Protocol Builder Feasibility Analysis

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Introduction

- Secure, web-based application to help Institutions create better quality investigator-initiated protocols faster and easier

- Developed by BRANY (Biomedical Research Alliance of New York)

- Designed to meet Federal/Industry Regulatory Standards
  - 16 various Protocol Types – Observation and Interventional
  - Expert Guidance icon – Detailed explanation of the requirements for each field
  - Smart Forms with Branching Logic – Predictive and reduces the need for double-entry of text
  - Resource Center – Provides commonly used Research forms and allows addition of supporting documentation

- Allows for development and review of document protocol by multiple individuals (Investigators, Coordinators, Administration, etc.)
Studies Evaluated

- 8 IRB-reviewed, Investigator-initiated Studies
  - Experienced Investigators purposely selected
  - Interventional FDA-Approved Drug/Biologic (2); Interventional FDA-approved drug w/repository (1); Interventional Drug - Investigational New Drug (2); Interventional Device - Non Sig. Risk (1); Observational Prospective (1); Interventional Behavioral (1)

Federally Funded (NIH - NIDDK, NCI, NHGRI, NICHD)
- Adoptive Transfer of Cord Blood T cells to Prevent and Treat CMV, EBV and Adenovirus Infections after Transplantation
- Multivirus-Specific Cytotoxic T-Lymphocytes for the Prophylaxis and Treatment of EBV, CMV, and Adenovirus Infections post Allogeneic Stem Cell Transplant
- Energy Expenditure and Metabolic Control Among Youth with T1 Diabetes
- Healthy Eating, Physical Activity, & Glycemic Control in Young Children with Type 1 diabetes (T1D) – Phase 1
- N-carbamylglutamate in the Treatment of Hyperammonemia
- Short-Term Outcome of N-Carbamylglutamate in the Treatment of Acute Hyperammonemia
- Reverse Transcriptase Inhibitors in Aicardi Goutières Syndrome

Internally Funded
- Integrated Control and Movement System to Enhance Flexible Ureteroscopy
Categories Evaluated

- **User Interface contains 150 total fields**
  - Number of fields per study dependent upon Protocol Type selected
  - 11 Primary fields – Cover Page, Synopsis, Introduction, Study Objectives, Study Design, references, etc.
  - 77 Secondary fields – Title, Investigational Product, Prior Experience, Risks/Benefits, Outcome Variables, Study Population, Funding Source, etc.
  - 62 Tertiary fields – Drug/Device Preclinical Experience, Primary Outcome Variable, Eligibility Criteria, Adverse Events Definition, etc.

- **Feasibility Study (N=8)**
  - 88 total Primary fields; 616 total secondary fields; 496 total Tertiary fields
  - Investigator’s official Protocol compared to associated fields within Protocol Builder

**Key**
- No Corresponding Section Present
- Similar Section Present/Out of Place but in similar section
- Corresponding Section Present
- Section Not Applicable
Results 1

<table>
<thead>
<tr>
<th>Category</th>
<th>Total (out of)</th>
<th>No Corresponding Section Present</th>
<th>Similar Section Present/Out of Place but in similar section</th>
<th>Corresponding Section Present</th>
<th>Section Not Applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Category</td>
<td>88 fields</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary Category</td>
<td>616 fields</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertiary Category</td>
<td>496 fields</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Results 2

- No Corresponding Section Present
- Similar Section Present/Out of Place but in similar section
- Corresponding Section Present
- Section Not Applicable

- Primary Category Total (out of 88 fields)
- Secondary Category Total (out of 616 fields)
- Tertiary Category Total (out of 496 fields)
Findings

<table>
<thead>
<tr>
<th>Field</th>
<th>No Corresponding Section Present</th>
<th>Similar Section Present/Out of Place but in similar section</th>
<th>Corresponding Section Present</th>
<th>Section Not Applicable</th>
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<tbody>
<tr>
<td>Primary</td>
<td>15.9%</td>
<td>34.1%</td>
<td>50.0%</td>
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<tr>
<td>Secondary</td>
<td>15.4%</td>
<td>32.0%</td>
<td>32.3%</td>
<td>20.3%</td>
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<tr>
<td>Tertiary</td>
<td>7.5%</td>
<td>36.7%</td>
<td>21.9%</td>
<td>33.9%</td>
</tr>
</tbody>
</table>
Findings

- Overall the majority of Primary, Secondary, and Tertiary fields are present

- However...
  1) A significant number are out of place or placed inconsistently throughout the protocol (i.e. there is very little organizational consistency among protocols)
  2) Many of the sections that are missing are essential (e.g. Protocol version/date; Adverse Events definition and reporting; IRB Review; Removal of subjects; Study discontinuation; Study monitoring; Handing of missing data; Appendix/References, etc.)

- Drug/Biologics studies (both FDA-approved and IND) are most consistent; Observational/Behavioral least consistent

- Studies reviewed and approved by NIH were most consistent
Benefits/Considerations

• Benefits
  • Quality Improvement
    • Improve consistency of protocol development institution-wide
    • Increase adherence to FDA, IRB, Sponsor, and Institutional regulations
  • Expedite Process
    • Guided experience saves Investigator’s time
    • Standardization decreases time and effort required for SRC, IRB, etc. review
  • Automatic Updates
    • Continuously updated to address changes in regulations, industry standards, and research trends
  • Web accessibility
    • Accessible anywhere, anytime

• Considerations
  • Cost
  • Adding a writer or reviewer to a protocol requires the use of an additional license
  • Current format may require some modifications to suit Institutional norms
Recommendations

• Should be considered a **template** protocol development tool
  • *Not final – Minor modifications can be made after completion to suit Sponsor, IRB, etc.*

• Conduct a 15 - 25 study pilot including junior and senior Researchers
  • *To confirm need and to obtain feedback (esp. regarding user interface changes)*

• Review of input fields by CNHS Research experts (Select senior Investigators, OPHS, QA/QI staff, etc.)
  • *Developers can modify user interface and input fields based on client feedback*
  • Consider adding: Confidentiality statement; Signature page; “N/A” option
  • Consider omitting: Study number; funding source; Health Economic Impact

• Insist that ad hoc modifications be allowable in contract