IRB and the Regulation of the Return of Genetic Research Results

Genetics in the Clinic Series

July 26, 2017

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Overview

- Introduction to the JAX Institutional Review Board
- Return of research genetic results -RoR
- IRB review of RoR
- CLIA and RoR
- SACHRP 2016 on RoR
- Informed consent for RoR, JAX IRB requirements
- Unintended consequences

Role of JAX IRB

Review of Human Subjects Research to ensure that it meets requirements of 45 CFR 46 “Common Rule” for Federally-funded research and equivalent protections for non-Federally funded research. To be HSR, must meet both definitions below:

- *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

- *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) Data through intervention or interaction with the individual, or (2) Identifiable **private information**

What is “private information”

- 45 CFR 56.102 (f) Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or *associated with the information*) in order for obtaining the information to constitute research involving human subjects
- *Private information* includes…information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record)

Return of research genetic results

- Primary goal of research is to develop generalizable knowledge
- "Resources for research should be primarily directed to scientific discovery, thus, researchers do not have a duty to look for actionable genetic findings beyond those uncovered in the normal process of their investigations"[1]

[1] Jarvik, et. al., Return of Genomic Results to Research Participants: The Floor, the Ceiling and the Choices in Between. The American Journal of Human Genetics 94, 818-826, June 5, 2014.

Guiding principles for RoR[2]

1. Research is different than clinical care
2. Resources for research should be directed to scientific discovery- no duty to search for clinically-actionable findings beyond planned analysis
3. Research needed to determine best practices for RoR in research and in clinical settings
4. Clinically valid information discovered during research should be offered to participant
5. Participant must have right to refuse to receive results

[2] CSER Consortium & eMERGE network 2013

IRB review of research with RoR

- There is no specific regulation of RoR in 45 CFR 46 “Common Rule”
- IRB reviews study protocol and informed consent form
- Protocol should address scope of research analysis and plans for RoR including CLIA confirmation of research results- executed agreement for CLIA testing prior to study initiation if results will be returned
- Consent form should include plan for RoR and should include subject opt out for receiving results, benefits and risks, plan for reporting significant new findings per 45 CFR 46.

Decision Points for RoR

- Clinical validity of result
- Clinical actionability of result
- Clinical significance of result
- Magnitude of harm related to non-disclosure
- Terms of Informed Consent- did the subject consent to RoR?
- COMPLIANCE WITH LAW (CLIA /HIPAA)

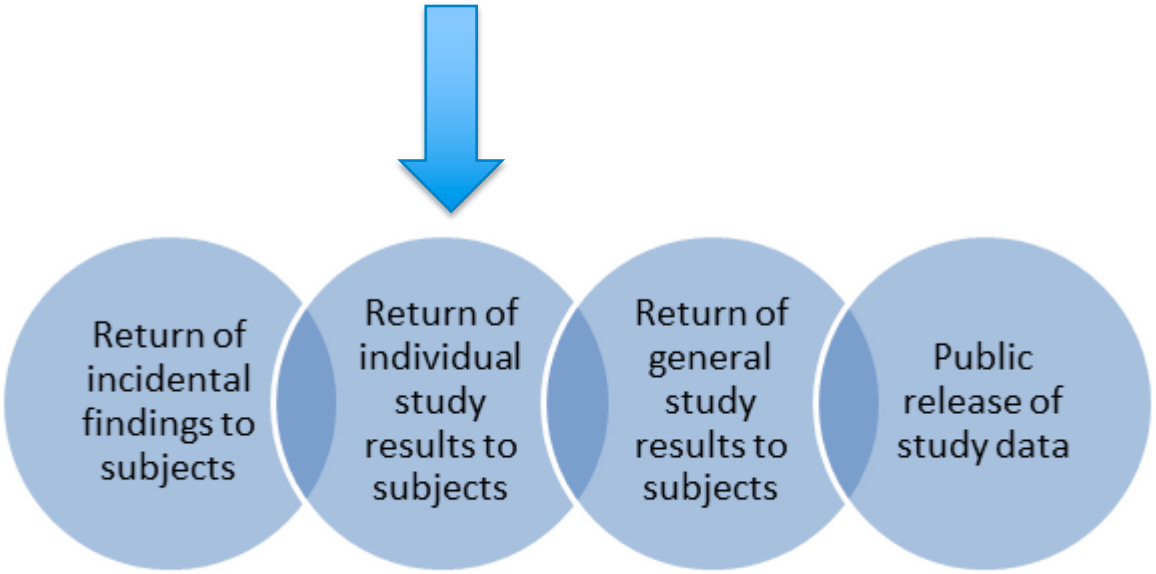
Clinical Laboratory Improvement Amendments (CLIA) and RoR

- CLIA applies when: (1) patient-specific results are reported from the laboratory to another entity AND (2) the results are made available for the diagnosis, prevention or treatment of any disease or impairment of, or the assessment of health of individual patients" 42 USC 263a(a)

- CLIA does not apply to research laboratories that DO NOT REPORT patient-specific results "for the diagnosis, prevention or treatment of any disease or impairment of, or the assessment of health of individual patients" Aggregate reporting is not subject to CLIA.

www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/Research-Testing-and-CLIA.pdf

SACHRP Recommendations 2016



SACHRP Attachment B, 7/21/2016

- **Individual Results** definition: Information linked to the identity of a research subject, pertains to that subject and is the focus of the study
- Three categories: Baseline, in study, end of study results
- Baseline findings can be shared (provided IRB approved and clinically validated)
- In study- carefully considered as not to bias study
- End of study: can be shared (provided clinically validated)- applicability of regulations questionable.

SACHRP: Justification & inclusion of research results reporting

	Validated	Not validated
Clinically actionable	Likely indicated	Possibly indicated
Not clinically-actionable	Possibly indicated	Likely not indicated

SACHRP- Admin Considerations

- Inclusion of plans for RoR in protocol
- Inclusion of plans for RoR in consent form and consent process
- Inform subjects if plan is that no results will be returned
- IRB review of plan per 45 CFR 46.111
- It is preferable to plan for return of results during protocol development and provide to IRB at initial review.

Informed Consent for RoR

- Include plan for RoR at the outset of research
- Provide option for participant not to receive research results in consent
- Only return CLIA confirmed results
- Consider plan to refer for genetic counseling, CLIA testing if research result is medically actionable
- Include: If CLIA test report validating research results will be provided to a clinician, it will be included in the medical record.

IC- continued

- Application of Genetic Information Non-discrimination Act (GINA) should be described as well as situations where GINA does not apply (life insurance, long-term care insurance applications-will be disclosed)

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New NIH, FDA, CMS Study with NAS

- National Academies-sponsored study to consider whether the current regulatory environment for return of individual-level results from analyses performed in research laboratories adequately minimize risks and maximize benefits both for individuals and society
- Will evaluate evidence of harms and benefits of return of results from research laboratories and consider if alternate approaches could achieve a more appropriate balance of risks and benefits

From: Under the Poliscope. A fresh look at returning research results. June 7, 2017. https://osp.od.nih.gov/2017/06/07/a-fresh-look-at-the-rules-for-returning-research-results/

Rare Disease Research and RoR

- Due to small population of individuals with each Rare Disease and ongoing longitudinal research to discover relevant genetic/genomic biomarkers, the line between research/clinician/patient may become blurred.
- It is critical for the JAX investigator to maintain a firm line between research and clinical care in these situations
- Protocols and consent language must be followed EXACTLY with any return of results to participants approved by IRB **before** it occurs.

Management of RoR at JAX

- Until regulations change or new guidance is issued, any return of research results that in a research protocol in which JAX is engaged will:

- Include in the protocol and informed consent the well-considered plan for RoR

- Any results obtained in a research laboratory that will be returned to subjects must be confirmed by a CLIA laboratory before the return. This information must be included in the IRB approved protocol and consent form.

Return of results from CLIA testing

- Return of results once confirmed by CLIA testing may only occur by providing the CLIA report from the testing
- No additional information or interpretation is to be provided beyond that included on the CLIA report
- Documentation of the return of results and a copy of the CLIA report must be included in the research record of the participant.

JAX IRB Requirements for RoR

- If research results will be confirmed in a CLIA lab and will be returned to consenting participants, an agreement between the investigator and a CLIA lab for this testing and resources to complete this testing must be provided to IRB before study initiation.
- CLIA reports are to be included in the research record with documentation of when they were provided to the participant and their provider, if applicable, and by whom.

Contact information for HRPP & IRB

- MyJax: https://myjax-p.jax.org/Committees/hsirb
- IRB@jax.org
- HRPP policies (includes IRB, QA, COI): https://myjax-p.jax.org/Committees/hsirb/Pages/Policies.aspx
- *Coming soon*: Handbook for Investigators: Summary of Human Research Protection Program (HRPP) policies with "need to know" information. Developed by Fayez Jawed, Clinical Research Specialist. In final revisions.

Unintended consequences

- “For Cholesterol study volunteer, an unsettling discovery in a *Science* paper: herself

www.sciencemag.org/news/2016/05/cholesterol-study-volunteer-unsettling-discovery-science-paper-herself


Congratulations

Questions?