal investigators and pharmaceutical companies; the technical enablers of data such as health information technology (HIT) companies; and others, PACeR is developing comprehensive solutions that benefit multiple stakeholders. Their combined subject matter expertise and multitude of perspectives in this distinctive initiative have ensured that PACeR remains ambitious, yet realistic as it progresses, and the participation of patient advocates ensures that the benefit to patients is the top priority.

PACeR strongly encourages participation of additional members in Phase 2. We welcome the perspectives of new members such as physician professional societies, community hospitals, device manufacturers, EMR vendors, disease societies, and others. The more comprehensive PACeR’s membership, the more sustainable its approach becomes.

II. PACeR PHASE 1 PARTICIPANTS, OBJECTIVES, AND GUIDING PRINCIPLES

PACeR Involves a Broad Range of Participants with an Interest in the Secondary Use of Clinical Data

PACeR was created under the auspices of the Healthcare Association of New York State (HANYs) and brought together global pharmaceutical companies, patient representatives, clinical research organizations, technology companies, hospital and ambulatory care networks, physicians, and patients. Their joint purpose is to develop a practical plan for improving the quality and efficiency of evidence-based clinical research by identifying and closing gaps in the ability to use EMR systems. PACeR participants are listed in the chart below.

PACeR is governed by a Project Leadership Committee drawn from participants, and is sponsored by HANYs. Project management has been provided by Booz & Company and Quintiles Consulting.

PACeR Has Practical Near-Term Objectives Informed by a Long-Term Vision

The PACeR collaboration was convened to:

- » support improvement in patient care and the research missions of participating institutions;
- » improve the operational efficiency and scientific integrity of clinical research;
- » establish a large-scale integrated electronic health capability across multiple institutions and organizations for clinical research purposes;
- » support the objectives of medical institutions regarding the primary and secondary use of clinical data;
- » operate in a way that is economically sustainable in the near and long term; and
- » serve as a viable, practical model for other states, regions, and the nation, that recommends solutions to relevant technical, legal, regulatory, economic, and operational issues.

PACeR's objectives are designed to be accomplished through a multi-year, iterative process of working with hospitals, physicians, and patients who generate clinical data and

PACeR IS A DIVERSE COLLABORATION OF MEDICAL CENTERS, INDUSTRY, PATIENT GROUPS, & ADVISORS

Sponsor/ Patient Advocacy	Academic Medical Centers		CRO*, Pharmaceutical, and Health Information Technology Companies	Advisors/Observers
HANYs	Albany Medical Center	Roswell Park Cancer Institute	Bayer	U.S. Food and Drug Administration
	Bassett Medical Center	Stony Brook University Medical Center	Johnson & Johnson	New York State Department of Health (DOH)
The Hastings Center	Continuum Health Partners (St. Luke's-Roosevelt, Beth Israel)	SUNY Downstate Medical Center	Merck	New York eHealth Collaborative (NYeC)
		SUNY Upstate University Hospital	Oracle	
Legal Action Center	New York Hospital Queens	University of Rochester Medical Center	Pfizer	CDISC and HL7
	North Shore-Long Island Jewish Health System	Weill Cornell Medical College	Quintiles	New York State Foundation for Science, Technology, and Innovation (NYSTAR)
	NYU Langone Medical Center	Westchester Medical Center	Roche	
Project Management	Booz & Company and Quintiles Consulting			

*CRO = clinical research organization

investigators who use high-quality clinical data for evidence-based research and improved care quality and outcomes.

PACeR's Phase 1 work focused on developing a practical, economically sustainable approach to strengthen clinical research capabilities in the near term. It targeted improvement in capturing the clinical data necessary for evidence-based medical research and testing the safety and efficacy of products in development by pharmaceutical and device manufacturers, as summarized in the following table.

PACeR PHASE 1 OBJECTIVES

- Identify gaps between current clinical research capabilities and those required to meet project goals for leveraging the secondary use of electronic clinical care data in:
 - clinical trial modeling;
 - identification of eligible patients for research;
 - patient recruitment and enrollment in evidence-based studies; and
 - clinical research standardized data capture.
- Identify legal and regulatory issues and implications for economic viability, data, and systems.
- Develop a practical, implementable plan for narrowing the gaps between current and needed capabilities to perform clinical research, accomplished by addressing the specific needs of all stakeholders – hospitals, physicians, patients, industry, and government.

PACeR focused initially on methods to improve the operational efficiency and scientific integrity of clinical trial research.

The cost, complexity, and time that it takes to bring a drug successfully to market has increased enormously over the course of the last 20 years and now exceeds eight years and \$1 billion. Failure rates are exceedingly high. The Tufts Center for the Study of Drug Development estimates that for every 10 potential drugs that enter clinical testing, only one is approved for marketing and sale.² In the long term, these failure rates can be reduced by using EMR systems designed for both patient care and clinical research.

Today, most EMR systems only capture summary care information for basic medical charting and billing purposes. Access to robust clinical data with detailed information

about disease states, diagnostic and therapeutic regimen, illness history, and patient population will improve the drug development process. It will also provide a means to perform post-market safety monitoring of drugs and devices, thereby improving quality and outcomes of medical care, while reducing costs.

Improved electronic clinical care data will:

- » enable better design, higher quality, and more rapid completion of clinical research studies at reduced cost;
- » enable researchers to refine clinical trial eligibility criteria to more accurately match existing patient populations; and
- » help identify potential patients for clinical studies and speed enrollment for participation in studies. This will ensure that pharmaceutical companies have a better, faster, and more predictable way to invest in the development of drugs.

Information and analysis based on interchangeable data from many clinical sites will also stimulate investment in research and development. A partnership among clinical sites that provides such information would create economic as well as clinical value for patients, hospitals, physicians, and government.

Improved efficiencies and revenue from clinical research for medical institutions and reduced costs of conducting clinical research for pharmaceutical and medical products companies encourage all stakeholders to invest in and develop clinical information systems that are capable of multiple uses, including patient care, clinical research, and outcomes research. Improved clinical data capture methods that expand the amount of information available for clinical research will benefit the health care system overall by creating a way to scientifically evaluate treatment options that yield the highest quality and best outcome at lowest cost for each patient.

PACeR will also serve the research mission of participating academic medical centers, as improved data will make them more competitive for grants and research projects sponsored by the National Institutes of Health (NIH) and industry, thereby attracting top clinicians involved in academic research to their institutions.

Most importantly, implementation will help patients by making innovative therapies and medical devices available more quickly

² DiMasi JA. "The price of innovation: new estimates of drug development costs." *Journal of Health Economics* 22 (2003): 151-185.

and cost-effectively, with greater safety.

The availability of more robust clinical data can also advance outcomes research, enabling institutions to meet their quality objectives. Complete, detailed clinical data, captured in a methodical and longitudinal manner, can augment research on the outcomes of health care practices.

This is a critical capability, given that the economic viability of institutions increasingly depends on health outcomes. The Centers for Medicare and Medicaid Services' (CMS) emphasis on value-based purchasing, which links payment with quality of care measures, indicates the importance of capturing and managing robust clinical data for public reporting programs and tracking outcomes improvement.³ Since CMS' core measures overlap with a subset of clinical trial protocol eligibility criteria in equivalent therapeutic areas, increasing the availability of clinical data can serve multiple objectives within an institution.⁴

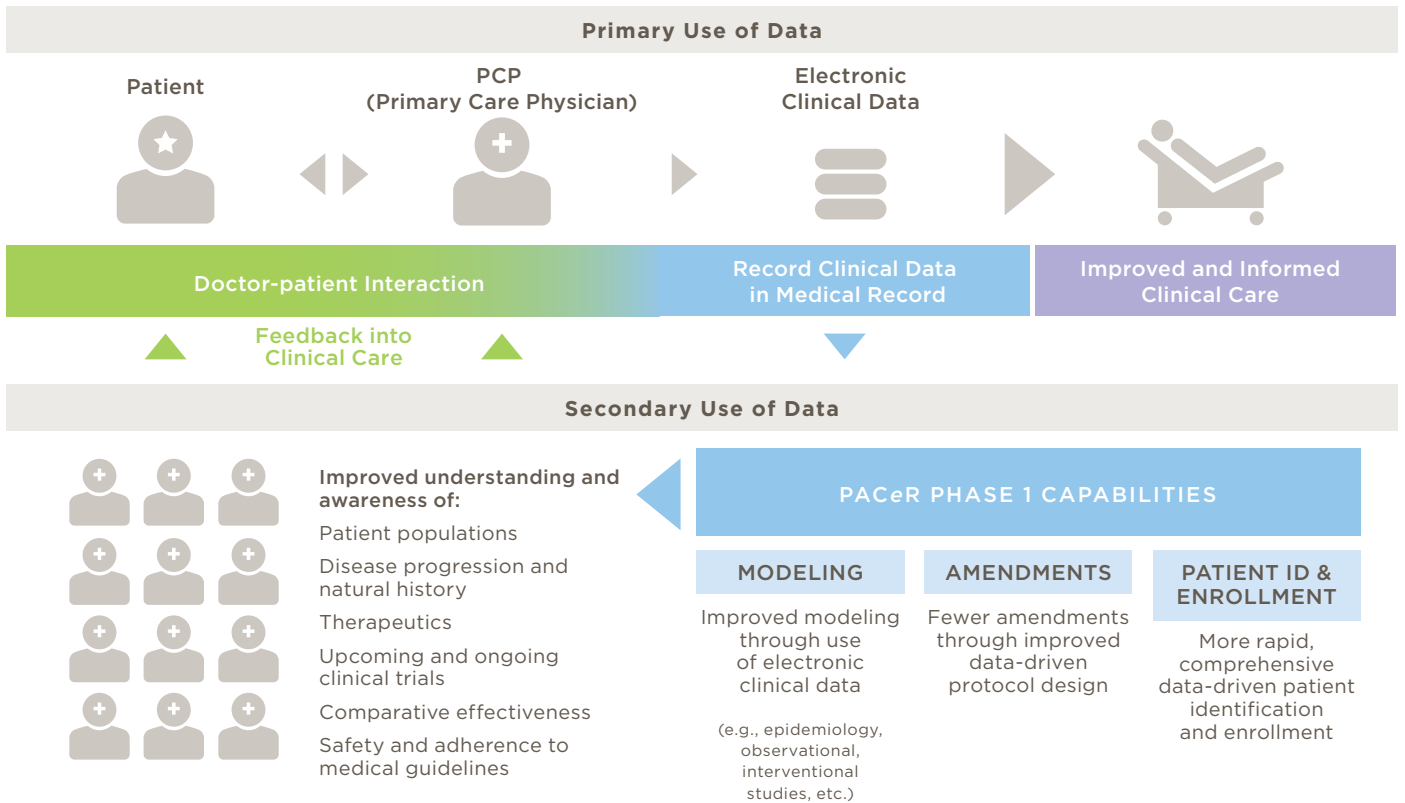
The electronic data captured to support clinical research will also support the long-term vision of improved delivery of clinical care. The chart below illustrates the dual impact of PACeR on the primary and secondary use of clinical data over the near term and long term.

PACeR's Breadth of Participation Enables it to Address Key Standardization and Sustainability Issues

PACeR's multi-stakeholder participation enables it to develop standardized approaches and establish a new research enterprise that is economically sustainable for all parties.

- » PACeR's members include major medical centers, health systems, and community hospitals in New York State, and major pharmaceutical companies and health information technology companies. PACeR is advised by regulators, standards-setting organizations, patient advocacy groups, and others.

PACeR ENABLES THE SECONDARY USE OF DATA TO BENEFIT PATIENTS, PCPS, & ULTIMATELY, CLINICAL CARE



³ "Roadmap for implementing value driven healthcare in the traditional Medicare fee-for-service program." Centers for Medicare and Medicaid Services. https://www.cms.gov/QualityInitiativesGenInfo/downloads/VBPRoadmap_OEA_1-16_508.pdf

⁴ "Eligible professional meaningful use core measures." 2010. <https://www.cms.gov/EHRIncentivePrograms/Downloads/EP-MU-TOC-Core-and-MenuSet-Objectives.pdf>

- » PACeR is defining standardized approaches to health data nomenclature that will streamline the analysis and use of health data through the use of common terminology across clinical networks.
- » PACeR is designed to maintain data ownership and control with medical centers, physicians, and patients.
 - PACeR’s design uses a federated database approach where participating institutions continue to own and control access to patient data.
 - PACeR’s design does not involve direct access to an institution’s health databases by users of data, but rather the use of database queries to answer specific questions.
 - Access to patient-specific data is through a uniform informed consent process controlled by individual patients and their physicians.
- » PACeR is an ongoing learning laboratory to develop additional sustainable models for the improvement of electronic data and its use to improve health care delivery and outcomes.
- » **Public/Private Initiatives Such as Regional Health Information Organizations (RHIOs):** PACeR offers a mechanism for clinical data nomenclature standardization and interoperability across hospitals and physician networks.
- » **New York State:** PACeR will enhance the state’s position as a center for medical research and home to some of the world’s most prominent academic medical centers, and attract a greater share of strategic investment in clinical research.

PACeR’s Guiding Principles Put the Patient First

PACeR’s guiding principles reflect the themes of sustained, long-term improvement in health care outcomes, benefit for all stakeholders, and the primacy of patients and individual control of their personal health information for use in clinical research through a rigorous informed consent process.

Generating benefits and safeguarding protections for patients remains PACeR’s top priority throughout Phase 1 and future phases.

New PACeR capabilities are designed to protect patient privacy:

PACeR is Designed to Provide Benefits to All Stakeholders

PACeR’s Phase 1 results point to significant benefits for major health care stakeholders, including:

- » **Patients:** PACeR will improve identification and matching of patients for clinical trials and accelerate the process of getting innovative medicines to the public.
- » **Academic Medical Centers, Community Hospitals, Principal Investigators, and Other Scientists:** PACeR identified opportunities to improve the underlying data and processes for conducting medical research and improving patient care.
- » **The Research Community:** Timely analysis of large amounts of high-quality clinical care data will streamline the clinical trial protocol development process.
- » **Health Information Technology Companies:** PACeR will develop functional specifications for health IT systems to capture and organize the data necessary to meet the needs of scientific, evidence-based research, observational research, and cost effectiveness analysis.
- » **Regulators:** Access to improved data and analysis will support safety surveillance initiatives and causal analysis of adverse events.

- » PACeR does not aim to create a centralized database. PACeR will adopt a federated model, where institutions continue to own and control access to their data.
- » Only data analyses using non-protected health information (non-PHI) will be shared with researchers in other hospitals and pharmaceutical companies (e.g., for protocol design) in accordance with the Health Insurance Portability and Accountability Act’s (HIPAA) “preparatory to research” provision.⁵
- » PHI data will only be used within the institution for patient recruitment by the designated principal investigator/clinician with HIPAA authorization, and after institutional review board (IRB) approval of the protocol, just as it is today.

PACeR generates benefits for patients, including:

- » accelerating the process of developing innovative treatment and management for medical conditions;
- » increasing awareness of upcoming and ongoing clinical trials through physicians and physician practices;
- » ensuring that researchers utilize a data-driven protocol

⁵ “Research repositories, databases, and the HIPAA privacy rule.” National Institutes of Health. 2004. http://privacyruleandresearch.nih.gov/research_repositories.asp

design process with accurate eligibility criteria, thereby reducing the likelihood of patients who are screened but fail to enroll in clinical trials; and

- » enabling academic medical centers that diagnose and treat patients to better manage outcomes and patient care through an increased availability of clinical data.

PACeR'S GUIDING PRINCIPLES

- Maintain the focus on patient benefit as the guiding “north star” of the project.
- Improve the state-of-the-art for clinical trials/research in a manner that benefits all stakeholders.
- Maintain institutional autonomy and achieve standardization through the benefits of participation.
- Develop a practical, actionable, and high-impact implementation program.
- Ensure that approaches and implementation programs benefit both investigator-initiated and industry-sponsored studies by considering the financial constraints and other distinguishing attributes of investigator-initiated studies.
- Aspire to comprehensive “reinvention” of clinical trials/research; accept meaningful incremental change.
- Establish a research system that is self-supporting and requires a minimum amount of government support.
- Create an accurate, high-quality, and complete clinical data capture system that can withstand the rigors of the scientific method for meaningful clinical research, evidence-based decision making, bio-surveillance, and protection of public health.

PACeR is Aligned with National Health Care Improvement and Economic Growth Objectives

The work accomplished by PACeR Phase 1 is consistent with the goals of the federal government to improve the quality and outcome of health care in the United States, while reducing the cost of patient care.

Nationally, PACeR is aligned with the goals of HITECH, which mandates the adoption of interoperable electronic medical record systems by hospitals and physicians by the end of 2015.⁶ The Office of the National Coordinator for Health Information Technology (ONC) within the U.S. Department of Health and Human Services (HHS) will invest approximately \$20 billion

to create HIPAA-compliant electronic health record systems.^{7,8} The law's stated long-term purpose is to improve health and health care through the best possible application of HIT. HHS “expects to harness the full potential of electronic technology to prevent and treat illnesses and improve health.”⁹

Through adoption and use of EMRs to treat all Americans, the stated strategic goals of ONC are: 1) to use information captured within patient medical records to “provide critical information to health care professionals to improve the quality of care delivery, reduce errors, and decrease costs,”¹⁰ and 2) “improve population health by simplifying the collection, aggregation, and analysis of anonymized health information for use to improve public health and safety.”¹¹

“Meaningful use” of electronic patient care systems requires that over the course of the HITECH four-year phase-in, providers implement systems that are capable of performing e-prescribing and that capture and exchange clinical care data necessary to measure and improve care quality. Clinical information will be submitted to CMS in sufficient granularity to perform an evidence-based evaluation of the quality and outcome of clinical care.¹² Additionally, the Medicare Improvements for Patients and Providers Act of 2008 (MIPPA) provides incentive payments from 2009 through 2013 to certain Medicare providers who adopt and use qualified electronic prescribing systems.

PACeR's objective is to build clinical data collection capabilities that are consistent with the goals of HITECH and ONC, as well as other organizations such as CMS dedicated to improving health outcomes. In particular, a core goal is enhancing the availability, exchange, and use of standardized high quality clinical data for evidence-based medical research.

PACeR is also aligned with regulatory goals, including those of FDA, as reflected in Dr. Sacks' comment on page 11.

PACeR is consistent with the goals and objectives of standards organizations such as CDISC and HL7, and both organizations have been involved in the PACeR program as advisors. PACeR does not anticipate creating new standards, but rather managing and coordinating the use of existing standards to which participating organizations will adhere.

⁶ Blumenthal D and Tavenner M. “The ‘meaningful use’ regulation for electronic health records.” *New England Journal of Medicine*. July 2010.

⁷ Federal J, Blumenthal D, Rishel W. “Federal health information policy: A case of arrested development.” *Health Affairs*. 4 (2003): 44-55.

⁸ “The push for nationwide use of EHRs.” *API Healthcare*. http://www.apihealthcare.com/_asset/trjg8w/WPEHR-1109--Push-for-Nationwide-Use-of-EHRs_nospread-2.pdf

⁹ “Statement by David Blumenthal on Health IT adoption and the new challenges faced by solo and small group healthcare practices.” 2009.

¹⁰ Mostashari F. “Aging in place: The national broadband plan and bringing healthcare technology home.” 2010. <http://www.hhs.gov/asi/testify/2010/04/t20100422e.html>

¹¹ “Office of the national coordinator for health information technology: Health Information Technology.” http://www.hhs.gov/recovery/reports/plans/onc_hit.pdf

¹² “Health policy brief: ‘Meaningful use’ of electronic health records.” *Health Affairs*. 2010. http://www.healthaffairs.org/healthpolicybriefs/brief.php?brief_id=24

**DR. LEONARD SACKS,
Acting Director for the U.S. Food and Drug
Administration's Office of Critical Path Programs**

"Harnessing information technology and novel scientific tools in the service of medical product development has been a central priority for FDA. These innovative tools provide a historic opportunity to move medical product development into the 21st century and to deal with the challenges of spiraling research and development costs in the face of diminishing returns. To accomplish these goals, FDA looks to all involved constituencies in the public, private, and academic sectors for scientific and practical expertise. In tackling such issues as the role of electronic health records in clinical research, the potential to personalize medicine using bioinformatics, and the safeguarding of medical privacy, HANYS' Partnership to Advance Clinical electronic Research has embraced the task and we enthusiastically support their effort." ¹³

PACeR can generate economic and employment benefits by creating a high-quality electronic clinical research network across New York State and solutions that can be migrated to other states. This will afford pharmaceutical and medical device companies and other researchers a more sophisticated and reliable research capability that can enhance the competitiveness of U.S. health care research. Improved clinical research will benefit the health care system overall and the American economy by helping increase the proportion of clinical research done in the United States versus other countries.

¹³"Broad-based health care collaborative to provide the next generation of clinical research for new medicines." HANYS 2010. http://www.hanys.org/communications/pr/2010/2010-06-14_pacer.pdf

III. PACeR PHASE 1 FINDINGS AND CONCLUSIONS

PACeR Phase 1 Findings are Based on Thorough Analysis by Participant Experts

As described in detail in the following sections of this document, the Phase 1 evaluation confirmed the feasibility of developing a sophisticated clinical data network across New York State that can be used for evidence-based research. Component pieces to develop this system exist within each of the participating medical networks, but much work will need to be done to build a statewide, standardized, consistent, and complete platform. That is PACeR’s goal and future work plan pending sufficient funding.

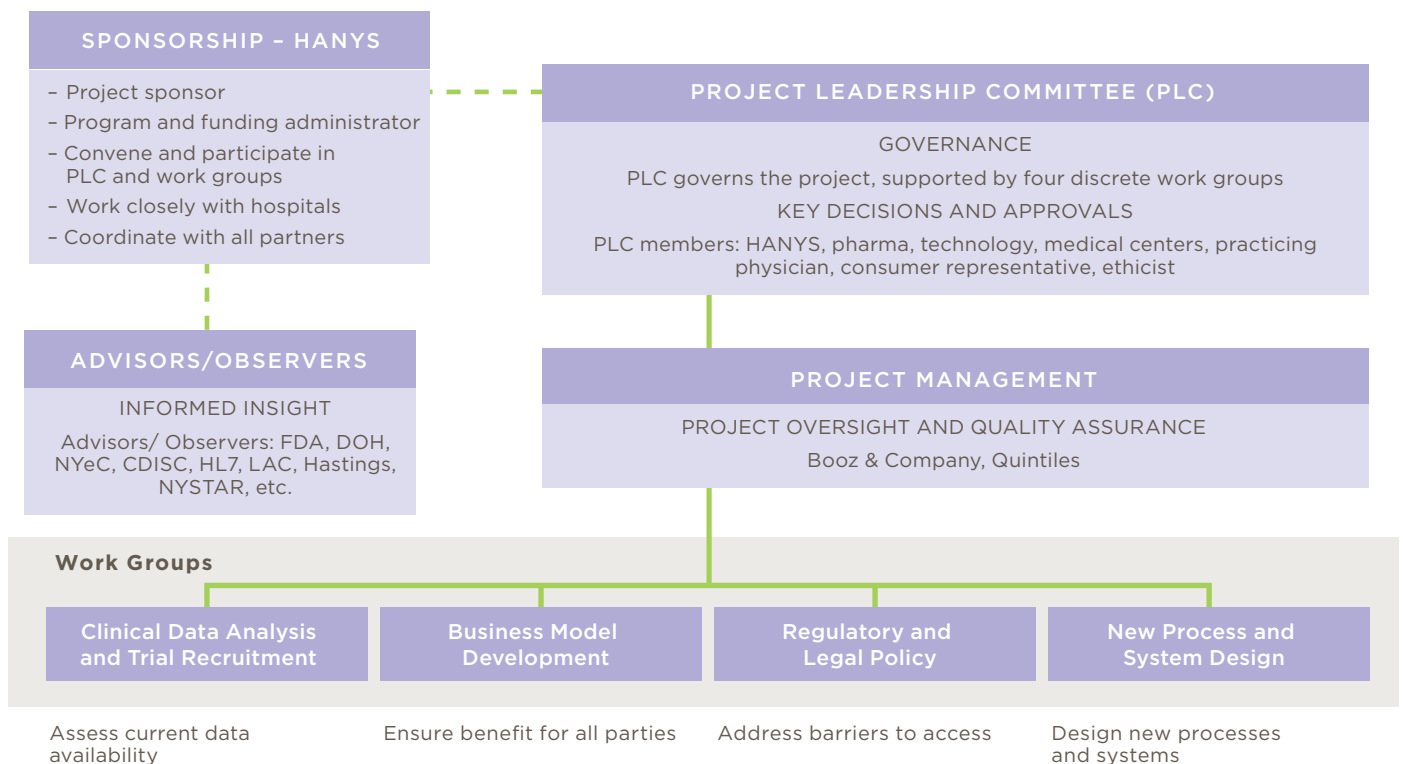
PACeR findings were developed by work groups comprised of members from participating organizations, under the direction of the PACeR Project Leadership Committee and supported by a project management team, as shown in the following chart.

The work groups addressed issues including the current availability of clinical data to support evidence-based clinical research, the regulatory and legal barriers to access and use of the data, economic and other benefits, and the design of new processes and systems.

PACeR focused initially on clinical research protocol modeling and trial recruitment, given the tremendous opportunity to create value by reducing the cost, complexity, and time associated with the clinical trials required to bring an innovative product to market.

Much of the success of each clinical trial depends on the design of the clinical trial protocol. Each protocol describes the scientific rationale for why the test product should produce the desired effect, the design of the clinical study, the disease state, the clinical therapeutic methodology, the statistical plan that will demonstrate effect, specific patient selection criteria, and an exact template for trial conduct by investigators at all locations so the study can be performed in exactly the same way by all participants.

PACeR’S GOVERNANCE AND TEAM STRUCTURE



PACeR's Phase 1 work group experts identified the gaps between currently available clinical data and what is needed to conduct high-quality clinical research; and explored issues related to data access, economics, and the design of new processes and systems required to build a practical capability to improve the conduct of clinical research and protocol design.

The findings of the work groups are discussed below. PACeR also designed solutions to address the major barriers identified, which are described later in this document.

A. Data Availability

PACeR Phase 1 Finding: The Availability and Quality of Electronic Clinical Data and Systems in PACeR Institutions Varies Significantly

Background

PACeR Phase 1 focused on improving capabilities to conduct evidence-based clinical research, a discipline that uses the scientific method to establish statistically significant relationships between the cause and effect of medical treatment. It seeks to determine the safety and benefit of treatment and diagnostic testing. Evidence-based clinical research requires a detailed and systematic set of highly granular data that are captured during the physician-patient clinical encounter. More broadly, evidence-based clinical research requires longitudinal data collection that encompasses a much larger set of lifestyle, environmental, employment, socio-economic, and other measures of health and well being across large populations.

FDA requires that prior to approval for sale in the U.S., all prescription drugs be subjected to a rigorous set of evidence-based clinical patient studies. Through randomized, controlled trials that compare groups of patients being treated with an experimental drug against control groups that are not receiving treatment (placebo or alternate therapy), drug scientists must prove safety and efficacy that is statistically significant (proving the medication has a positive effect that is unlikely to occur by chance).

To develop a clinical trial drug protocol according to the scientific method, pharmaceutical scientists need to identify clinical end points that will be affected by the drug being tested and demonstrate that the candidate drug does, in fact,

statistically alter the end points as predicted. In designing a study protocol, the scientific team must consider variables associated with the patient population, the disease state, the therapeutic plan, and other influences that might confound analysis and make it impossible to prove safety and efficacy.

Evidence-based drug trials begin with a Phase I evaluation of safety (tens of patients) and, if successful, proceed to a Phase II (hundreds of patients) demonstration of efficacy, which, if successful, allows the candidate to proceed to a large-scale Phase III (thousands of patients) randomized clinical trial that, if successful, proves safety and efficacy for general use. Once a drug is approved for sale, FDA requires ongoing study of the medication in the general population to identify adverse consequences not discovered during the controlled trial (Phase IV pharmacovigilance/post-market surveillance).

To be able to demonstrate a cause-and-effect relationship, it is critically important that scientists designing the trial study protocols have detailed and accurate information about the disease state, the patient population, current therapeutic approaches, and clinical end points with empiric values.

The processes of research often overlap with clinical care when performing retrospective analysis of population databases, measures of public health, disease risk factors, and causal inference from meta-analysis. However, controlled scientific evaluation of clinical cause-and-effect requires an added level of rigor and data granularity that sometimes goes beyond what is needed in the standard practice of medicine and observational research.

In a drug trial, using placebo cohorts is an attempt to ensure that clinicians studying a drug do not bias the study. The key to evidence-based clinical research is the ability to capture all of the study variables that are determined to be causally associated with the hypothesized outcome. Through controlled comparison with a cohort without the causal variable(s) it is possible to show statistically that cause and outcome are associated. If the study can be replicated by others, it is considered to be a valid finding and a new scientific truth. A drug that cures a disease in a population of patients with a statistical level of significance above the placebo cohort is considered by FDA to be approvable, subject to safety.

An important PACeR Phase 1 finding is that there are significant gaps in capability and design of currently available EMR solutions to support clinical research that meets FDA requirements. The systems do not capture much of the information necessary to perform evidence-based clinical research. In many instances, data might reside in an electronic format, but not in a form that can be easily used for clinical research.

In addition, EMR implementations are not standardized across hospital and ambulatory care settings and in many instances, not even standardized across applications within institutions. This lack of consistency undermines the ability to conduct scientifically valid comparative research.

There is also a work flow and information collection gap associated with capturing clinical data; electronic systems are not designed to automatically capture clinical data. Without better software design and new approaches to data gathering that reduce the time needed to collect patient-specific information, the use of clinical EMR software for research purposes will be limited.

In a number of instances, hospitals and health systems within the PACeR network have developed customized clinical systems that do have significant evidence-based research capabilities. These highly-developed systems tend to be designed to treat a specific disease state (for example, cancer) or for a specific purpose (such as surgical quality, tumor registry, diabetic compliance, etc.).

Findings

Phase 1 findings are based on results from an extensive and detailed questionnaire that provided an inventory of all software applications installed for inpatient and outpatient data capture. In addition to the physical inventory of all software installed, the survey collected information concerning the current capability of each application to provide the clinical data necessary to be useful for electronic, evidence-based clinical research.

Several key questions were analyzed:

- » What are the capabilities and levels of sophistication within clinical information systems across institutions in New York State?
- » Is the current information that is captured useful for evidence-based pharmaceutical and medical device research?
- » If the information is useful, how can it be used and what are the legal, regulatory, and technical parameters impacting its use?
- » What are the limitations and shortcomings of currently installed health care data repositories?
- » Given the limited ability of existing clinical information systems to facilitate evidence-based research, how can additional functionality and standardization be made available today to limit the need to make new, redundant expenditures to replace software currently being sold and installed?

Other measures of system capability were also captured to evaluate security, privacy, ability to monitor record access, and the like. The survey responses from each institution are treated in strict confidence; therefore, results from these surveys are summarized and blinded in this white paper.

PACeR institutions reported a wide variety of hospital information and clinical information system installations representing nearly every major vendor selling software today, including: Allscripts, Cerner, Eclipsys, Epic, General Electric, HBO-McKesson, Meditech, and Siemens. Additionally, a wide variety of specialty software systems for specific clinical care were interfaced with the hospital sample. No two institutions reported the same combination of installed software.

Results demonstrated that there is a wide range in the maturity of clinical systems across the study hospitals' population. The most advanced networks have clinical data repositories that are fed clinical and financial data from the health information system, departmental, and EMR applications. These networks collect patient information from inpatient and ambulatory systems. In a small number of institutions, separate clinical trial management applications are installed and used for evidence-based research and clinical trial purposes.

The typical hospital within our study has a mature information management system to capture information about admissions, discharges and transfers, orders and results, medication and laboratory results, diagnostic coding, patient billing,

accounting, and finance. Most have or are in the process of implementing computerized provider order entry (CPOE). While all hospitals are exploring EMRs, they are in various stages of evaluation and implementation. A number of PACeR institutions are also adding clinical data repositories.

After the clinical system inventory survey, the PACeR team performed a more detailed analysis of the content of electronic data within a subset of institutions, as described above. This analysis focused on the availability of clinical data needed to model and validate six detailed and complex research protocols. The protocols addressed the following therapeutic areas:

- » Chronic Lymphocytic Leukemia;
- » Colorectal Cancer;
- » Melanoma;
- » Type 2 Diabetes (two protocols targeted this condition); and
- » Obesity.

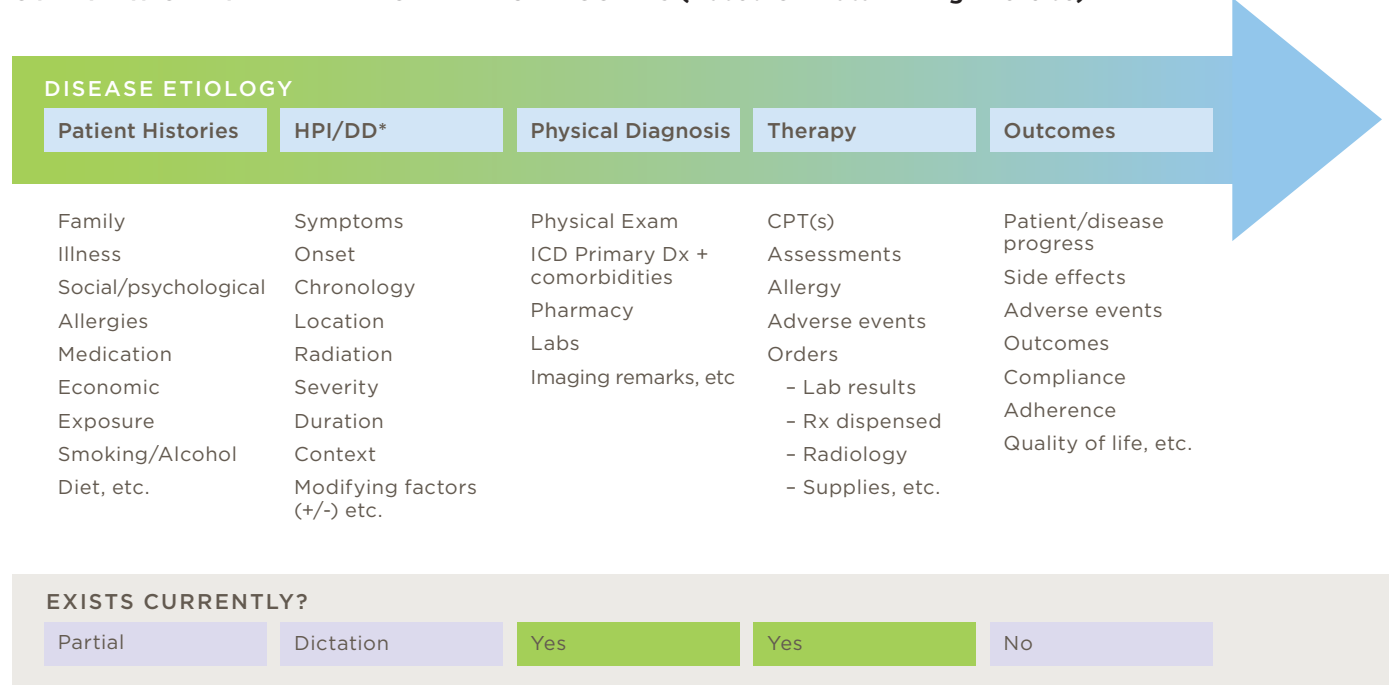
The following chart indicates the elements of clinical data included in the detailed protocol review. Clinical research requires extensive clinical investigation and evaluation of patient disease state, including the history of the illness. For each

patient encounter, the physical examination, laboratory results, diagnostic images, and advanced testing are electronically charted to ensure that all clinical end points can be evaluated.

The PACeR Clinical Data Analysis Work Group assessment of the availability and content of electronic clinical data within five PACeR health networks, their EMRs, and other applications, for use in clinical trial modeling and other scientific evidence-based research, revealed that:

- » Only one hospital was capturing “most” (approximately 80%) of the information within its inpatient and ambulatory applications and clinical data repository necessary for evidence-based research.
- » One hospital was capturing more than half (approximately 60%) of the information within its inpatient and ambulatory applications and clinical data repository necessary for evidence-based research.
- » Two hospitals were capable of capturing 35% to 40% of the information necessary for evidence-based research.
- » One hospital was capturing perhaps 25% of the necessary data.
- » Most institutions have interfaced applications so they can “communicate” through a standard known as

OVERVIEW OF AVAILABILITY OF DATA CATEGORIES (Based On Data Mining Exercise)



*HPI/DD = history of present illness/differential diagnosis

CURRENT STATE OF DATA QUALITY AT PACeR-PARTICIPATING INSTITUTIONS

Based on Data Mining Exercise and Hospital Site Visits

Average portion of trial protocol query completed on first pass ¹	Number of PACeR-participating institutions	Number of patients ² (not longitudinal, not distinct patient record)	State of existing querying capability ³
90%	1 (one therapeutic area only)	~5,000	<ul style="list-style-type: none"> - Sophisticated query tools exist, primarily automatic - Speed for 80% querying completion: 1-2 days
60%	2	~500,000	<ul style="list-style-type: none"> - Query tools exist, but delays due to need to query several databases - Manual data querying process required - Speed for 80% querying completion: 2-4 weeks
40%	9	~980,000	<ul style="list-style-type: none"> - Basic query tools, with severe delays - Extensive manual data querying process required - Speed for 80% querying completion: 1-2 months
25%	1	~530,000	<ul style="list-style-type: none"> - No query tools - Querying process is primarily manual - Speed for 80% querying completion: 8-12 months

1) Qualitative result, based on metabolic and non-metabolic protocols from PACeR participating pharmaceutical/clinical research organizations.

2) Includes inpatient discharges, ambulatory visits, emergency department visits per annum; master patient index required to align patient data nomenclature/terminology.

3) Timing for querying completion is illustrative; further testing/accuracy required.

HL-7 messaging, but HL-7 does not standardize the nomenclature used within disparate vendor products. CDISC, LOINC, SNOMED, MedDRA, and MEDCIN are examples of attempts by standards organizations and companies to create clinical data standards that vendors can use to create a common vocabulary for clinical care, but the PACeR survey revealed that only a few of the participating networks have uniformly implemented one or more of these standards.

- » No two institutions were capturing information (clinical controlled nomenclature) in a form that would allow for automated direct comparison of disease state or the clinical care process between them.
- » Cross-institutional analysis using standardized data sets such as Diagnosis Related Groups (DRGs), International Classification of Disease (ICD), Current Procedural Terminology (CPT), etc., can be performed in those instances where vendor systems are standardized. However, these cross-institution comparisons yielded disparate information. For example, one institution used more than 50 ICD codes to qualify diagnosis and comorbid conditions in the patient medical record. Most institutions used no more than 12. *Note: most cross-institutional data that are comparable are submitted to the Department of Health through the Statewide Planning and Research Cooperative System (SPARCS).*
- » Much of the information in an EMR cannot be easily analyzed because it is stored in a form that is unstructured

(i.e., voice dictation, FAX, BMP, GIF, TIF, etc.) and requires manual review. Physicians' notes, operative notes, discharge plans, pathology, and radiology findings are dictated and transcribed. Opportunities might exist for text mining using optical character recognition-enabled software to extract clinical findings; however, much of the data extracted would not be in a standardized nomenclature that could be relied upon.

- » The EMRs reviewed in Phase 1 record patient care in a form that allows for review of summaries of health, prescriptions, lab values, and basic diagnoses. They are not designed to capture data with the granularity necessary for clinical research. EMRs contain basic coded information concerning ICD diagnoses, DRGs, CPTs, Healthcare Common Procedure Coding System (HCPCS), and other data needed to record summary patient record histories and to bill for care. Detailed coded patient histories, illness histories, chief complaint-differential diagnosis, physical examination findings, and longitudinal assessment of restoration to health and well being are generally not captured.
- » EMR systems that are useful to assist a clinician during the care process are of limited use for clinical research, in part because clinical research is by nature non-standard. Each research hypothesis requires its own scientific method and set of clinical variables for evaluation. It relies on longitudinal, retrospective information as a baseline measure, but it requires highly discrete, granular data

captured in a controlled way to ensure uniformity of input and validity of findings.

- » Future phases of PACeR must include data collected in the ambulatory care setting, as these data are critical for multiple uses.

While PACeR Phase 1 identified important gaps in the availability of the electronic clinical data required to perform scientific, evidence-based research, Phase 1 findings also demonstrate that the current data are at least as sufficient as current alternatives, and can be improved significantly in the short term.

PACeR Phase 1 Finding: Currently Available Electronic Data are Useful for Protocol Modeling Despite Being Incomplete

Pharmaceutical and device companies, as well as clinical investigators, have very few sources of comprehensive electronic clinical data today. Data that are available for use are derived from claims databases, data purchased from third-party sources, or from individual institutions through research partnerships. Claims data are limited in scope, timeliness, and accuracy, generally containing only diagnoses, procedures, and medications billed to insurance companies. These data sources have limited usefulness and cannot be relied on to model clinical research protocols or identify patient availability in specific institutions.

As a result, despite PACeR's Phase 1 finding that there are gaps in EMR and health information system data and capabilities in participating institutions, the data mining exercise also demonstrated that there is still much useful data that can be used to model disease state, therapeutic processes, and population health for drug/device trials. Institutions with 60% or more of the data needed to model protocols provide a viable alternative to other existing databases, particularly since the clinical databases of the institutions participating in PACeR include millions of patients of above-average diversity. PACeR's advantages over alternatives for trial protocol modeling and patient selection are shown in the following table.

PACeR's advantages with respect to data quality, comprehensiveness, and institution-specific understanding of patient availability provide multiple benefits including cost and lead time reductions. The cost reductions can amount to

PACeR'S VALUE IS ENABLING "ONE-STOP" ACCESS TO LARGE QUANTITY OF HIGH-QUALITY DATA

Comparing Data Sources for Trial Modeling and Patient Enrollment

Value proposition is "one-stop" access to:	Current Data Sources for Researchers (PIs and Pharma)		
	PACeR	Hospital databases ¹ (Individual institutions)	Commercial databases (Primarily claims-based)
Higher quality clinical data	✓	✓	X
Large statewide population	✓	X	X
Institution-specific understanding of patient availability	✓+ multiple institutions	X	X

¹ Access to database includes institutional data expertise (e.g. epidemiologists, biostatisticians, etc.)

millions of dollars per protocol from reductions in the number of amendments, lower patient screening costs, and fewer, more productive sites. Lead time reductions from fewer protocol amendments, as well as more rapid patient recruitment and enrollment, can result in earlier product launches, with multi-million dollar financial benefits to pharmaceutical companies, and significant benefits to patients from earlier access to innovative therapies.

In addition to its current advantages, PACeR designed processes and systems to supplement the availability of standardized electronic clinical data in the near-term to increase its usefulness compared to other alternatives. The data that can be made available will serve not only clinical trial modeling and patient selection purposes, but also will support pharmacovigilance/safety surveillance, cost effectiveness, and benefit of care assessments, base level quality measurement, procedural outcome evaluations, and other research.

PACeR Phase 1 Finding: There are Feasible Solutions to Improving Data Quality in the Near Term

Recognizing the value and importance of improving the quality of electronic clinical data in the near term, the PACeR Clinical Data Analysis and New Process and System Design Work

Groups jointly designed processes and systems to capture the balance of the required data for protocol modeling and patient identification for trial eligibility, while protecting patient privacy. The process involves two stages, A and B, described in the diagram below. Stage C, shown for completeness, addresses post-protocol modeling activity associated with clinical trial enrollment, which is addressed later in this document.

In Stage A, the first activity is conversion of protocol eligibility criteria to a series of queries, most likely by PACeR staff. Subsequently, institutions use their own query application software, or software provided by PACeR to mine their databases and yield the number of potentially eligible patients.

Based on the findings from the Phase 1 data mining exercise, only a portion of the information in the queries can be addressed by this automated process, ranging from 90% to 25%, depending on the institution (as described above), and protocol requirements.

Key aspects of Stage A include:

- » The “mining” activity will occur within the confines of the health care entity, in keeping with PACeR’s federated model approach where health care entities are the custodians of their own data and no PHI will be accessed, used, or

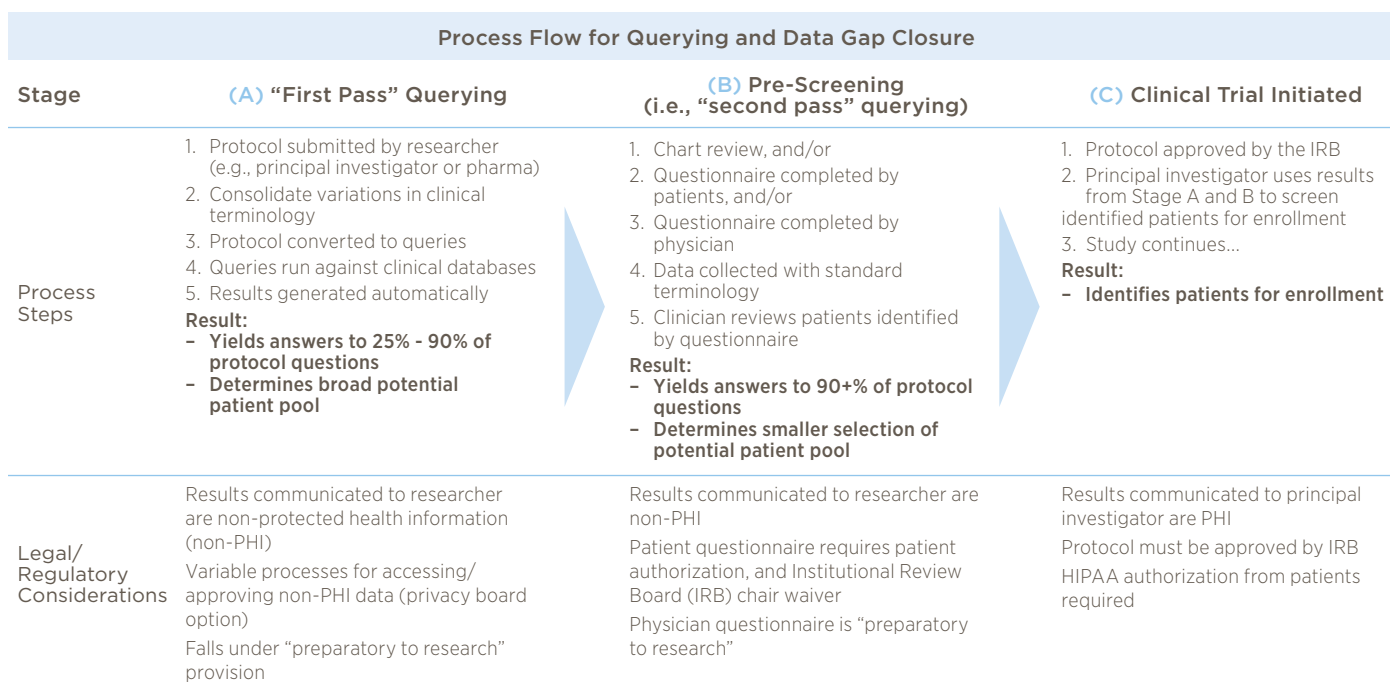
disclosed outside the health care entity.

- » The mining activity is initiated by the health care entity’s clinicians and completed by health care entity-employed information technology (IT) staff, who will be compensated by PACeR.
- » Much of the mining activity falls under the “preparatory for research” provision in HIPAA, given that the protocol remains in the design phase and no PHI is shared outside the health care entity.
- » At no time will PHI data be shared outside the health care entity. Answers to the queries (the data) will only be shared as de-identified data analyses (no PHI).
- » This process step will likely require repetition, as the protocol is continually refined with more appropriate/feasible eligibility criteria and clinical end points, thereby yielding a higher potential patient population that matches the protocol.

Stage B represents a semi-automated process step, where the purpose is to close the clinical data gaps identified in Stage A.

PACeR Phase 1 economic analysis demonstrates that it is not financially viable to close data gaps for all patients who pass through the initial automated screen – unless 90% or more of

A DYNAMIC DATA COLLECTION CAPABILITY HAS BEEN DESIGNED TO CLOSE GAPS IN THE NEAR-TERM



the data required for protocol modeling are available for the first screen. In instances of diseases with very low prevalence, it may be possible to economically gather data on all patients identified in the first screen. However, for most diseases a sampling process will be needed.

Therefore, PACeR designed a process to capture additional data for a statistically valid sample of patients.

PACeR envisions that data for the sample of patients will be gathered from the patients themselves (at the request of their physicians), and/or by a physician or nurse. The detailed design of the process for gathering additional data is described in Appendix A. The core of the data gathering process is an automated, Web-based capability to send questionnaires to patients, via their physicians, requesting needed information. Information supplied by patients would be supplemented by the physician or other health care professionals.

Stage B will result in a statistically valid estimate of the number of patients meeting protocol eligibility criteria.

Key aspects of Stage B include:

- » As in Stage A, the activities are conducted by the health care entity and an affiliated physician, in keeping with PACeR's federated model approach.
- » Although PACeR will provide appropriate tools and processes for completing this stage, the majority of activity will be conducted by clinical, IT, and administrative staff, which will be appropriately compensated by PACeR.
- » Patient questionnaires, even if sent directly from physician offices to patients, require institutional authorization. In addition, many PACeR participant institutions require IRB chair exemption for the questionnaires.
- » At no time will data containing PHI be shared outside the health care entity. Answers to the queries (the data) will only be shared via de-identified data analyses.
- » Ideally, this stage should only be conducted once per protocol, due to the more significant financial and human resources required to accomplish this activity. These limitations emphasize the importance of using an automated and analytical approach in the first stage to yield answers to as many protocol questions as possible.

Stage B design highlights an important issue for PACeR going forward. It will be useful as the PACeR Phase 2 Demonstration Project progresses to identify data that are needed only for a specific protocol versus those required for multiple clinical protocols and for routine clinical care. For data required for multiple uses, health care entities can prioritize data capture electronically, creating benefits for routine care as well as clinical research.

In the third stage (Stage C), the final protocol is approved by the IRB, and the clinical trial is initiated. During this stage, the principal investigator uses the patient population results from the first two stages to identify patients for screening and enrollment, with the aim of increasing the efficiency of patient enrollment with a data-driven approach. After IRB approval, and full, specific consent authorization from patients, the principal investigator has access to PHI results.

To be explicit, with respect to contacting individual patients for potential participation in a clinical trial and the associated access to PHI, PACeR envisions no change from the processes currently employed by health care entities (e.g., hospitals). Patients would be contacted through their treating physicians and/or principal investigators, and any and all consent requirements would be managed no differently than they would be absent PACeR.

The stages and process steps described above will be tested and refined during the Phase 2 Demonstration Project (see "PACeR Recommendations and Phase 2 Plan").

The next sections of this white paper address the findings of the PACeR Legal and Regulatory Policy Work Group focusing on access to clinical data for secondary research, and on clinical data nomenclature standardization.

B. Legal and Regulatory Constraints

PACeR Phase 1 Finding: Institutional Policy Constraints Associated with Access to Data for Clinical Trial Protocol Modeling Can be Addressed

The PACeR Legal and Regulatory Policy Work Group found no significant legal or regulatory constraints to using the data PACeR would require for clinical trial protocol modeling. HIPAA authorization is not legally required for sharing data

that are de-identified in accordance with HIPAA regulations. Activities required for protocol modeling, including mining clinical databases for protocol refinement and sharing de-identified data outside the health care entity, are consistent with HIPAA.

The work group also found that many institutions place policy and practice constraints on the use of data required for protocol modeling. These include:

- » The majority of institutions use HIPAA's safe harbor method to de-identify PHI. The alternative, which is a statistical method, is rarely used by institutions due to the imprecise wording of the HIPAA regulations, and in some cases the lack of statistical expertise at institutions. Because the safe harbor method limits the number of data fields, the statistical method is more beneficial to researchers. For example, dates directly related to an individual – which are often critical for effective analyses – may be not allowed by the safe harbor method, but may be allowed by the statistical method.
- » Most institutions participating in PACeR allow researchers within their institutions to access PHI for the purpose of review preparatory to research; for example, to help collect de-identified data to model or design a research study or aid in study recruitment. However, most of these institutions do not permit external researchers to access PHI to prepare for research, and some do not allow external researchers access to results from analysis of de-identified data unless there is a principal investigator within the institution involved in the research.
- » The process for approving access by researchers within the institution to analytical results using de-identifiable data and limited data sets varies considerably by institution, and is sometimes more restrictive than legal requirements. Privacy officers at some institutions approve requests to use non-PHI data, whereas other institutions utilize IRB review, even though de-identified data are not part of IRBs' authorized jurisdiction, according to regulations.
- » Independent of PACeR-participating institutions, PACeR-participating pharmaceutical companies and clinical research organizations use contractual agreements for accessing non-PHI data, including external data transfer agreements for research preparation.
- » The timing for approving requests to access analytical results from de-identified data also varies by institution, from two to three days, to up to three weeks.

Historical policies and procedures, risk of liability, and institutional culture account for the variability described above. PACeR Phase 1 recommendations include approaches to address these institutional practice and policy constraints. In the best case scenario, a single solution will be adopted by most participating institutions. PACeR's understanding of each institution's current process will enable required approvals for secondary use of data to be addressed expeditiously. Nevertheless, institutions will justifiably be deliberate in adopting new approaches, and the process will take time.

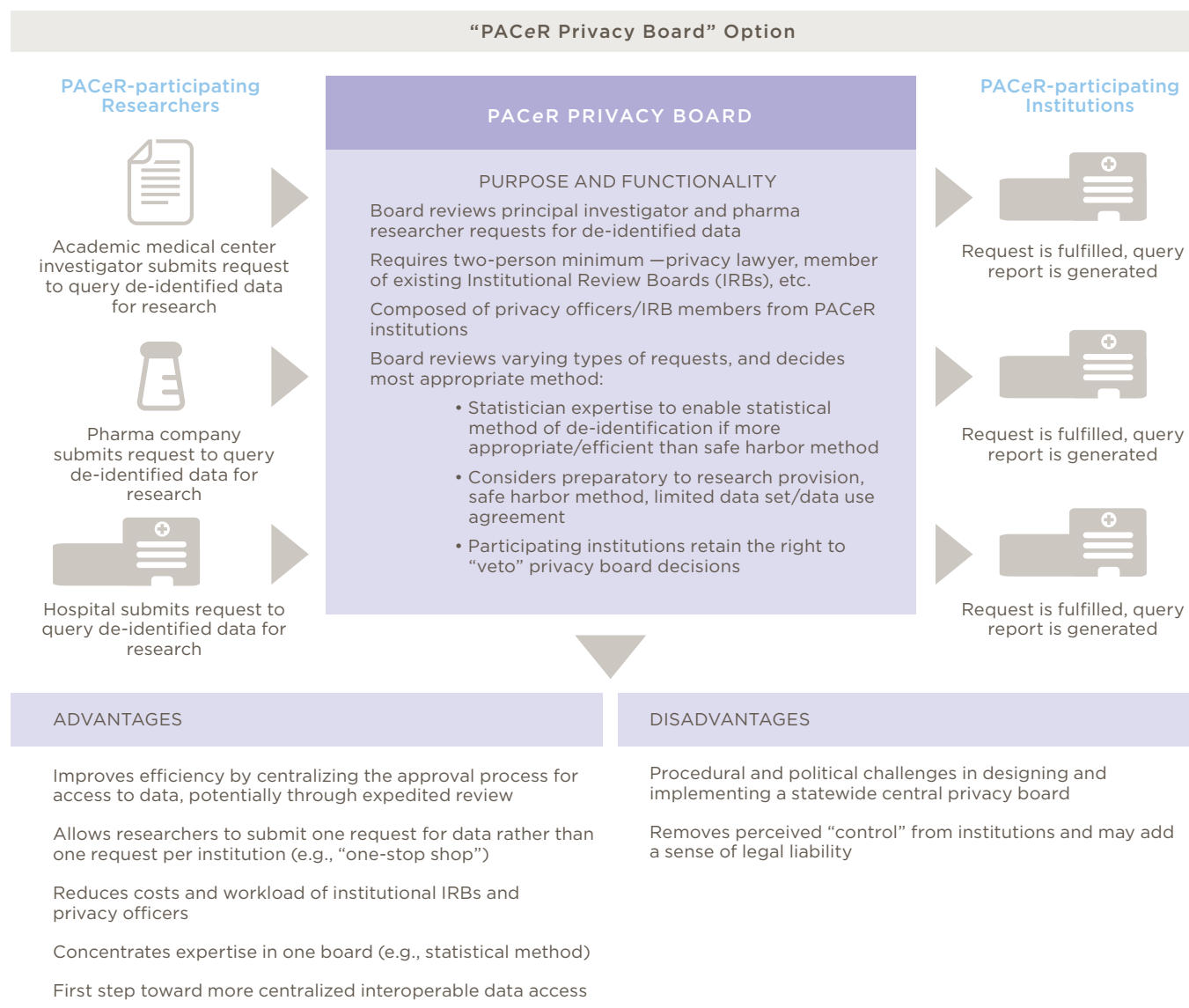
One approach to addressing institutional policy constraints is formation of a PACeR privacy board to approve access to de-identified data results on behalf of institutions. Its purpose, functionality, advantages, and disadvantages are described in the diagram on page 21.

Currently, PACeR-participating institutions have varied reactions to the privacy board concept. An important activity in Phase 2 is to further review the idea with various stakeholders within institutions.

Key PACeR privacy board concepts include:

- » The privacy board concept has the potential to streamline access to de-identified data. Using the current process would lead to every IRB and/or privacy officer conducting duplicate reviews, so that even if most were quick, delays would result from even one slow review.
- » The risk of institutional liability would be minimal, given that the privacy board's activities would only relate to de-identified data. However, even if risk is minimal, it must be addressed through contracts between the institution and PACeR, whereby PACeR assumes liability for the decisions made by the privacy board in accordance with standards established by the privacy board.
- » The privacy board's purpose would be to approve requests, but in addition, it will likely include a group of experts who help institutions de-identify data and update datasets. In particular, a qualified statistician would be needed to conduct the statistical method.

THE “PACeR PRIVACY BOARD” IS ONE OPTION FOR STREAMLINING & FACILITATING ACCESS TO NON-PHI DATA



- » The role, if any, of pharmaceutical companies and clinical research organizations in the design and participation of the privacy board needs to be considered, from a practical standpoint and in terms of perception and potential misunderstanding.

Another approach to addressing institutional policy constraints is pre-approval of “standardized” inquiries for pre-defined sets of de-identified data. This effectively creates a “hard-coded” query tool (an anonymous cohort identification tool) that would only query de-identified data. It would ensure privacy,

with appropriate security checks and regular review, and may obviate the need for privacy officer, IRB, and/or privacy board review of trial modeling requests. For example, a researcher could submit a request through a Web portal, and he/she could only select criteria that exclude the 18 identifiers as specified by HIPAA’s safe harbor method. The query tool would have specific algorithms built in to ensure that the data provided to the researcher are de-identified under the statistical method.

However, certain issues arise with this option:

- » For the statistical method, challenges include developing a robust algorithm(s) that is accurate and reliable in handling all population sizes and complexity of data elements.
- » Administrative procedures, audits, and other quality and accuracy checks would need to be established for quality assurance.
- » Unique identifying characteristics are required to be eliminated under the HIPAA safe harbor de-identification standard. This is particularly challenging with rare diseases and/or small populations.
- » The efficiency of this approach would need to be compared with current methods, and with the PACeR privacy board option. In particular, the technical and resource challenges associated with de-identifying multiple databases will likely be a constraint.

While there are a number of options for addressing patient privacy issues and policies, PACeR's Phase 1 found that these issues can be addressed, and are not a barrier to realizing PACeR's goals.

PACeR Phase 1 Finding: PACeR Institutions are Amenable to a Standard Method to Map Institutional Data to a Common Terminology, and a Key Role of PACeR is to Define and Monitor Compliance with the Method

A significant finding from the PACeR institutional survey is that there is not a common structure (ontology) and standard use of terminology (clinical nomenclature) in clinical applications and clinical databases across institutions.

One of PACeR's major roles, and a differentiating feature of the PACeR initiative, will be to define a standard method to map institutional data to a common terminology across participating New York State institutions, and to monitor compliance with the method. PACeR will maintain quality control of nomenclatures used by participating research sites and "certify" compliance with standards. This section describes how the PACeR role in defining and enforcing standards is likely to evolve, given Phase 1 findings.

Most institutions adhere to ICD (diagnostic) and CPT (treatment) standards, so the precedent for using standard terminology exists. Terms not covered by these standards differ,

and although terminology standards exist, including MedDRA, SNOMED, and MEDCIN, different standards are used by PACeR-participating institutions.

A key finding from PACeR Phase 1 data mining is that there is good, although not complete, adherence to one or more of the terminology standards. In the short run, where institutions have a significant amount of "legacy" data that do not use nomenclature from any of the standards above, PACeR has designed processes in which "experts" map data into one of the standard nomenclatures. Phase 1 data analysis results suggest that most institutions use one of the major existing nomenclature standards today, and the amount of mapping work necessary will be manageable.

This finding, coupled with the fact that there are existing information technology applications that "map" various standards to each other, underlie the PACeR plan to accommodate the three to five major standards in use today, and to design an automated capability to aggregate data across medical institutions.

Going forward, PACeR will work with participating medical centers and community hospitals to adopt a more narrow set of standards, but the current situation in which several standards are in use is not a barrier to PACeR success. PACeR will "certify" adherence to one of the accepted range of standards today, and update the information as the standards evolve.

In addition to working to define a more narrow set of terminology standards, PACeR will monitor the extent to which institutions adhere to standards, and may also provide IT applications that help individual institutions comply.

C. Economic Sustainability Considerations

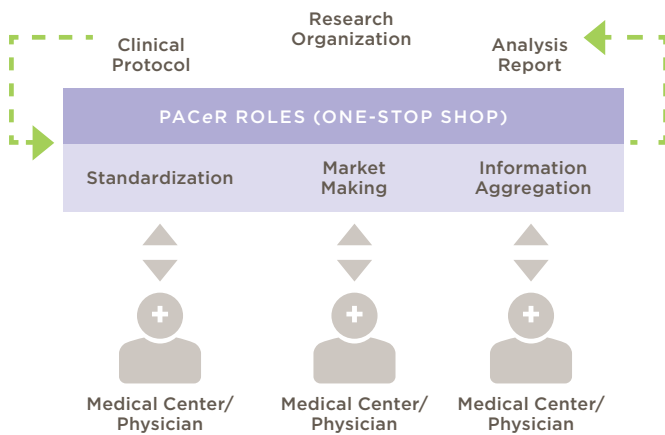
PACeR Phase 1 Finding: A PACeR Economic Model Featuring a "Market-Making" Capability for Protocol Modeling and Patient Selection is Viable

The PACeR Business Model Work Group developed a near-term business approach for PACeR consistent with PACeR's long-term objective to be a self-sustaining entity enabling the secondary use of electronic clinical data for a variety of purposes. The initial PACeR economic model was developed

to meet PACeR's Phase 1 objectives to support clinical trial modeling and patient selection.

PACeR economics as defined in Phase 1 are based on compensation for services that return query results and perform related analyses for clinical trial modeling and patient selection. PACeR does not provide direct access to or "sell" data directly. Rather, PACeR is a "one-stop shop" for analytical services based on analysis of data aggregated across participating institutions. PACeR also plays a role in enforcing standardization, as described above. PACeR's overall role is illustrated in the following diagram.

PACeR ROLE AND SERVICES OVERVIEW



The analysis reports provided by PACeR will include extracts of the (de-identified) data received from participating institutions, available to users for a specified period to test the impact of changes in protocols and the like.

PACeR will also provide a mechanism for sponsors and medical centers to engage in discussions about clinical protocol design. PACeR will be more than just a vehicle for exchange of analytical results. It will also enable protocol developers and clinicians at participating institutions to engage in "what-if" discussions about protocol design. It is a one-stop exchange to facilitate protocol modeling dialogue among interested parties.

In its role as a one-stop exchange and market maker, PACeR will establish compensation and pricing levels, working with the institutions supplying data used in analyses, and those using the analyses to model clinical trials. The level of compensation

will be determined on the basis of the value of the service to users, as well as the cost to institutions of providing the data. The structure of compensation will be designed to reward institutions with high-quality data, and to encourage other institutions to improve the quality of their data.

Rewards will be established to ensure that institutions that provide high-quality data earn increased revenue. PACeR Phase 1 analysis shows that the cost of gathering additional data not currently captured electronically is the major driver of PACeR's costs. Pricing set at the cost for an "average" institution will result in the rewards described above for institutions that capture above-average amounts of data electronically.

Note that as PACeR institutions gather additional electronic clinical data over time, costs of gathering additional data will decline.

PACeR Phase 1 analysis of the cost of providing services included a thorough assessment of all components of cost, including:

- » A one-time review of clinical systems for each institution. This may be done by a small team (five to eight) of clinicians, IT personnel, and clinical informatics staff within two days. They review the overall structure and design of institutional databases with PACeR personnel to better understand the infrastructure, tools, and processes necessary to capture data to answer customer requests (e.g., protocol questions).
- » Consolidation of variations in clinical terminology between researcher requests (e.g., protocol) and nomenclature utilized in institutional databases. This may be completed by clinical personnel in a few days, but must be completed for each request for data.
- » An automated query of clinical databases, usually by institutional IT personnel. Depending on the complexity of the request, the granularity and robustness of the clinical databases and the sophistication of the query tools, completing the request and obtaining results may take a few days.
- » For patients who pass the initial automated screen, an automated questionnaire is sent to the patients via the physician office. Although there is time and expense in the initial set-up of the questionnaire software, hardware, and

PRELIMINARY PACeR BREAK-EVEN ANALYSIS FOR A PARTICIPATING INSTITUTION (Operating costs only, excludes one-time investments)

	DEBIT	CREDIT	ASSUMPTIONS (DIABETES)
<i>Gross Revenue (approximate break-even)</i>		\$40,000	One protocol payment per institution
<i>Expenses</i>			
Consolidate variations in clinical terminology in clinical query results (nomenclature mapping)	\$1,000		Completed by clinical personnel Eight hours per query per institution @ \$125 per hour
Conduct initial automated database screen/query	\$2,000		Completed by information technology (IT) personnel Requires approximately two days @ \$125 per hour
For patients passing initial screen, send automated questionnaire to patient via physician office for secondary screen	\$2,000		Operating costs for hosting and maintenance of questionnaire IT infrastructure (e.g., servers, firewalls, databases, etc.) No payment to patients Automated process based on initial query results
For patients passing initial and secondary screens, send automated questionnaire to be completed by physician or nurse	\$31,250		Completed by clinical personnel 250 hours per query (30 minutes per patient, 500 patients reviewed) @ \$125 per hour
Total Expenses		\$(36,250)*	

* Excludes one-time investments such as: institution's clinical systems configuration review (2 days with 5 managers @ \$125 per hour, approximately \$10,000); nomenclature and data aggregation applications hosting and deployment (will likely be done by PACeR); query tool licensing and deployment.

Institutions with high data quality have lower secondary screening costs, and higher net income

- storage and collation of results, the day-to-day operation of this process step requires minimal institutional personnel time. The current PACeR business model does not compensate patients for completing the questionnaire, but this is subject to change as the process is implemented.
- » For patients who pass the initial and secondary screens, an automated questionnaire is sent to the patients' clinicians for completion. The assumptions are based on an estimate of completing questionnaires for only a subset of patients (e.g., 500 patients). The timing and number of patients is dependent on the complexity of protocol questions. As more questionnaires are completed, this growing collection of answers will mitigate the need to repeat identical protocol questions in the future.
 - » Most importantly, the increased availability of data in clinical databases for the automatic answering of queries will greatly reduce the time and costs required for clinicians to manually answer questions. Therefore, institutional capacity requirements for participating in PACeR are relatively minimal if improvements in data quality and granularity are achieved.

While actual pricing levels will be determined in discussions with interested parties in Phase 2, Phase 1 analysis suggests that the costs of providing protocol modeling input based on

COMPARING DATA SOURCES FOR TRIAL MODELING AND PATIENT ENROLLMENT

Value proposition is "one-stop" access to:	Current Data Sources for Researchers (PIs and Pharma)		
	PACeR	Hospital databases ¹ (Individual institutions)	Commercial databases (Mostly claims-based)
Higher quality clinical data	✓	✓	X
Large statewide population	✓	X	X
Institution-specific understanding of patient availability	✓+ multiple institutions	✓	X
Current pharmaceutical company cost to access data and/or data analyses	~\$140,000 per protocol includes: Three institutions @ \$40,000 per institution \$20,000 for PACeR services (e.g., aggregation of query reports, standards maintenance, market maker services, etc.)	\$150,000 to \$1.5 million per protocol includes: Three institutions @ \$50K to \$500K per institution No aggregation services, no standards maintenance	\$250,000 to \$2.5 million includes: – Access to entire database – Primarily claims data, minimal clinical data – Data are not institution- or geographic-specific

¹ Access to database includes institutional data expertise (e.g. epidemiologists, biostatisticians, etc.)

TOTAL REVENUE OF A NYS DATA QUERYING CAPABILITY FOR TRIAL MODELING (Assuming Institution Data are Complete)

1. Revenue analysis based on number of protocols in NYS and current access to institutional databases

Variable	No. of industry-sponsored new protocols in NYS per year	50% of protocols can potentially use institutional databases	Cost to pharma for accessing health system database	Maximum annual revenue (protocols in NYS multiplied by the cost to access institutional database)
Numerical Value	-1,500 protocols ¹	-750 protocols	-\$100K per protocol ²	\$75 Million

2. Revenue analysis based on current subscription costs of commercial databases in NYS

Variable	Average subscription fee per commercial database	Average annual cost of commercial databases per pharma company	Number of NYS pharma companies	Max. annual revenue (cost of commercial database multiplied by the number of NYS pharma companies)
Numerical Value	\$250K - \$2.5M	-\$3.75M ³	-20	\$75 Million

1) 1,000 protocols implemented, 500 protocols developed but not implemented. 100 to 200 protocols for clinical operations, epidemiology, disease outcomes research per large pharmaceutical company per year.
 2) Range is \$50K to \$200K per protocol
 3) Commercial database resides within pharmaceutical company - can be directly mined/manipulated by pharmaceutical company information technology team.
 Sources: Site Visits, Work Group Member Interviews, www.clinicaltrials.gov, PACeR Team analysis

high-quality data across multiple institutions is in the same “ballpark” as the value the input will deliver to users, illustrated in the exhibit on page 24.

A “ballpark” top-down analysis suggests that PACeR’s revenue potential for protocol modeling alone is substantial, more than \$50 million annually.

PACeR’S ROLE IS TO DELIVER FOUR KEY SERVICES TO CAPTURE VALUE

PACeR’s Role Based on Minimum Functions to Deliver Core PACeR Value: “One-Stop” Access to Analysis of Clinical Data for Trial Modeling and Patient Selection

PACeR Function/Service	Purpose
Provide options and enable methods for ontology mapping and implementation of clinical data nomenclature standards used by institutions (uses existing standards, e.g., SNOMED, MedDRA, HL7, etc., aligning with state and national initiatives, e.g., meaningful use criteria)	Enables cross-institutional data aggregation and “one-stop, single query report” generation
Provide capability to aggregate queries across institutions, and provide query tools to institutions, as needed	Performs cross-institutional data aggregation and “one-stop, single query report” generation
Develop (through a combination of contracting and internal development) options for process and informatics methodologies and approaches for dynamic data collection/enhancement	Improves data quality and modeling/patient selection results Assists New York state institutions with limited resources through tool/process provision Ensures quality of tools/processes through certification
PACeR serves as a transparent “market maker” for interested parties within a competitive context	Enables “one-stop” access to multiple institutions with a consistent pricing mechanism that reacts to market forces

PACeR services described above are key to generating value for stakeholders, as summarized in the exhibit at bottom left.

Over time, PACeR can provide additional analytical and other services related to the secondary use of high-quality aggregated electronic clinical data; for example, comparative effectiveness studies, safety surveillance studies, best practice sharing with respect to the conduct of clinical trials, patient education about clinical trials, and the like. These additional sources of value will significantly enhance PACeR’s economic viability.

PACeR will require investment funding to continue design, development, and implementation activity. Investment funding will likely come from a variety of sources, including sponsors, government agencies, and foundations, as discussed in more detail in the following section.

Several key stakeholders are part of PACeR’s business model and service delivery, ensuring that all participants contribute to and benefit from a viable and sustainable approach.

As PACeR development progresses, the role, value, and future responsibilities described below are subject to change.

Providers (including academic medical centers, community hospitals, and physician practices):

- » Roles and responsibilities: Systematically capture, store, and maintain institutional clinical databases. Although the current state of data capture varies considerably between

ONE-TIME INVESTMENTS REQUIRED FOR PHASE 2 (One-time costs only, excludes Operating Costs)

Investment Description	Approximate Investment	Assumptions
PACeR infrastructure design and prototyping (data integration/federation, nomenclature standardization, "market-making," etc.)	\$8.5 - \$4 million \$5 - \$10 million data integration/federation software \$2.5 - \$3.0 million PACeR organization and process design \$1.0 million program management	Participating medical centers have existing data repositories Existing and supplemental data integrated using modified versions of existing software
PACeR "start-up" support for initial 10-20 use cases	\$1 - \$2 million	-\$100,000 over and above revenue realized from use cases
Institution clinical systems configuration review	\$10,000 per institution	Two days with five managers @ \$125 per hour per institution (institution and PACeR personnel)
Query tool licensing and deployment	\$250,000 one-time licensing costs Additional costs for deployment and training per institution	License cost of existing query tool currently utilized by PACeR-participating pharmaceutical companies
Questionnaire software and hardware (to gather supplemental data)	\$150,000 total or \$10,000 per institution	Costs include development, distribution, storage, and collation of questionnaires
Additional hardware requirements at institution (e.g., computers, wireless routers, hubs, etc.)	\$50,000 per institution	Assumes that existing hardware at institution is insufficient to run PACeR applications (e.g., querying capabilities, questionnaires, etc.)

institutions, the data remain crucial for protocol modeling and patient selection in clinical trials, in addition to other secondary uses.

- » Economic value to stakeholder: Institutions will benefit from revenue generated by PACeR data analyses and services, and from revenue generated by increased clinical trial patient enrollment and improved capabilities from other secondary data uses (e.g., outcomes research, comparative effectiveness, etc.). Non-economic benefits such as furthering the research mission of providers also accrue.
- » Ongoing improvement in value: Providers have multiple motivations to improve their data quality, one of which is that data quality is directly linked to pricing and compensation from PACeR. A key component of the PACeR business model in the future is that as an

institution's clinical data improve, the value of the data increases. PACeR's standardization service aims to assist institutions with improving data quality.

Patients and patient advocacy groups:

- » Roles and responsibilities: Patients are the ultimate "source" of the data, although PACeR primarily relies on providers to capture data. PACeR safeguards patient protection by design – incorporating patient advocacy groups in PACeR's participation and governance ensures that their role and benefits remain a top priority.
- » Value to stakeholder: PACeR services, which will benefit providers and industry, ultimately benefit clinical care. PACeR aims to accelerate the development of innovative treatments for patients' medical conditions and enhance opportunities for patient participation in clinical trials.
- » Ongoing improvement in value: Patients' incorporation in PACeR's current and future governance body ensures that patient benefits are not compromised by other stakeholders.

Principal investigators:

- » Roles and responsibilities: Clinicians serve as principal investigators for industry-sponsored research and develop and implement investigator-initiated research. They also use PACeR services directly for their own research programs. This is in keeping with the guiding principle that PACeR benefits investigator-initiated research, in addition to industry-sponsored research.
- » Value to stakeholder: Principal investigators can use PACeR services to identify patients for enrollment and to more accurately model their protocols.
- » Ongoing improvement in value: The dialogue between principal investigators and researchers in pharmaceutical companies will likely increase, as it is key to the protocol modification and refinement process.

Pharmaceutical and medical device companies:

- » Roles and responsibilities: Multiple departments within these companies can benefit from PACeR services, including clinical trial operations, safety surveillance, epidemiology, and disease outcomes. They represent the "demand" for high-quality clinical data from multiple institutions. Their role is to request (and pay for) PACeR services to meet their multiple needs, such as a specific

protocol that requires refinement of eligibility criteria based on clinical data. PACeR's business model also accommodates a "dialogue" between researchers in these companies and data experts and clinicians within these institutions as protocols are continually refined. As more requests are made and more protocols analyzed, PACeR can begin creating a repository of common protocol questions that in the long term may be incorporated into routine clinical care.

- » Economic value to stakeholder: PACeR will provide access to a large quantity of clinical data analyses from multiple institutions through an efficient "one-stop shop." Aggregated clinical data analyses from multiple institutions provide information about a large patient population through an iterative process, and are more valuable than current data sources used by researchers, including single hospitals and commercial databases that are largely claims-based.
- » Ongoing improvement in value: Pharmaceutical companies will learn to modify protocol questions so they are more aligned with clinical care, and more generalized across multiple protocols, thereby streamlining the collection of data at the point of care.

Health information technology companies:

- » Roles and responsibilities: HIT companies will develop the infrastructure and tools necessary to enable PACeR's service provision, including the functional specification for the collection and aggregation of data, and analysis and reporting to address queries. In addition, they will provide input to the standardization of clinical software design and implementation that meets the needs of clinical research. The development process will be a hybrid approach (e.g., developed in-house and through contracts), as determined by PACeR's governance body.
- » Economic value to stakeholder: By taking part in the design of innovative capabilities and working simultaneously with the providers and users of data, HIT companies serve the demands of their key clients.
- » Ongoing improvement in value: HIT companies will further improve the technical specifications of data collection to supplement potential process and clinical workflow changes within hospitals.

PACeR's Business Model Work Group developed key principles for PACeR's governance and financing mechanisms to guide the formation of a PACeR entity in Phase 2. They are summarized in the exhibits below, and focus on broad participation in ongoing governance and a "federated" approach to financing.

BROAD PARTICIPATION IN GOVERNANCE, INCLUDING PHARMA, HIT, AND HOSPITALS, IS INTEGRAL TO SUCCESS GOING FORWARD

Guiding Principles of PACeR's Governance

Includes insight from the Business Model Development Work Group

Principle	Purpose
PACeR-participating institutions (or a subset) must have a role in decision-making (e.g., for standards maintenance, pricing, service provider decisions) with the ability to opt out	Encourages current and future hospital participation Acknowledges that hospitals are the current custodians of clinical data Ensures that institutions' PIs are represented, enabling benefit for investigator-initiated studies
PACeR-participating pharmaceutical and HIT companies must have a role in decision-making with ability to opt out	Encourages current and future pharmaceutical and HIT company participation
Need to develop rules of governance and establish mechanisms and criteria for founding board members, and additional board members (e.g., consider lessons learned from existing models)	Ensures transparency and opportunities for PACeR participants to influence decisions
Need to accommodate external investors in PACeR, and determine magnitude and restrictions of their role in governance; investors reviewed on case-by-case basis	Ensures that PACeR's objectives are not compromised by need for ROI
Include patient advocates and ethicists in governance	Ensures broad participation

Note: The "transition phase" governance structure will differ from long term (e.g., continue with Project Leadership Committee)

IV. PACeR RECOMMENDATIONS AND PHASE 2 PLAN

Having confirmed the feasibility of PACeR's Phase 1 objectives, the primary PACeR Phase 1 recommendation is to continue the PACeR initiative with a Phase 2 program to demonstrate PACeR's value in practice, while building PACeR capabilities. The overall philosophy and intent of Phase 2 is to "learn by doing," recognizing that the Phase 1 plan will require modification as it is tested.

PACeR Phase 2 is a demonstration program composed of multiple projects. It could be governed and led by HANYS and a Project Leadership Committee, essentially continuing the structure from Phase 1 with minor changes. Funding for Phase 2 is still being finalized, but will likely come from a variety of sources, including PACeR participants. Plan details are subject to change pending available resources.

PACeR's Phase 2 Will Continue to be Led by a Broadly Representative Leadership Committee

The current Project Leadership Committee members remain committed to PACeR and its goals, and have agreed to continue to lead Phase 2. The Project Leadership Committee will determine when and how leadership and governance will change, including how PACeR will evolve as an independent entity.

PACeR Phase 2 is a Demonstration Program Consisting of Multiple Projects

PACeR's Phase 2 includes multiple projects of interest to PACeR participants. Consistent with PACeR's objectives, the projects will all involve more than one academic medical center to demonstrate the capability to provide protocol modeling input across many institutions.

The projects will take place over the course of approximately one year. In order to "learn by doing," there will be no more than three to four projects initiated as Phase 2 begins. Subsequent project timing and volume will be determined based on the results and findings from the initial projects.

The specific projects that will initiate Phase 2 are still being finalized, but they are likely to include protocol modeling and safety surveillance initiatives.

The projects that comprise Phase 2 will help advance the design, construction, and testing of critical PACeR components. This capability-building will include creating PACeR institutional infrastructure that will endure over time, including:

- » A statewide Center for the Support of Clinical Terminology and Ontology Mapping will be created to oversee use of a common set of standards by participating institutions. The entity will work with participants to select the common standards that will work with existing standards, to add terms to standards dictionaries over time, and to certify compliance with standards by PACeR members.
- » Over time, the PACeR entity will also take on more of the leadership and governance roles now filled by the PACeR Project Leadership Committee and will increasingly oversee other aspects of the PACeR initiative, including the provision of services such as data queries/analyses, and gathering of additional clinical data.
- » PACeR will develop "market making" capability to deliver protocol modeling and patient selection services using data from multiple institutions. Query tools and related analytical tools to answer protocol modeling questions will be needed to support this capability.
- » PACeR will establish data aggregation and reporting capability to support the "one-stop shop" role of delivering analytical services spanning multiple institutions. The data aggregation capability will be designed to accommodate input from multiple institutions.
- » Processes and tools will be established within medical centers and ambulatory care settings to capture additional data needed for protocol modeling and other uses. The Phase 2 approach will be to deploy clinical software solutions that "wrap around" currently deployed EMR systems, where those systems will not accommodate the capture of data required for clinical research.
- » PACeR will educate the public about the responsible use of personal clinical information for the treatment and cure of disease and for the development of new diagnostics, medications, and medical devices. The program will emphasize that participation in evidence-based research can

dramatically improve the overall health of the population and improve the safety of the care that they receive, if done ethically and with fully informed consent.

Throughout Phase 2, PACeR will continue to engage the full range of stakeholders, including practicing physicians and patients who will be affected by, and will benefit from, PACeR. PACeR will continue to put patients first and will ensure that all solutions deployed will allow patients to decide how their personal medical information will be used.

PACeR Phase 2 Represents the Next Step of a Bold and Innovative Initiative

PACeR represents a multi-stakeholder, collaborative initiative to improve clinical research and benefit patients and all other participants. Its distinguishing characteristics include the collaboration of hospitals, principal investigators, and pharmaceutical and device companies, and a sustainable, scalable business model that aspires to expand beyond New York State and beyond clinical research to multiple secondary uses of data. Phase 2 is an opportunity to demonstrate and implement unique PACeR capabilities, including the standardization of data, the market making service, and the dynamic collection of data directly from physicians and patients. The dedication, expertise, and breadth of PACeR's participants will enable the collaboration to succeed.

PACeR Phase 2 is Open to New Participants

As PACeR embarks on Phase 2, it welcomes and encourages participation by additional organizations, including pharmaceutical, device, and information technology companies; academic medical centers; patient advocacy groups; professional physician societies; disease societies; and others.

Interested organizations should contact HANYS for information on funding and participation requirements.

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APPENDIX A: PROCESS FOR CAPTURING ADDITIONAL CLINICAL DATA

The PACeR Future State Work Group determined that it can implement a set of technologies, workflows, and policies that can be wrapped around existing EMR systems to add the flexibility, functionality, and clinical data necessary to perform evidence-based research. The diagram below explains the concept.

Health care institutions and ambulatory networks are represented by the three blue boxes. A few highly developed health information systems and clinical EMR systems capture upwards of 80% of the information necessary for scientific study of clinical and pharmaceutical research. These systems have been customized by the individual institutions to obtain this level of function. More commonly, institutions across New York State are capable of collecting between 35% and 55% of the required information within their developing EMR applications.

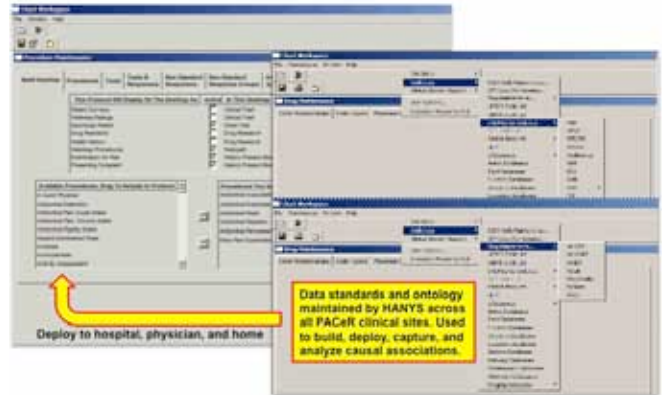
Recognizing that there is an opportunity for hospitals and physician networks to collaborate with industry and improve the research capabilities of all clinical systems being installed, PACeR Phase 2 recommendations include the design and development of a set of solutions and prototypes that will capture the additional data required for scientific, evidence-based clinical research. These solutions will not only be useful in New York State, but will also help inform regulatory and other health data standard bodies of methods that can be applied across the U.S. health system to achieve future

meaningful use of EMR systems and support scientific clinical research of all types.

A Conceptual Prototype for Deployment in PACeR Phase 2

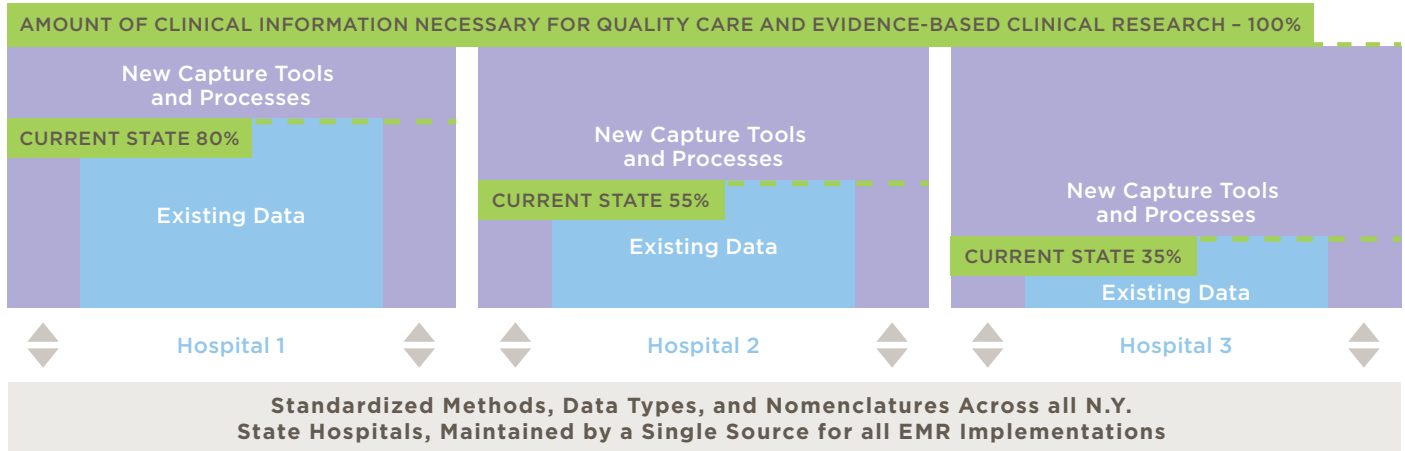
The Center for Support of Clinical Terminology and Ontology Mapping will develop a prototype clinical nomenclature foundation to support PACeR as it implements evidence-based pharmaceutical and medical device research systems. Shown as the gray box in the diagram at the bottom this page, the standardized terminology engine provides the foundation for the software “wrapper” applications that will capture the clinical data necessary for evidence-based research.

DATA STANDARDS AND ONTOLOGY ACROSS ALL CLINICAL SITES



The application displayed above maintains an ontological data construct that spans all standard body terminologies used for science and medicine. The complexity of data across this broad domain requires a lexicon to support every aspect of clinical

DATA COMPLETENESS



medicine – including genetics, disease state, clinical practice, and even the disciplines of economic and social science.

By establishing a central location and agreed-upon terminology that health care providers can use to establish and maintain EMR systems, New York State can create a uniform, cross-institution, and ambulatory research network that will lead the nation in evidence-based medical research capabilities.

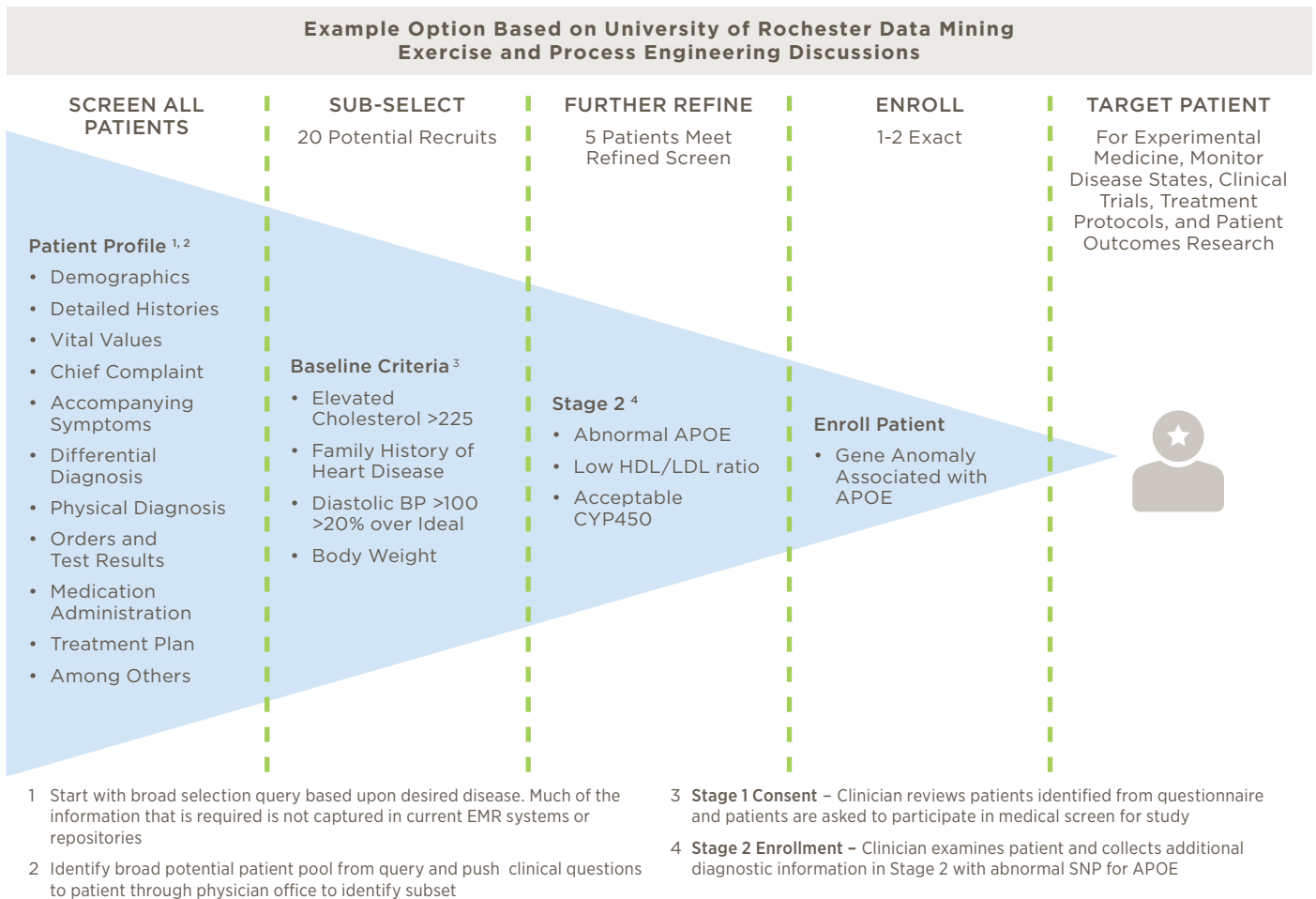
Expansion of EMR Functionality

Clinical science requires that a software system be flexible and adaptable to the methodological requirements of each trial. For example, when the PACeR Clinical Analysis Work Group analyzed the ability of installed EMRs to capture the data necessary, researchers determined that some of the questions that were required to complete the study are not routinely asked

or captured in the clinical record. A question such as “are you planning to become pregnant within the next two years” was a requirement of the study, but not part of the electronic data collection for any EMR.

In addition, clinical science requires in-depth assessments of patient histories, capture of current illness assessment, and additional clinical data during the clinical encounter that are not contained within existing EMR applications. The functionality of a pharmaceutical Electronic Data Capture (EDC) system is needed in addition to the functionality contained in the standard EMR. The caveat is that clinicians and their extenders in the ordinary practice of medicine do not have the time and are not compensated to take the time to collect all of the information needed to assemble the data for evidence-based pharmaceutical research.

FOR PATIENT ENROLLMENT, WE HAVE BEGUN TO DEVELOP APPROACHES FOR FILLING ELECTRONIC DATA GAPS



The diagram on page 31 demonstrates the concept of how a real-time EMR system coupled with a real-time EDC system would improve that ability to perform pharmaceutical research and find the right patients for a clinical trial. In this example, a drug company is interested in developing a medication that targets an APoE mutation.

ApoE 4 is a specific gene variant that is present in approximately 5% of people between the ages of 30 and 60 who develop Alzheimer's disease. Current EMR systems only capture some of the basic elements shown in the screening column. To trial a specific drug, the pharmaceutical company needs to find patients who have this gene anomaly. By working with the physician practice to engage patients at risk and using clinical wrapper technology that is pushed to the home by the physician, detailed histories and unusual questions that are not ordinarily captured during an office visit can be answered. This process might begin with a retrospective analysis of all patients who are between the ages of 30 and 60 who have elevated cholesterol and blood pressure, and other screening questions. By mining existing clinical databases, a population of patients of interest can be developed.

Additional clinical data are captured by pushing detailed questionnaires via secure Internet to the sub-population. Patients who agree to participate in the research fill out the detailed information needed to find and refine the study cohort. After review by a clinician, patients who have been identified as potential study participants are provided with consent forms and asked to participate in a detailed physical examination. Clinical information captured within the EMR or clinical research wrapper is then used to evaluate each individual, identify specific clinical criteria that meet the study requirements, and find patients who are closely matched to the study methodology and requirements for participation in the drug trial.

The diagram on page 30 shows how the clinical wrapper technology envisioned for PACeR is constructed on top of the nomenclature foundation managed by Center for Support of Clinical Terminology and Ontology Mapping.

This prototyping exercise is designed to:

- » standardize all scientific data collection that is currently outside existing EMRs' functional capability to capture, across all locations performing clinical evidence-based pharmaceutical research;
- » automate the collection of data by engaging the patient in new ways that improve the data gathering capabilities of clinical sites and the content of clinical electronic records in a manner that reduces the burden and cost of data capture on the practicing physician; and
- » deploy a clinical software wrapper system that is functionally malleable so that it can be modified "on the fly" by clinical and pharmaceutical research scientists to capture clinical data that are not built into the static design and function of deployed EMR systems. Again, because the wrapper is deployed using clinical terminology that has been standardized through the Center's nomenclature foundation, evidence-based research will be performed using fully normalized data across all PACeR institutions.

APPENDIX B: BUSINESS MODEL WORK GROUP SUPPORTING ANALYSIS

PACeR’s Phase 1 economic sustainability derives from the value it provides to pharmaceutical and medical device companies, as well as medical institutions and principal investigators, by improving their ability to model clinical trials and identify and enroll eligible patients in clinical trials.

PACeR’s Phase 1 value has been estimated based on the benefit for those conducting clinical research, as well as what they are paying today for comparable services and information.

Major PACeR benefits, including fewer protocol amendments and more rapid identification and enrollment of eligible patients in clinical trials, are shown in the following chart.

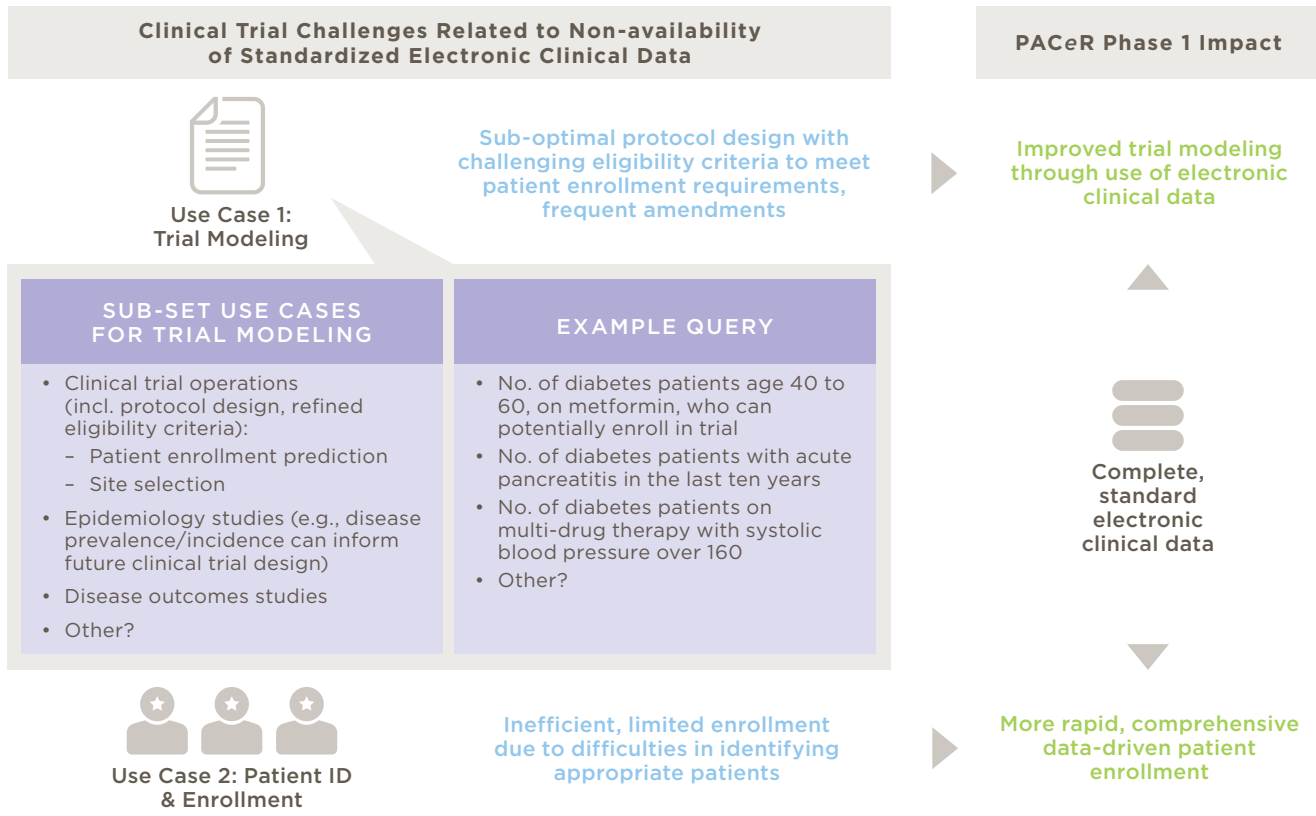
More detailed analysis of the value created by PACeR incorporates all the important sources of benefit from the

analytical services PACeR provides. The key drivers of PACeR value for all participants are shown in the following chart.

An analysis of these drivers of value shows that value is derived primarily from more rapid identification and enrollment of patients in clinical trials. Value from clinical trial modeling is significant, but less than the value associated with the conduct of trials.

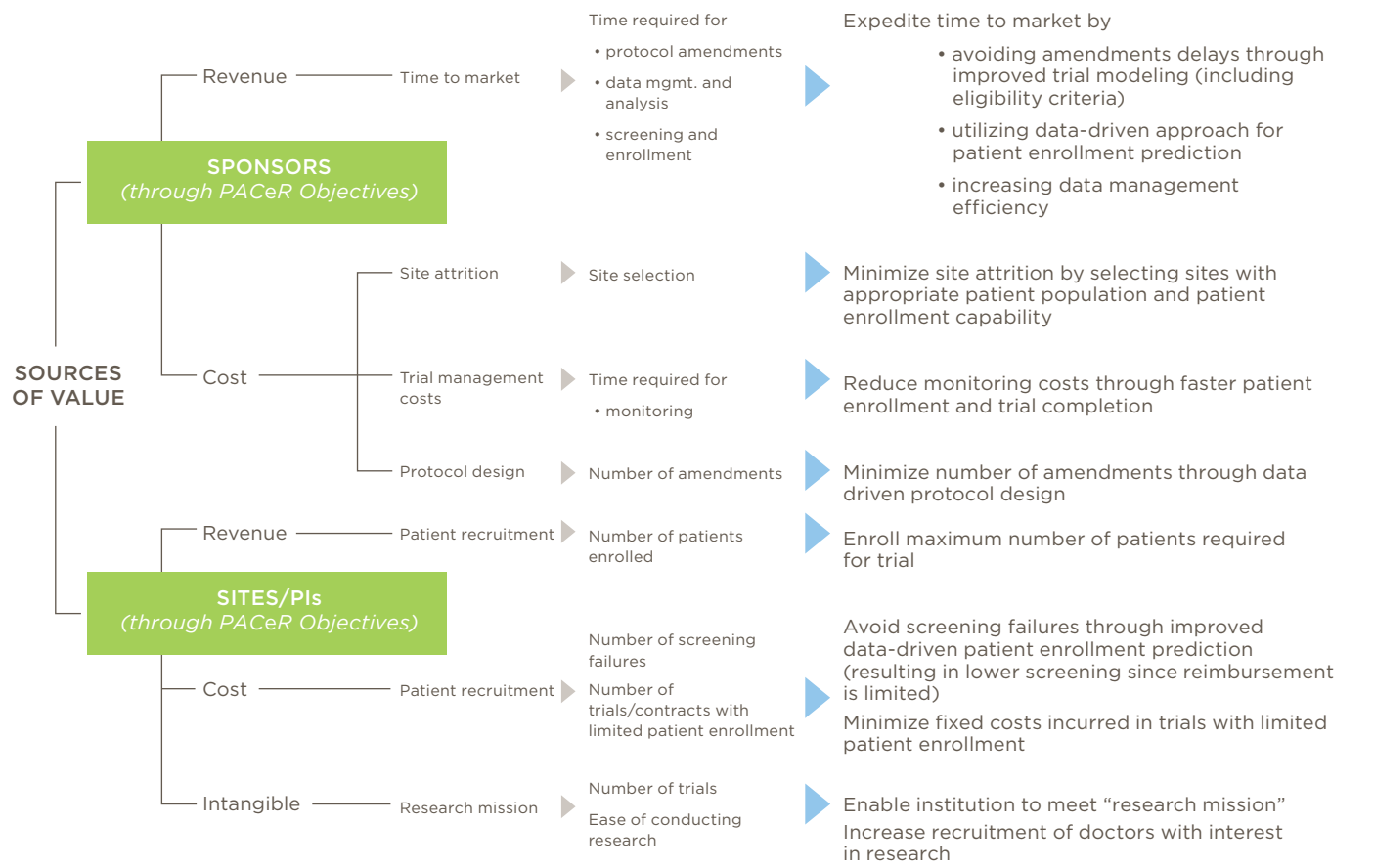
PACeR Phase 1 estimates show that for an average protocol, modeling, and amendments savings will range from \$100,000 to \$200,000 per protocol, and cost reductions associated with trial conduct will range from \$400,000 to \$500,000. In addition, to the extent that more rapid enrollment in New York State enables an earlier product launch, benefits on a net present value basis can be tens of millions of dollars (based on reducing lead time by one year, from 48 to 36 months).

THERE ARE TWO MAIN USE CASES FOR PACeR PHASE 1 IMPACT: TRIAL MODELING AND PATIENT ENROLLMENT



WHAT IS THE VALUE OF NEW YORK STATE DATA FOR CLINICAL TRIAL MODELING AND PATIENT ENROLLMENT?

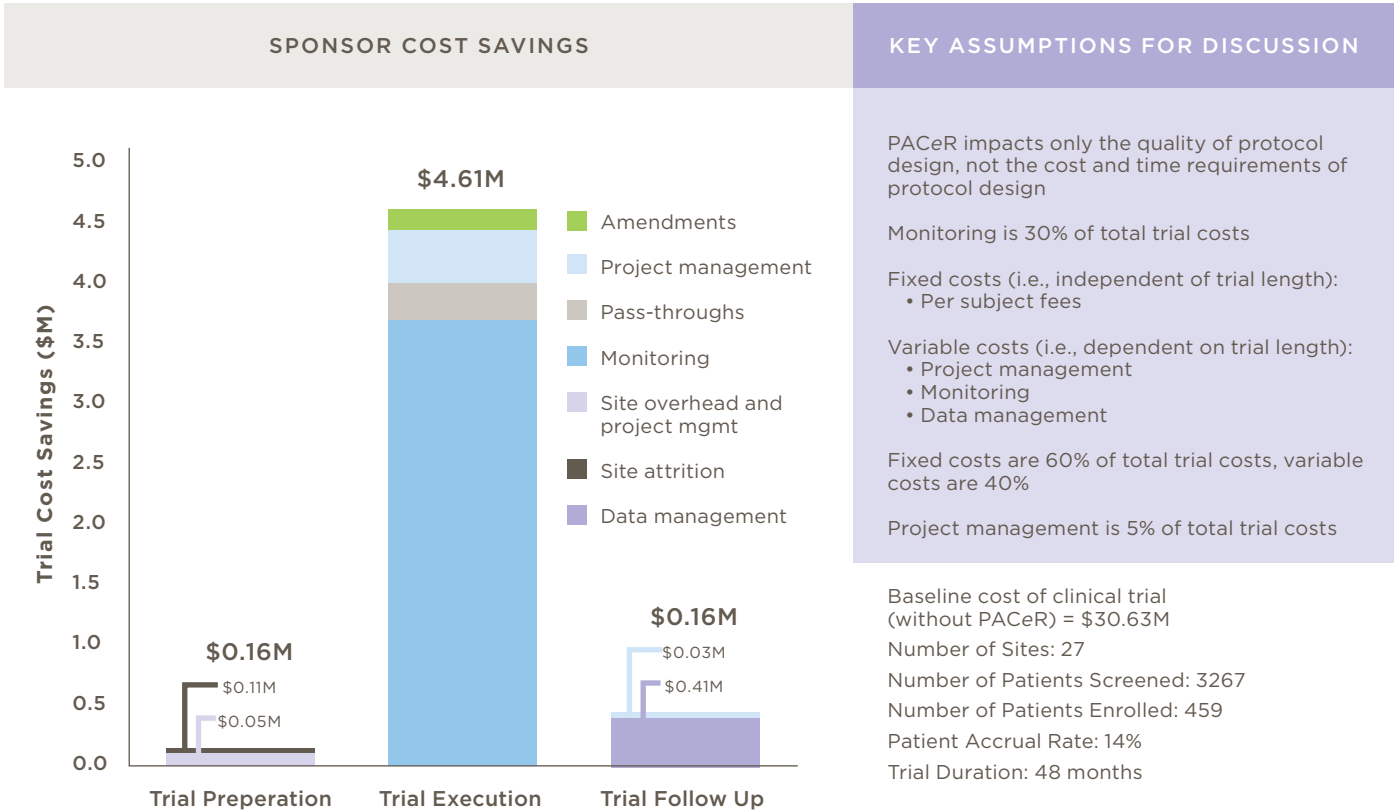
**PACeR's Objective Is to Create Value for Sponsors and Sites
(Including Principal Investigators) Where Clinical Trials are Performed**



Estimates of PACeR value are roughly consistent with comparable alternatives used today. To support clinical trial modeling, sponsors typically pay between \$50,000 and \$250,000 for access to claims databases from health plans and for clinical data from individual hospitals. These alternatives are

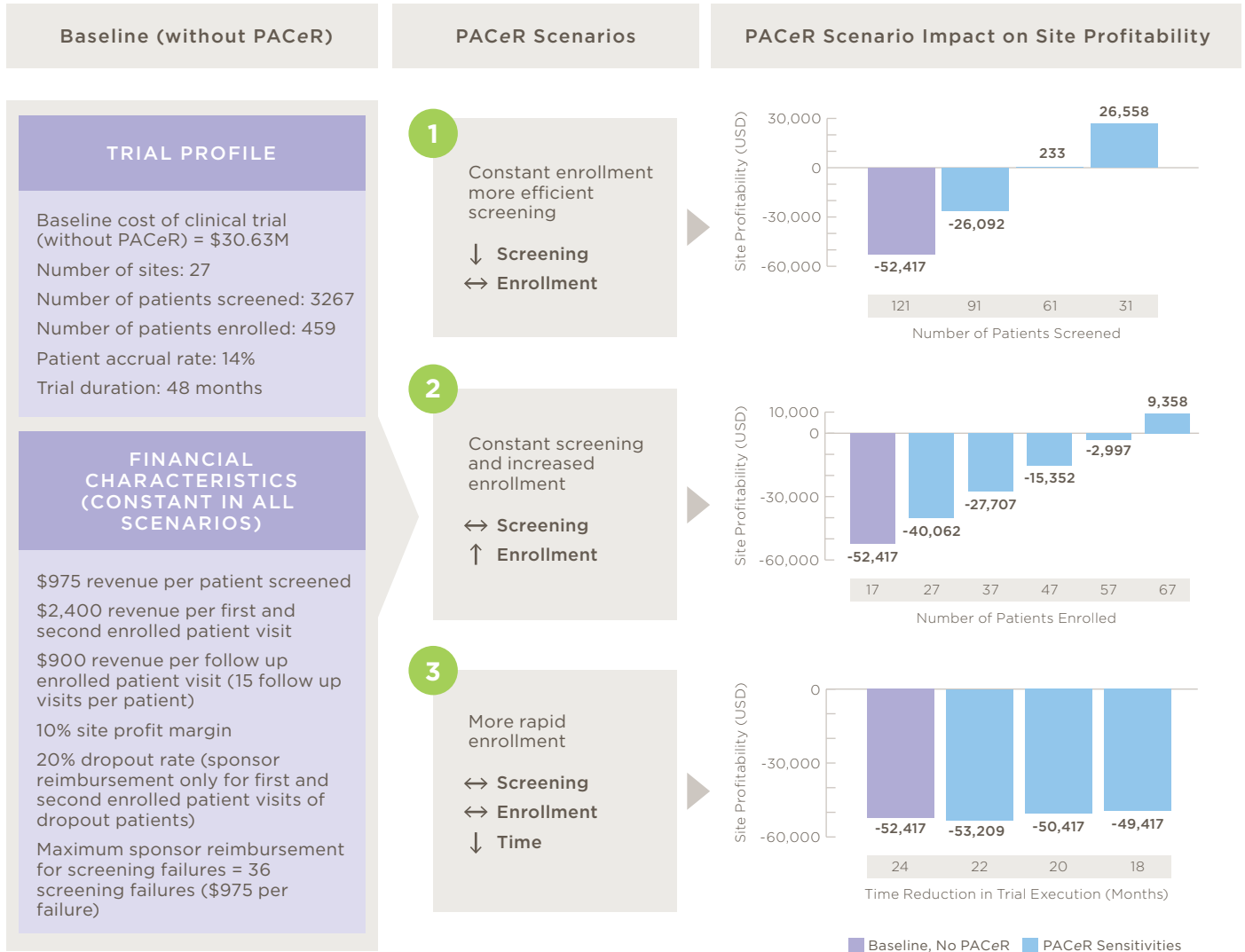
not strictly comparable, since the access is typically an actual database, as opposed to the analyses PACeR would provide. However, unlike the alternatives, PACeR has significant data quality advantages, and enables sponsors to follow up with all participating institutions.

PACeR IMPACT AND COST SAVINGS ASSUMPTIONS FOR SPONSORS ACROSS THE CLINICAL TRIAL PROCESS



Representative Trial Profile: Phase III, Oncology, Randomized, 27 sites with 121 patients screened per site, 15 follow-up visits per patient, three amendments per trial, 36 months required to screen/enroll patients.
 Sources: Site Budget Reports from Vanderbilt University Medical Center, Weill Cornell Medical College, University of California San Francisco Medical Center; "Effective financial management of Clinical Trials: Issues and Challenges" Lampasona, et al. Emory University; "Developing an investigator site budget for clinical trials" American Society of Clinical Oncology, 2007; "Prospective Evaluation of Cancer Clinical Trial Accrual Patterns: Identifying Potential Barriers to Enrollment" Lara, et al. *Journal of Clinical Oncology* 2001; "The Phase III Trial in the Era of Targeted Therapy: Unraveling the "Go or No Go" Decision" Roberts et al. *Journal of Clinical Oncology* 2003; Quintiles CRO budget .

POTENTIAL PACeR SCREENING AND ENROLLMENT SCENARIOS HAVE VARYING IMPACT ON SITE PROFITABILITY



1. Representative Trial Profile: Phase III, Oncology, Randomized, 27 sites with 121 patients screened per site, 15 follow-up visits per patient, three amendments per trial, 36 months required to screen/enroll patients.

Sources: Site Budget Reports from Vanderbilt University Medical Center, Weill Cornell Medical College, University of California San Francisco Medical Center; "Effective financial management of Clinical Trials: Issues and Challenges" Lampasona, et al. Emory University; "Developing an investigator site budget for clinical trials" American Society of Clinical Oncology, 2007; "Prospective Evaluation of Cancer Clinical Trial Accrual Patterns: Identifying Potential Barriers to Enrollment" Lara, et al. *Journal of Clinical Oncology* 2001; "The Phase III Trial in the Era of Targeted Therapy: Unraveling the "Go or No Go" Decision" Roberts et al. *Journal of Clinical Oncology* 2003; Quintiles CRO budget.

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FUNDERS

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F. Hoffmann-La Roche, Ltd.

Johnson and Johnson

Merck & Co., Inc.

Oracle

Pfizer, Inc.

Quintiles

ACADEMIC MEDICAL CENTERS/HOSPITALS

Albany Medical Center

Bassett Medical Center

Continuum Health Partners

New York Hospital Queens

North Shore-Long Island Jewish Health System

NYU Langone Medical Center

Roswell Park Cancer Institute Corporation

Stony Brook University Medical Center

SUNY Downstate Medical Center

SUNY Upstate University Hospital

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