Concept Clearance – Continuation of the Gabriella Miller Kids First Pediatric Research Program (Kids First).

Description: Kids First was initiated in response to the 2014 Gabriella Miller Kids First Research Act. The Act and this program were named in honor of a young Northern Virginia girl who in her short life became a persuasive advocate for pediatric research. The Act authorized an appropriation of $12.6 million per year for ten years to be used to support pediatric research specifically to "supplement, not supplant" existing research efforts. The first appropriation for Kids First was for fiscal year 2015.

Kids First has been a Common Fund trans-NIH Program administered by NICHD with the help of NCI, NHLBI, NHGRI, and additional colleagues from numerous NIH institutes and the CDC. The Kids First Working Group was tasked with building a data resource to advance collaborative research and data sharing for childhood cancer and structural birth defects. These conditions are leading causes of death in childhood, and while collectively are far too common, individual conditions are mostly rare, and collecting sufficient patient populations for genomic studies has been challenging. It makes sense to study these conditions together, since shared genomic variants and signaling pathways have been identified; and a child born with a birth defect faces an increased risk of also developing cancer.

Phases 1 and 2 Major Accomplishments: To populate the Kids First resource, whole genome sequence data was generated from cohorts of children and their families with pediatric cancer and/or structural birth defects. This data has been harmonized along with relevant clinical and phenotypic data, and been made available to the research community through the Kids First Data Resource Portal. In the portal, researchers can visualize and search the clinical and phenotypic data to find individual-level genomic data of interest, and then bring together and analyze genomic data from multiple data sets and even from across multiple NIH Data efforts. The portal enables analysis across conditions and allows researchers to bring in their own data to analyze alongside Kids First data. Genomic, phenotypic, and clinical data from 22 birth defects and 11 pediatric cancers, are available. This data is being used: more than 3,800 users are registered on the data resource portal and there have been more than 650 data access requests approved for secondary use of Kid First genomic data. Kids First actively collaborates with other data efforts such as the Childhood Cancer Data Initiative, INCLUDE, the Common Fund Data Ecosystem, and NIH's Cloud-based Platforms for Interoperability**,** and with other partnerships and pilot efforts**.** The availability of this large resource of genomic, phenotypic and clinical data along with a researcher-friendly data platform and analysis tools empowers basic mechanistic and gene regulatory studies, accelerates discoveries of biomarkers and targets for precision medicine, and transforms pediatric research.

Phase 3 Concepts: Legislation (H.R. 3391 and S.1624) to authorize an extension of the Kids First Program is currently before Congress. These bills differ in duration and authorized funding levels, but each specifies Kids First is to be a DPCPSI program that "shall prioritize such pediatric research that does not duplicate existing research activities of the National Institutes of Health."

The Kids First Working Group has proposed the following activities for consideration if there is an extension of the Kids First program:

- Enable addition of data to the resource including clinic-based data generation and new –Omics Data.
- Enhance Development of Data Resources.
- Support expert-driven activities to increase the value of Kids First data.

At a high level, these activities follow the same themes that successfully guided phase 2 of the Kids First program's prior years. However, in detail there are new aspects and areas of emphasis stemming from experience of the program and input from the research and patient community. New areas of proposed emphasis include:

- Expansion of data generation to include individuals from clinical settings or patient registries.
- Increased emphasis on prioritization of a diversity of conditions and participants for cohort-based sequencing.
- Additional data types as scientifically justified, and technologies mature.
- Training and tool development emphasizing utilization of Kids First data by non-bioinformatics researchers.
- Facilitation of electronic health record inclusion and establishment of FHIR-based standards for pediatric data.
- Development of comprehensive variant curation methodologies and annotation of Kids First data.

These high-level conceptual activities will be translated into specific initiatives by the Working Group as appropriate for the number of years the program is extended, and the levels of funding provided. This request for Concept Clearance for the potential extension of Kids First is submitted on behalf of the Gabriella Miller Kids First Working Group.