

## CONCEPT CLEARANCE RECORD

### FY 2016 RESEARCH INITIATIVE – NCATS

TITLE: R&D Contract Support for NCATS Translational Sciences

INITIATIVE TYPE: Request for Proposals

OBJECTIVE(S): To obtain long-term contract laboratory services in support of the mission of the NCATS Division of Pre-Clinical Innovation (DPI).

DESCRIPTION: NCATS uses both internal and contract resources to advance collaborative research projects across the phases of the translational science spectrum. These research projects are designed to overcome key obstacles and inefficiencies in the translational process. While the mechanisms for overcoming obstacles differ, multiple NCATS programs require access to contract resources to achieve their missions. For example, the Therapeutics for Rare and Neglected Diseases (TRND) and Bridging International Development Gaps (BrIDGs) programs heavily rely on contract research organizations (CROs) to provide manufacturing, pharmacology, toxicology, regulatory and clinical operations services to achieve milestones of their projects. All projects within TRND and BrIDGs programs require Good Manufacturing Practice– and Good Labor Practice–compliant services, which cannot be performed within NCATS' own laboratories. Other NCATS programs, such as Chemistry Technology and Matrix Combination Screening, regularly use CROs to profile molecules that are being investigated internally.

This clearance proposes to request proposals from vendors to provide long-term contract services for NCATS programs in various pre-clinical and clinical therapeutic development areas. A myriad reputable CROs operate in the drug development space and provide needed services to government customers. These services may include:

- Optimizing the chemical structure of promising drug compounds to maximize their activity and minimize their toxicities;
- Developing animal disease models;
- Conducting Investigational New Drug (IND)-enabling safety studies;
- Conducting Chemistry, Manufacturing and Controls (CMC) development studies;
- Manufacturing biologic products, gene vectors and cell therapies;
- Designing and validating assays and processes;
- Providing regulatory strategy and assembling materials for pre-IND and IND submissions;
- Conducting clinical trials in accordance with the NCATS mission and authorization; and
- Providing quality assurance and quality control information for all studies.

IMPORTANCE: The short-term goal of this research and development (R&D) activity is the development, demonstration and dissemination of new translational technologies and approaches. In the long term, the contracts will enable the identification of new candidate therapeutics, the filing of INDs with the U.S. Food and Drug Administration and the generation of clinical data that may allow NCATS collaborators and other researchers to market new therapeutics.

NCATS programs have historically used CROs to meet these goals. For example, the TRND program notably used external resources to develop promising sickle cell and Niemann-Pick disease type C therapeutics. Due to CRO-generated data, NCATS facilitated multimillion-dollar investments into these therapeutics by industry.

To generate those data and others, NCATS leveraged the contract capabilities of other NIH Institutes and Centers (ICs). While use of other programs' resources was initially beneficial, reliance upon non-NCATS contracts has become untenable for many reasons. First, those contracts have statements of work that are limited by the scope of the programs they serve. The Statements of Work may restrict the use of the contract to a limited number of ICs or to a limited range of therapeutic modalities, disease areas and route of administrations or study durations. Further issues arise when other ICs are unable to accept work,

even when in scope, due to the impact that additional funding has on their contract ceilings. Finally, another IC's ability to make timely contract awards during critical fiscal year periods can be limited. Such limitations put NCATS' ability to innovate at risk.

NCATS programs onboard new collaborations annually through formal and informal means, leading to a regular need for contract resources to be in place. The NCATS DPI budget is allocated for programs like TRND, BRIDGs, Chemistry Technology and Matrix Screening that establish and nurture these collaborations. Because of NCATS' strong interest in de-risking translational opportunities, especially in the rare and neglected disease space, it is important for the Center to have its own contracts and the ability to independently advance promising science forward when the private sector has demonstrated a lack of interest in doing so.

Under NCATS direction, preclinical research will be conducted in compliance with applicable regulatory and agency policies and regulations. Likewise, while the interest in the rare and neglected disease therapies may limit the diversity of patients enrolled in NCATS-sponsored clinical research, best practices (e.g., the inclusion of women, minorities and children as appropriate) will be followed when possible.

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