The National Academies of
SCIENCES • ENGINEERING • MEDICINE

HEALTH AND MEDICINE DIVISION

Returning Individual Research Results to Participants

Guidance for a New Research Paradigm

Committee members

- **Jeffrey R. Botkin, (*Chair*),** University of Utah School of Medicine
- **Paul S. Appelbaum,** Columbia University
- **Suzanne Bakken,** Columbia University
- **Chester Brown,** University of Tennessee Health Science Center
- **Wylie Burke,** University of Washington
- **Richard Fabsitz,** George Mason University
- **Vanessa Northington Gamble,** The George Washington University
- **Gregg Gonsalves,** Yale University
- **Rhonda Kost,** The Rockefeller University Center for Clinical Translational Science
- **Debra Leonard,** University of Vermont
- **Amy McGuire,** Baylor University
- **James Nichols,** Vanderbilt University School of Medicine
- **Bray Patrick-Lake,** Duke University
- **Consuelo Wilkins,** Vanderbilt University Medical Center
- **Brian Zikmund-Fisher,** University of Michigan

National Academies of Sciences, Engineering, and Medicine Staff: Michelle Mancher, Emily Busta, Autumn Downey, Olivia Yost, Caroline Cilio, Andrew Pope

Consultants: Christi Guerrini, Rebecca Davies, Haavi Morreim

Sponsors


CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES


FDA
U.S. FOOD & DRUG
ADMINISTRATION


NIH
National Institutes of Health

Historically, return of individual research results has not been a standard or common practice

- Risks associated with return of inaccurate results
- Research is for benefit of society not individuals
- Concerns about blurring the line between research and clinical care and fostering the ‘therapeutic misconception’

Two HHS regulations provide conflicting guidance

Clinical Laboratory Improvement Amendments of 1988 (CLIA)

- Ensures the quality of results from clinical laboratories
- According to CMS, only allows the sharing of test results with participants if they are generated in CLIA-certified laboratories

Health Insurance Portability and Accountability Act of 1996 (HIPAA)

- Protects personal health information (medical records and other info included in designated record set (DRS))
- Requires the return of results requested by a participant (when part of HIPAA-covered entity), regardless of whether they were generated in a CLIA-certified laboratory

Charge to the committee

Determine if and when it is appropriate to return individual research results to research participants through

- Reviewing of current practices
- Examining evidence on the benefits, risks, and costs
- Considering the ethical, social, operational, and regulatory aspects of return

Outside of Scope

- Results not generated from human biospecimens (e.g., social and behavioral, imaging)
- Anonymized/de-identified results
- Aggregate results
- Analysis of CMS' interpretation of CLIA
- LDT regulations

Key Messages

Potential benefits of return of individual research results

- Better relationships between investigators and participants
- More transparency and trust
- Better recruitment and retention, which could lead to cost savings
- Improvements in efficiency, generalizability and participant-centeredness of research

Risks and costs of return of individual research results

- Participants make decisions based on inaccurate or misinterpreted information
- Adverse psychosocial effects
- Legal liabilities for research institutions
- Time, personnel and resources
- Opportunity costs

Balancing benefits vs. risks and costs

Early evidence suggests benefits have been understated and risks overstated (or can be mitigated against)

- But, lack of conclusive evidence overall
- Costs are real but very variable

Ethical considerations

- Obligation to return when reliable results suggest imminent danger (i.e., ‘duty to warn’)
- Opportunity to demonstrate the ethical principles of respect for persons, beneficence and justice.
- Research demonstrates that many participants want and expect their results
- Return of individual results may be inappropriate in many circumstances
  - However, other actions (e.g., return of aggregate results) may be appropriate

Guiding principles for the return of individual research results

1. Because **research results have value to many participants**, return of results should be routinely considered as a matter of reciprocity, respect, transparency and trust.

2. When assessing value of returning results, **trade-offs for all stakeholders** should be considered.

Guiding principles cont'd

3. When results are offered, **participants can decide** whether to receive or to share their results.

4. **Communication is key** to promote understanding of the meaning and limitations of information.

Guiding principles cont'd

5. **Validity and reliability** of results is crucial to provide value to investigators, participants, and society.

6. **Inclusion of diverse populations is critical** to the conduct of high-quality research. Researchers should seek input from participants and communities, to accommodate the full spectrum of needs and preferences.

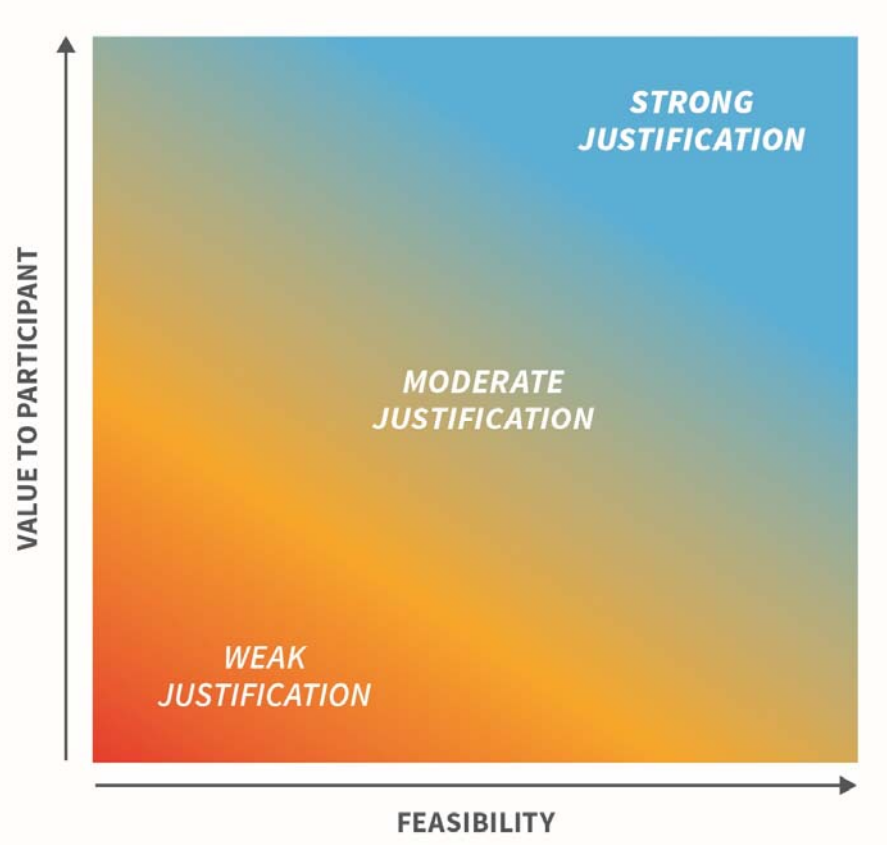
Decision making on a study-by-study basis

- Decisions on return will vary depending on the characteristics of the research, the nature of the results, and the interests of participants.

- Investigators should prepare for three scenarios for return:
  - Planned investigator **offer**.
  - Upon participant **request**.
  - In the event of **unanticipated findings**.

Feasibility and value framework

The justification for return becomes stronger as the potential **value** of the result to participants and the **feasibility** of return increase.



Need for a Quality Management System (QMS) for research laboratories

- Confidence in the validity of individual research results is critical
- **Many research laboratories do not have the systems** in place
- Without a QMS, it is difficult to know which laboratories can generate accurate and reliable results.
- BUT, **CLIA requirements are not always a good fit**

It would be a worthwhile effort for government agencies to develop an externally accountable QMS for research laboratories.

Need to harmonize federal regulations

- HIPAA/CLIA conflict cause **variable interpretation and action** across IRBs and research sites
- FDA regulations are unclear regarding how return of results impacts the IDE process
- Regulatory conflicts create
  - **Inconsistent and inequitable access** for participants
  - Dilemmas for laboratories, investigators, and institutions

Recommendations

Determine conditions under which individual research results will be returned

Investigators and institutions (Rec. 1)

- Should **routinely consider** whether and how to return individual research results on a **study specific basis** through a thoughtful decision-making process.

Include plans in study protocols

Investigators (Rec. 6)

- Should include plans in protocols that describe whether results will be returned and, if so, when and how.

Research sponsors and funding agencies (Rec. 7)

- Should require that applications for funding consistently address the issue.

Institutions and IRBs (Rec. 8)

- Should develop policies to support the review of plans to return research results.

Develop a QMS for research laboratories

The National Institutes of Health (Rec. 2)

- Should lead an interagency effort, including nongovernmental stakeholders, to **develop an externally accountable QMS** for non-CLIA certified research laboratories.

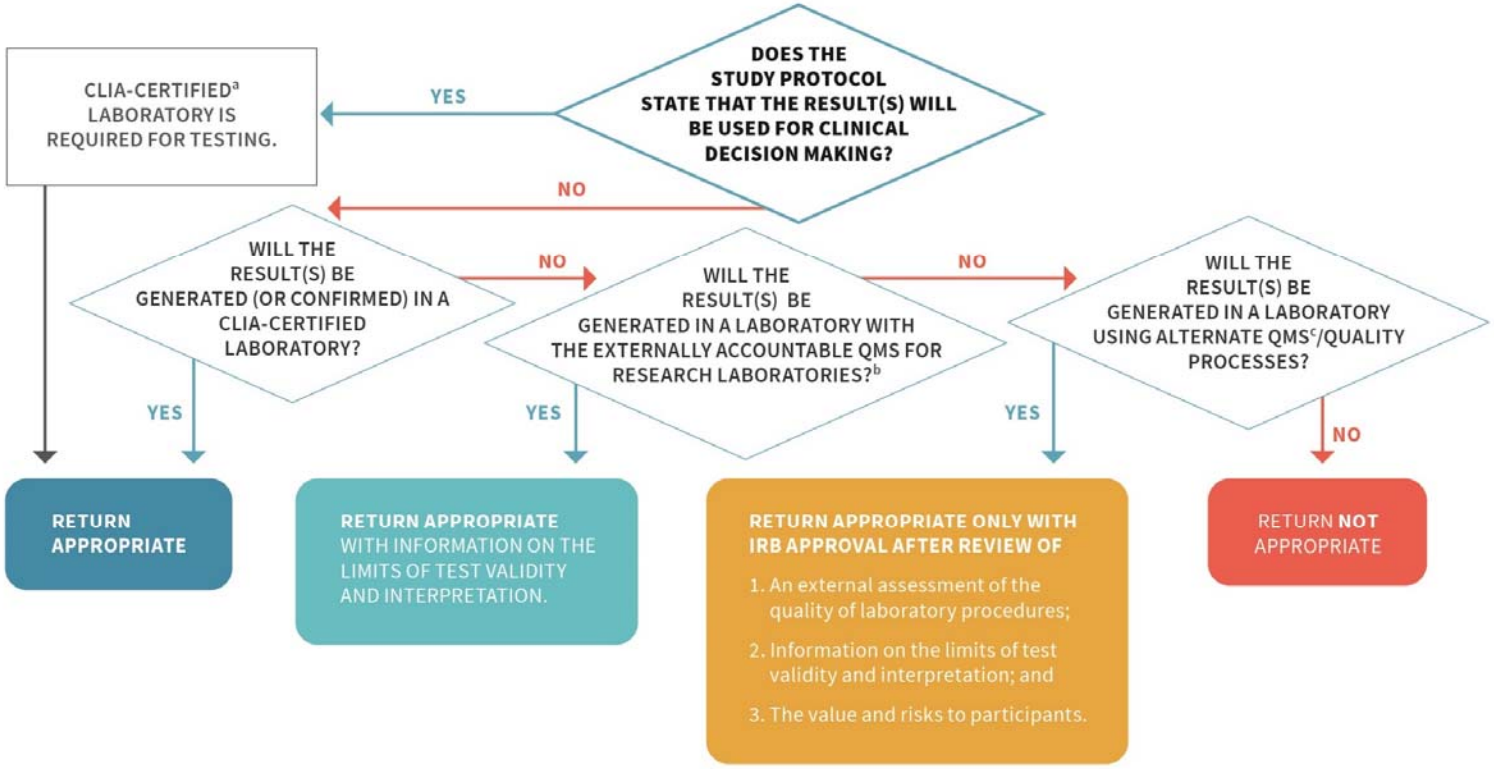
Ensure the high quality of individual research results

Institutions and their IRBs (Rec. 3)

Should permit investigators to return individual research results if**:**

- Testing is conducted in a **CLIA-certified laboratory**; or
- Results are not intended for clinical decision making in the study protocol
  - and testing is conducted under the **externally accountable QMS** for research laboratories; or,
  - the **IRB determines** that:
    - o **Potential benefits** are sufficiently high and **risks of harm** are sufficiently low;
    - o **Quality** of analysis is sufficient; and
    - o Information will be provided **regarding limits on test validity and interpretation.**

Determining whether laboratory quality is sufficient for investigators to return individual research results



Incorporate participant needs and preferences

Investigators (Rec. 5A)

- **Should seek information** (e.g., reviewing published literature, consulting advisory boards, and/or engaging community and participant groups)

Research institutions and sponsors (Rec. 5B)

- Should **facilitate investigator access to relevant community** and participant groups

Sponsors (Rec. 5C)

- Should **engage community and participant representatives** in the development of policy and guidance

Ensure transparency in the consent process

Investigators should communicate in clear language to research participants (Rec. 9A&B)

- Which individual research results participants can **access** (incl. under HIPAA)
- Which, if any, results will be **offered**.

Ensure transparency in the consent process cont'd

If results will be offered, consent should state (Rec. 9C)

- **Risks and benefits** associated with receiving results.
- Conditions under which researchers will alert participants of **urgent results**.
- **Time and process** by which results will be communicated.
- Whether results will be placed in a medical record and/or communicated to the participant's clinician.
- When relevant, the participant's option to have results shared with family members if participant becomes incapacitated or deceased.

Implement effective communication strategies

Investigators and institutions (Rec. 10)

- Should communicate results in ways that explicitly convey **clear takeaway messages** that include **statements of actionability** (or lack thereof)
- Should pair results communications with **reference information** to foster participants' understanding of the meaning of results.
- Should **include caveat statements** addressing uncertainties and the limitations to result validity
- Should align communication approaches to the different needs, capabilities, resources, and backgrounds of participants.

Expand the evidence-base

Sponsors and funding agencies (Rec. 11)

- Should support additional research to **better understand the benefits and harms** of return of individual research results, as well as participant needs, preferences and values, and to **enable the development of best practices** and guidance.

Revise and harmonize current regulations

Regulators and policy makers (Rec. 12)

- Should revise and harmonize the relevant regulations in a way that **respects the interests of participants** and **balances the competing considerations of safety, quality, and burdens** on the research enterprise.

Refer to research “participants” not “subjects”

The Department of Health and Human Services (HHS) (Rec. 12G)

- Should ensure that all regulations refer to research “participants” rather than research “subjects” in accordance with ethical principles of autonomy and respect for persons.

Address the CLIA/HIPAA conflict

Office for Civil Rights (OCR) (Rec. 12A&B)

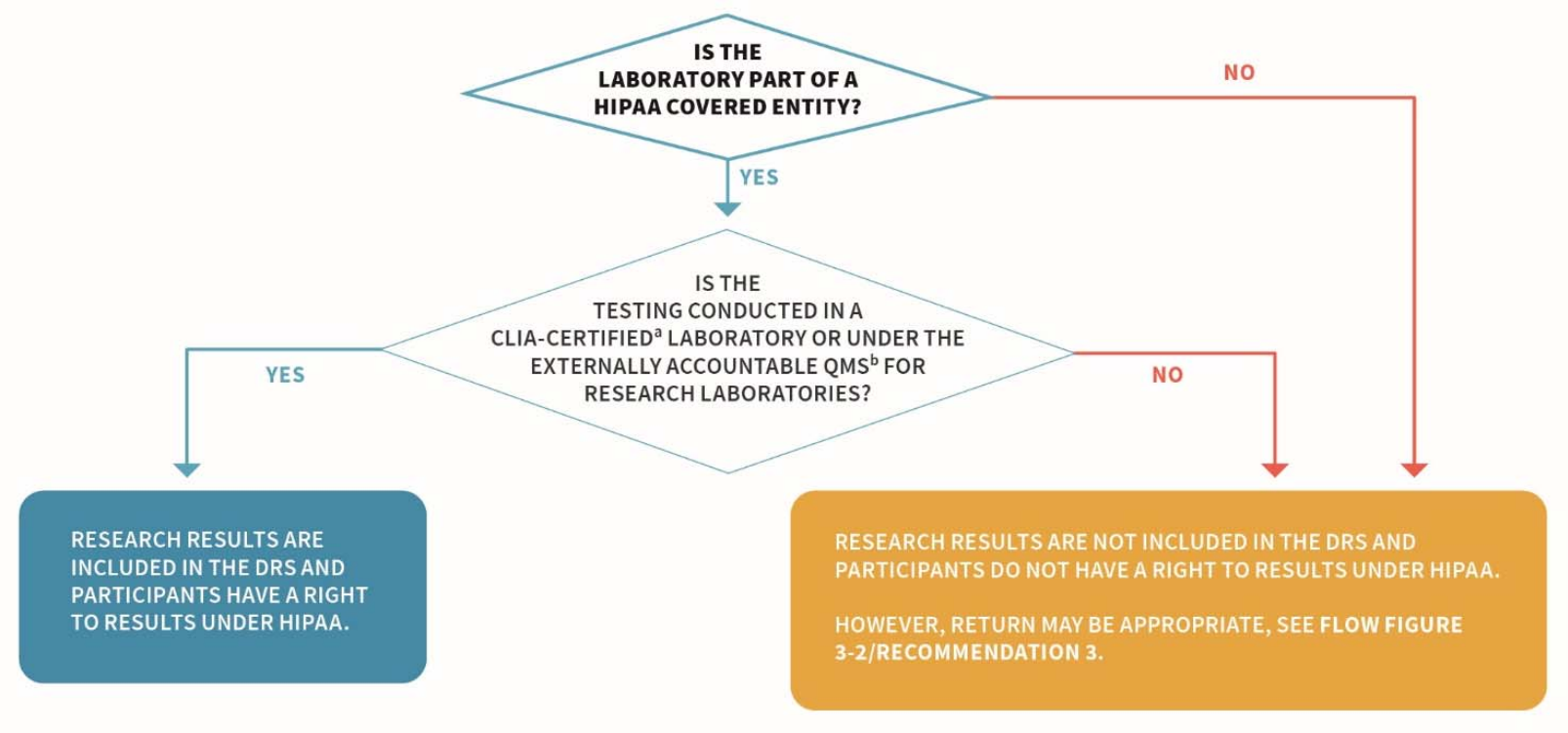
- Should **define DRS** to include only individual research results generated in a CLIA-certified laboratory or under the externally accountable QMS for research laboratories.
- Require HIPAA-covered entities that conduct research on human biospecimens to **develop a plan for the release of individual results** in the DRS to participants.

Address the CLIA/HIPAA conflict cont'd

Centers for Medicare and Medicaid Services (CMS) (Rec 12C&D)

- **Should Revise CLIA**, such that when there is a legal obligation under the HIPAA access right to return research results, a laboratory will not be considered in violation of CLIA and need not obtain CLIA-certification before satisfying this legal obligation.
- **Should allow research results to be returned from a non-CLIA certified laboratory** when they are not intended in clinical decision making in the study protocol and the laboratory conducts its testing under a QMS with external accountability or an IRB approved quality process.

Determining whether participants have the right to access their individual research results under HIPAA



Final thoughts

The recommendations in this report

- Promote a **process-oriented approach** to returning individual research results that considers the value to the participant, the risks and feasibility of return, and the quality of the research laboratory.
- Permit an increase in the return of individual research results over time as stakeholders develop the necessary expertise, infrastructure, policies, and resources.

Final thoughts

The initial investments will likely be significant, but ultimately the return on those investments in terms of **increased participant trust** and **engagement** with the research enterprise and higher quality standards for research laboratories will be worthwhile.

Free PDF available at
nationalacademies.org/ReturnofResults

Response to date (9/19): 4673 downloads