



Agenda

September 24-25

The Food and Drug Administration (FDA) is announcing a public conference entitled **“Next-generation sequencing (NGS) technology, data formats standardization and promotion of interoperability protocols.”** The goal of the conference is to engage stakeholders in discussions to identify the benefits and limitations of NGS technology as it pertains to FDA-regulated products. FDA would like to involve the broader NGS community, including relevant representatives of other government agencies, academia, industry developers of sequencing and bioinformatics platforms, and end-users of the technology, to discuss these and other relevant questions in an effort to move forward in a more informed manner to better provide guidance to sponsors on these and other issues.

SESSIONS

The meeting will last two days and consist of 7 main sessions to address the diverse needs of different organizational units within FDA and the wider NGS community as they pertain to regulation of medical products involving this technology:

Next-Generation Sequencing Standards (Chaired by Dr. Vahan Simonyan/FDA)

Perspectives of FDA and select government representatives will be highlighted in this section as they pertain to the submission of NGS data and validation of analytical protocols. The purpose of this session is to assemble working groups for the development of guidance for a versatile platform of next-generation sequencing technology verification, standardization of data formats and bioinformatics analysis provenance, and promotion of interoperability protocols.

The immediate motivation for the proposed standards is to promote confidence in all data delivered by various technologies to users and regulatory staff, and to ensure the suitability of such data for high-stakes research including but not limited to studies resulting in regulated products. To better support regulatory staff to make best decisions regarding public interests, there is a need to implement a set of self-imposed standards that will not only guarantee data of the highest quality, but to further ensure the provenance of such data and all bioinformatics approaches from which NGS information is generated. Short term goals and the focus of this conference are centered on the quality of the information and uniform meta-information submission. Future workshops will proceed to open the dialogue on harmonization of various computational protocols and provenance of the bioinformatics pipelines.



Potential stakeholder and perspectives:

- Center representatives will have a chance to outline the need for FDA to develop a consistent set of formats, computational protocols, and submission procedures to promote the usage of HTS data for research and regulatory sciences.
- National and international institutes providing infrastructure services such as NCBI, NIST, CDC, EBI, DDBJ and ICGC will be able to communicate their perspectives on HTS data formats standards and protocols
- Representatives from previously established standardization consortiums will be able to present success stories and challenges encountered during attempts to systematize HTS platforms.

Big Data Administration and Compute Infrastructure (Chaired by Dr. Eugene Yaschenko/NCBI)

Platforms for NGS data storage and analysis will be the key subject of this session. Stakeholders will be able to represent their perspectives on storage hardware, large data transfer networking, and distributed compute platforms capable of supporting HTS based research and regulatory sciences.

Different platforms and providers will have the opportunity to present their respective environments in order to gain a better understanding of what they envision as the appropriate resources to best enable NGS stakeholders to successfully complete their tasks. The goal is to determine which resources are available, necessary and/or most appropriate.

In addition to introducing diverse platforms, current and developing computing infrastructures will be introduced. This topic will be discussed by various developers whose main focus is NGS analysis. This will help to identify the tools which are prominently used within the community and to ensure that these are the optimal tools for producing accurate and reliable results.

Potential stakeholders:

- Public and private cloud computing platform providers such as Amazon, Google clouds, etc.
- Bioinformatics platform developers such as HIVE, dna-nexus, Galaxy, SevenBridges, CLC-bio, NCBI, etc.
- Large infrastructure hardware providers: Internet2, IBM, Dell, etc.

Database development (Chaired by Dr. Raja Mazumder/George Washington University)

This session will focus on the need for the development of databases that address all the requirements of NGS data stakeholders. Discussion of the validation and integration protocols necessary to maintain the integrity of the data and database will also be encouraged keeping in mind the goals of developing a database that includes model organism information as well as the integration of existing commonly used databases such as NCBI and Uniprot. The hope is



to establish the resources that must be incorporated when developing an NGS database and the curation steps needed to produce a viable and reliable database that facilitates collaboration and research.

Biologics Product Evaluation (Chaired by Dr. Konstantin Chumakov/FDA, Dr. Arifa Khan/FDA)

This section will be headed by CBER. It will present a chance for industry manufacturers of biologics to communicate their perspectives to FDA's NGS initiative.

This session will review different applications of NGS in development, evaluation, and quality control of biological products. The applications include adventitious virus detection in cellular substrates and products manufactured using *ex vivo* ingredients, characterization and identity testing of complex biologicals, and assessment of genetic stability and molecular consistency of live and inactivated vaccines. The talks will describe current efforts for addressing gaps in sample preparations, standards, data analysis pipelines, and virus databases. Additionally, approaches for data collection, format, and transfer and standardization of protocols will be discussed. Speakers will be encouraged to share their vision of utility and expectations for the NGS-based methods and discuss challenges in making the results comparable and easily transferrable to alternative analysis platforms.

The session will provide an opportunity to initiate discussions to formulate the best strategies to meet the needs for preparing data for regulatory submissions.

Biomarkers and Personalized Medicine (Chaired by Dr. Eric Donaldson/FDA, Dr. Raja Mazumder/GWU)

Attention will be directed to clinical research using next-generation sequencing technology as a method to validate the efficacy of drugs, detection of biomarkers, personalized medicine and other bio-medicine centric disciplines.

In order to establish the trust of NGS technology in this field, we must first discuss the security and privacy measures involved. Of particular interest will be the needs of FDA and CDER in evaluating NGS data, as well as the needs of the hospitals that are actually implementing HTS pipelines and cancer research.

As new technology is developed and used, it is crucial to establish appropriate protocols for its use. This session should promote the establishment of certain benchmarks and test measurements that can be used to verify the validity of NGS data submissions while maintaining its integrity.

Food Safety and Pathogen Detection (Chaired by Errol Strain/FDA, Dr. Heike Sichtig/FDA)

This session will concentrate on food safety and pathogen detection technologies based on next-generation sequencing. The subjects of environmental sample collection and analysis,



study of outbreaks, food quality and pathogen control will be highlighted in this section as related to food and veterinary medicine.

The goal is to provide an overview of the use of NGS in public health and molecular epidemiological settings, focusing on outbreak cluster detection and source tracking of infectious bacteria/viruses and foodborne pathogens. Multiple studies have shown the ability of NGS to deliver high-resolution data that allows us to unambiguously link clinical isolates from affected individuals to contaminated food, medical instruments, environmental sources, etc. Standardization of pathogen NGS databases and their associated analysis pipelines is critical to widespread participation by public health organizations.

Next-Generation Sequencing Devices and Clinical Applications (Chaired by Dr. Zivana Tezak / FDA, Dr. Justin Zook / NIST and Dr. Heike Sichtig)

The key area of this section is the development and validation of NGS hardware, protocols and applications. A description of the current regulatory approval pathway and requirements for NGS platforms will illuminate the challenges posed to the industry from the regulatory perspective. Conversely, an approved NGS platform representative will share his/her perspective and vision for the future. Applications of human microbiological research and clinical use will highlight the efforts of existing platforms in current research efforts, and a brief discussion of the status with input from the major industry platforms will provide an outlook for the future.