ISTAND Qualification Letter of Intent (LOI) Model Content Elements

FDA is providing a model content outline describing the information that should be included in an Innovative Science and Technology Approaches for New Drugs (ISTAND) Pilot Program letter of intent (LOI), which should be accompanied by a cover letter and include the following information. If literature is cited, please cite using the number assigned to the source in a numbered reference list.

Note: Certain information contained in submissions will be made publicly available as per section 507, as described in greater detail HERE upon acceptance into the pilot program. Section 507 refers to section 507 of the Federal Food, Drug, and Cosmetic Act [FD&C Act] which was created by Section 3011 of the 21st Century Cures Act.

1. **Submission Title**: One sentence description of the submission.

2. **Requesting Organization**:

- Name of Organization: Physical Address; Phone Number; Website address
- Primary Point of Contact: Name; Job Title; Address; Phone Number; Email
- Alternate Point of Contact: Name; Job Title; Address; Phone Number, Email
- Supporting or participating organizations or individuals

3. **Drug Development Need Statement:** Describe the drug development need that submission is intended to address, including (if applicable) the proposed benefit over currently used tools in similar contexts of uses (COUs). (200 words maximum target)

4. I**STAND Applicability Statement:** This program is designed to support drug development tools that are not biomarkers or clinical outcome assessments (COAs). A drug development tool is a method, material, or measure that has the potential to facilitate drug development; biomarkers and COAs are defined in the BEST Glossary. Please indicate how this submission is a drug development tool that does not meet the definition of a biomarker or COA. (250 words)

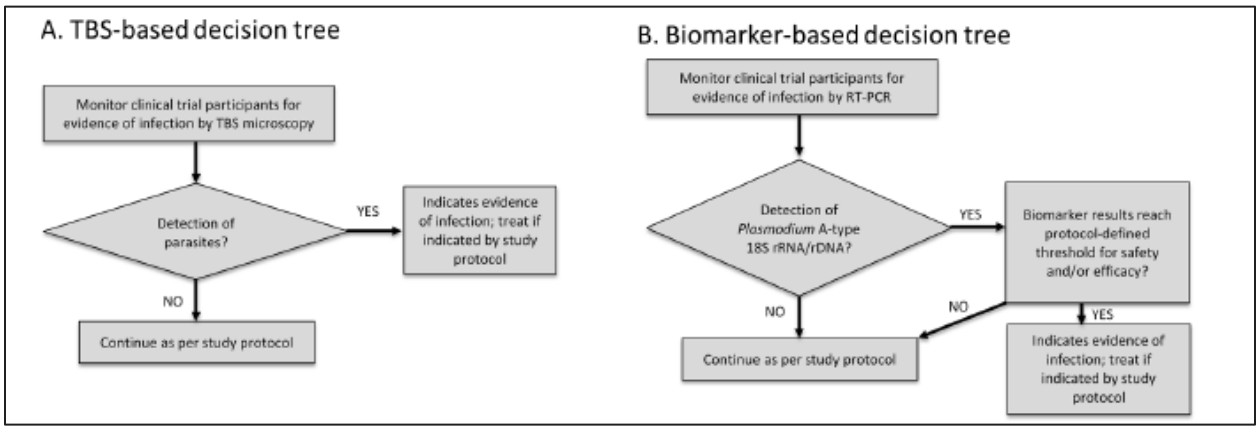
5. **Context of Use Statement:** A statement that fully and clearly describes the way the drug development tool will be used and the drug development-related purpose of the use. Examples of COU statements are available on the Biomarker Qualification Submissions and the Qualified Biomarkers web pages. Please note that drug development tools are qualified as tools to aid in drug development. While such tools may be used for other purposes (e.g., to aid in clinical decision making), COUs that do not address a specified drug development use are outside the scope of the program. Only a single COU should be included in your LOI. (250 words)

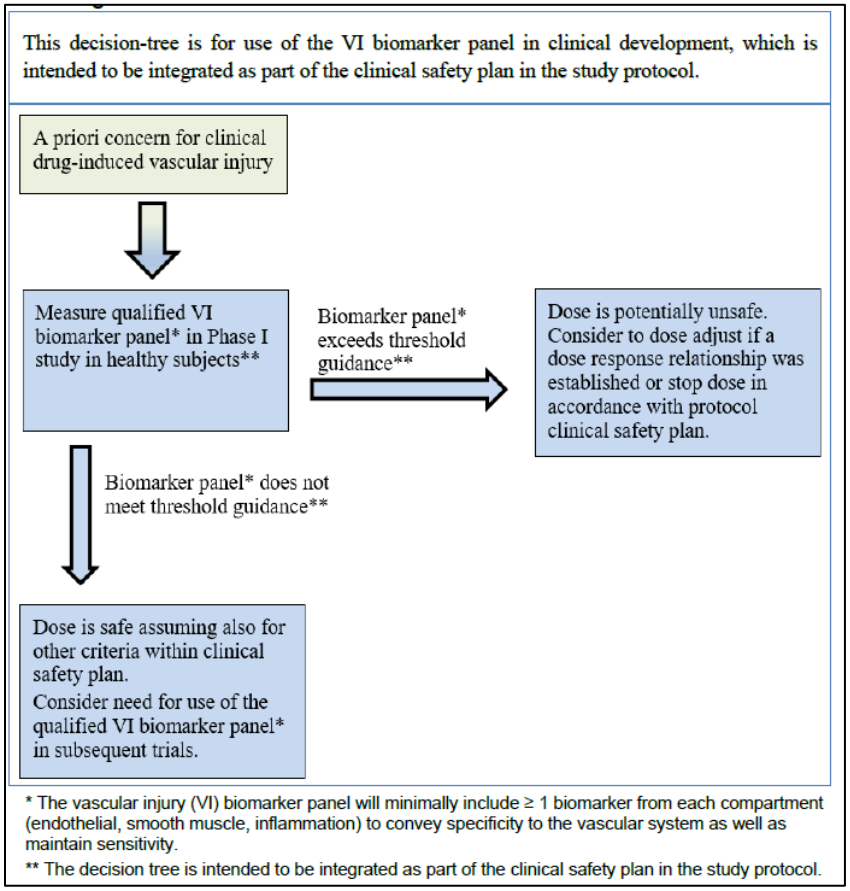
6. **Drug Development Use:** Describe the specific drug development use for the tool in the context of the current-state. Provide a flow diagram with decision tree (e.g., what is the current paradigm the drug development need the tool is targeting, how would the ISTAND tool be triggered and change the current paradigm, including changing a specified regulatory outcome). See example flow diagrams here.

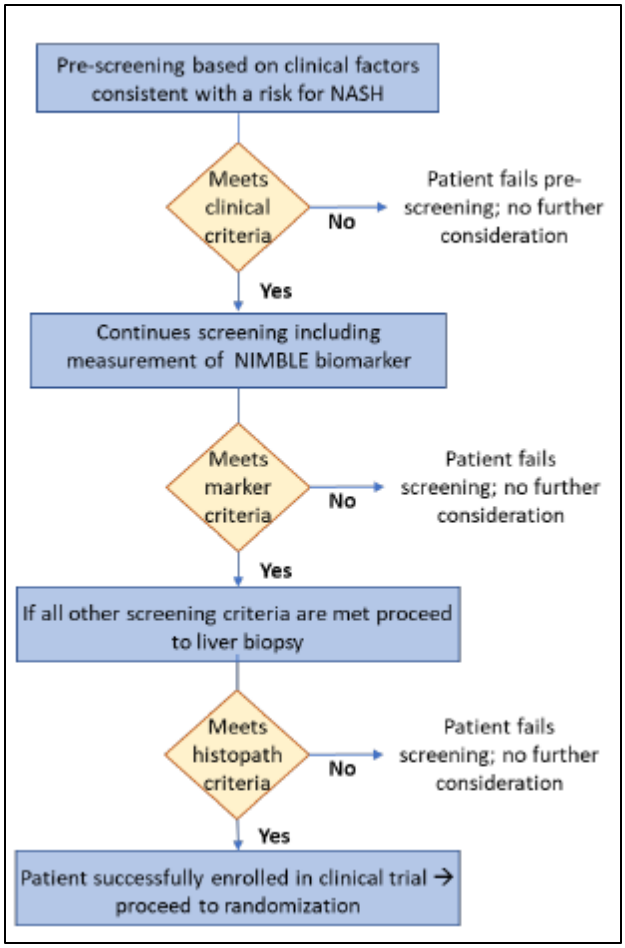
7. **Technical Description:** Provide a technical description of the science or technology approach, its operating characteristics, and its realized and potential uses in drug development. Provide information on the clinical and analytical validity of the tool, or plans to establish the validity, if applicable. (5 pages plus references)

8. **Previous Regulatory Interactions:** Please describe any previous or concurrent interactions with FDA or ex-US regulators (e.g., EMA, PMDA) regarding this submission. Include information about the timing and nature of the interaction and any outcomes. (1 page)

Example Drug Development Use Flow Diagrams






Pre-screening based on clinical factors consistent with a risk for NASH
Meets clinical criteria
No
Patient fails pre-screening; no further consideration
Yes
Continues screening including measurement of NIMBLE biomarker
Meets marker criteria
No
Patient fails screening; no further consideration
Yes
If all other screening criteria are met proceed to liver biopsy
Meets histopath criteria
No
Patient fails screening; no further consideration
Yes
Patient successfully enrolled in clinical trial → proceed to randomization