Complement Animal Research in Experimentation (Complement-ARIE) – A Common Fund Proposal

Background: The 21st century has been a time of accelerated technological advancement. With the recent adoption of the FDA Modernization Act 2.0, drugs are no longer required to go through animal studies to be registered. NAMs, which broadly span *in chemico, in vitro*, and *in silico* approaches, have proven to be valuable tools in basic, clinical, and toxicology research, and have been used to study the efficacy and toxicity of novel therapeutics. The trans-NIH Complement Animal Research In Experimentation (Complement-ARIE) working group (WG) has been engaged in robust strategic planning activities and stakeholder outreach focused on developing a unifying vision for building on ongoing efforts to develop, standardize, validate, and use NAMs, and identifying opportunities for innovation and coordination.

Program Goal: To catalyze the development, standardization, validation, and use of **human-based new approach methodologies (NAMs)** that will transform the way we do basic, translational, and clinical sciences.

Proposed Initiatives based on Strategic Planning Outcome and aligned with ACD Recommendations:

- **Technology development projects/centers** – stimulate the development of NAMs to fill in areas of greatest need, with emphasis on increased biological complexity and throughput, innovative combinatorial approaches, and data sharing. Training component required.
- **Data & NAM resource coordinating center** – create integrated data structures, including standards for model credibility, improve FAIRness (Findability, Accessibility, Interoperability, and Reusability) of NAM-relevant data, create searchable NAMs repository.
- **Validation network for regulatory implementation** – establish common data elements and standardized reporting, apply validation/qualification frameworks, accelerate deployment and regulatory implementation of NAMs.
- **Community engagement and training** – promote the development of an inclusive, diverse biomedical research workforce with the skills to build/use new NAMs, and community engagement, including societal and ethical considerations.
- **Strategic engagement** – ~2-5% of program funds to engage with emerging opportunities.

Deliverables: Complement-ARIE will significantly advance understanding of human health and etiology of human disease, have near-term application in fields such as mechanism elucidation, personalized precision medicine, safety pharmacology, predictive toxicology, and efficacy evaluation of candidate therapeutics, and provide a range of ready and standardized models for health and disease biology.

Budget: 10-year initiative, consisting of two five-year phases. Includes direct & indirect costs ($M).

Initiatives	FY25	FY26	FY27	FY28	FY29	FY30	FY31	FY32	FY33	FY34	TOTAL
1) Projects/Centers	24	24	25	25	25	25	25	25	25	25	248
2) Data Coordination	5	5	5	5	5	5	5	5	5	5	50
3) Validation network	2.95	2.95	3.4	3.4	3.4	3.4	3.4	3.4	3.4	3.4	33.1
4) Training	0	0	3.4	3.4	3.4	3.4	3.4	3.4	3.4	3.4	27.2
5) Engagement	2	2	2	2	2	2	2	2	2	2	20
RMS	1.05	1.05	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	11.7
Total	35	35	40	40	40	40	40	40	40	40	**390**