Developing Novel Endpoints, Generated using Mobile Technology, for use in Clinical Trials: A Clinical Trials Transformation Initiative (CTTI) Project

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Background

Efficient and reliable assessment of meaningful endpoints is critical to the ability of a clinical trial to detect important treatment effects.

- Mobile technology offers new ways to capture functional performance over prolonged periods and as trial participants go about their daily lives.
- There is uncertainty about the approach required to develop and use mobile technology-derived novel endpoints to support regulatory approval and labeling claims.
- In June, CTTI will recommendations and tools that describe the pathway to technology-derived novel endpoint acceptance, including guiding principles for endpoint selection and suggested approaches for optimizing the efficiency of novel endpoint development. These recommendations and tools are summarized here.

Methods

CTTI established a project team to develop recommendations on the selection, development, and application of novel mobile endpoints.

- This project team defined novel endpoints as either (a) new endpoints that have not previously been possible to assess (e.g., tremor), or (b) existing endpoints that can be measured in new and possibly better ways.
- The team comprised individuals from regulatory agencies, pharmaceutical & technology industries, academia, and patient advocacy organizations.

Recommendations

Optimizing Novel Endpoint Selection

Focus on measures that are meaningful to patients.

When selecting outcome assessments for development, the approach should be patient-centered with the patient voice included as standard in the work of clinician experts in the therapeutic area.

- Select the device after selecting an outcome assessment.
- Selecting a suitable mobile device for data capture should occur only after the clinical outcome assessment or biomarker is identified.

Use a systematic approach to identify key novel endpoints.

CTTI has developed a Selection Tool that may be helpful when deciding between viable novel endpoints for development.

Anticipated Benefits of Developing Novel Endpoints for Use in Clinical Trials

<table>
<thead>
<tr>
<th>SPECIFIC BENEFITS</th>
<th>SHORT-TERM</th>
<th>MEDIUM-TERM</th>
<th>LONG-TERM</th>
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</thead>
<tbody>
<tr>
<td><strong>Patient Centricity</strong></td>
<td>Development of high-quality, patient-centric, mobile technology-derived endpoints</td>
<td>Increased in clinical trials that yield more complete information on how therapies affect disease most important to patients</td>
<td>Reduced participation burden (patient and caregiver) in clinical trials</td>
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<tr>
<td>Enhanced technology for use for observational cohort studies</td>
<td>Increased in clinical trials that yield more complete information on how therapies affect disease most important to patients</td>
<td>Reduced participation burden (patient and caregiver) in clinical trials</td>
<td>Increased in clinical trials that yield more complete information on how therapies affect disease most important to patients</td>
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<td><strong>Efficacy</strong></td>
<td>Improved probability rates for advanced trials phase II to phase III trials in clinical trials</td>
<td>Increased efficiency of postmarket surveillance</td>
<td>Increased in number of potentially successful treatments taken forward for testing in phase III trials, particularly in high-risk therapeutic areas</td>
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<tr>
<td>Decreased dropout rate by patients in phase I/II trials through use of mobile technology in clinical trials</td>
<td>Increased efficiency of postmarket surveillance</td>
<td>Increased in number of potentially successful treatments taken forward for testing in phase III trials, particularly in high-risk therapeutic areas</td>
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<tr>
<td><strong>Safety</strong></td>
<td>Use of mobile technology to enhance safety in clinical trials</td>
<td>Increased in number of potentially successful treatments taken forward for testing in phase III trials, particularly in high-risk therapeutic areas</td>
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Practical Approaches to the Novel Endpoint Development Process

Foster collaboration among key stakeholders.

Sponsors, patients, clinicians, technology companies, and regulators should collaborate in a pre-competitive environment to identify and advance consensus on the mobile technology-derived outcome measures that are most valuable and warrant development.

Create technical standards for mobile technology-derived assessments.

Technical standards are required for the efficient development and rapid adoption of any technology.

Engage with regulators.

Regulators can and should provide critical input throughout the process of developing novel endpoints.

Include novel endpoints as exploratory endpoints in existing clinical trials and observational cohort studies.

Including novel endpoints in clinical trials as exploratory assessments is the best way to understand what value they offer as well as how to further refine the endpoint.

Think critically about how to optimally position novel endpoints in interventional trials.

Where novel endpoints address unmet need, they may be uniquely important as primary efficacy endpoints. However, where well-established endpoints that effectively demonstrate clinical benefit already exist, novel endpoints may be valuable as complementary assessments.

Next Steps

The recommendations will be launched during a CTTI webinar on Monday, June 26 at noon ET.

For more information or questions please contact the CTTI project manager for this effort, Jennifer Goldsack at Jennifer.Goldsack@duke.edu.