

GWAS

Challenges of Local Implementation

P. Pearl O'Rourke, MD
Partners HealthCare
Boston, MA

Local implementation

- The Players
 - Investigator
 - IRB
 - Institutional Official
- The tasks
 - Submission of data into the NIH GWAS Repository
 - Accessing data from the NIH GWAS Repository

Submission Challenges

- Identifying who is covered by the policy
- Assessing adequacy of informed consent
 - Prospective collections
 - Existing datasets
- Risk assessment
- Assessing adequacy of de-identification
- Return of research results
- Multi-center research

Submission Challenge:

Who is covered by the policy

- NIH funding for GWAS analysis on or after January 25, 2008
- Questions:
 - NIH funds for specimen collection and maintenance – but non-NIH funds for GWAS

Submission Challenge:

Assessing Adequacy of Consent

- Prospective collections: consent ideally should include:
 - Broad scope of research
 - Clear inclusion of GWAS
 - Sharing of coded research results with the NIH GWAS Repository

N.b., ongoing complaints that consent forms are too long and too complex

Submission Challenge:

Assessing Adequacy of Consent

- Existing collections: consent must be assessed for:
 - Scope of research: broad or limited?
 - Any mention of genetic research: is it adequate?
 - Sharing of research results
 - Allowed
 - Expressly not allowed
 - Silent

Submission Challenge:

Example of consent review

“Your tissue and data will be used to study asthma and other lung diseases. Some of the research will involve a study of the genes that may cause asthma. “

Institutional Option:

- Rather than say no - limit any use to lung diseases

Submission Challenge:

Example of consent review

“Your research data will not be shared with any commercial entity. “

Institutional Option:

- Rather than say no - limit access of data from the NIH GWAS Repository to exclude use by commercial companies

Submission Challenge:

Assessing Adequacy of Consent

- Re-consent as an alternative
 - Logistics and expense
- Deceased subjects (legacy collections)
 - Can a waiver of informed consent be used?
- How to handle samples obtained from pediatric subjects
 - Include? Do not include?
 - If include: re-consent at age of majority?

Submission Challenge:

Risk Assessment

- Institutions (IRBs) are asked to consider risks to individuals, families, groups or populations
 - Is this possible when future use of the data accessed from the NIH GWAS Repository is **not** under the control of the local IRB?
 - Local IRB can only assess risk of placement of data into the NIH GWAS Repository
 - Can place limits on use of data submitted

Submission Challenge:

Risk Assessment

- Assessment of group risk is problematic
 - How to define a group
 - How to consider any attendant risk/s
 - When is group consent recommended?

Submission Challenge:

Adequacy of De-identification

- Can the data be de-identified?
 - Is it possible to de-identify this data?
 - Does today's technology render phenotype-genotype pairs identifiable?
 - Has the threshold for identifiability changed?
 - How to deal with state laws that consider genetic information is identifiable?

Submission Challenge:

Adequacy of De-identification

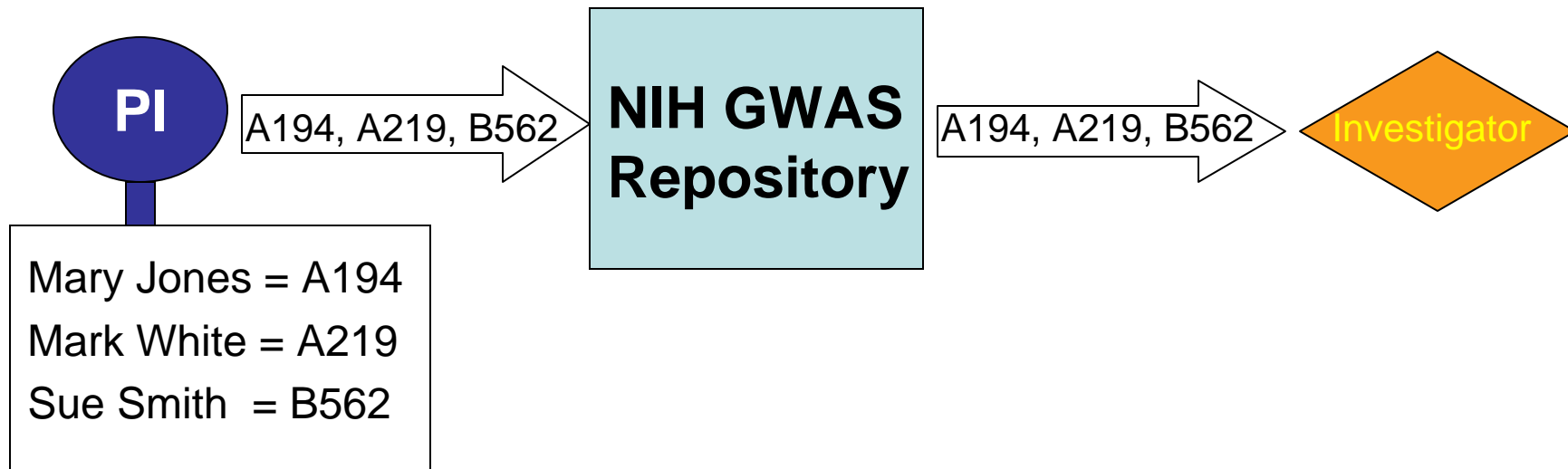
- If your institution considers 'coded-GWAS-data' to be identifiable....
 - You should NOT submit the data to the NIH GWAS Repository.
 - The NIH GWAS Repository does NOT consider itself *involved* in human subjects research

Submission Challenge:

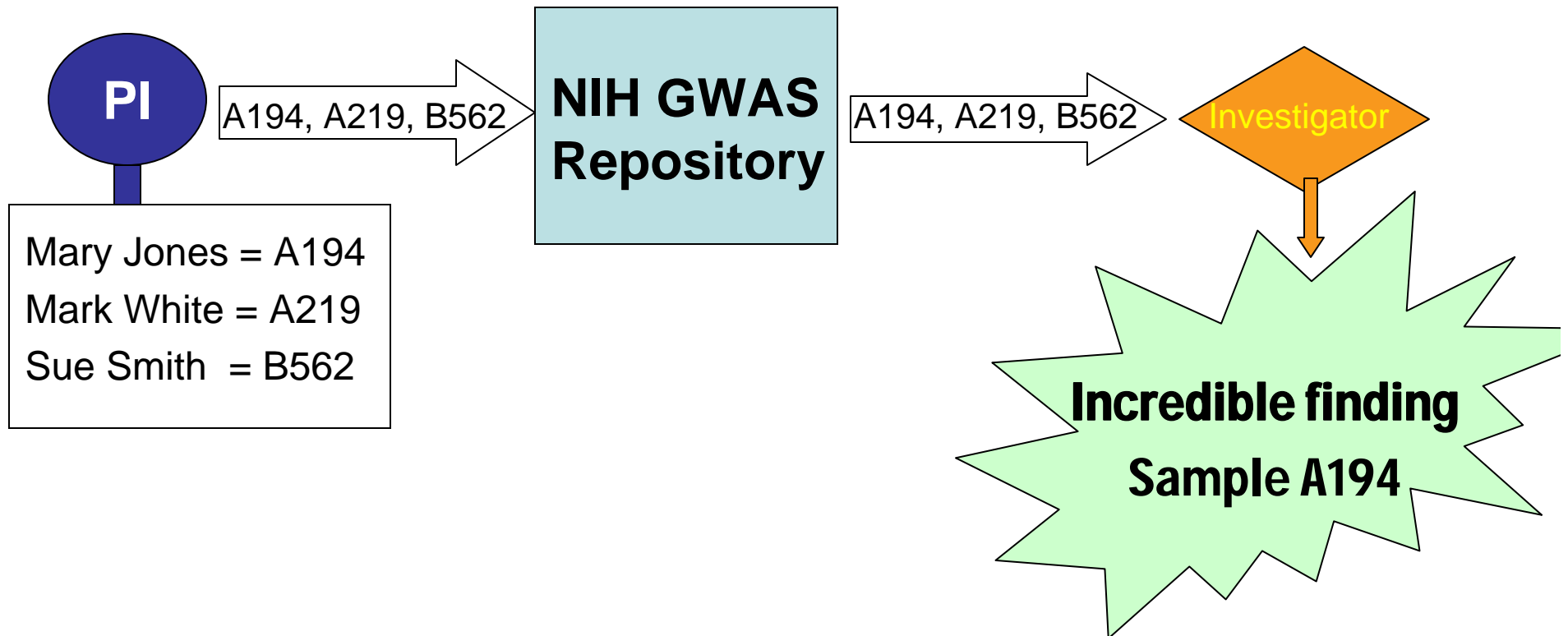
Return of Research Results

- Return of research results:
 - “Secondary investigators may share their findings with primary investigators, who may determine whether it is appropriate to return individual or aggregate research results to participants whose health may be affected, following established institutional procedures (e.g., IRB approval) and specific parameters defined in the original study.”

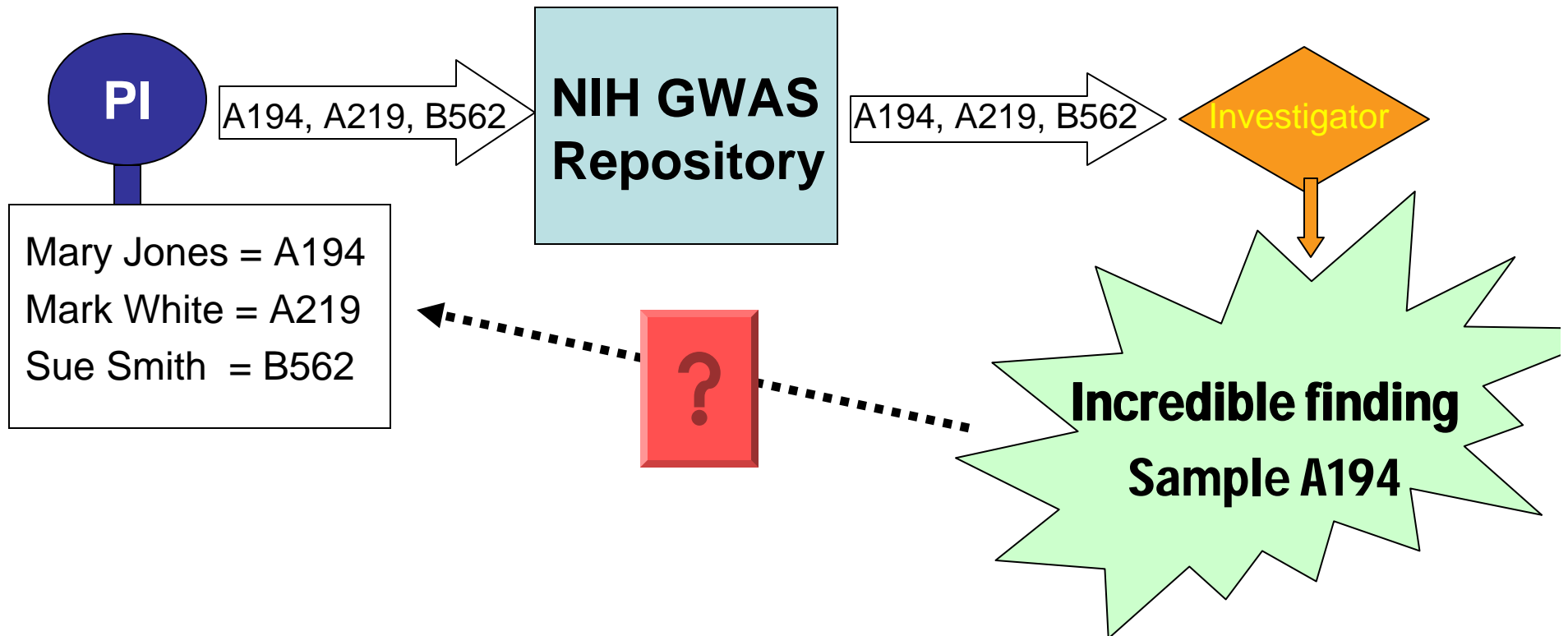
Return of Research Results



Return of Research Results

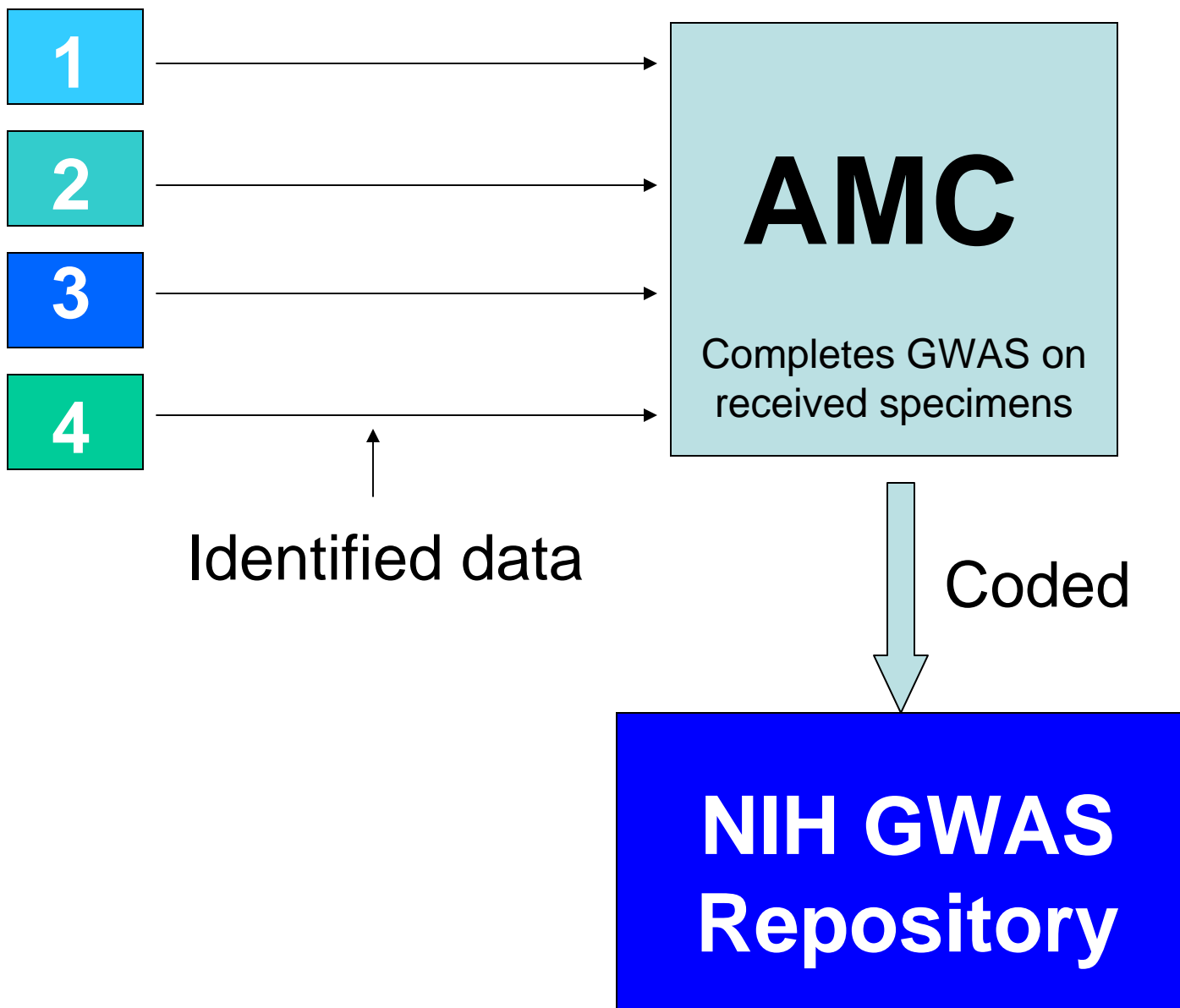


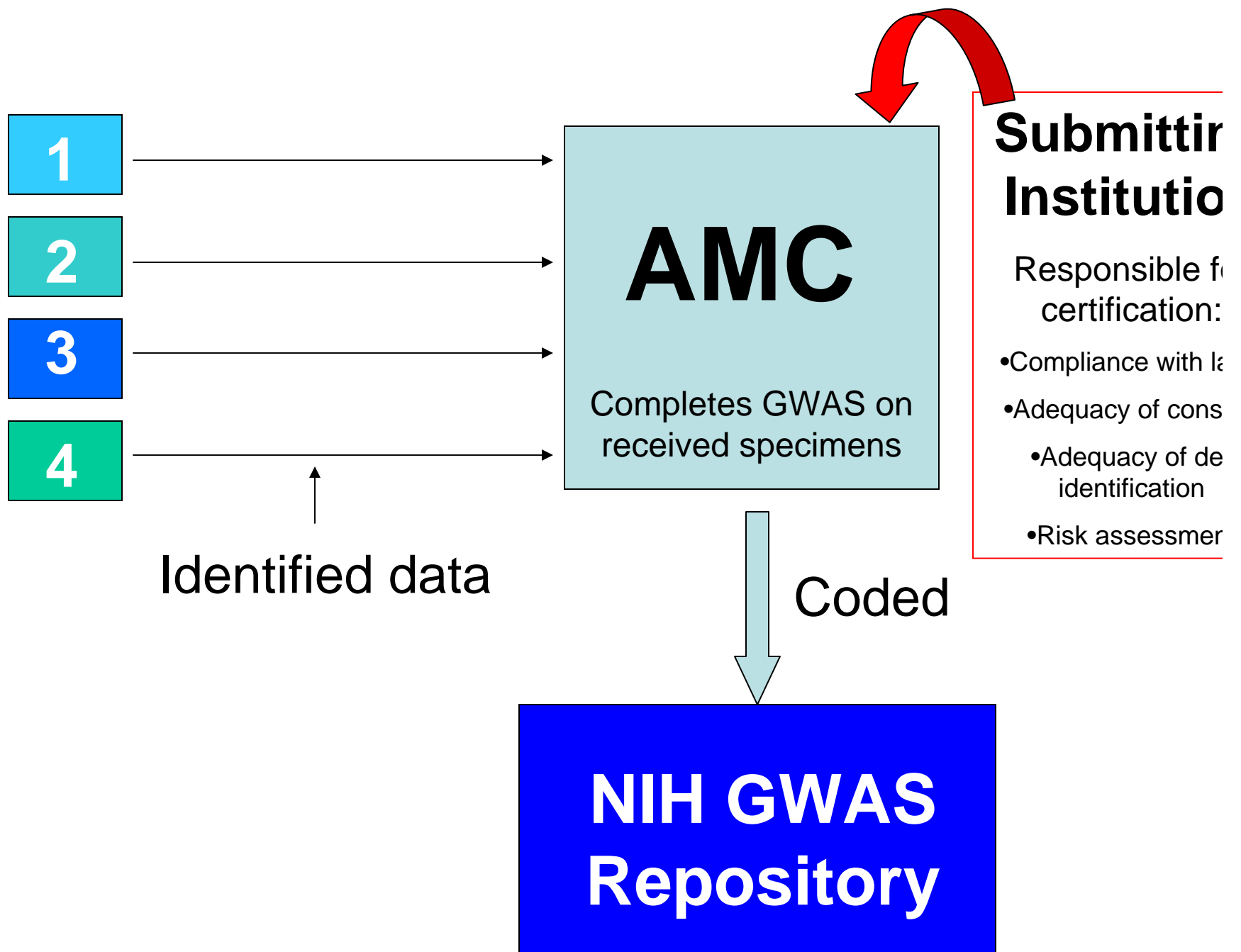
Return of Research Results



Submission Challenge:

Multi-center Research





Submission challenge:

Multi-center Research

- Realities:
 - Other sites may have altered the informed consent form in response to their own IRB
 - In a single multi-year, multi-site study: each site may have numerous consent forms

Submission challenge:

Multi-center Research

- Question:
 - Must the AMC certify for all participating sites?
 - NO.
 - The submitting institution is responsible for all participating institutions
 - Can rely on certifications from each of the participating institutions
 - But submitting institution must obtain and keep copies of local certifications

Submission challenge:

Multi-center Research

- More Difficult Question:
 - What if there is no consensus across sites?

Submission challenge:

Multi-center Research

- Example:
 - Site 1 wants to limit GWAS use to asthma research only
 - Site 2 wants to limit GWAS use to any pulmonary condition
 - Site 4 determines that the consent is not adequate for submission of data to the NIH GWAS Repository
 - Site 3 and the AMC see no need to limit

Access Challenges

- “OHRP has confirmed that secondary data users will not be conducting human subjects research”
- Will the institution conduct any form of ethical review?
- What if the institution considers GWAS data to be identifiable?
 - Will IRB and/or HIPAA actions be required?