eMERGE Network Steering Committee Meeting
February 9-10
Bethesda, MD

Attendance

Network Members in Attendance

Geisinger	David Carey
Geisinger	Robert Elston
Geisinger	Andy Faucett
Geisinger	Samantha Fetterolf
Geisinger	Glenn Gerhard
Geisinger	Helena Kuivaniemi
Geisinger	Gerard Tromp
Geisinger	Diane Smelser
Geisinger	Janet Williams
Geisinger	Marc Williams
GH/U WA	Malia Fullerton
GH/U WA	Gail Jarvik
GH/U WA	Eric Larson
GH/U WA	Kathleen Leppig
GH/U WA	James Ralston
Marshfield	Murray Brilliant
Marshfield	Jay Fuehrer
Marshfield	Simon Lin
Marshfield	Cathy McCarty
Marshfield	Peggy Peissig
Mayo	Sue Bielinski
Mayo	Chris Chute
Mayo	Mariza de Andrade
Mayo	Matt Durski
Mayo	John Heit
Mayo	Iftikhar Kullo
Mayo	Jyoti Pathak
Mount Sinai	Erwin Bottinger
Mount Sinai	Steve Ellis
Mount Sinai	Omri Gottesman
Mount Sinai	Carol Horowitz
Mount Sinai	Yolanda Keppel
Mount Sinai	Kash Patel
Mount Sinai	Saskia Sanderson
Mount Sinai	Chunhua Weng
Northwestern	Rex Chisholm
Northwestern	Abel Kho
Northwestern	Laura Rasmussen-Torvik
Northwestern	Luke Rasmussen
Northwestern	Maureen Smith
NHGRI	Joy Boyer
NHGRI	Lucia Hindorff
NHGRI	Rongling Li
NHGRI	Nicole Lockhart
NHGRI	Teri Manolio
NHGRI	Ian Marpuri
NHGRI	Jean McEwen
NHGRI	Brad Ozenberger
NHGRI	Erin Ramos
NHGRI	Karen Rothenberg
NHGRI	Laura Rodriguez
NICHD	Roz King
NCI	Laura Buccini
NCBI	Mike Feolo
Penn State	Gretta Armstrong
Penn State	Marylyn Ritchie
Penn State	Shefali Setia
Vanderbilt	Ellen Clayton
Vanderbilt	Dana Crawford
Vanderbilt	Josh Denny
Vanderbilt	Dan Roden
CC	Melissa Basford
CC	Jonathan Haines
CC	Brad Malin
CC	Lauren Melancon

Network Invitees and Guests

Aurora Healthcare	Michael Michalkiewicz
Children's Hospital Boston	Ingrid A. Holm
Johns Hopkins	Michelle Huckaby Lewis
Children's Hospital Of Philadelphia	John Connolly
Children's Hospital Of Philadelphia	Brendan Keating
Cincinnati Children's Hospital	Beth Cobb
Cincinnati Children's Hospital	John Harley
Complete Genomics	Rick Leach
Complete Genomics	Raith Erickson
Complete Genomics	Damon Hostin
USAF	Jeff Lin
USAF	Ronald Miller
USAF	Cecili Session

Decisions and discussion

NHGRI Program Office Report – Rongling Li

Although NIH funding will be unchanged for FY12, NHGRI will see a slight budget increase for FY12. Rongling also reported on NHGRI's proposed reorganization into seven divisions. NHGRI is currently holding public meetings to discuss this plan. She highlighted two meetings held by NHGRI in December- Characterizing and Displaying Genetic Variants for Clinical Action (co-sponsored with Wellcome Trust) and Genomic Medicine II. She reported that the applications in response to the RFA for eMERGE Phase II – Pediatric Study Investigators will be discussed at Council in February, with the earliest funding date in May as stated in the RFA.

Goals for the meeting:

- Interact among sites and workgroups to identify potential new network-wide projects
- Initiate possible interactions or collaborations with relevant networks in phenotyping, discovery of new genomic variants, and clinical implementation
- Discuss responses to the ESP recommendations

Takeaways for the meeting:

- Refine goals, milestones, and timelines of the workgroups
- Build relationships with other networks, particularly the Return of Results Consortium and Air Force PC2Z program, and possibly identify new projects
- Determine next steps for the eMERGE PGx collaboration
- Approve the responses to the ESP recommendations

Return of Results Consortium – Jean McEwen (NHGRI)

The newly formed Return of Results Consortium is studying issues associated with whether, when, or how to return research results and incidental findings in genomics studies or clinical care. NHGRI, NCI, and NICHD all help to fund four categories of projects. R21 grants fund analytical research on normative and legal issues. R01 grants fund empirical research with direct interactions with research participants or others in current genomics projects. U01 Clinical Sequencing Exploratory awards study the generation, interpretation, and return of research results in clinical care. Lastly, there are investigator-initiated projects that did not fall into a specific RFA. The studies all encompass a wide range of methodologies and research populations. The consortium hopes to address common issues around RoR, explore opportunities for synergy among studies, develop joint publications and presentations, and identify areas of consensus that could be used for policy recommendations. The consortium has many overlapping study areas and investigators with eMERGE. The CERC co-chairs regularly participate in consortium activities. The RoR consortium will support the CC to help facilitate collaborations.

eMERGE PGx Initiative – Dan Roden

Theoretically, each site would identify about 1000 target patients to consent. These individuals would be sequenced on the VIPgx platform which covers 84 pharmacogenes. Some group (like PGRN) would develop a list of actionable variants. eMERGE would then develop a validation platform, interface the variants in the EMR, figure out how to display the data, and create decision support. Outcomes include performance metrics for the assay and the clinicians as well as healthcare impact. Variants of unknown significance could be reinterfaced with the system.

Dan compared this initiative to Vanderbilt's PREDICT program, where decision support for specific medications fires when prescribed to a patient. Issues include target patient set, identification of actionable variants, validation steps, EMR deposit, decision support, tracking outcomes, variants of unknown significance (VOUS), and budgets.

eMERGE PGx Discussion

The probes are still under construction in Iceland, but should be shipped by the end of February. The probes would be validated against a panel of 48 HapMap samples, then a group of 32 trios containing 33% of each Caucasian, African-American, and Latino populations. Sites thought we should identify general internal medicine patients who are at high risk for receiving a drug that would be considered actionable. We should not underestimate the amount of resources needed for EMR deposit, as well as the price of sequencing. The group generally agreed that we need to run a parallel validation step using something like the Illumina ADME chip or an Ion Torrent platform, but we would like to eventually move away from this. Decision support will also need to determine where, when, and how to display results. Luckily, for PGx variants, once you input the first gene/drug pair, similar architecture can be used for other gene/drug pairs. In terms of budget, sequencing could take up a large portion of the budget and affect the amount left for validation. Teri suggested that the project should be designed and then scaled to meet budgetary restrictions. Outcomes measured could include how often genotyping is successful, how often data enters the chart, whether physicians utilize data in the chart, how often decision support fires, and medication usage.

Site Presentations

Marshfield Clinic- Cathy McCarty

Marshfield has developed electronic algorithms for glaucoma/ocular hypertension, dry eye, and acute macular degeneration. Obstacles include a lack of eye-specific PGx data and certain ophthalmic data that is hard to extract into the EMR. GWAS will begin in year 2, and the community advisory group has started focus groups with physicians and patients. Marshfield is currently redesigning its EMR so that the right information is available at any time on any device, including tablets. This will help align the EMR interface with the current clinical workflow so that it is searchable, intelligent, data-driven, and actionable. Pilot testing should be done by the end of 2012. Marshfield is also designing a new web form for data capture of ophthalmology information (like IOP and visual acuity) that will be shared with the Network. Another study is working on identifying individuals with braf and kras mutations – they can narrow down who has this, but then they have to look through scanned records. The site is working on integrating PhenX measures into its site to look at GxE interactions. They will also be using physical activity and food frequency questionnaires to do GxE. The initial phenotype will be cataracts. They are now trying to add regulatory and conserved regions to Biofilter. ATHENA will also use environmental covariates to look at higher order effects.

Vanderbilt –Josh Denny

Vanderbilt has completed its phenotyping algorithms for ACEI-related cough, LDL response to statins, C. diff colitis, and VTE. ACEI cough allergies are documented in the chart. LDL response is the difference between LDL before statin and the median LDL within 18 months after starting on statins. As a replication exercise, Vanderbilt ran a PheWAS on the GWAS

catalog. 173/516 (33.5%) of all matching proper genome-wide associations were replicated. SNPs with lower p-values were more likely to replicate. For genetic risk scores, they have conducted literature reviews to look for variants identified in GWAS or meta-analyses. These variants are then classified by population, and risk scores would be used to classify cases and non-cases. Preliminary analyses have used PAGE, PubMed, and the GWAS catalog to find variants. Ethical considerations for PREDICT include decision support to change clopidogrel prescriptions to prasugrel. Focus groups have shown that patients like the idea of pharmacogenomics and do not feel reassured by GINA. Patients also have a wide range of preferences on their desire to know about their genetic risk, but they want to decide what they find out. They are also mapping the incidentalome to see what genes and variants those studied in PREDICT are associated with.

Geisinger - David Carey
Geisinger has completed the AAA algorithm which is now being internally validated. They are testing NLP to extract aortic diameter values over time to look at aortic diameter expansion. Ocular hypertension/glaucoma, PAD, resistant hypertension, and cardiorespiratory fitness are all in progress. Children are now beginning to be enrolled in their biobank. They have submitted a concept sheet for an AAA GWAS which was approved by all 7 sites. This data will help the site participate in an international AAA GWAS meta-analysis. Geisinger is now starting implementation of IL28B genotyping for chronic hepatitis C management. Specific IL28B genotypes have been found to help clear HCV infection more quickly and predict response to standard drug therapies. Treatment-naïve patients have HCV genotyped determined. Based on this genotype, they will then be genotyped for IL28B. IL28B genotype will determine the treatment protocol the patient receives. Patients that do not respond well can be switched back to standard protocol. Another study uses patients who previously received the standard of care and uses genotyping to determine whether to continue therapy. Workflows are being developed, and their goal is to go live with this project by the second quarter of 2012.

Mayo Clinic – Iftikhar Kullo and Chris Chute
Mayo has completed phenotyping algorithms for cardiorespiratory fitness and VTE and is still working on heart failure. They published a paper on a genetic risk score for coronary heart disease which resulted in 30% risk reclassification. They are now working on tools for communication of genetic risk such as pictograms. In terms of EMR integration, Mayo's strategy is to develop a system where a collaborative knowledge resource base can integrate with decision support, EMR, and genetic information. Enhanced order and support for the EMR, lab, and pharmacy will be developed in addition to improved decision support, integration with AskMayoExpert, and increased infrastructure for genomic data integration. Mayo will also be conducting a RCT for genomic risk of CHD. 150 patients from eMERGE I with intermediate 10-year CHD risk will be enrolled and have blood drawn. They will be randomized to genotype-informed risk and Framingham risk arms, and both arms will meet with genetic counselors. Outcomes measured include understanding of test results and risk, emotional response to results, and motivation for behavioral change. Enrollment and genotyping will start this summer. They have been meeting with genetic counselors frequently to talk to them about returning risk results to patients. Family history could potentially be added at a later point.

Mt. Sinai – Erwin Bottinger
Mt. Sinai has enrolled over 20,000 patients in its biobank and seeks to sequence 20,000 people on the OmniExpress and exome chip. Yolanda Keppel has joined as program manager, and Jean-

Sebastien Hulot and Stuart Scott will work with pharmacogenomics after previous experience with PGRN. They have completed phenotyping algorithms for hypertension-associated CKD and diabetes-associated CKD and have implemented the resistant hypertension algorithm from Phase I. They are also working on an algorithm for drug-induced liver injury. They have conducted many focus groups and recently published a paper showing that minorities are aware of the role of genetics in chronic disease and want to know risk results for multiple diseases. Validation of possible clinical SNPs is now ongoing in multiple populations. Mt. Sinai has been working with Epic to improve its EMR functionality, including real-time decision support two-way HL7 message transport, SmartSet order advice, and best practice alerts. Their pilot project for pharmacogenomics in decision support is pending IRB submission. Their project on risk advice for individuals with hypertensive kidney disease of African ancestry is also in initial phases.

Group Health – Gail Jarvik and Eric Larson

Group Health is currently working on C. diff, onychomycosis, and shingles under its BuGWAS phenotypes. It is also participating in collaborations for hemochromatosis penetrance and CAD. For EMR integration, they plan on participant-observation of the Genomics Improvement Project to improve the efficiency of how we evaluate evidence for genomic findings before they enter clinical care. Automated decision support is complete for Stevens-Johnson syndrome, with warfarin and clopidogrel support on the way. Eleven qualitative needs assessment interviews with health system leaders have been completed to discuss attitudes towards integration at GHC. Guides are being finalized for focus groups with GHC physicians and patients. They are working on developing prototypes to support POC decisions for ordering genetic testing for HLA-related adverse drug reactions and prescribing carbamazepine, allopurinol, and abacavir. Pop-ups would appear in the Epic EMR for both orders and prescriptions.

Northwestern - Maureen Smith and Luke Rasmussen

Northwestern is working on NLP for its lower GI algorithms. It is also in the process of validating algorithms from Vanderbilt and Group Health. Manual chart review showed that the colon polyp algorithm had a PPV of 94% and the diverticulosis algorithm had a PPV of 86%. More covariate data such as age, BMI, and other diagnoses will be collected. Phase II data has been sent to the Coordinating Center already. Their lipids GWAS paper is currently under review. For EMR integration, year one will focus on simple representation of variants in Epic using HL7 with simpler decision support, while Y2/Y3 will focus on more sophisticated data using a data integration workflow with logging and auditing framework and integration with MyChart. Design of the decision support system is underway. Northwestern has also conducted physician surveys on awareness of genomic risk profiling. 92% of physicians had heard of genomic risk profiling, but 85% had never ordered it for a patient. Physicians thought clinical validity, testing limitations, and disease prevention were the three most important topics to discuss alongside GRP, but 60% of them felt unprepared to discuss ELSI implications of GRP results. They cited cost, lack of testing knowledge, and unproven clinical validity as barriers to ordering GRP.

Coordinating Center – Josh Denny

The Coordinating Center presented a cross-site Record Counter (RC) based off of a similar product developed at Vanderbilt. The RC can give estimates of phenotype counts across the Network. The current version uses demographic data, ICD9 codes, and site. Access to the RC would be restricted to Network members. Users are able to query the data using and, or and not

statements and the tool returns counts stratified by demographics and site. The system could help prioritize certain diseases based on sample sizes and study feasibility. To use the tool, all sites will need to give approval to use the data. The DUA covers usage of Network data is this way. Issues around sharing the Record Counter externally would need to be explored. More ICD9 codes and data would update the system and increase its utility.

The CC also presented PheKB.org, a collaborative, searchable home for ePhenotyping that would allow for the collection of algorithms at different stages of completion, capture of performance data, annotation of site-specific implementation issues, version control, and algorithm sharing. It would also provide email updates when an algorithm has been changed.

Air Force PC2Z Program – Cecili Sessions

The Patient-Centered Precision Care (PC2Z) Program seeks to advance personalized medicine for active duty members of the Air Force. Funded through 2018, the program has collaborations with NIH and other institutions. For knowledge generation, they seek to create a biobank of full sequence and clinical data to expand evidence for clinical utility of genomic data. They are developing a medical informatics system that can be incorporated into current and future DoD tools. Education for physicians, patients, and medical school students is also a part of the program. ELSI research considers data privacy and psychological issues related to many common psychiatric disorders that soldiers face. Lastly, they will develop a diagnostic system that enables the delivery of genomic data into the workflow. There are ~35,000 active duty personnel and 2.6 million eligible beneficiaries. The Military Health System has extensive health records for tracking patients. Medical record data is recorded at all military treatment facilities worldwide and includes external care if the patient presented military identification. PC2Z uses Coriell's standards for genotyping and uses the Affy 6.0 chip. They also phenotype for the same traits as Coriell – obesity, T2D, hypertension, and some PGx traits. The plan is to enroll 2000 active duty Air Force personnel by Q1 of 2013. Individuals enrolled in the study were consented for Whole Genome Sequencing (WGS). Data limitations include a relatively healthy active duty population without diseases that aren't compatible with service. Air Force physicians can only see deidentified data so that patients will not worry that data will be used against them. They are not allowed to incorporate this data into the EMR or make it available to superiors. GINA also does not apply to servicemen. There are additional regulations with contacting non-governmental organizations. If the Air Force were to become a Network member, position papers would have to be drafted for Air Force counsel which hinders their speed.

Privacy Update – Brad Malin

Right now, data privacy has three big issues – how data gets de-identified according to federal policy, how we can assess re-identification risk, and how data can be formally protected if you want to share more than federal policy allows. OMB (Office of Management and Budget) has cleared the OCR (Office for Civil Rights) /HHS Guidance on De-Identification via the HIPAA Privacy Rule. This guidance will hopefully clear up questions around Safe Harbor. Two papers have been published on anonymization of longitudinal EMR data and attacks on health systems. To study phenotype trajectories for patients, there is a tradeoff between knowing age and diagnosis that needs to be understood better. In the systematic review of actual EMR re-identification events, most events concerned data that was not properly de-identified to begin with. They are now using VDART to find re-identification policies of demographics and evaluate clinical profile anonymization strategies.

Review of ESP Recommendations to the Network – Rex Chisholm
The ESP provided recommendations for network improvement in multiple areas – visibility, external linkages, research beyond GWAS, leadership and integration, network functioning, and ethics. eMERGE needs to continue to put out publications (particularly cross-network) and deliverables to maintain visibility. We have begun exploring external collaborations with CTSAs, SHARP, and UK Biobank, as well as external groups who have attended prior Steering Committee meetings. Sites have worked extensively with EMR vendors since the panel at the last SC meeting. The eMERGE PGx project is an example of a collaboration outside of GWAS. Dr. Charis Eng was added as an ESP member to replace Dr. Marc Williams, who is now engaged with eMERGE as one of the PIs at Geisinger Clinic. Senior leadership has been retained, and the Network will work to think of projects to better integrate the pediatric sites. Working groups have developed charters and timelines, and some of the groups have even begun to meet together at SC meetings. CERC is working to address its broad portfolio with other partners like RoR Consortium and Clinical Sequencing Exploratory centers. Marshfield is collaborating with other sites to expand their eye phenotypes, and the new sites have added more minorities for better phenotype validation. Overall, the sites and workgroups need to connect more to expand beyond GWAS, and the Network as a whole needs to maintain a high output level.

Workgroup Updates

EHR Integration – Erwin Bottinger
The EHR Integration (EHRI) workgroup will develop eMERGE II consensus and concepts for EMR integration of genomic information and delivery of clinical genomic decision support utilizing EMR. They will develop decision support tools and best practices for them, address challenges and approaches for using WGS/WES data in EMR, interact with EMR vendors, and support usage of CDS in clinical implementation projects. EHRI will work to develop a shared knowledge base by engaging PGRN/CPIC to translate CPIC guidelines into "executable rules" (reproducible algorithms that make decisions for what the rule is and when CDS fires). They will also compile a knowledge base for implementation projects around common diseases risk genetics projects. EHRI will be involved with creating standards with other leading groups such as HL7, CDSC, and ISO. Another proposal is to propose an expert eMERGE panel at the next AMIA meeting led by Joseph Kannry. The panelists would cover knowledge bases, decision support, implementation issues, and standards creation. EHRI will also advise local sites on creating decision support for actionable variants and measuring outcomes.

Actionable Variants – Gail Jarvik and Iftikhar Kullo
In eMERGE Phase I, the Network concluded that Turner and Klinefelter's syndrome and Factor V Leiden homozygotes genotypes could be returned, while HFE mutations were more troublesome. Actionability and clinical utility depend on individual context and local politics. The Phase II Actionable Variants group seeks to define an initial set of variants that are potentially useful for clinical practice, focusing on common disease risk variants and PGx variants. The group will look at levels of evidence for the variants and the cost/benefit of using them in care. Current priorities include risk scores for CVD, AAA, PheRISK, macular degeneration, CKD progression in African-Americans, and possibly atrial fibrillation. The group will assess whether risk scores improve current classification of risk and impact physician and patient behaviors. They will also develop tools to help implement risk scores like communication devices. PGx variants will be headed by PGRN. Limitations include imprecision, usage of an additive model, adding new variants to risk scores, restriction to European populations, and odds

ratios vs relative risk. Other ideas from the sites included assessing where a person is on the behavioral continuum of change and seeing if they move post communication of genetic risk, using risk scores to increase precision for those who are and aren't at risk for disease progression, and determining what to do with VOUS. We also need to be aware of what patients actually want to find out and differentiate between risk for a disease and risk for disease progression. The group also expressed interest in "how" results such as risk and risk scores are best returned, given that most work has been done with return of Mendelian genetics. The workgroup also received comments concerning the appropriateness of the workgroup name. A suggestion was made that the workgroup should be called Return of Results rather than Actionable Variants to better define the mission of the workgroup.

Genomics – Dana Crawford and Marylyn Ritchie

The current focus of the Genomics group has been to complete imputation. The current reference set is a cosmopolitan panel from the 1000 Genomes released at ASHG in October 2011. The panel has 14 million variant calls/phased genotypes and includes SNPs, indels, and deletions for 1092 individuals. eMERGE I data is being imputed using the same panel without indels via BEAGLE, although they are considering switching to IMPUTE2 in the future. Data was randomized by site, sex, and race. Out of ten data groups, nine have finished running. The eMERGE I dataset will be combined and analyzed for various quality metrics and stored in multiple data file types. 15 million imputed SNPs are currently in the eMERGE I dataset. For Phase II, sites will send their data to the CC in the spring to be imputed. CC will merge the imputed Phase I and II datasets for QC. The first data freeze will take place in Spring 2012, resulting in v1 of the Phase II dataset. CC will decide whether to merge all data that comes in after the Spring 2012 freeze with v1 or create v2. The group will be discussing how to integrate phenotype data with the samples – the Phase II data will have 21 new phenotypes and 4 Phase I phenotypes. The exome chip is also being considered.

The resistant hypertension GWAS was underpowered to find anything in coding regions, but the new site data and new data from the Phase I sites could be added for discovery. We could also look at known blood pressure variants and see where they appear in the current GWAS. Possible replication would be in another consortium site with blood pressure data. Geisinger is leading work with an AAA consortium where the other sites could be collaborators. Another meta-analysis opportunity involved Wellcome Trust and will need the imputed eMERGE dataset. The group recommends prioritizing phenotype data. The group may also collaborate with the Actionable Variants WG on genetic risk score and possibly write a methods paper.

Consent, Education, Regulation, and Consultation – Andy Faucett and Maureen Smith

The CERC group now holds both a regular monthly call and a monthly call on physician interactions. They are working actively with the Return of Results Consortium to figure out how the two groups can integrate their projects. It might also be helpful to have a call with NHGRI to further discuss this issue. CERC is focusing on using algorithms for RoR, exploring the interface between research and clinical care, and return of multiple results. The eMERGE PGx project would be another opportunity where CERC could help design education tools, study return of results, create common protocols for behavioral outcomes for patients and physicians, and elucidate the patient's perspective throughout the process.

Phenotyping – Josh Denny and Peggy Peissig

The first round phenotypes (AAA, C. diff, cardiorespiratory fitness, diabetic/hypertension-associated CKD, non-syndromic polyps, ocular hypertension, ACEI cough) are all in revision or validated at their primary sites, and 4/7 have been implemented at secondary sites. Four algorithms had PPV >95%. All sites have started with their second round phenotypes (BMI, onchomychosis, VTE, DILI, diverticulosis, glaucoma, response to lipid-lowering agents), with 4/7 implemented and validated at the primary site. Three sites have started their 3rd round phenotypes. Current Network phenotypes include resistant hypertension and PAD, T2D, and lipids, all of which are in progress. Work in progress meetings are held on calls to discuss algorithms with the entire workgroup. The group has developed best practices, including validation of the condition at multiple sites and spot-checking fidelity of the algorithm. The group's recommendation is to evaluate >50 cases/50 controls randomly sorted with physician/nurse/trained chart abstractor, limiting cases to those in the EMR. The CC will get formal approval from each PI to use data in the Record Counter, after which sites will update or contribute demographic data and ICD9 codes for genotyped individuals. The group has also prioritized phenotype representation, which currently is being done through Word documents. They may start using National Quality Forum standards to represent text documents as XML; unfortunately this method does not support NLP. KNIME and DROOLS can also be used for implementation. The Network's progress has been noted in a recent issue of JAMIA.

Physicians' Focus Group – Ellen Wright Clayton

At Vanderbilt, the PREDCT project seeks to identify patients likely to receive target medications in the next 3 years, genetically test the patients, and then tailor drug therapy based on genetic test results. Although these conversations were not under IRB-approved protocols, these can still be seen as considerations. Patients at Vanderbilt knew about GINA, with some knowing how it interacts with HIPAA. Patients were divided on what data should be in the EMR, as some want everything that doctors have. At present, significant results go into a box at the top of the patient summary and can be found in other parts of the EMR. No matter what results are returned, all genes tested are listed in the record. HEO/Wiz POC decision support brings up a large pop-up window when a particular drug is prescribed for a certain genotype, with the option to bypass DS advice and a box where the doctor can enter why he/she is not following the guidelines. There is even a separate tab or genomic information. Statins have been implemented, and TPMT/azathriopine is in the pipeline. Physicians differed in how much info they want, and part of this depended on if they had used PGx data before. Assessing what results are actionable also was complex, not only for genotype but also for drug type and length of dose. Staff hand-curated prior test results for SLCO1B1. Physicians also differed in their reception to getting subsequently revealed results. Different doctors ordered different amounts of tests, and they may find results that they were not expecting. Physicians also had issues with tracking people who receive external primary care. The physicians also discussed concepts of quality, improvement, and dissemination. Marc Williams will share dissemination science principles with CERC.

dbGaP Overview for Data Request and Submission of Analysis Results after Publication – Mike Feolo

There have been 123 eMERGE data requests from 76 investigators at 48 institutes across 8 countries. NCBI would like all primary eMERGE publications to have dbGaP accession numbers. dbGaP would also like investigators to submit analysis results after publication so that they can create a permanent archive of published results. End users would be able to see individual level data that the PI actually published on, which are often different from initial QC results. The public can now view and download all p-values without direction of the data, data

which can then be downloaded to programs like LocusZoom and PheGeni. When submitting data, dbGaP would like a description of analysis and methods, as well as an analysis results file with genotype counts, pHWE, testing statistics, risk allele, and OR/beta values in one row for each SNP. P-values can also be aligned to the current genome. For secondary studies, the primary study accession number should be listed. dbGaP has not worked on any enhancements such as making navigation easier or showing allele frequency annotations, but comments should be submitted to Mike Feolo. NIH is looking into changes to the Common Rule on identifiability of biospecimens. Any rulings will then be communicated to dbGaP.

Closing Remarks and Final Discussion – Rex Chisholm
Everyone agreed that the breakout sessions were very important and useful and should be maintained for future meetings. The group also appreciated that meetings between workgroups were able to be facilitated.

Action Items:

1) Marc Williams will send out principles of dissemination science and information on the NIH Conference on the Science of Dissemination and Implementation to the CERC WG.
2) Network members were encouraged to send comments about dbGaP improvements to Mike Feolo.
3) The CC will contact PIs to get permission to use site date in the eMERGE Record Counter.
4) Rongling will work with Joy Boyer, Jean McEwen, and Brad Ozenberger to coordinate Return of Results Consortium, Clinical Sequencing Exploratory Research, and eMERGE Steering Committee portfolios and meetings.
5) Marc Williams will contact the HL7 Clinical Genomics WG about establishing joint activities with the EHR Integration WG.
6) Chris Chute will contact CDSC and ISO to discuss standards with the EHR Integration WG.
7) The Actionable Variants workgroup will further discuss changing the workgroup name to Return of Results to better represent the mission and goals of the workgroup.