Investigational Device Exemption Case Studies

- These case studies were developed by NHGRI and DO NOT REPRESENT official guidance for FDA regulations.
- IDE risk determinations will always depend on the specifics of the study. Risk determinations PRESENTED HERE have been made based solely on the information presented.
- For more information please contact NHGRI's Policy and Program Analysis Branch.

Protocol 1

- 100 healthy middle-aged adults
  - Randomized to family history or family history plus WGS
    - WGS results entered into participants' EMR
- 100 cardiomyopathy patients
  - Randomized to family history or family history plus WGS
    - WGS results entered into participants' EMR
- WGS conducted in a CLIA-certified laboratory.
- Following (actionable) results disclosure, participants surveyed for anxiety and depression. Follow up at 6 weeks and 6 months includes behavioral, economic, and health outcomes.
- Participants with elevated scores will be referred to a genetic counselor

Protocol 1

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  - Randomized to family history or family history plus WGS
    - WGS results entered into participants' EMR
- 100 cardiomyopathy patients
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    - WGS results entered into participants' EMR
- WGS conducted in a CLIA-certified laboratory.
- Following results disclosure, participants surveyed for

In this protocol, the device may be be all the physical components, reagents, and software that are operated under a single SOP to convert a patient's sample into a result.

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  - Randomized to family history or family history plus WGS
    - WGS results entered into participants' EMR
- 100 cardiomyopathy patients
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- [illegible]
- [illegible]d for [illegible] 6 [illegible]h [illegible]
- Participants with elevated scores will be referred to a genetic counselor

The inclusion of healthy volunteers who would not normally receive the test may increase the risk of the study.

Protocol 1

- 100 healthy middle-aged adults
- [illegible]
- [illegible]
- [illegible]
- outcomes.
- Participants with elevated scores will be referred to a genetic counselor

The risk to participants is mitigated somewhat thanks to appropriate counseling in cases where return of results results in increased stress or potentially inappropriate treatment decisions.

Protocol 1

This study would likely be significant risk.

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    - WGS results entered into participants' EMR
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- Participants with elevated scores will be referred to a genetic counselor

Protocol 2

- Diabetic patients with high likelihood of monogenic diabetes
  - Targeted Ion Torrent panel
  - Pathogenic (for diabetes) mutations confirmed in CLIA-certified laboratory by FDA-approved immunoassay
  - Only confirmed pathogenic sequencing results returned to physicians (no incidental findings)
  - Pre- and post-test genetic counseling

Protocol 2

- Diabetic patients with high likelihood of monogenic diabetes
  - Targeted Ion Torrent panel
  - Pathogenic mutations confirmed in CLIA-certified
  - Pre- and post-test genetic counseling

Here the device is the targeted Ion Torrent Panel.

Protocol 2

The use of an FDA-approved—and therefore "medically established"—diagnostic may make this study exempt, or nonsignificant risk at most.

(performed in a research laboratory)

- Pathogenic mutations confirmed in CLIA-certified laboratory by FDA-approved immunoassay
- Only confirmed pathogenic sequencing results returned to physicians (no incidental findings)
- Pre- and post-test genetic counseling

Protocol 2

- Diabetic patients with high likelihood of
  - laboratory [illegible] FDA-approved immunoassay
  - Only confirmed pathogenic sequencing results returned to physicians (no incidental findings)
  - Pre- and post-test genetic counseling

Restricting return of results to known, confirmed pathogenic findings would likely make this study nonsignificant risk.

Protocol 2

- Diabetic patients with high likelihood of monogenic diabetes
  - Targeted Ion Torrent panel
  - Pathogenic mutations confirmed in CLIA-certified
  - Pre- and post-test genetic counseling

The risk to participants is mitigated somewhat by the inclusion of counseling.

Protocol 2

This study would likely be exempt.

- Diabetic patients with high likelihood of monogenic diabetes
  - Targeted Ion Torrent panel
  - Pathogenic mutations confirmed in CLIA-certified laboratory by immunoassay
  - Only confirmed sequencing results returned to physicians (no incidental findings)
  - Pre- and post-test genetic counseling

Protocol 3

- 6000 adults:
  - Subjects will be enrolled if they have ≥ 30% risk of receiving warfarin, clopidogrel, or statins, or documented adverse event to receiving warfarin, clopidogrel, or statins
  - 84 widely-accepted (PharmGKB) pharmacogenes will be sequenced on a research platform
  - Clinically actionable variants validated with Sanger sequencing in a CLIA-certified laboratory
  - Participants may consent to have clinically actionable variants returned.
  - No return of incidental findings
  - Data will be archived and used for future research, and to make treatment decisions through an existing clinical protocol

Protocol 3

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The device here is the research platform and the panel of 84 pharmacogenes.

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Confining the study to variants with strong evidence of clinical validity mitigates risks to participants in this study.

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  - Participants may consent to have clinically actionable variants

Confirming investigational device results with a "medically established" technique usually exempts a study from requiring an IDE.

Protocol 3

- [redacted]

Restricting return of results to known, confirmed pathogenic findings may make this study nonsignificant risk.

  - Clinically [redacted] variants validated with Sanger sequencing in a CLIA-certified laboratory
  - Participants may consent to have clinically actionable variants returned.
  - No return of incidental findings
  - Data will be archived and used for future research, and to make treatment decisions through an existing clinical protocol

Protocol 3

This study would likely be Nonsignificant risk or exempt.

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