International Liquid Biopsy Standardization Alliance Charter

Effective June 10, 2020

The International Liquid Biopsy Standardization Alliance (ILSA) comprises organizations that recognize the importance of working towards the global use of liquid biopsy and common reference standards in oncology and seek to promote their use in the broader medical community. The ILSA partners are thus aligned in their common vision to bring about the ubiquitous and meritorious use of liquid biopsy to support clinical decision making and regulatory considerations, which will ultimately reduce the need for unnecessary and invasive solid tumor biopsies. ILSA efforts are synergistic and address the spectrum of unmet needs to bring liquid biopsy into routine clinical application. Organizations joining the ILSA group intend to share the scope of their work, discuss lessons learned, and disseminate the tools and data they develop as a coordinated effort.

Mission: *The International Liquid Biopsy Standardization Alliance (ILSA) brings together complementary efforts around liquid biopsy standardization, focused on circulating tumor DNA (ctDNA), to promote its use as a broadly functional biomarker in cancer. These efforts aim to provide guidance on the development of universally recognized reference samples and best practices, which will increase assurance that assay testing steps are executed appropriately and provide harmonized and accurate results. The alliance consists of multiple stakeholders representing the public and private sectors, including academia, industry, government, patients, and end users.*

Meetings: The ILSA partners place value in the exercise of information exchange through quarterly in-person meetings and teleconferences. These meetings are intended to provide updates across membership on recent activities and to coordinate the scope and exercise of their collective efforts. All decisions made by the group are supported democratically through a simple majority vote with dispute adjudication exercised before the full alliance. Minutes are taken from each meeting and disseminated to the full group for review and edit before archival at FNIH.

Scope: The group believes in the value of disseminating accounts of its collective efforts to the broader field. The group will publicize its alliance through educational outreach to the scientific community and seek to make gathered resources broadly available. These activities may include but are not limited to development of:

- Pre-analytical variables;
- Material use and naming convention;
- Appropriate standards for collection and data coordination;
- Guidance documents;
- Educational material across diseases and clinically relevant applications;
- Ring studies, protocols, and clinical trials;
- Clinical collection standards;
- Infrastructure for laboratories to collaborate and build complementary data sets;
- Qualified reference materials for real-world-use testing in the field;
- Recommendations and pathways for qualification of standards and assays;

- SOPs, lessons learned, and best practices; *and*
- A connection point and open venue for commercial vendors, clinical centers, diagnostic laboratories, and other consortia for further engagement.

Membership: The alliance is open to all those working in liquid biopsy, reference standards, or standardization who wish to join, but is likely most suitable to public- and private-sector actors from academia, industry, and government, as well as patients and end users of genetic testing. Members are expected to join teleconferences and face-to-face meetings and to provide input and feedback to inquiries from their colleagues. Members are free to leave the group at any time.

ILSA is sponsored and hosted by the Foundation for the National Institutes of Health (FNIH) and is an organization of equals. It is expected that the alliance will find utility in developing workstreams and subgroups to facilitate progress, however. Subgroups, administered through occasional additional teleconferences, are expected to convene around issues related to repository buildout, data collection and quality; collation of lessons learned and best practices; communications, outreach and promotion; and guidance and standards review. Subgroup recommendations will be reviewed by the entire alliance and subgroup membership is voluntary.

Present membership includes representatives from BloodPAC, CANCER-ID, the European Liquid Biopsy Society (ELBS), the International Society of Liquid Biopsy (ISLB), the FNIH Biomarkers Consortium ctDNA Quality Control Materials Project, the Friends of Cancer Research ctDNA to MONItor Treatment Response (ctMoniTR) Project, JMAC, the Medical Device Innovation Consortium (MDIC), and the National Institute for Biological Standards and Control (NIBSC, UK), with observance and participation from Food and Drug Administration (FDA) and European Medicines Agency (EMA) staff.

Objectives: ILSA members strive to develop the infrastructure needed for continued communication of ongoing efforts. To that end, the ILSA group has proactively linked partner efforts on their websites to promote and disseminate each other's work. ILSA members have also committed to building a central repository for information sharing hosted by the BloodPAC Data Commons. The platform will share links to each organization to help researchers and clinicians recognize existing collaborations and avoid initiating duplicative efforts. Future development of the repository is planned to host reference development and testing protocols, white papers that highlight best practices, relevant policies for different countries and regions, and eventually de-identified data sets from studies that can be utilized in continued research.

Goal: The ILSA members wish to encourage others in the liquid biopsy field to join the group to help harmonize the many disparate efforts that strive towards progress in achieving full "clinical utility" of liquid biopsy in the many contexts of use in which it is applicable. Progress in achieving harmonization of the field will be evaluated periodically by the group to assess effectiveness and additional needed efforts.

Eventually, ILSA would like to identify and develop a uniform end-to-end process from pre-analytic capture through technology and assay validation to clinical collection and analysis. The group would then hope to promote the use of this process to allow for standardized data capture for liquid biopsy to build the necessary level of evidence required to have multiple contexts of use qualified by regulatory agencies for clinical implementation.

Charter Signatories

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