Office of the National Coordinator for Health Information Technology

Sharing Genomic Data and Information for Patient Care via Application Programming Interfaces

FINAL REPORT

Prepared on behalf of the U.S. Department of Health and Human Services (HHS), Office of the National Coordinator for Health Information Technology (ONC) under Contract: HHSP233201600031I, JBS International, Inc. and Carradora Health

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Executive Summary

SYNC FOR GENES

The Sync for Genes program, launched in 2017 by the Office of the National Coordinator for Health Information Technology (ONC) initially in partnership with the National Institutes of Health, is designed to enable the sharing of standardized genomic information among laboratories, providers, patients, and researchers by advancing the development and use of industry supported genomic standards. Progress on this goal is realized through a series of phases that demonstrate how technology can address the challenges to development, implementation, and adoption of genomics standards. The work conducted in Phase 4 furthers the work of earlier phases and was designed to generate insights that will guide Phase 5.

Sync for Genes Phase 1 focused on pilot site testing of standards in a number of use cases that were included in the Health Level Seven® (HL7®) Clinical Genomics Work Group's Domain Analysis Model and contributed to the successful publication of the Genomics Reporting Implementation Guide as part of Fast Health Interoperability Resources® (FHIR®) Release 3.0. Pilot sites in Sync for Genes Phase 2 expanded on the Phase 1 work by demonstrating the exchange and integration of genomic test results at point of care. Connectivity and exchange of clinical genomic data was demonstrated by these sites during a FHIR® Connectathon, using the FHIR® Clinical Genomics specification and their own genomic diagnostic reports. Sync for Genes Phase 3 pilot projects identified gaps in the FHIR® Clinical Genomics specification, as applied to the sharing and integration of genomic data generated by laboratories in the healthcare setting.

This report covers the work and recommendations of **Sync for Genes Phase 4: *Sharing Genomic Data and Information for Patient Care via Application Programming Interfaces* (APIs).** Phase 4 built on the work in Phases 1 through 3 but also looked comprehensively at the challenges to widespread implementation and adoption of interoperable genomics standards. Phase 4 included:

- Two demonstration projects, formerly referred to as pilot projects, which added further insight into the use of APIs for sharing genomic data.
- A Technical Expert Panel (TEP), facilitated by a subject matter expert (SME) in the field of genomics, identified implementation and adoption challenges.
- Findings informed a set of recommendations that considered the challenges, as well as their dependencies, timeframes, and the resources required to maximize the effectiveness of further Sync for Genes phases.

DEMONSTRATION PROJECTS: KEY FINDINGS

The two Phase 4 demonstration projects centered on providing genomic information for patient care purposes through HL7®-FHIR®-based genomics APIs.

Children's Hospital of Philadelphia (CHOP)

Pediatric brain tumors are the leading cause of disease-related death in children in the United States. CHOP's Center for Data-Driven Discovery in Biomedicine and the University of California, San Francisco (UCSF) are part the Children's Brain Tumor Network and the Pacific Pediatric Neuro-Oncology Consortium.

Existing agreements among all entities were leveraged for sharing clinical genomic testing data. The objective of this demonstration project was for genomic data, including variants, from CHOP patients with brain tumors to be mapped to FHIR® and made available to the UCSF team for query and retrieval using a prototype FHIR® API.

State of Utah Newborn Screening Program (NBS)

The overarching goal of the Utah NBS is to expand screening and to improve the care of newborns at risk of developing gene-mediated diseases. The NBS participated in Sync for Genes Phase 2 to prepare methods to the transfer genomic variant results to healthcare providers. The deliverable for the Phase 2 project was a set of FHIR® resources containing genomic variant results, including raw sequence data in Variant Call Format (VCF), that modeled newborns who screened positive for NBS disorders (e.g., cystic fibrosis and phenylketonuria). The Phase 4 project expanded on this work by tailoring a genomic variant report to clinical specialists to whom newborns are referred and by developing a proof-of-concept API to deliver genomic variant results to healthcare providers.

Key Findings

Both demonstration sites provided valuable insight for future Sync for Genes demonstration projects and for the Phase 4 recommendations. There was synergistic value in sites meeting regularly with each other and in working with similar populations, since both sites brought different prior experience to the table and were experienced with FHIR®. Both projects were advanced by open-source support: sandbox environments and a vcf2fhir conversion tool. The project team also learned that much of the bioinformatics workflow to do the clinical sequencing, processing, and variant calling that may be necessary is done in systems completely outside of the electronic health record. More work is needed on integrating genomic information within the clinical record.

THE TECHNICAL EXPERT PANEL (TEP): IDENTIFYING THE CHALLENGES

The 12 members of the TEP represented diverse backgrounds, institutions, and populations. Over the course of five virtual meetings, the TEP identified specific challenges in each of six categories:

1) Standards Development and Content
2) Implementation of Genomic Standards
3) Infrastructure to Support Genomics
4) Utilization of Genomic Data
5) Educational Needs of Both Patients and Providers
6) Policy Issues

TEP RECOMMENDATIONS

Insights from previous phases of Sync for Genes; the TEP; demonstration projects; a literature review; and the project SME, who is engaged both nationally and internationally on multiple efforts to advance the field of genomics, were collated and analyzed to develop five comprehensive recommendations that could advance the Sync for Genes program through future phases.

1) Develop a set of interoperable genomic standards by convening a diverse set of stakeholders to develop and document use cases that include both the research and clinical perspectives and support harmonization of selected standards that result in a set of interoperable genomic standards
2) Develop a publicly accessible, centrally maintained sandbox environment that includes a server, implemented genomic standards, example data sets, test scripts, and related tooling
3) Support the implementation and adoption of genomic standards by exploring incentives that could positively influence decision-making related to the implementation and adoption of standards and by providing technical support for potential users.
4) Explore opportunities to improve the delivery of educational content that is developed and maintained by researchers and clinical experts in the field of genetics

Final Report

INTRODUCTION AND BACKGROUND

Sync for Genes, launched in 2017 by the Office of the National Coordinator for Health Information Technology (ONC) in partnership with the National Institutes of Health (NIH), aims to enable the sharing of standardized genomic information among laboratories, providers, patients, and researchers. The project advances the development and use of industry-supported standards for the consistent sharing and integration of genomic information, such as the Health Level Seven International® (HL7®) Fast Healthcare Interoperability Resources® (FHIR®) standard, for use in research, in clinical care, and by patients and their caregivers.

NIH and ONC, support the sharing of genomic data because they are critical to the All of Us Research Program and the Precision Medicine Initiative. Together these efforts will allow a new wave of investigators to drive the future of precision medicine research.

Sync for Genes builds on knowledge gained from Sync for Science (S4S), a public-private collaboration among ONC, the Harvard Medical School Department of Biomedical Informatics, and NIH's All of Us Research Program to develop a simplified, scalable, and secure way for individuals to access and share their electronic health record (EHR) data with researchers. S4S uses and works with open-source standards that allow researchers to securely receive EHR data from a third-party application programming interface (API) as directed by a patient.

The Sync for Genes project is designed to advance knowledge gained through work conducted in a series of phases, each building on those previously completed. This report summarizes Phases 1 through 3, presents the work of Phase 4, and makes recommendations for future phases of the program.

SYNC FOR GENES PHASES

Sync for Genes Phase 1: Standardizing Genomic Data

Sync for Genes Phase 1 (S4G1) was the first step toward integrating clinical genomic data into point of care. Five organizations pilot tested use cases that were included in the HL7® Clinical Genomics Workgroup's Domain Analysis Model. In addition to providing a real-world test bed for standards development and for proof of concept for specific use cases, S4G1 articulated several areas for future demonstration projects and contributed to the Workgroup's FHIR® Release 3.0 of the Genomics Reporting Implementation Guide.

Sync for Genes Phase 2: Integrating Genomic Data

Sync for Genes Phase 2 (S4G2) expanded on the work done in S4G1 to advance the standardized sharing of genomic data using the FHIR® standard, including demonstrating the exchange of genomic test results and the integration of those results into a healthcare environment. Four organizations participated in Phase 2 and conducted projects with different focus areas. Feedback from project activities was provided to the HL7® Clinical Genomics Workgroup to support the further refinement of the FHIR® Clinical Genomics specification. The pilot sites also participated in a FHIR® Connectathon, where they successfully

demonstrated connectivity and exchange of clinical genomic data using the FHIR® Clinical Genomics specification and their own genomic diagnostic reports.

Lessons learned included the importance of appropriately scaled and scoped projects related to the exchange of genomic data, assurance that participating entities have working knowledge of both FHIR® and genomics, group interaction, and opportunities to apply the FHIR® specification to clinical genomic use cases in a guided environment. S4G2 also introduced the need to address industrywide challenges to meeting the overall project goal. Challenges identified included variable FHIR adoption by developers and gaps in security and data provenance.

Sync for Genes Phase 3: Engaging Laboratories

Sync for Genes Phase 3 (S4G3) explored challenges and potential solutions to the adoption of FHIR® by laboratories that produce clinical genomic data. This phase identified gaps in the FHIR® Clinical Genomics specification, as applied to this new setting, and developed a common format for exchanging genomic results among participating sites.

Sync for Genes Phase 4: Sharing Genomic Data and Information for Patient Care via APIs

Sync for Genes Phase 4 (S4G4) offered the opportunity to review the work and results of the previous phases and to develop a set of recommendations designed to support a comprehensive environment that can address the major challenges to the development of genomics standards, implementation, adoption, and use. These recommendations were designed to also meet the needs of researchers, clinicians, patients and their caregivers, and all other relevant stakeholders in the health information technology industry. They were informed by

- the work of two demonstration projects that focused on the development and use of APIs to share genomic information among interested parties;
- a Technical Expert Panel (TEP) facilitated by the project subject matter expert (SME), who is co-chair of HL7's® Clinical Genomics Workgroup and an active member in the Global Alliance for Genomics and Health (GA4GH); and
- a targeted literature review.

DEMONSTRATION PROJECTS

Overview

Building on the success of the first three Sync for Genes phases, a call for Phase 4 demonstration site proposals was announced in late November 2020. The call included the need to use of HL7® FHIR®-based genomics APIs to integrate genomic data in clinical and research settings to support providers, researchers, patients, and caregivers in accessing genomic information.

Respondents were independently evaluated by four field experts, using a standardized weighted evaluation matrix, and recommendations for two sites were presented to ONC. The two projects were conducted in parallel to TEP meetings, and their findings contributed to the development of the final recommendations.

Children's Hospital of Philadelphia (CHOP) Center for Data-Driven Discovery in Biomedicine

Pediatric brain tumors are the leading cause of disease-related death in children in the United States. Both CHOP and the University of California, San Francisco (UCSF) are part the Children's Brain Tumor Network and the Pacific Pediatric Neuro-Oncology Consortium. All entities were able to leverage existing agreements to share clinical genomic testing data.

The current approach to exchanging somatic testing results among clinical sites across the consortium is typically done manually, via phone and email exchanges, creating bottlenecks for a wide variety of use cases. The objective of this demonstration project was to use HL7® FHIR® to make CHOP's patient data available to the UCSF team for query and retrieval of clinical tests of interest in a more effective and self-service manner.

To achieve this objective, the CHOP team first identified a set of pediatric brain tumor patients and structured their genomic data as recommended by the FHIR® Release 4 (R4) genomics standard. The data were loaded into a FHIR® server to provide the ability to query and to retrieve clinical genomic data via the FHIR® API. Utilizing a FHIR® API, a prototype app was developed that provided a user interface specifically for this use case. This app was then provided to the UCSF team to query and retrieve the data.

State of Utah Newborn Screening Program (NBS)

The overarching goal of the NBS is to expand screening and to improve the care of newborns at risk of developing gene-mediated diseases. To develop scalable and universal second-tier and confirmatory testing solutions, The NBS team recently completed validation of an exome-sequencing-based analysis pipeline that allows for analysis restriction to a variant panel, gene panel, or full exome. The NBS participated in S4G2 to prepare for the transfer of genomic variant results to healthcare providers participating in the NBS program. Deliverables for the Phase 2 project included a set of FHIR® resources containing genomic variant results, such as raw sequence data in Variant Call Format (VCF), that modeled newborns who screened positive for disorders that are typically screened in newborns (e.g., cystic fibrosis and phenylketonuria).

In Phase 4, NBS expanded on this work by tailoring a genomic variant report for clinical specialists to whom newborns are referred and by developing a proof-of-concept API to deliver genomic variant results to healthcare providers, such as clinical specialists (e.g., pediatric pulmonologists, neurologists, endocrinologists, and metabolic specialists).

KEY FINDINGS

The two demonstration projects generated insight into both the processes and technology that can foster success.

Process

- There is synergistic value in meeting regularly and in working with similar populations.
  - As both teams were in the pediatric realm, sharing of use cases and cross-pollination about using the FHIR® standards supported both participants.
- Previous experience enables success within the allotted timeframe.
  - Experience with both FHIR® and R Shiny® apps on FHIR® allowed the CHOP team to move forward quickly. The R Shiny® framework allowed for rapid prototyping and confidence that this approach could ultimately be deployed for others to use.
  - Previous work on S4G2 allowed the NBS team to refine and reorganize the Observation resource, using the Implication, Interpretation, Variant, and Genotype profiles to better describe genomic variant results.
- Surveying potential recipients of a genomic report enables the development of a generalizable report with greater usability for relevant clinicians.
  - The NBS team is developing a genomic variant report based on its national survey that other state newborn screening programs throughout the country can use.

Technology

- Access to open-source tooling supports more efficient use of internal resources.
  - A vcf2fhir tool allowed CHOP to convert many of the VCFs into the FHIR® R4 Genomics Diagnostic Report profile, which is part of the FHIR® R4 Genomics standard.
  - VCFs were fed into the tool, resulting in initial mapping of the VCF elements into FHIR®. Many of the key elements were readily translated. Custom scripts were built on top of the vcf2fhir tool to address the remaining gaps. The open-source nature of the tool empowered the technical team to understand its logic and opened the door to future contributions.
- Access to a sandbox environment enables implementation of genomics standards.
  - The NBS used the public Logica FHIR® Sandbox as its FHIR® server.
- Much of the bioinformatics workflow of clinical sequencing, processing, and variant calling related to genomic data is done in systems external to an EHR.
  - Only final reports that are signed by a pathologist are included in the EHR. To get the structured data required for FHIR®, a comprehensive VCF file needs to be created.

THE TECHNICAL EXPERT PANEL

The TEP consisted of 11 members, plus the project SME as the facilitator, representing multiple diverse areas and interests: academic research; clinical care; research and development; laboratories; patient advocacy; and federal programs, such as NIH's *All of Us*. The goal of the TEP was to identify and prioritize

challenges to the exchange and integration of genomic data and how to address them. Input and feedback from the TEP was gathered over a series of five virtual meetings.

The TEP identified and discussed a wide array of challenges inhibiting the generation and exchange of standardized genomic data at the first meeting, after which participants provided feedback that distilled the challenges into six major categories. Subsequent meetings entailed in-depth discussions regarding each challenge. Analysis of TEP discussions, along with lessons learned from the two demonstration projects and a literature review, informed the recommendations included in this report for advancing the goal of seamless sharing of genomic data.

CHALLENGES

1) **Standards Development and Content.** Standards are needed to support the integration and use of genomic data into both clinical and research systems. They are developed by standards development organizations (SDOs), member-supported organizations using a lengthy process that fosters consensus through formal balloting, ensures content is fit for purpose through well-formed use cases and is implementable, and assures ongoing maintenance of the standard.
2) **Implementation of Genomic Standards.** The implementation of standards requires technical expertise and domain resources in both the standard development and implementation environments. Implementation, however, requires adoption by potential users to be effective within an organization and can support interoperability only when it is adopted by a community.
3) **Infrastructure to Support Genomics.** The complexity of genomic data and its clinical use require specialized infrastructure. Strategies are needed to integrate, manage, and deliver genomic data, test results, and interpretations in ways that are consumable by end users, who may not be trained in genomics.
4) **Utilization of Genomic Data.** The value of genomic data can only be realized if they can be accessed and used effectively by different end users. Researchers utilize genomic data for discovery of disease mechanisms and treatments; clinicians to diagnosis and treat patients; and patients to understand hereditary risks, make lifestyle choices, and assist with family planning.
5) **Educational Needs of Both Patients and Providers.** The educational needs of both providers and patients fall into two primary categories: the need for reliable content and for systems that can effectively deliver that content. The TEP focused on delivery of content that is developed elsewhere, primarily by specialty societies, to both clinicians and patients.
6) **Policy Issues.** Policies can inadvertently pose challenges to the collection and use of genomic data. For example, regulatory requirements can impose significant burden on the acquisition and exchange of genomic information, as can intellectual property rights of various proprietary systems.

The following table outlines the specific examples identified and associated with each of the six challenges.

Challenge Category	Specific Examples of Issues to be Considered
Standards Development and Content	• Lengthy timelines for standards development by standard development organizations (SDOs) can lead to local development of isolated standards. • Differing domain content used in research and clinical care lead to separate, often incompatible, standards used by these two communities. • Lack of metadata inhibits use across communities. • New data types are generated faster than formal standards development can process them. • Replacing a working implementation with one that is based on another standard is resource intensive. • Contextualization is needed to express the nuance that is required to capture and convey how this type of data can best be used. • Adoption of standards by both a sender and receiver, which is frequently not the case, is needed for messaging. • The value of standards may not be understood at all levels of an organization, inhibiting not only their development, but also their testing, implementation, and adoption.
Implementation of Genomics Standards	• Validation (conformance) is needed to demonstrate that standards function as anticipated. • Limited access to open-source, sandbox environments to test conformance, tooling, and protocols limits implementation. • Use cases need more pragmatism to be valuable to those that need them. • Adoption may require converters (i.e., into FHIR® format) and educational support. • Vendors may be slow to adopt standards in their software. • Vendors may implement standards differently so interoperability cannot be realized. • Implementation can be resource intensive.

Challenge Category	Specific Examples of Issues to be Considered
Infrastructure to Support Genomics	• The vast amounts of data generated by genomic testing exceeds EHR storage capacity. • Genomic information is not static, so updating mechanisms for standards must be included. • Genomic data on an individual will be associated with that individual throughout the individual's lifetime. • Genomic data can come from multiple sources, which do not contain the same level of detail, complicating integration. • The ability to audit decision-making by determining what information was known at the time of a decision is needed. • Standards do not support all stages of workflows along the continuum. • A standardized infrastructure could support data transfer, including metadata (e.g., data provenance), along with a standardized approach to storing raw data versus annotated data.
Utilization of Genomic Data	• The continuous evolution of genomic information and its complexity can lead to outdated or discordant interpretations. • Information systems must represent data in semantically accurate and computationally unambiguous forms. • Data governance polices are needed to preserve the integrity of data, how they can be accessed, and support subsequent re-interpretations within a clinical environment. • Genomic data alone are not enough to make meaningful clinical decisions. • Data sets from genomic tests may not be harmonized in a way that can be used by research. • Patient-facing applications will require additional data, standards, and educational material. • Patient context and knowledge are evolving.
Educational Needs of Both Patients and Providers	• Patients are overwhelmed by the sheer volume of genomic testing results. • Clinicians are generally not trained in genomics and lack both knowledge and facility with associated clinical workflows. • Lack of information on the quality and trustworthiness of the genomic information provided from external partners is an issue for all potential users. • Patients find it difficult to evaluate the relative importance of the information provided. • Providers find it difficult to incorporate new and evolving genomic data. • Laboratory reports may not be helpful to clinicians if results are presented without implications or supporting data (e.g., date, methodology, and clinical context).

Challenge Category	Specific Examples of Issues to be Considered
Policy Issues	• Technology needs more flexibility to support the changing regulatory environment • Some regulations are not compatible with functional workflows.

TEP RECOMMENDATIONS

Below are the five recommendations the TEP identified as priority areas to address the six challenges previously discussed. The first two recommendations and parts of the third are foundational, while others are more future oriented. Each is recommendation includes a description, goal, background, approach, and impact on the genomics community.

Recommendations

1. Develop a set of interoperable genomic standards
2. Develop a sandbox environment for genomic standards
3. Support the implementation and adoption of genomic standards
4. Explore opportunities to improve educational content
5. Explore opportunities to address gaps in policy

Recommendation 1: Develop a Set of Interoperable Genomic Standards that Serves Both the Clinical and Research Communities

Description and Goal

Description: develop a set of interoperable genomic standards by documenting a diverse set of use cases, directly supporting the development and improvement of standards, and harmonizing standards on key elements

Goal: meet the specific needs of different communities for genomics standards and support the sharing of genomic data among them

Background and Rationale

Many standards are developed independently for use in the genomics domain, but none are sufficient to be used alone, and few standards work well together. Therefore, a fundamental need exists for a set of interoperable standards that serves both research and clinical use cases. Those standards need to be developed for the long term and must be rigorous, computable, expressive, and pre-harmonized to meet the needs of both the clinical and research domains.

Approach

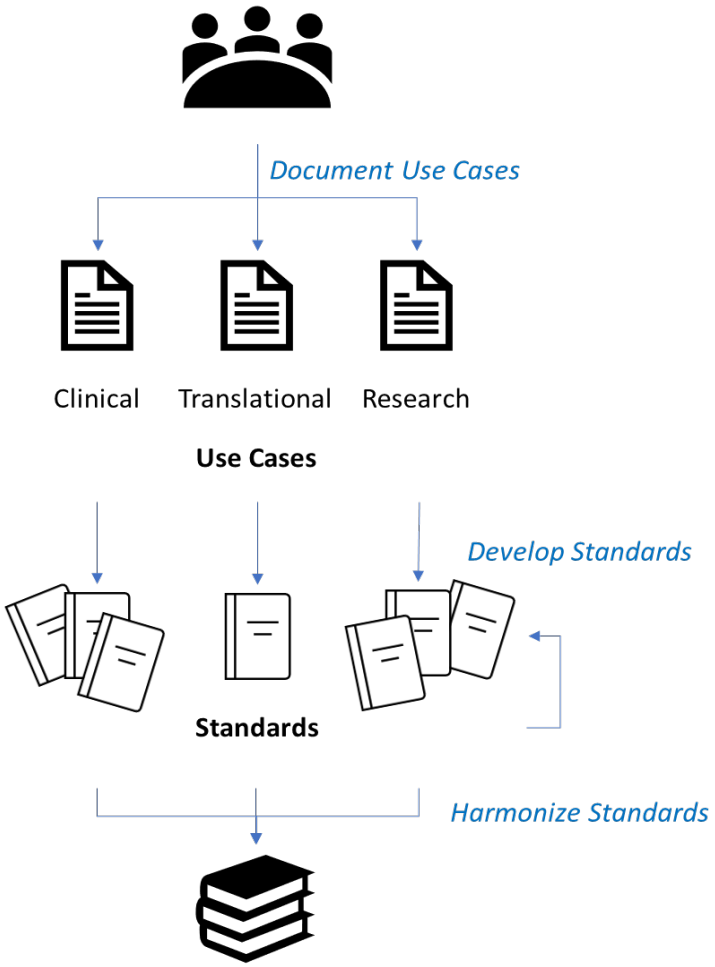
The following could significantly enhance more timely development of needed genomics standards.

- **Convene a diverse set of stakeholders to develop and document use cases that include both research and clinical perspectives**. Existing clinical and research use cases could be leveraged when possible but may require formalization. Use cases could reflect the complexity of real-world scenarios, include relevant metadata and provenance, and be reviewed periodically to address gaps related to advances in technology and in uses of genomic data.
- **Support further development of existing standards that are based on a common data model**. Increasing coverage and formalism will better manage evolving knowledge and interpretations. Ongoing work in key standards organizations (e.g., HL7® and GA4GH®) can be leveraged to drive new releases of existing standards that take iterative steps towards harmonization. Standards could be prioritized based on use cases and level of adoption.
- **Support harmonization of standards** by harmonizing key touch points between disparate standards to improve the exchange and use of genomic data in different contexts (e.g., clinical, research) and to result in a set of interoperable genomic standards that will enable deeper and richer integration between knowledge bases and among genomic data sets

Impact

The development of well-documented use cases that guide the development of a set of robust, interoperable genomic standards will improve the accurate expression of genomic data and associated interpretations, increase interoperability, and promote convergence within a fragmented domain.

It is important to note that the process is iterative. After each the cycle of standards development, depicted below, is completed, the list of known gaps can be prioritized to inform the next round of development.



Recommendation 2: Develop and Support a Sandbox Environment for Genomics Standards

Description and Goal

Description: develop and support an open-source, sandbox environment that includes properly implemented standards, corresponding example data sets, and test scripts

Goal: incorporate more widespread implementation and adoption of standards by providing an efficient way for potential adopters to evaluate a standard before directing resources to its implementation

Background and Rationale

Potential adopters of a standard need to explore its capabilities and limitations, preferably with example data sets and scripts. Unfortunately, that type of environment does not exist for most standards, so potential adopters must create one locally—a process that can require significant time and resources, as well as technical expertise that may not be available.

Approach

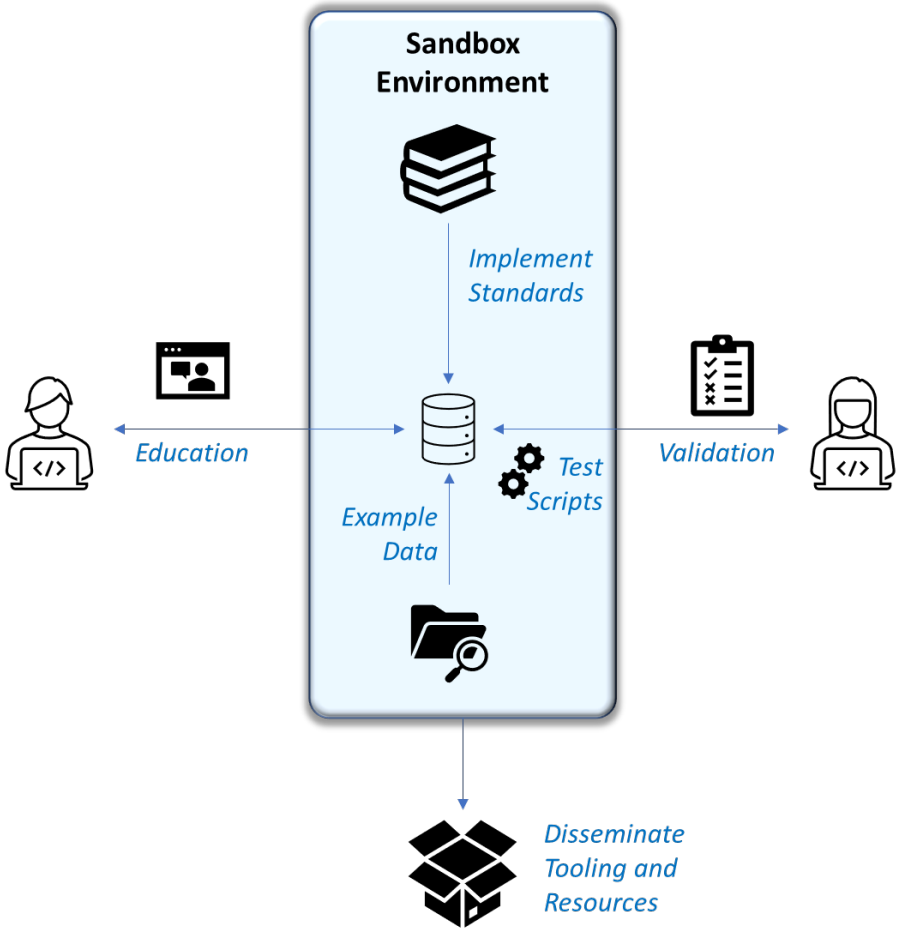
The following steps could enable more efficient implementations of genomics standards.

- **Build and maintain the technical aspects of a publicly accessible, centrally managed sandbox environment.** The environment would include a server, implemented standard(s), database(s), example data sets, test scripts, and relevant tooling. Documentation would provide examples of API calls and file formats and link to the relevant authoritative sites for each standard.
- **Identify a relevant set of standards for implementation testing.** Ideally, this set would align closely with the standards developed as part of Recommendation 1.
- **Develop example data sets and test scripts.** Data and messaging standards define the structure and semantic meaning of data, but specifications often contain limited to no example data. Public or synthetic data could be used to create example data sets that demonstrate how those data would be represented using selected standards. Test scripts that demonstrate APIs (if applicable) and validate the returned data could also be developed.
- **Consider public dissemination.** This would allow adopters to easily install a replica of the environment on internal systems and behind firewalls, enabling it to be used to test the integration of standards within existing clinical and/or proprietary systems.
- **Consider related tooling.** A web page that lists community-developed utilities, such as format converters, might provide a path for implementers from legacy formats and conventions currently in use to the standards identified in Recommendation 1. This resource could be developed in conjunction with a standards concierge service (see Recommendation 3).

Impact

The development of a sandbox environment that includes developed standards and corresponding example data sets will lower barriers to implementation and adoption of standards by providing a resource-efficient approach to assessing the cost/benefit of implementation.

The following graphic depicts a high-level workflow process in a sandbox environment.



Recommendation 3: Support the Implementation and Adoption of Genomic Standards

Description and Goal

Description: recognize that a sandbox environment is foundational for assessing the costs/benefits of technical implementation of standards, but more is needed to further support local implementation and adoption of genomics standards in multiple environments.

Goal: achieve more widespread implementation and adoption of genomics standards through support and incentives for local implementation and adoption

Background and Rationale

The “implementation” of a standard refers to its deployment in an environment in which it could be used, while “adoption” refers to its use in practice. Both require a cost/benefit analysis and a clear value proposition. While the specific details of those considerations might differ among institutions, common barriers could be reduced through technical and strategic support for both implementation and adoption.

Approach

The following actions could be considered to support the efficient and effective implementation and subsequent adoption of genomic standards.

- **Explore incentives.** Examples include providing direct funding to assist low-resource settings and common technical infrastructure and tooling that lowers cost (e.g., a sandbox environment, see Recommendation 2). Additional examples include advocacy and/or policies related to federal funding or regulations.
- **Support a "concierge service" for standards.** This would connect potential adopters to points of contact in a standards organization who can answer questions about a standard. The service would be able to recommend candidate standards for a given use case (see Recommendation 1) and help potential adopters who are unfamiliar with a standard or its organization to locate communication channels to address questions that may arise.
- **Support engagement with SDOs during local implementations.** This would help required localizations and/or extensions to be more consistent and to provide feedback to the standards organization about potential gaps in the specification that could be considered for the next iteration of the standard (see Recommendation 1).
- **Facilitate conformance testing.** Develop tooling, including test data and test scripts, that could be used to provide a base level of conformance testing for an implemented standard, if such tooling does not already exist. It should cover common use cases and could be deployed within the sandbox environment (see Recommendation 2).

Impact

Standards that are not implemented properly or widely adopted will fail to improve interoperability. Efforts to support the proper implementation and subsequent adoption of genomic standards will foster more widespread adoption and help to establish a minimum level of interoperability, by decreasing heterogeneity among implementations.

Recommendation 4: Explore Opportunities to Improve Access to Educational Content

Description and Goal

Description: recognize that patients and providers are often overwhelmed by the amount of information produced by genomic testing and the different approaches to understanding the long- and short-term impact that data may have on patients and families

Goal: support provider and patient/caregiver understanding of genomic data and the implications they have on clinical care and personal decisions, through the efficient and effective delivery of reliable genomic content that is developed by specialists and experts in the field. This is a long-term goal that is dependent on multiple public and private resources and institutions.

Background and Rationale

Genomic data and information need to be accompanied by explanatory and educational materials that are focused and accessible to providers and easily digestible by patients and caregivers. This requires engaging with end users to gather information on how educational materials can best be presented. Once requirements are collected, utilization of existing resources could help curate potential knowledge and delivery mechanisms for genomics and precision medicine.

Approach

The following approaches could be considered to support the delivery of educational resources to both patients and providers.

- **Evaluate and leverage existing educational resources** for effect on target audiences.
- **Create a repository** of resources with a standardized format/header and metadata, including some federally hosted resources that are kept up to date.
- **Develop technologies and draft policies** related to the technical infrastructure for the delivery of valid, externally developed genomics educational material.
- **Deliver structured, standardized, context-aware genomic content** through existing frameworks (e.g., Infobuttons, clinical practice guidelines, and clinical decision support hooks).
- **Design user interfaces based on requirements (e.g., navigation of content and delivery to target audiences) collected directly from potential users**. This would include ways to assess the reliability of the presented content.
- **Assist organizations in adopting standards** to help develop and deploy educational content.

Impact

The value of data and information is in their interpretation and use. Reliable and trustworthy educational resources must be available and easily accessible for providers and patients/caregivers to understand genomic data and the implications they have on clinical care and personal decisions.

Recommendation 5: Explore Opportunities To Address Gaps In Policy Development

Description and Goal

Description: recognize that policies take many forms and include statutes, regulations, guidance, and funding priorities; the timeframe for them to come to fruition can be lengthy. They do not always align with rapidly evolving technology, rapidly expanding knowledge base in the field of genomics, or state of the art clinical practices. This recommendation addresses the need for better alignment of policy with genomics-related technology, knowledge, and practice.

Goal: raise awareness among policy makers of the key implications of a given policy on the field of genomics and on those that access and use genomic data; this is a long-term goal with many dependencies.

Background and Rationale

Policies that affect the presentation, use, and sharing of genomic data to protect patient and family privacy must also recognize the value that data may provide to research into their possible disease processes and of clearly presenting the implications of these data in their diagnoses and treatments. This holistic approach to policymaking may require more emphasis on educational processes before specific policies become generalized requirements, thus allowing for greater flexibility with respect to informed patient choice and information systems. Policies related to genomics need to maintain privacy and protections of patients and their families while allowing for more technical efficiency when obtaining consent for use of genomic data for research purposes and clinical care decisions.

Approach

While the goal of this recommendation is long term, a number of approaches could be considered as starting points.

- **Develop white papers and educational materials** to foster implementation of existing policies by providing greater clarity as they relate to genomics; one example where this could be helpful is the 21st Century Cures Act.
- **Increase the efficiency of obtaining consent** to share genomic data by establishing broader, standardized consent language, with clarification about when additional consent may be required to share genomic information for research purposes and clinical care decisions.
- **Make information available on the potential risks of harm** related to sharing of sensitive data versus the advantages of such sharing.
- **Increase specificity regarding patients' rights and responsibilities.**
- **Convene stakeholders** (e.g., the Food and Drug Administration, Centers for Medicare & Medicaid Services, and certification bodies for lab testing at both federal and state levels) to identify issues and ways to address them.

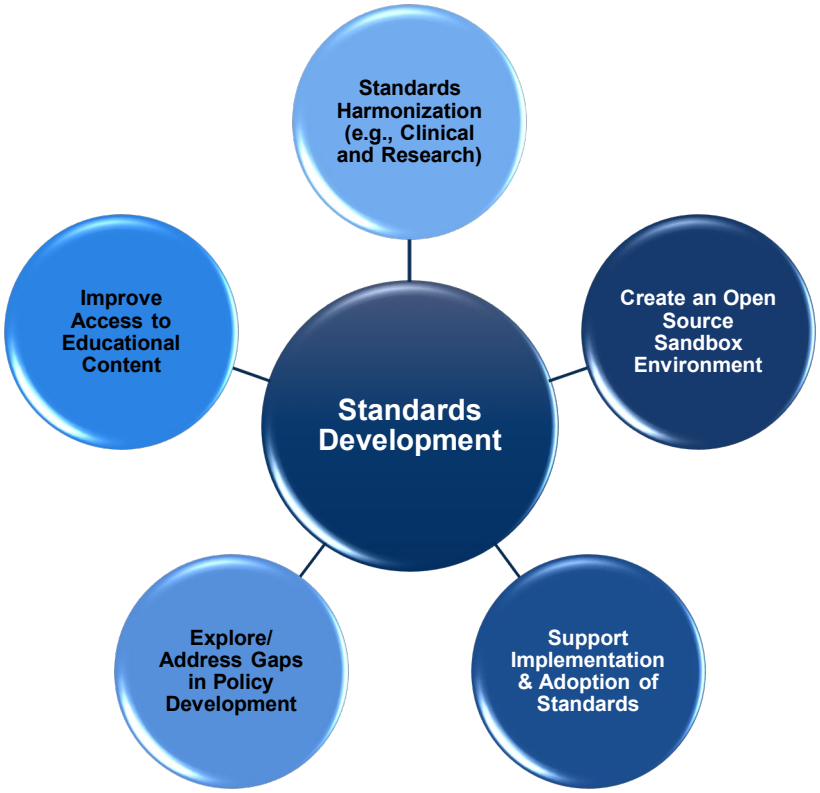
Impact

Policies that affect the field of genomics have significant impact on the generation and use of genomic information—so much so that the topic could be addressed more comprehensively in a separate venue.

CONCLUSION

Sync for Genes Phase 4 offered the opportunity to review progress made in earlier phases, advance the program through the work of two additional demonstration site projects, and identify outstanding challenges to interoperability of genomic data and to integration into patient care workflows. The work culminated in a set of comprehensive recommendations, depicted below, that considered dependencies, timelines, and the practical needs of potential developers and users of genomic information.

These recommendations include the need to focus initially on development of interoperable genomics standards and their implementation, emphasize the need for support for local implementation and adoption, and address the longer-term opportunities to address access to reliable educational materials and to policies that align with the rapidly evolving field of genomics.



These recommendations were designed to inform further phases in the Sync for Genes program, recognizing that the field of genomics is rapidly evolving. It is critical that the recommendations are not considered or implemented in silos but are addressed in collaboration with all relevant stakeholders. It is also important to recognize that developing initiatives that cut across the traditional boundaries among standards development organizations may address issues more comprehensively.

Glossary of Acronyms and Terms

Acronym	Description
API	Application Programming Interface
CHOP	Children's Hospital of Philadelphia
EHR	Electronic Health Record
FHIR	Fast Healthcare Interoperability Resources
GA4GH	Global Alliance for Genomics and Health
HL7	Health Level 7
NIH	National Institutes of Health
NBS	Utah Newborn Screening Program
ONC	Office of the National Coordinator for Health Information Technology
S4G1-2	Sync for Genes Phases 1-2
S4S	Sync for Science
SDOs	Standards Development Organizations
SME	Subject Matter Expert
TEP	Technical Expert Panel
UCSF	University of California, San Francisco
VCF	Variant Call Format

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