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Prerequisites to Implementing a Pharmacogenomics Program in a Large Healthcare System

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Introduction

Pharmacogenomics (PGx) technology is advancing rapidly; however, clinical adoption is lagging. The Indiana Institute of Personalized Medicine (IIPM) places a strong focus on translating PGx research into clinical practice. We will describe what have been found to be the key requirements that must be delivered in order to ensure a successful and enduring PGx implementation within a large healthcare system.

Over the past 5 years, a technological revolution of new devices has helped to move PGx from the research bench to CLIA-approved laboratories while costs of performing PGx testing have substantially declined. In 2001 Francis Collins projected that by 2020 PGx would be the standard practice for predicting drug responsiveness for many disorders and drugs[1]. A review of published PGx articles demonstrates that clinical research has been rapidly expanding[2], however as AR Shuldiner, et.al noted “there are a number of substantial barriers to the adoption of pharmacogenetic tests into clinical practice”. Two key drivers that are holding back the adoption of PGx testing are the lack of expansive, strong clinical evidence supporting the routine and prospective use of genetic testing and the void of health economic data linking genetic testing with reductions in cost of care. In 2009 the Clinical

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Conflicts of Interest

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Pharmacogenetics Implementation Consortium (CPIC) was organized with the first guideline published in 2011. Since that time 12 different guidelines and 4 updates have been published covering over 26 medications. Despite this extensive and ongoing work there remain a significant number of drugs without dosing guidelines that contain FDA issued drug-gene "Black Box" warnings[3]. It is also important to recognize that any change to clinical standards of care takes time. The National Institute for Health and Clinical Excellence reported that a new clinical procedure can take up to 3 years to become standard of care. The time required for clinical translation (research to clinical adoption) often exceeds 10 years (range of 10 to 25 years).

The IIPM serves both the Indiana University Health System (over 2.5 million outpatient visits and 145,000 admissions annually) and the Eskenazi Health System (a safety-net health care system which handles over 1.2 million outpatient visits and 15,000 admissions annually). The successful clinical implementation of a PGx program at a large healthcare system requires alignment of clinical and administrative stakeholders including: Senior executive leadership (CEO/President, Chief Medical Officer, Chief Information Officer, Chief Financial Officer and Chief Legal Officer), senior clinical leaders (clinical divisions, nursing and pharmacy), pathology, Pharmacy and Therapeutics committee members, patient advocates and third party payers. Prior to implementation, committees should be established representing these stakeholders. Alignment of common interests and concerns must be obtained within and across administrative and clinical stakeholders groups. This alignment is crucial if the PGx initiative is to be funded and clinically adopted into the standard of care (see figure 1)

The IIPM PGx implementation team worked with key stakeholders and identified critical deliverables for each of the groups. After soliciting team members from within the institution's stakeholder domains, strategically important working groups (aligned with critical deliverables) were created.

- **Clinical Implementation**: Comprised of scientists, physicians, nurses and clinical pharmacists, this team's objective was to select which gene-drug pairs would be implemented and prepare the clinical direction to be provided. CPIC guidelines on gene/drug pairs were used to help select targeted medications and the micro-array architecture. Decisions were based on the clinical evidence associated with each reportable SNP. Based on the above analysis and a review of new prescriptions written within the Eskenazi Health System, 24 targeted medications, 16 genes and 51 clinically validated allele variants were selected for implementation. The clinical implementation team is an evergreen group that continues to meet and review new scientific and clinical evidence.
- **Laboratory Implementation**: This working group included individuals experienced in PGx testing and establishing a clinical genetics laboratory. They were tasked with identifying and selecting the state of the art equipment required for the genetics lab, staffing the laboratory with highly qualified personnel familiar with CLIA requirements, laboratory reporting and capital/operating budgets. Within the new 1,000 square foot laboratory, the team, after extensive research,

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selected state of the art micro-array, automated DNA extraction and sample handling systems.

- **Education and Marketing**: Basic education on clinical genetics and the evolving science of PGx must be provided to the clinical teams (physicians, advanced practice nurses, registered nurses and pharmacists) if a successful implementation is to occur. Clinicians who treat outpatients must also clearly understand the tests that are available, when to order them and what to do in the event of receiving "clinical alerts". A multifaceted approach was applied. We invited nationally known experts to take part in a symposium to address clinical implementation challenges. Nurses were provided with internally created on-line education with more than 500 completing the course. IIPM staff conducted Grand Rounds focused on PGx and held a full day CME program for physicians, nurses and clinical pharmacists. In addition to clinical training, lay-education and a public relations campaign are also paramount to a program's success. With today's direct-to-consumer advertising about genomic testing, consumers are trying to understand the benefits and risks and look to their healthcare professionals for answers. Because dissemination of somewhat "uncontrolled" and sometimes misleading information creates challenges for the healthcare professional, a successful system-wide pharmacogenomics program must also address patient and community member education[4].
- **Administration**: The administration of a clinical PGx program requires a multi-disciplinary approach with a specific focus on financial, legal, and regulatory issues. Having a team member with strong financial modeling skills is very important for project success. An individual with current knowledge of the rapidly changing reimbursement and local, state and federal regulatory requirements is critical to address the difficult questions frequently asked by the system's senior leadership teams. By using real cost and reimbursement information and system-based clinical and financial outcomes data, modeling short and long-term cash flow and return on investment is often required to justify up-front start-up costs. In addition, as part of Indiana University, the IIPM has access to faculty and graduate students from the IU Kelly School of Business who assisted in financial modeling of the program, thus helping to cost-justify the establishment of the new laboratory (space, equipment and staff).
- **IT/Workflow**: IT solutions must consider clinical workflows and facilitate the process for caregivers to order appropriate pharmacogenomic tests. In addition, test results must be easy to understand, include clinically validated guidelines, if available, and be integrated into the medical record system. By including clinical pharmacists, physicians and nurses into the decision making process, the IT/Workflow team can identify "blind spots" and implementation traps. PGx testing must be integrally linked to the EMR (especially for ICD-9 diagnosis coding) and to the pharmacy ordering system (linking Rx orders to alerts for pharmacogenomic tests). These links are not commonly found in most commercial hospital IT systems. Thus, a successful PGx implementation must plan for the cost and time to build these links and create the clinician alerts and test results that include the

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approved therapy guidelines. Within the Eskenazi Healthcare System, the hospital information system was created and is maintained by the Regenstrief Institute. The Regenstrief Medical Record System compiles laboratory results, orders, medications, registration information, nursing assessments, EKGs and other clinical data. By working with the Regenstrief team, PGx alerts and result reporting can be seamlessly incorporated into current processes and clinical workflow patterns. An example of a typical PGx alert is depicted in figure 2.

The IT/Workflow team also provided access to system-wide data on the Rx and test frequency along with costs associated with adverse events related to targeted medications. These data can then be used for health economic modeling, thus balancing the total financial picture associated with the adoption of PGx testing[5].

In conclusion, the technology to perform high quality PGx testing is readily available, able to be incorporated into a CLIA certified laboratory and is increasingly affordable. However, these factors alone do not guarantee a successful implementation of a PGx program. Careful planning, data collection and clarity in understanding and addressing stakeholder concerns must all be considered. Clinical workflows and system-wide education are essential to support an enduring program. A high priority in the early planning stages must be selecting PGx tests that are relevant to the patient population. These tests must provide clear, evidence-based, well documented direction for therapy changes. In addition, the PGx program must be dynamic; ongoing scientific and clinical reviews of the literature must be iteratively incorporated into the program. Once implemented, it is also important to continue to capture data on medication changes, adverse events and costs associated with targeted medication efficacy failures, as these data can be used to validate the cost effectiveness of a PGx program.

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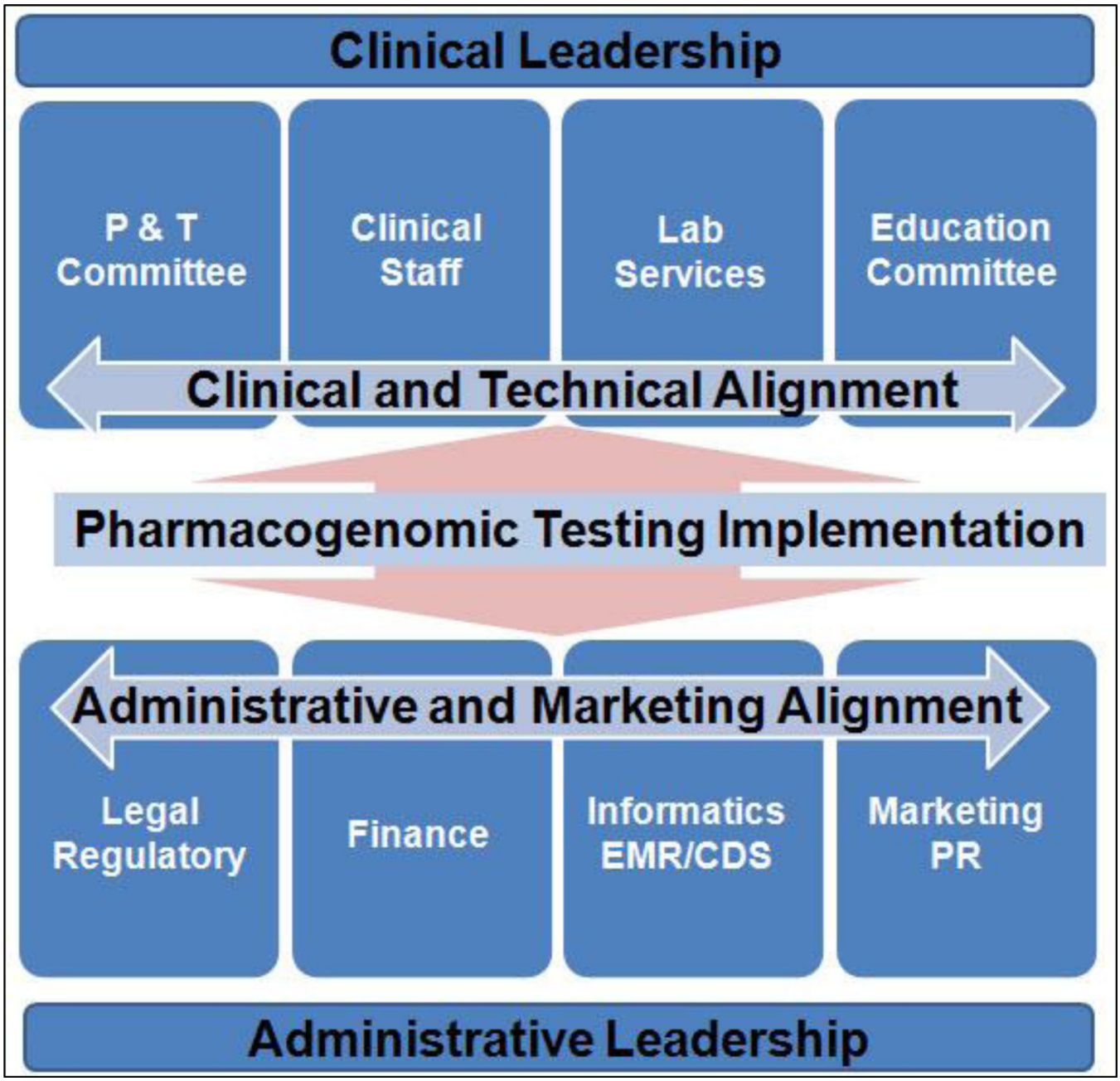

Figure 1.
Alignment required within Clinical and Administrative groups in order to facilitate PGx Implementation that is effective and enduring

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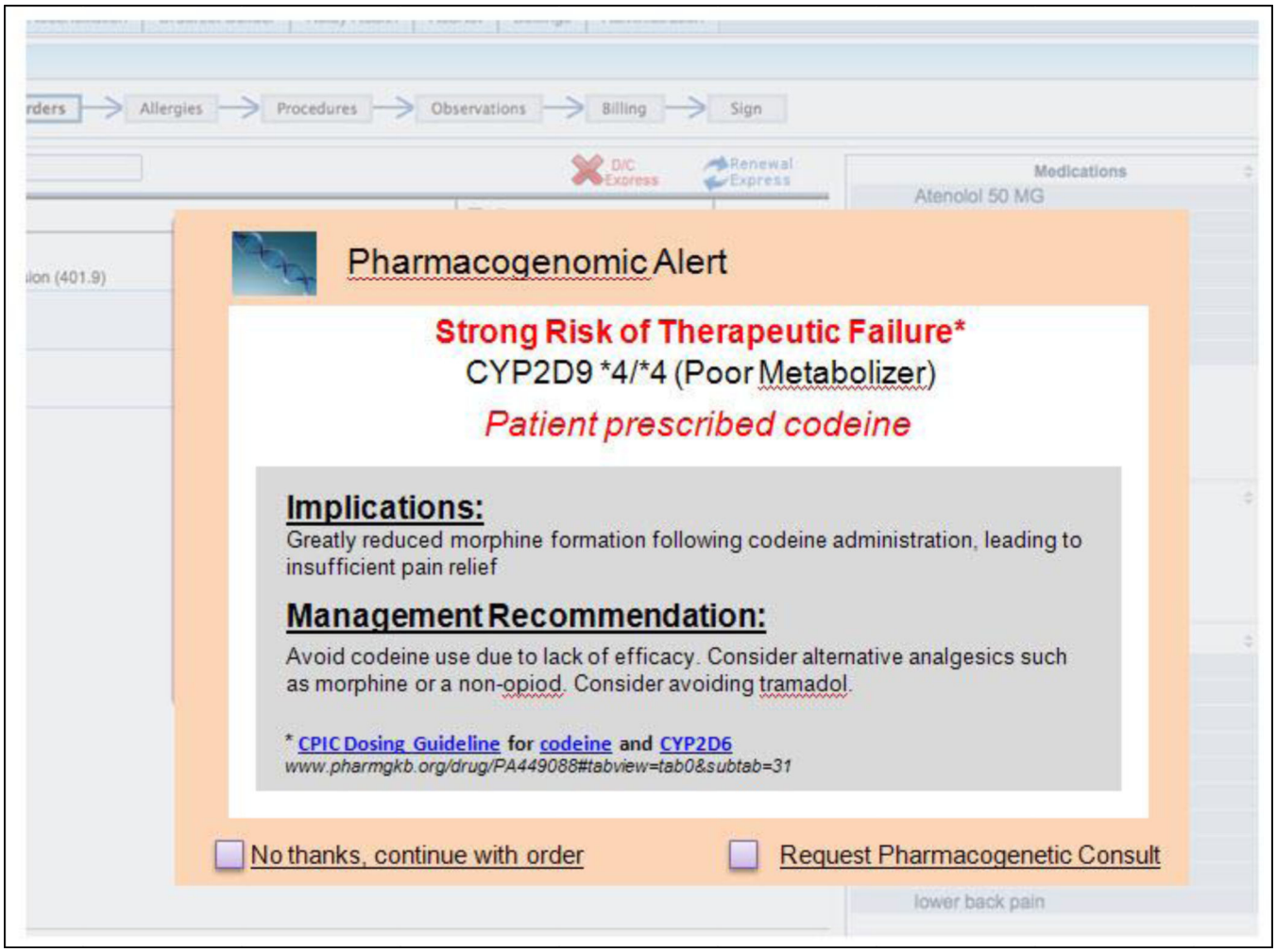

Figure 2.
Is an example of how the Eskenazi EMR PGx Alert may appear when fully implemented