National Human Genome Research Institute

National Institutes of Health

U.S. Department of Health and Human Services

ClinAction: Unifying Efforts to Identify Potentially Actionable Genetic Variants

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National Advisory Council for Human Genome Research

February 13, 2012

ClinAction: Potentially Actionable Genetic Variants

- Genomic studies increasingly identifying variants with potential implications for clinical care
- Unavoidable in genomic-scale research, DTC testing, sequencing for clinical care
- Current genomic medicine efforts need paradigm-setting examples to drive ethical deliberations and infrastructure development

Published 2006 Wiley-Liss, Inc. American Journal of Medical Genetics Part A 140A:1033–1040 (2006)
†This article is a US Government work and, as such, is in the public domain in the United States of America.

Special Reports

Circ Cardiovasc Genet 2010;3;574-80.

Ethical and Practical Guidelines for Reporting Genetic Research Results to Study Participants

Updated Guidelines From a National Heart, Lung, and Blood Institute

"…an independent, national central advisory committee should be established to review evidence for genetic risk factors to offer guidance to investigators, research institutions, and IRBs regarding when a genetic result is well enough understood and has sufficiently serious clinical implications to justify an obligation to return genetic research results to study participants."

Abstract—In January 2009, the National Heart, Lung, and Blood Institute convened a 28-member multidisciplinary Working Group to update the recommendations of a 2004 National Heart, Lung, and Blood Institute Working Group focused on Guidelines to the Return of Genetic Research Results. Changes in the genetic and societal landscape over

Other Related Workshops

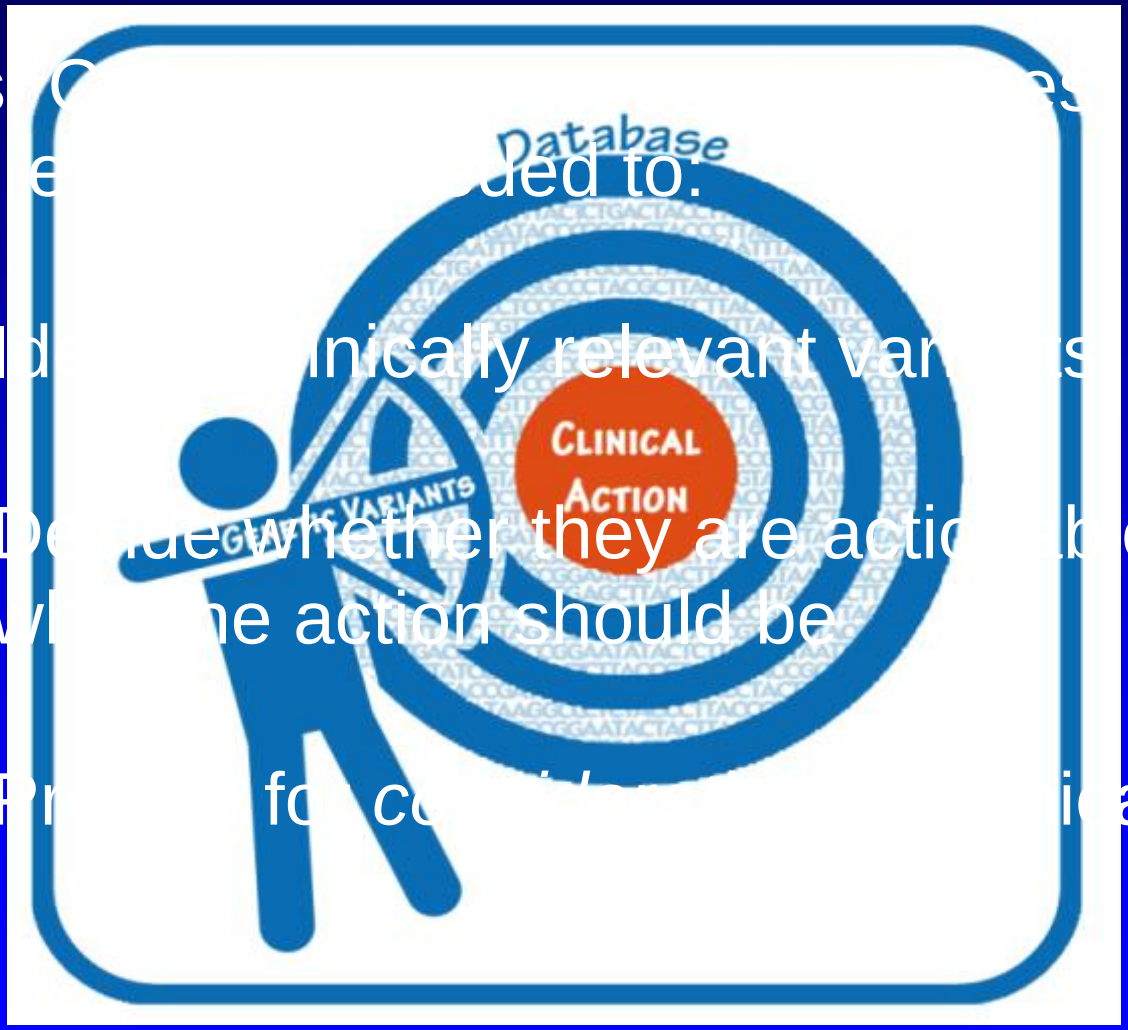
- Genomics and Health Information Technology Systems: Exploring the issues (Apr 2011)
- Genomic Medicine Colloquium (June 2011)
- IOM Workshop on Integrating Large-scale Genomic Information into Clinical Practice (July 2011)
- NHLBI Workshop on Integration and Display of Genetic Test Results within EHRs (August 2011)
- Genomic Medicine II (December 2011)

Characterizing and Displaying Genetic Variants for Clinical Action

December 1-2, 2011

Goals: C[illegible]es and other [illegible]ded to:

- Id[illegible]nically relevant variants
- De[illegible]whether they are actio[illegible]e and wh[illegible]e action should be
- Pr[illegible] fo[illegible]al use



Characterizing and Displaying Genetic Variants for Clinical Action

December 1-2, 2011

Goals: Consider processes, databases, and other resources needed to:

- Identify clinically relevant variants
- Decide whether they are actionable and what the action should be
- Provide for *consideration* for clinical use

Clinical Utility and "Actionability"

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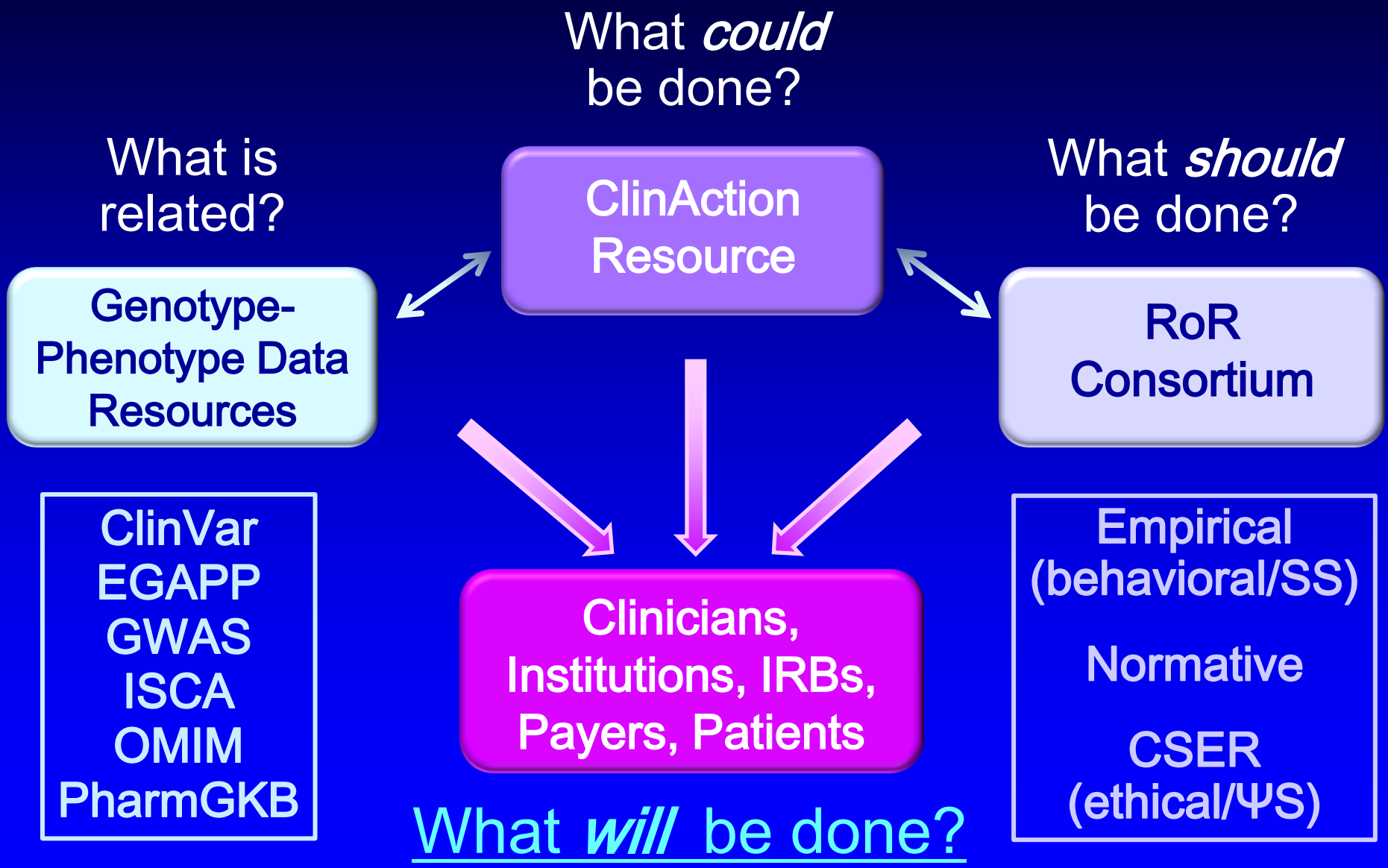
- Can be informed by expert consensus

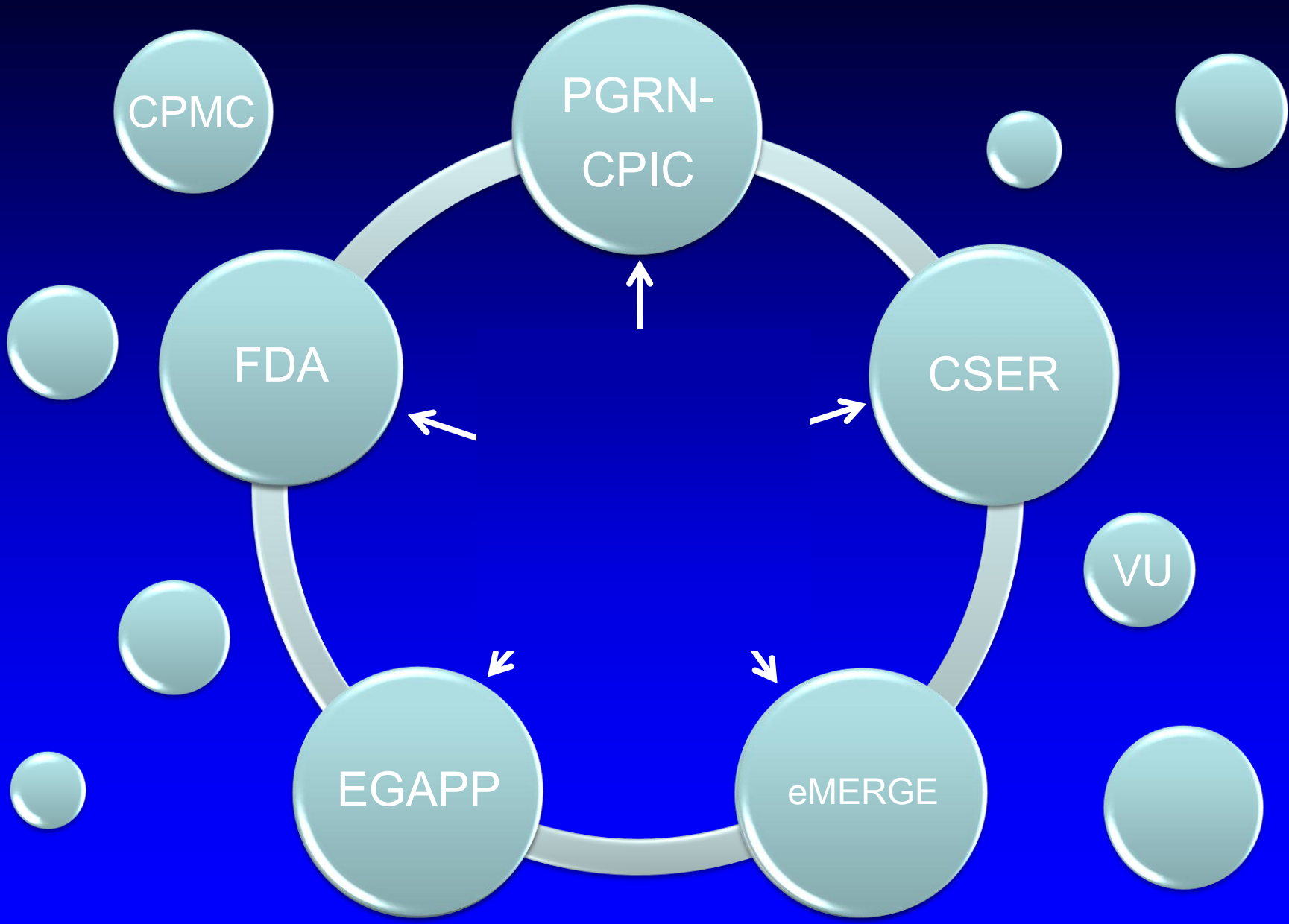
What We Mean by "Actionable"

- Evidence not sufficient for unequivocal CU
- Sufficient to determine how already available information could be used in clinical context
- Intermediate stage between CV and CU ("If you had it, would you use it?")
- May allow consideration of ethics, law, and policy in RoR to move to appropriate expertise
- Allows more flexibility for clinicians, institutions to tailor use of variant information to patient, clinical setting, and local standards of practice

Complex Matrix of Decision-Making



Ensuring Coordination with Related Efforts



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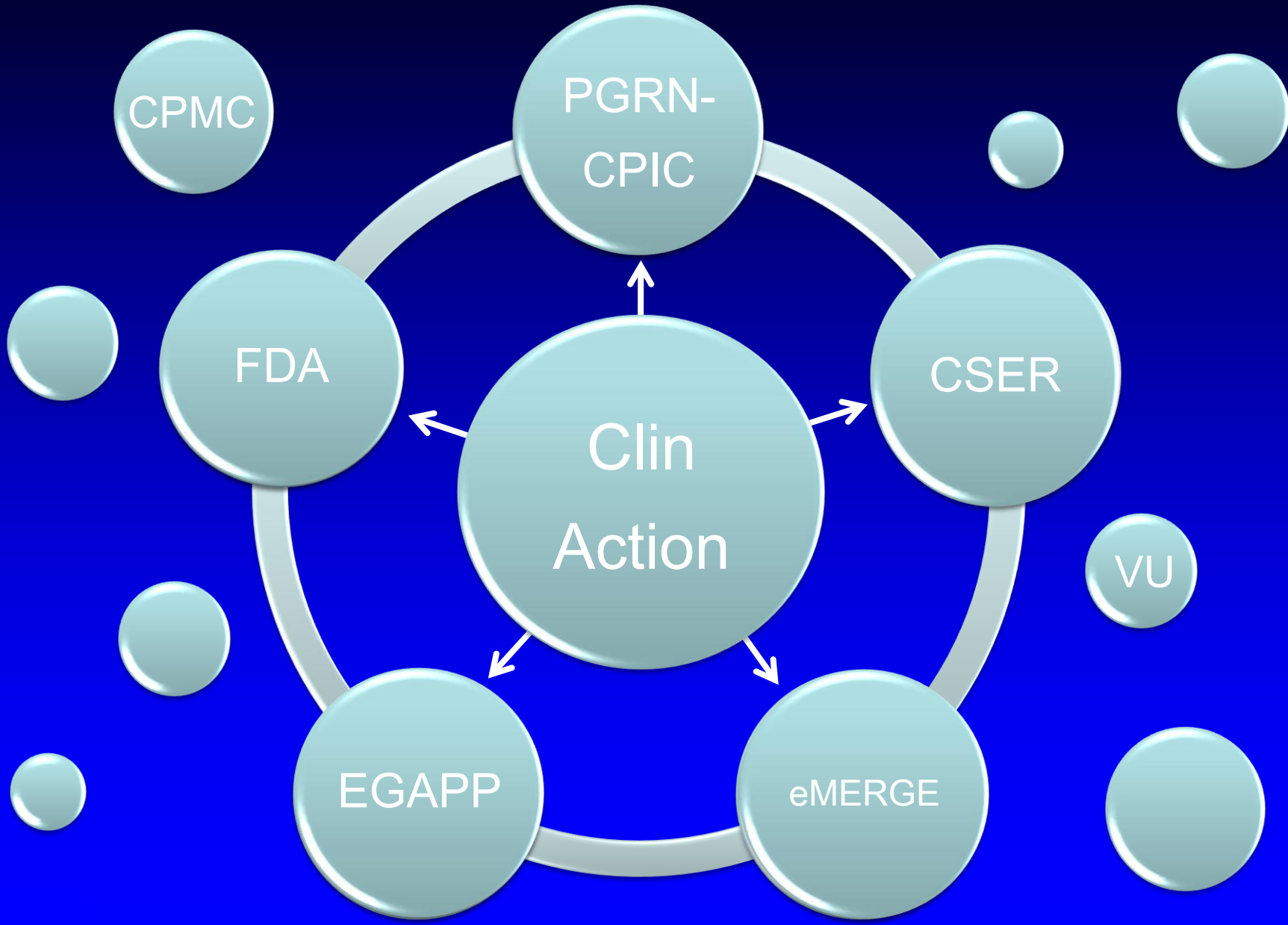
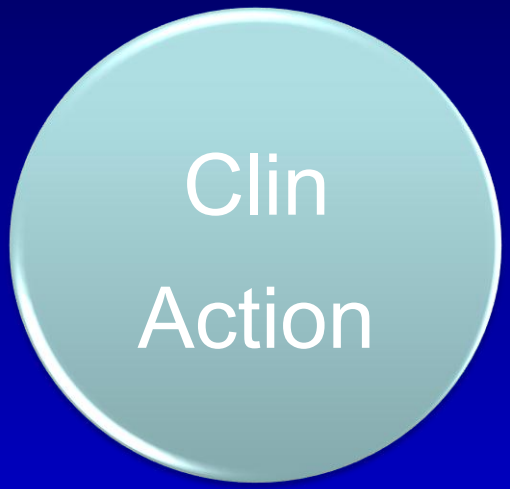


Ensuring Coordination with Related Efforts



ClinAction: Potentially Actionable Variants

Proposal: Support identification and dissemination of consensus information on potentially actionable genetic variants in clinical care.

Goals:

1. Identify genetic variants with implications for clinical care and disseminate evidence
2. Develop clinical decision support systems for incorporating these variants into clinical care
3. Build upon existing programs, unify, reduce duplicative efforts across numerous research and clinical organizations

Research Scope and Objectives

- Single awardee to collect and evaluate clinical relevance of variants associated with clinically important traits
- Multicomponent approach including:
  - Synthesis, curation
  - Consensus development, integration with ongoing efforts
  - Dissemination

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Research Scope and Objectives

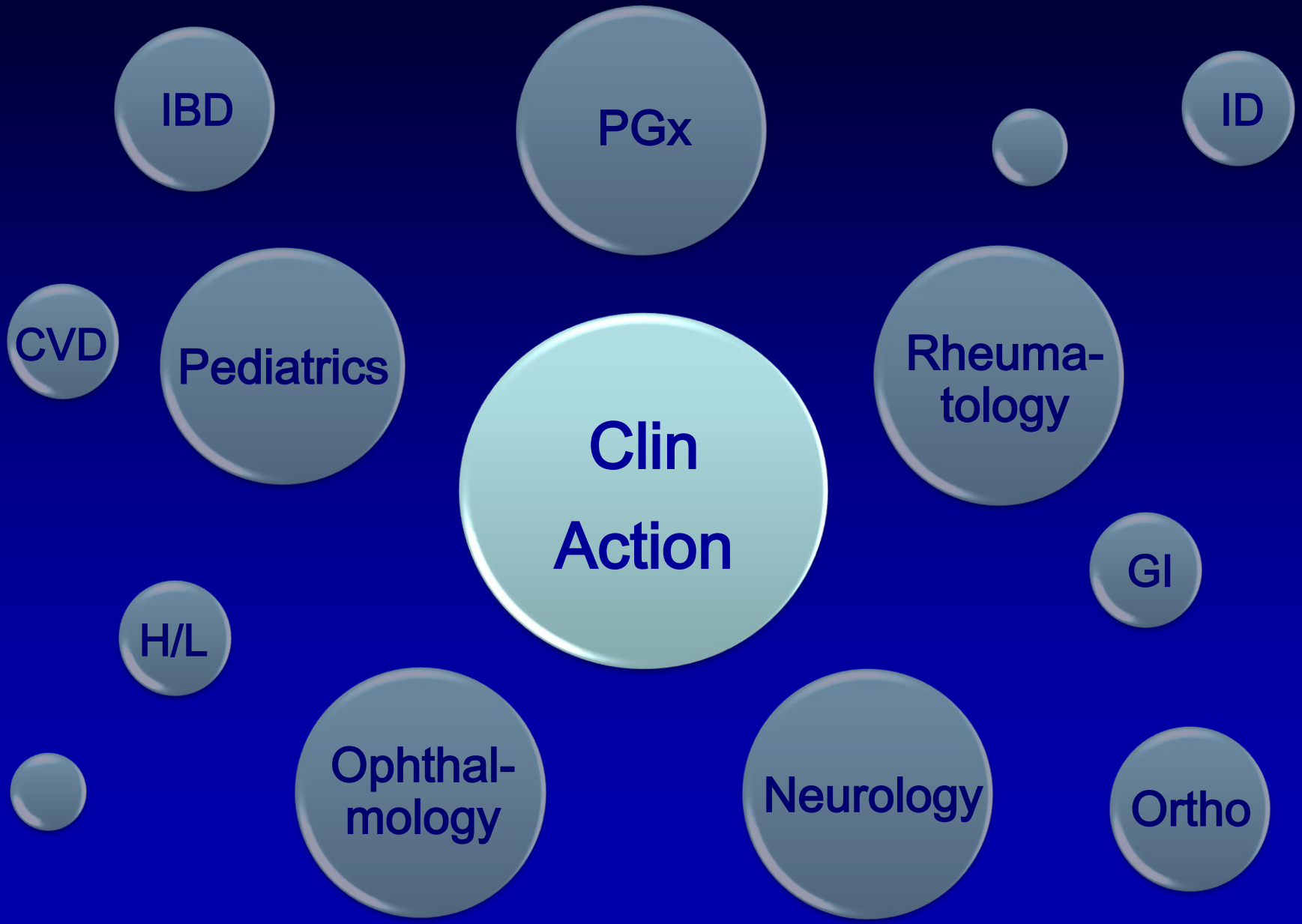
- Not providing screening recommendations
- Rather providing evidence on which screening recommendations could be made

- Not whether clinicians should be advised to *order* a particular assay
- Rather what could or should be considered if a patient's genetic results were *already* available

Consensus Development and Integration

- Invite existing groups to join or interact
- Develop framework for review and evaluation
- Define domains to group variants for evaluation
- Apply review framework and reach consensus on variants and actions to be recommended
- Bring deliberations to consensus, or address (rare?) inability to do so
- Obtain input on draft recommendations
- Ensure consistency of domain-specific recommendations with framework

Consider Distributing Curation/Consensus Efforts



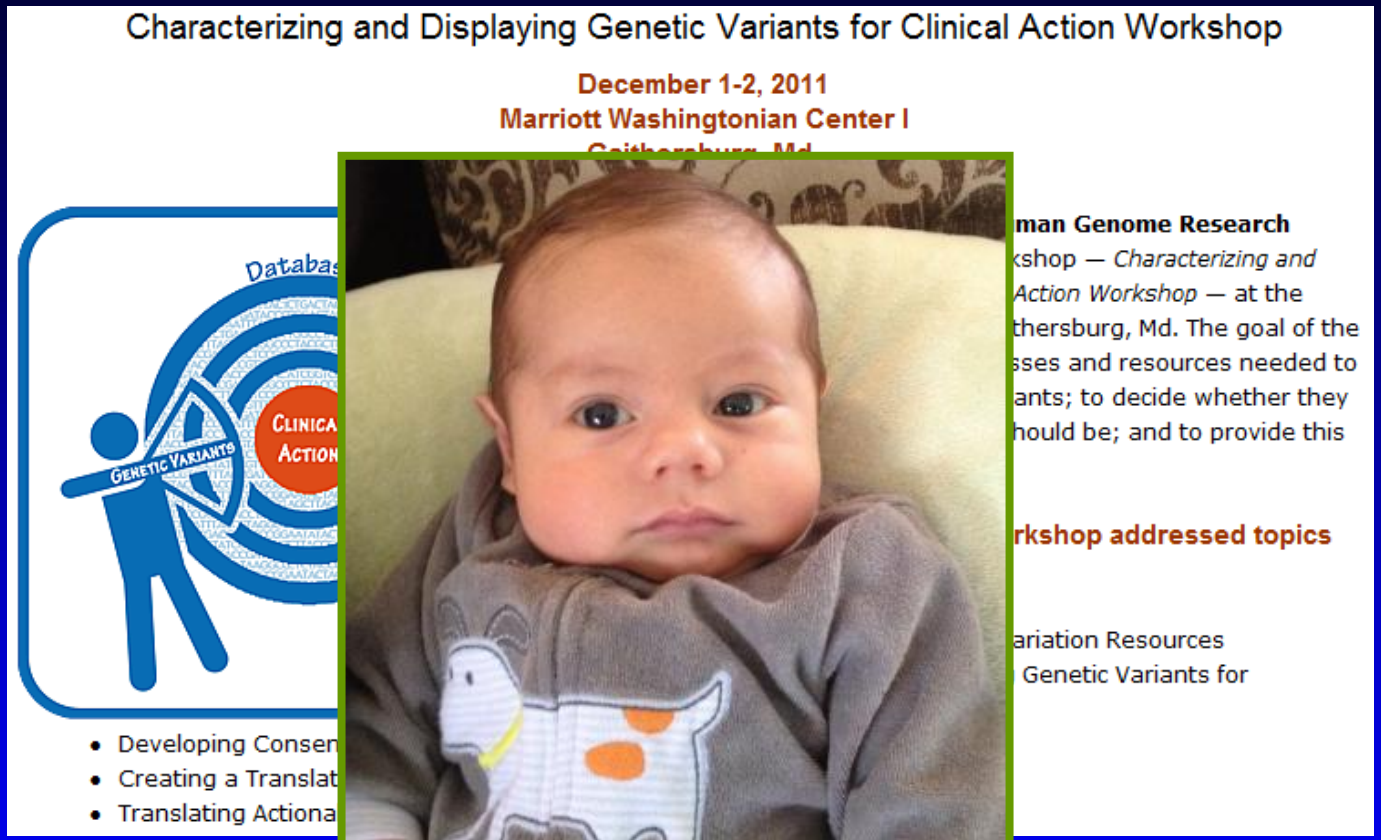
Dissemination and Clinical Decision Support

- Provide consensus recommendations on actionable variants and actions to be considered
  - Supporting evidence
  - Documentation of consensus process
- Develop and distribute CDS rules and tools for adoption in EMRs and other clinical systems
  - User-friendly tools for clinicians without access to such systems
  - Distribute to other health systems, especially non-US systems, to consider and adapt

Anticipated Funding

- $2M in FY13, $4M/yr for FY14-FY16
- 2-3 domains yr 1, 5-8 domains annually yrs 2-4
- Consider continuation if effectively developed and increasingly used, re-consider at 3-5 years
- Cooperative Agreement (U01)
- Support sought from other ICs and other sources

Many thanks…



Lisa Brooks
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http://www.genome.gov/27546581

Characterizing and Displaying Genetic Variants for Clinical Action, Dec 1-2, 2011

- Serve as “convener” with other NIH Institutes, professional organizations, and others to develop, prioritize and publicize recommendations regarding clinical actionability of genetic variants
- Create coordinated resource to extend current databases for use in clinical care by providing recommendations regarding clinical actionability
- Develop and disseminate user-friendly clinical decision support tools and/or an EHR integration layer for ready use of these data in clinical care

Characterizing and Displaying Genetic Variants for Clinical Action, Dec 1-2, 2011

- Encourage dissemination of decision support logic and interpretive tools, including a publicly available library, to enable diverse EHR systems to use the same logic and tools when developing CDS
- Coordinate with US and UK agencies (AHRQ, ONC, DVA, NHS), EHR vendors, and others to address data interoperability and viable approaches for integrating genomic information and actionable variants into EHR systems