Trusted Regulatory Spaces (TRS) for Dynamic Submission Management (DSM)

Design Principles for Global Cloud-Based Regulatory Collaboration

DNAnexus®

Lorenz
LIFE SCIENCES GROUP

Executive Summary

In the realm of global healthcare, the advent of cloud technology and AI heralds a new era of regulatory collaboration. Imagine a world where the barriers of geographical boundaries dissolve within the digital clouds, enabling a seamless exchange of regulatory information. This is a vision shared by industry and agencies as demonstrated by the FDA's Orbis and PRISM projects, the multi-agency Access project out of Health Canada, and this vision is supported by the World Health Organization and the International Federation of Pharmaceutical Manufacturers and Associations. As demonstrated by the global response to the COVID-19 pandemic, work-sharing and reliance among countries played a crucial role in the timely delivery of safe and effective drugs to patients, while fostering global regulatory synergy and convergence.

Using the cloud can reduce regulatory burden and timelines, but collaboration faces significant challenges posed by the security, privacy, and quality controls required to exchange regulatory information. These challenges span global, regional, national, industry, and agency boundaries, presenting a daunting array of control and qualification requirements. However, there are significant rewards to overcoming these challenges using Trusted Regulatory Spaces (TRS) in the cloud where sponsors, health agencies, and standards development organizations collaboratively advance the interchange of regulatory information.

Countries would share their expertise, experiences, and resources with others, enabling them to adapt more effectively to common capacity gaps they face, such as resource limitations, scientific knowledge, or regulatory disparities. Trusted Regulatory Spaces would also be used to advance the digitization, normalization, and harmonization of regulatory information through the collaborative evolution and implementation of structured data standards, producing AI-ready information relevant to all stakeholders.

Picture a future where the submission of regulatory documents is no longer a cumbersome process, but rather a streamlined operation conducted through a network of cloud platforms. Envision intelligent algorithms sifting through the deluge of data from clinical trials and manufacturing processes to refine trial methodologies and scrutinize safety protocols. As this tapestry of technology weaves its way into the fabric of pharmaceutical strategies, companies are awakening to the potential of regulatory reliance and Real-World Data. Firms will opt for simultaneous, multi-regional submissions, leveraging the power of regional Trusted Regulatory Spaces to abandon the slow march of sequential filings. They would use an agency-authorized process to include Real-World Data in submissions for confirmatory analysis and have a globally harmonized submission process for post approval changes to chemistry, manufacturing, and controls.

This paper proposes a cloud architecture for a Trusted Regulatory Spaces Network for Dynamic Submission Management using open-source and commercial off-the-shelf software to deliver a unified user experience on diverse cloud service providers, with capabilities for establishing collaboration contracts, and sharing data, analyses, and results. Thus, the narrative unfolds, where cloud technology and AI become the twin pillars supporting a more cohesive, efficient, and accessible healthcare landscape, and transforming global medicinal regulation.

Figures

Introduction

Objectives

The intended audience is described followed by a brief description of the sponsoring companies' backgrounds and the origin of Trusted Regulatory Spaces (TRS). Regulatory use cases that will benefit from cloud-based collaboration are described, and foundational design principles for regulatory cloud design are proposed. An archetypical regulatory information system model is proposed with relevant citations for regulatory cloud requirements.

A TRS Network (TRSnet) design comprised of using open-source and commercial off-the-shelf software running on diverse cloud service providers (CSPs) is proposed to enable a regulatory-grade distributed submission object management system that supports collaboration between sponsors, Real-World Data (RWDs) providers, Standards Development Organization (SDOs), and regulatory agencies. The cited regulatory use cases are mapped to the proposed design, and next steps for the development of TRSnet are considered.

This paper focuses on a pragmatic technical and implementation-oriented approach to define, deploy, and refine a cloud network for reliance and work-sharing, standards development acceleration, and use of RWD in submissions. The proposed design and reference implementation is informed by previous collaborative regulatory interaction projects and is intended to provide a cloud-based governance and services foundation to support ongoing and future regulatory research projects and the production workflows that emerge from them.

Intended Audience

This paper presents a design for a secure cloud-based regulatory research and review network that can be built today from existing open-source and commercial cloud services. The intended audience is pharmaceutical and health agency regulatory leaders, regulatory operations and policy decision makers, IT system architects, and risk management specialists, as they consider, define, and implement cloud-based solutions for interactive regulatory data management and analysis.

Pharmaceutical and biopharma companies and their RWD providers can consider how a TRSnet will address the current regulatory hurdles encountered when incorporating RWD-derived datasets into submissions. Health agencies can consider the proposed designs to enable global, regional, and national interactions with sponsors and SDOs. Multi-sponsor/agency regulatory research projects can consider the TRSnet design to efficiently and securely enable the pursuit of their objectives by providing a cloud network upon which to build, test, and deliver collaborative regulatory workflows.

Sponsoring Companies' Backgrounds

WOLFGANG WITZEL
President
LORENZ Life Sciences Group

LORENZ Life Sciences Group

LORENZ Life Sciences Group (www.LORENZ.cc) has been developing and marketing software solutions for the Life Sciences market for over 30 years. LORENZ Regulatory Information Management solutions address industry, health authorities and academia to ensure compliance enforcement worldwide. LORENZ' proven portfolio offers Product Registration/IDMP, Submission Assembly, Validation and Management, Publishing/eCTD, Regulatory Planning, Tracking and Submission Review products and related services. Interoperability between LORENZ products and third-party solutions, as well as the ability to automate processes, allow LORENZ customers to enhance operational efficiencies. LORENZ has a strong customer base worldwide, with over 1800 installations in 48 countries, including 19 agencies.

OMAR SERANG
Chief Cloud Officer
DNAnexus

DNAnexus

The DNAnexus Precision Health Cloud delivers robust, scalable solutions across global diagnostic testing, therapeutic development, healthcare delivery, population biobanks, and governmental health initiatives. Under contract with the U.S. Food and Drug Administration (FDA), DNAnexus powers precisionFDA, a secure, cloud-based collaborative research and review platform designed to advance regulatory science and enable rapid innovation. As a FedRAMP-authorized platform, DNAnexus meets stringent security, privacy, and quality standards essential for regulatory environments, supporting transformative cloud-based initiatives like the precisionFDA Regulatory Information Services Module (PRISM). With deployments across AWS and Azure regions in the U.S., Frankfurt, London, Amsterdam, and Sydney, the DNAnexus Precision Health Cloud drives regulatory collaboration and accelerates advancements in precision health on a global scale.

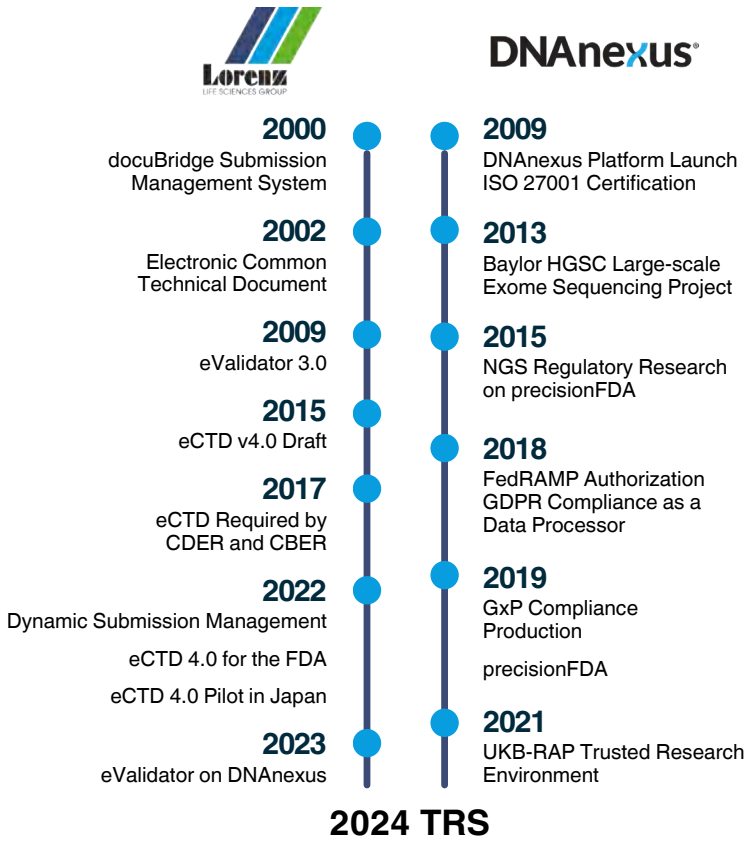


Figure 1: Origin of Trusted Regulatory Spaces

The Origin of Trusted Regulatory Spaces

LORENZ' and DNAnexus' paths to the origin of TRS (Figure 1) converged when LORENZ created a Linux version of their eValidator eCTD validation software for deployment on DNAnexus.

LORENZ pioneered regulatory submission management with its docuBridge system in 2000, and later enhanced global compliance with eValidator version 3 for ICH eCTD validation in 2009. When eCTD v4.0 was piloted in 2017 by the FDA, LORENZ' solutions enabled seamless validation and review. Japan has adopted eCTD v4.0, planning for mandatory use by 2026, ahead of the FDA's 2029 deadline. In 2022, LORENZ introduced Dynamic Submission Management (DSM), focusing on streamlining content, stakeholder processes, and technology for regulatory submissions.

DNAnexus launched its cloud-based genomic analysis platform in 2009, gaining FDA recognition in 2015 to build precisionFDA, a Next Generation Sequencing (NGS) regulatory research platform. With FedRAMP and GDPR compliance added in 2018, DNAnexus strengthened security for handling PHI and PII, enabling regulatory innovations like the production precisionFDA platform. In 2021, the UK Biobank engaged DNAnexus to create its Trusted Research Environment (TRE) for privacy-protected research.

In 2023, LORENZ and DNAnexus integrated eValidator into DNAnexus' FedRAMP environment. Leveraging DSM concepts and DNAnexus' secure cloud infrastructure, they partnered in 2024 to launch Trusted Regulatory Spaces for collaborative regulatory validation and review.

Sponsoring Companies' Cloud Services

LORENZ Cloud

The LORENZ Cloud is a commercial Software-as-a-Service (SaaS) solution providing customers with a managed AWS account provisioned with LORENZ RIM software (Figure 2). A system security plan is provided to present customers with the security controls applied to the system. All development and operations work is performed under a LORENZ QMS with an internal Product Development Life Cycle framework (PDLC). User authentication is via username and password, and access is controlled at the application level. AWS account residency is globally flexible, and AWS-based telemetry and reporting systems are used to manage cost. The LORENZ RIM software is accessed by the end users via a web interface.

This service is suitable for customers that do not require privacy impact assessments, or auditability, authorizations, and quality certifications.

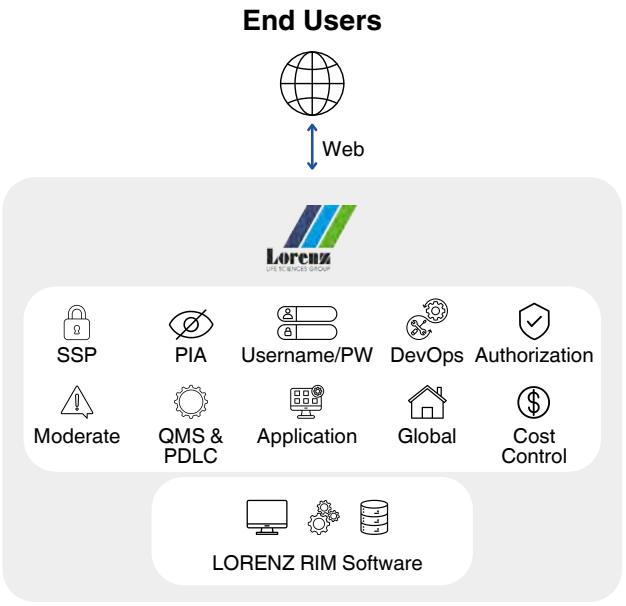


Figure 2: LORENZ Cloud

DNAnexus Precision Health Cloud

The DNAnexus Precision Health Cloud is a commercial global multi-tenant cloud Platform-as-a-Service (PaaS) for collaborative management and analysis of scientific and healthcare data (Figure 3). DNAnexus manages moderate risk category data, with a FedRAMP authorization that enables precisionFDA to connect to it. The FedRAMP authorization artifacts include a System Security Plan and a Privacy Impact Assessment. All development and operations work is performed under a DNAnexus QMS incorporating an FDA-compliant Enterprise Performance Life Cycle framework (EPLC).
DNAnexus is accessed by end users and external systems like the UKB-RAP Trusted Research Environment via the web interface or API. Connections are authenticated using Multi-factor Authentication (MFA) or Single Sign-on (SSO). Access is managed using DNAnexus Projects that enable members-only access to resources. Systems are audited and authorized in accordance with FedRAMP, ISO 27001, and GDPR, and data residency is controlled and configurable globally. The platform provides user and organization-based cost governance controls through the web interface and API. LORENZ RIM software is delivered on secure web-accessible workstations.

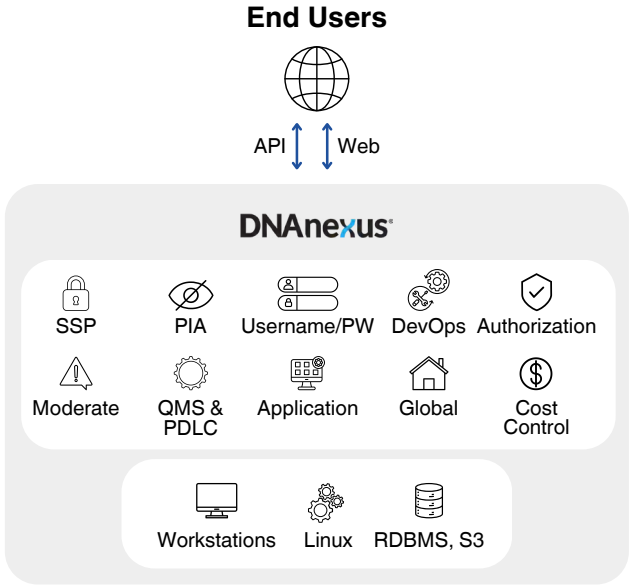


Figure 3: DNAnexus Enterprise Cloud for Precision Health

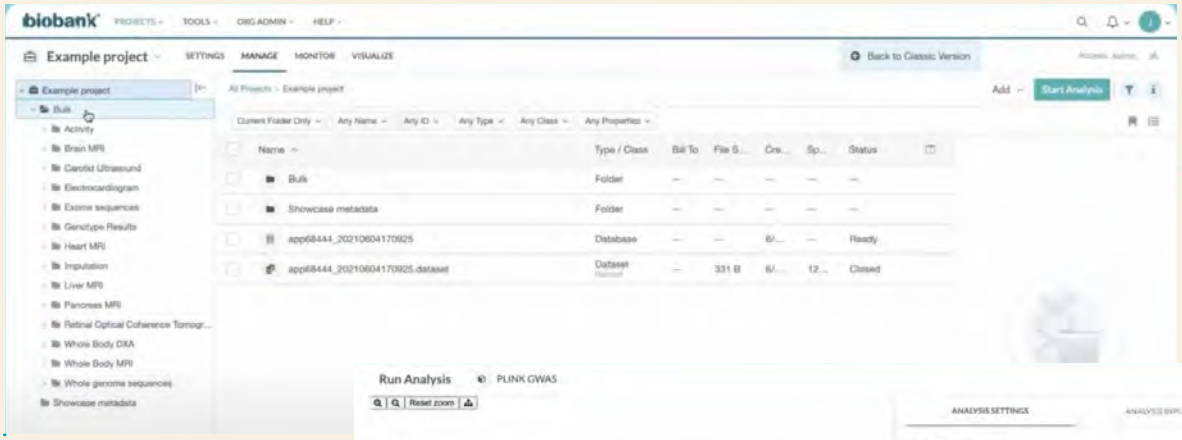
This service is suitable for customers requiring higher levels of security, privacy, and quality controls and authorizations, and the ability to support global collaboration.

UKB-RAP Trusted Research Environment

The UK Biobank Research Analysis Platform (https://www.ukbiobank.ac.uk/enable-your-research/research-analysis-platform) has been in production for three years enabling global researchers to work with UK Biobank's large-scale biomedical database in the cloud, under the control of Trusted Research Environments (Figure 4a). Access to this unprecedentedly large-scale biomedical database is requested on a per-project basis by global researchers via UK Biobank's Access Management System (AMS).

An authorized researcher's project is limited to only the data relevant to their proposal, and analysis of the data can only be performed in the TRE on UKB-RAP (Figure 4b), and certain data modalities are not allowed to be extracted from the platform. Technology controls exist to prevent data copying and other interactions across projects associated with different research proposals to ensure adherence to data use terms and reduce the risk of participant re-identification. Additionally, if a volunteer participant withdraws from the UK Biobank, their individual-level data must be removed from the UKB-RAP.

Designed and implemented by DNAnexus, the TRE data interchange contract and control mechanisms, data vending and management systems, and locked-down analysis environment, inform the proposed design of a TRSnet.



A. Research Project in the Trusted Research Environment

B. UKB-RAP Analysis Pipeline

Figure 4: UKB-RAP TRE

Regulatory Cloud Platform Value and Use Cases

The motivations and use cases for enhancing regulatory submission in the cloud are presented.

WHY A CLOUD-BASED REGULATORY PLATFORM?

- **Accelerating Therapies to Patients** – Establishing a streamlined information highway enables sponsors and regulators worldwide to collaborate efficiently. By sharing visibility and reusing data, they can support each other as key opinion leaders throughout the submission process, all while preserving their unique regulatory jurisdictions.
- **Reducing Burden** – Drug development is a complex and resource-intensive process for both industry and society. A cloud-based ecosystem minimizes redundancies, delivering time and cost efficiencies through globally accessible streamlined workflows. A cloud-based submission workflow reduces burden along the following dimensions:
    - **Technology:** Ensures secure, compliant information exchange tailored to regional and sponsor requirements, safeguarding sensitive data.
    - **Data & Content:** By applying FAIR principles (Findable, Accessible, Interoperable, Reusable) to data and content, this approach centralizes information exchange, significantly reducing costs associated with managing large amounts of duplicate data across sponsor and regulatory systems.
    - **People:** Frees up human resources to focus on high-value tasks by using AI and automation to handle repetitive processes like adapting submissions to regional formats and retrieving past interaction records.
    - **Process:** Streamlines workflows with cloud-enabled capabilities, allowing parallel submissions across regions to accelerate review timelines and reduce bottlenecks.

This cohesive approach enhances productivity, supports innovation, and reduces the overall burden of drug development.

Modernizing regulatory pathways is crucial to accelerate scientific discoveries. While cloud adoption has been ubiquitous within sponsors and agencies, the pace of adoption for global regulatory collaboration has been slow. Real-time reviews and cloud-based interactions would streamline communication, enabling faster, more responsive collaboration without the delays associated with establishing trusted interactions across traditional systems.

> **A cloud-based regulatory collaboration platform streamlines regulatory reliance and work-sharing and democratizes access to regulatory decision resources.**

REGULATORY COLLABORATION CLOUD USE CASES

- **Reliance and Work-Sharing:** Given the acceleration of complexity in the science and technology of drug development, and the globalization of patients and supply chains, even well-resourced regulators can be overwhelmed ensuring safety and quality. A cloud-based regulatory collaboration platform streamlines regulatory reliance and work-sharing and democratizes access to regulatory decision resources. Centralization of tools and processes reduces workloads for global sponsors and regulators enabling efficient, secure collaboration. This allows multiple regulators to evaluate submissions concurrently with controlled data access, immutable tracking, and streamlined decision-making.

- **Real-World Data in Submissions:** A trusted broker in the cloud enables secure access and lineage tracking of RWD and RWE to support drug safety and efficacy claims. Connecting sponsors, RWD providers, and agencies, it ensures data provenance and manages data use agreements, facilitating compliance with evolving standards and enabling efficient confirmatory analysis.

- **Standards Development, Digitization, and AI:** A collaborative cloud platform supports regulatory standards development, advancing data harmonization for AI insights. It helps standardize workflows, share resources, and promote AI readiness, enabling stakeholders to adopt the latest tools and AI models for enhanced regulatory analysis.

- **AI-Powered Submission Validation:** AI models presented on the platform validate submissions for compliance, consistency, and quality. By automating validation, the platform speeds up the review cycle in alignment with regulatory standards while maintaining security and privacy, thus enabling AI to efficiently augment human review.

Design Principles for Cloud-Based Regulatory Collaboration

Drawing on extensive experience in delivering advanced technologies such as RIM solutions and regulatory-grade cloud platforms and recognizing the unmet needs in the highly regulated and regionally specific drug development and maintenance processes, the following key design principles are proposed for a regulatory cloud platform.

- **Regulatory Decisions, Data, Analysis, and System Quality:** If a reviewer is analyzing submitted data, it must be done on agency-authorized systems to ensure the integrity of the data and analysis. This ensures confidence in data provenance, change control, and system validation, and the analytic results.
- **Data Risk Categorization:** Data should be appropriately categorized by risk. Overly conservative risk categorization can create unnecessary barriers and costs. Highly sensitive data should be managed with higher security, while less sensitive data can be handled with more efficient, lower-risk systems.
- **Data Distribution:** Data should be moved infrequently. Instead, analysis should be conducted where the data resides, via the exchange of access information and metadata rather than physically moving the data. This enables secure, authorized analysis while maintaining data security and privacy.
- **Data Sharing:** Data sharing between sponsors and regulators will be governed by bi-lateral usage agreements, ensuring compliance with global, regional, national, industry, and agency security, privacy, residency, and compliance requirements.
- **Digitization, Normalization, Harmonization, and AI:** Through the efforts of SDOs in concert with sponsors and agencies, regulatory data and metadata is being digitized, normalized, and harmonized to align with evolving standards. This facilitates the use of AI and supports collaboration across agencies and sponsors by ensuring consistent and interoperable data formats and structures.
- **Cost Controls:** Cloud resources must be procurable, and expended costs must be tracked and allocated to the users and organizations consuming them. This is essential for sustainable operations of both multi-agency systems and single-tenant enterprise systems, enabling transparency and efficient cost management.

Archetypical Regulatory Information System Attributes

This section proposes attributes that will be required for any system supporting regulatory interactions. A regulatory information system is defined by its boundary and governance and services layers and will be implemented with consideration for each of the components of the proposed Archetypical Regulatory Information System Architecture (Figure 5). For systems to interact in a network, system boundary, governance, services, interconnection, and interchange contract considerations must be addressed.

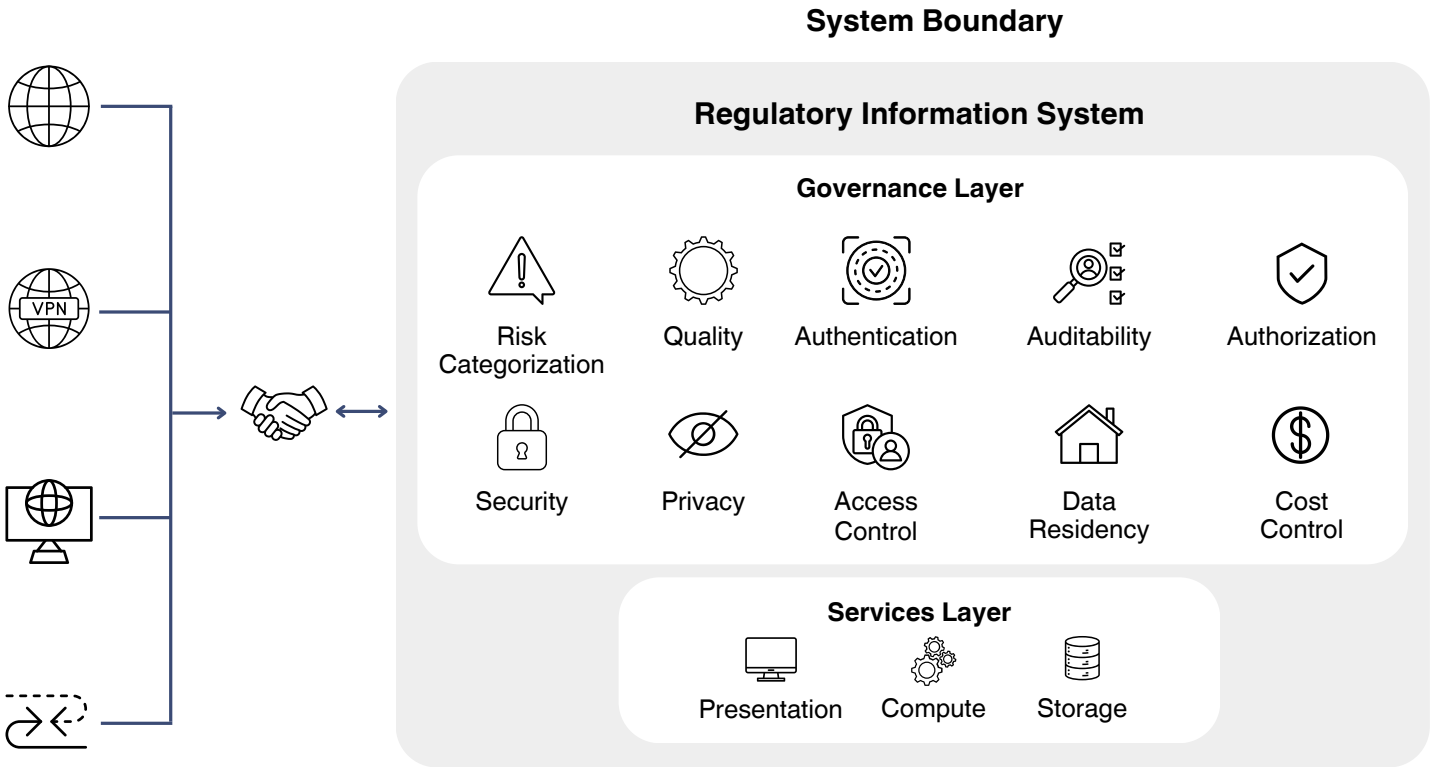


Figure 5: Archetypical Regulatory Information System Architecture

Regulatory Information System Boundary, Governance, and Service Delivery

This section outlines the key features needed for systems supporting regulatory interactions, focusing on boundaries, governance, and service delivery.

- **System Boundary and Access:** A regulatory system has a defined boundary where the system owner controls services and governance. External access to the system through methods like the internet or a virtual private network (VPN), is controlled under interchange contracts such as firewall rules or data use agreements. All information passing through the system boundary is governed under the terms of some form of interchange contract.

- **Governance:** The system has controls to ensure it can be audited and meets regulatory requirements. This includes managing user access and ensuring compliance with regulations.

- **Risk, Security, Privacy, and Quality**
  - **Risk:** Systems are categorized based on data sensitivity. Higher-risk systems handle more sensitive information such as proprietary drug formulation information.
  - **Security:** Protects data confidentiality, integrity, and availability of information managed by the system through encryption and tracking.
  - **Privacy:** Ensures personal data is handled according to privacy laws governing the acquisition, use, distribution, and removal of PII.
  - **Quality:** Ensures the system meets regulatory standards for quality and validation like FDA 21 CFR Part 11 requirements for validated computer systems (Annex 11 in the EU), and ICH GxP guidelines. These controls ensure that the system is fit for regulatory review purposes and that system changes are well understood.

- **Authentication and Access Control:** Systems use secure methods like Single Sign-On (SSO) and Multi-Factor Authentication (MFA) to ensure users only access authorized resources in accordance with the Zero Trust strategy of least-privilege access.

- **Authorization, Audit, and Data Residency:** Regulatory information systems must meet specific compliance standards.
  - An authorization enables the system to interact with other systems under interchange contracts that are readily executed without requiring additional diligence such as audits or network penetration testing.
  - Regulatory systems that do not obtain authorization under a specific compliance regime must be auditable in order to be trusted by other regulatory information systems.
  - Data residency controls govern the physical location of data and its distribution across national, regional, and state borders. These controls ensure that data resides within statutorily mandated borders.

- **Cost Control:** Cost controls provide administrative capabilities to govern users' resource consumption, and to visualize on a per-user and per-organization usage cost over time. Resource procurement capabilities enable users to request and manage cloud services under this cost governance.

- **Service Delivery:** Services are presented using underlying compute and storage resources through either batch applications (non-interactive) or interactive workstations with a user-friendly Graphic User Interface (GUI).

Citations for Regulatory Cloud Requirements

Publications regarding cloud-based regulatory systems are cited to provide context for the proposed regulatory information system attributes.

- **Nature Reviews | Drug Discovery:** Research on cloud-based systems in drug regulation highlights the benefits of cloud-enabled innovation. These include faster reviews, AI integration, globally coordinated reviews, improved security, real-time data access, and cross-study analysis. The value of a cloud platform in regulatory assessment lies in coordination between global regulatory authorities and the pharmaceutical industry, simplifying data sharing, application submission, and dossier management. "The true value of a cloud platform in regulatory assessment and review relies on a coordinated strategy between global regulatory authorities and the pharmaceutical industry. Globally, it is important that regulatory authorities adopt a compatible, ideally singular, platform, as coordination would greatly simplify data sharing, application submission and dossier management."

- **Therapeutic Innovation & Regulatory Science:** A study on cloud-based data tracking systems for gene and cell therapies proposes a cloud infrastructure for multiple stakeholders to share data. Key benefits of cloud characteristics include:
  - Consistent, state-of-the-art security.
  - Scalability for large data and computing needs.
  - Lower operational costs.

A hybrid cloud approach enables secure private clouds for proprietary data and shared clouds for collaborative data access.

> "Cloud characteristics are ideal for multi-party co-ownership: (1) access to consistent, state-of-the-art security that reduces the importance of the 'weakest link' among stakeholder systems; (2) scalability, in the computing and data size sense; and (3) lower operational costs. A hybrid cloud approach would also permit interfaces between private, proprietary clouds that individual stake- holders own to keep their data and a publicly shared cloud where the stakeholders release certain data in a controlled manner."

- **ICMRA-ICH-PIC/S-IPRP Joint Reflection Paper:** This paper recommends a virtual repository for a Regulatory Pharmaceutical Quality Knowledge Management System (PQ KMS), which would be used by multiple agencies to improve medicine availability and quality. It highlights the need for secure, controlled access to information, maintaining confidentiality, protecting against cyber threats, and interfacing with existing systems.

Secure and controlled authorized access to information and regulatory assessments to maintain confidentiality agreements and trade secrets, information security and protection from cyber threats, an ability to leverage current technologies to interface with existing regulatory authority and sponsor/ market authorization holder systems.

TRSnet Design

Now that an archetypical regulatory information system architecture has been described, the requirements for a TRSnet are explored, and a design is proposed. The proposed design incorporates open-source and commercial software running on diverse cloud service providers to provide implementation flexibility. In consideration of the proposed foundational design principles and cited requirements for regulatory clouds, a TRSnet design is proposed to enable distributed regulatory object management (Figure 6).

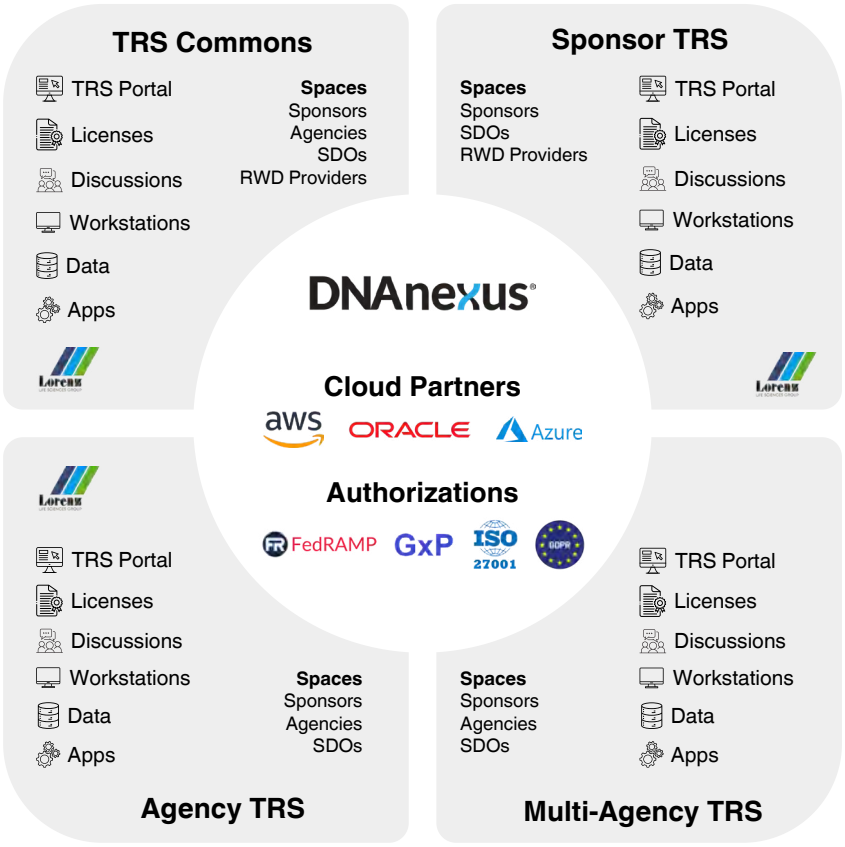


Figure 6: TRSnet Design

A TRSnet is made up of multiple internet-connected sponsor and agency nodes, and a single multi-agency node, enabling collaborative cloud-based interactions across system boundaries between drug and device sponsors, RWD providers, SDOs, and agencies. Each node supports the required regulatory information system governance and services layers attributes described in the Archetypical Regulatory Information System Architecture. An agency may deploy separate nodes for High and Moderate risk categories of data in order to efficiently and cost effectively manage submissions based on their specific risk categorization.

Internode interactions are governed through bi-lateral interchange contracts established between stakeholders and managed with licenses attached to shared resources. Provenance of data, applications, and executions is tracked across TRS node boundaries, to provide a clear picture of true source data and any transformations that have been applied. TRS Spaces on each node enable secure sharing of data, tools, and communications, between groups of named users across TRS boundaries. Discussion threads in Spaces provide a secure and auditable communications mechanism for stakeholder interaction within the TRSnet boundary. A TRS command line interface (CLI) enables the programmatic exchange of data, discussions, and other artifacts across nodes, and the TRS web interface presents user-friendly access to all TRS capabilities.

Electronic Submission Gateways, each serving one or more agencies, are used to transfer completed packages from sponsors, but the TRSnet could potentially support delivery of submissions in Spaces.

Authorized Cloud Service Providers

Each TRS node uses an underlying authorized CSP to enable the functional capabilities presented through the web and command line interfaces. PaaS providers like DNAnexus present an API upon which a TRS node can be built using underlying AWS, Oracle, and Azure cloud resources. CSPs provide region-relevant compliance strategies that TRS nodes inherit including ISO 27001, GDPR, and GxP internationally, and FedRAMP in the US.

DNAnexus provides TRS-compatible API services in North America, Frankfurt, London, Amsterdam, and Australia using multiple cloud partners to accommodate stakeholder data security, privacy, and residency requirements. SDOs and industry agencies like CDISC, ICH, and ICMRA will need to consider a suitable service deployment location for a multi-agency TRS node in order to address the requirements of their constituencies. Regulators deploying a High-risk categorization TRS will need to consider any underlying PaaS, IaaS and commercial software for authorization to operate under the controls required for this risk category.

TRS Command Line Interface

The TRS CLI supports inter-node discovery to create a TRSnet and provides connected nodes with the ability to request user accounts from sibling nodes. The multi-node aware CLI enables authenticated and authorized users to list, create, and access objects in other TRS nodes using globally unique TRS node and object IDs. The commands for listing, downloading, and uploading files, reading and writing threads, and for listing apps, executions, and spaces, all support internode access.

TRS Web Interface

The TRS Web Interface presents capabilities to navigate across authorized TRSnet nodes to access data and tools in a trusted manner. The web interface presents members-only collaboration spaces, discussion threads, and custom web portals, built on a foundation of file and folder management, version-controlled applications, interactive workstations, and relational databases.

TRS Nodes and Regulatory Object Management

Each TRS node abstracts its underlying authorized CSP's Infrastructure-as-a-Service to present web and command line interfaces harmonized across nodes regardless of the underlying CSP. This supports uniformity of processes, technology, and projects across all stakeholders to enable efficiencies in regulatory workflows. Each TRS node has a unique name, and all users, data, applications, and executions have unique identifiers, enabling internode addressing to support a distributed regulatory object management system. Data can be shared through the exchange of access information and metadata rather than via actual data movement, and all transactions and provenance are tracked and reported. Using these unique identifiers, LORENZ eValidator-DSM and docuBridge-DSM solutions enable seamless management of regulatory objects wherever they reside in the TRSnet.

There are four TRS node types, Sponsor, Agency Moderate and High, and Multi-Agency. The sponsor node enables interaction between sponsors, agencies, RWD providers, and SDOs. The Agency Moderate node connects agencies with sponsors, SDOs, and other agencies. The Agency High node is dedicated to sponsor-reviewer interactions. The multi-agency node doesn't manage submission data but instead manages the interchange contracts, licenses, and other metadata that connect sponsors and agencies for reliance and work-sharing use cases, and connect SDOs, sponsors, and agencies for collaborative development of standards. All TRS nodes provide a "de-militarized zone" that enables facile collaboration without exposing internal systems and data.

The TRS Commons Cloud Platform

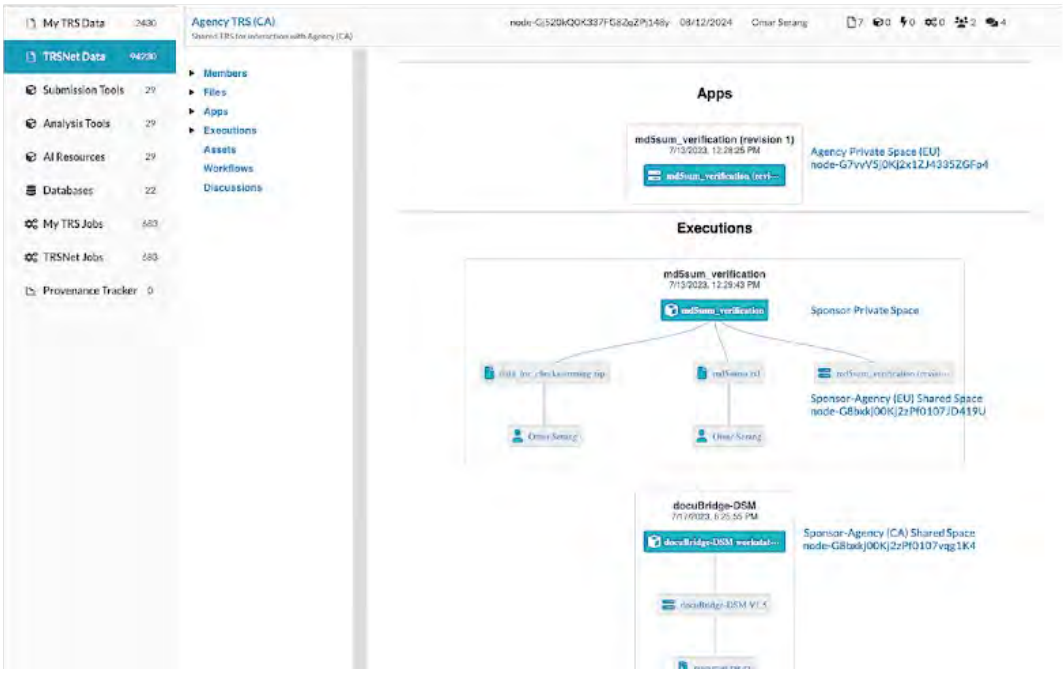
Additionally, a LORENZ-sponsored TRS Commons node on DNAnexus will be launched in early 2025 to provide a secure platform in the AWS Frankfurt region demonstrating TRS capabilities and supporting collaboration between regulatory stakeholders. The TRS Commons is based on a multi-agency node design to present tools and use cases unifying and accelerating the joint objectives of industry, agencies, and SDOs. This goes beyond a document-oriented collaboration model by providing data management, discussion threads, and on-platform tools in a regulatory-grade environment to enable the rapid development and execution of global regulatory use cases.

TRS Spaces and Discussion Threads

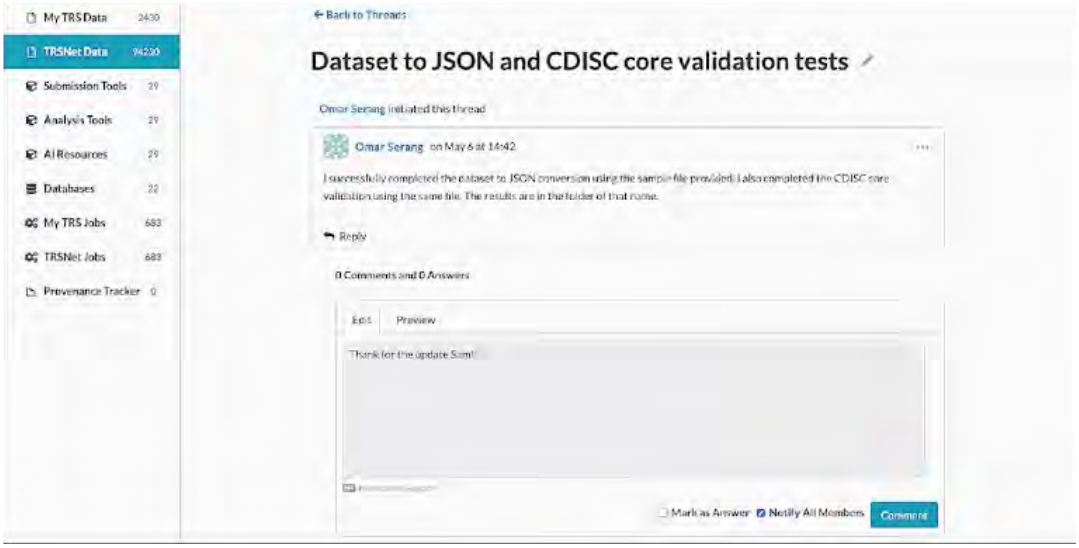
TRS Nodes enable secure sharing of data and applications with a selected list of other users in Spaces (Figure 7a). Spaces are created for multi-lateral collaboration between stakeholders and bi-lateral interactions between sponsors and reviewers. Spaces are accessible only to specified users and are self-administered by Space leads who can add, assign roles, or disable, members. Space members can communicate securely amongst each other directly within the Space using discussion threads with attached files and optional email alerts (Figure 7b). All artifacts within a Space including files, applications, workstations, databases, executions, membership, and discussion threads, are tracked for provenance, and a TRS report can be generated to present this information (Figure 7c).

DNAnexus provides TRS-compatible API services in North America, Frankfurt, London, Amsterdam, and Australia using multiple cloud partners to accommodate stakeholder data security, privacy, and residency requirements.

A. TRSNet Nodes Listing



B. TRS Message Thread



C. TRS Report

Figure 7: TRS Spaces and Discussion Threads

TRS Portals

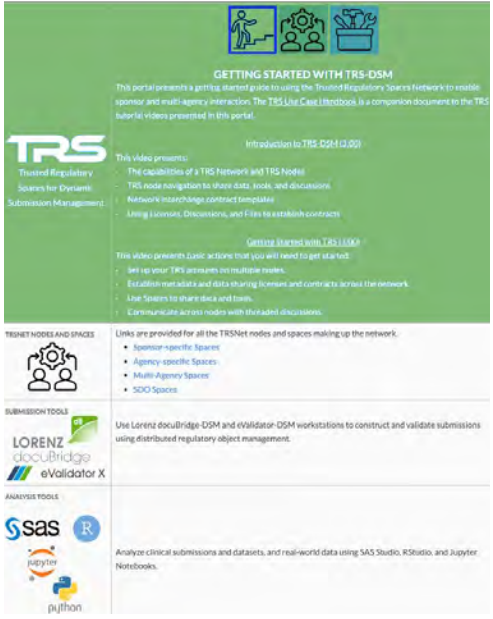
A TRS Portal is available for each node type, offering both common and specific workflows for applications, workstations, and data. It provides a unified user experience across all TRS nodes, allowing users to easily manage interchange contracts, access data, and communicate with network members. Common workflows include collaboration with Spaces, account management, data sharing, and utilizing submission and analysis tools.

- All TRS Node Portals share some common Getting Started workflows for TRSnet collaboration and account management; establishing interchange contracts for user access and data sharing; using Spaces to connect sponsors, RWD providers, SDOs, and agencies; and using submission and analysis tools (Figure 8a).

- The Sponsor Node Portal helps manage data use agreements, multi-agency communications, RWD provider and SDO integration, and information sharing for reliance and knowledge management systems (Figure 8b).

- The Agency Moderate Risk Node Portal mirrors sponsor workflows for communication, submission planning, and information requests, with a focus on multi-agency coordination (Figure 8c). The High-Risk Category Portal offers stricter workflows for network data exchange and contract management.

- The Multi-Agency Portal emphasizes collaborative interchange contract development, reliance information and knowledge management system maintenance, along with joint standards development (Figure 8d).



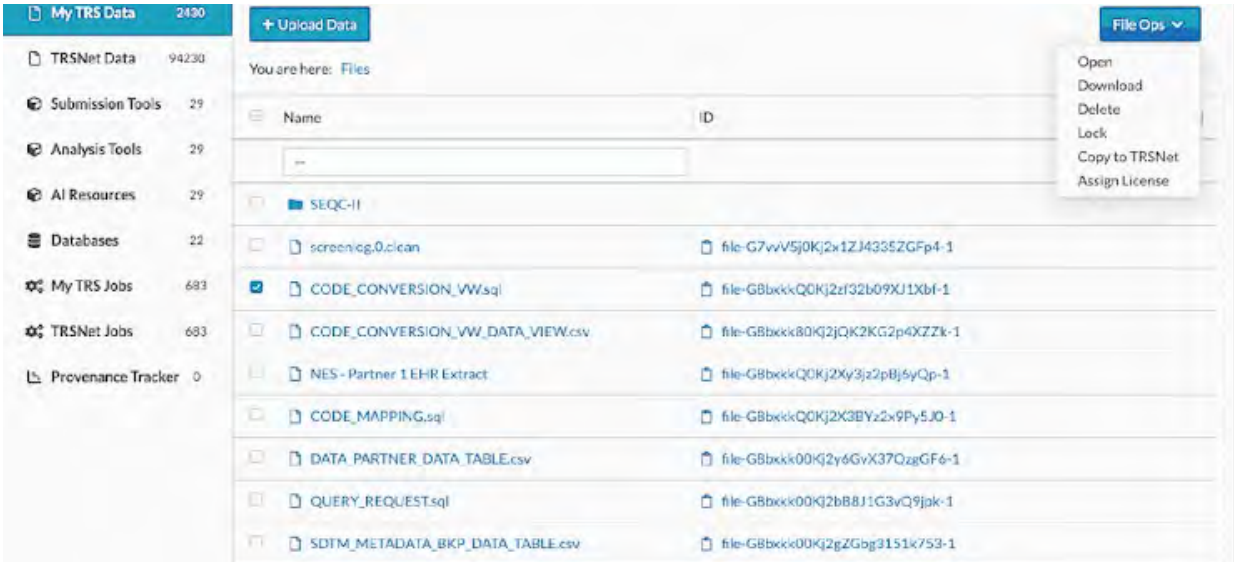
A. TRS-DSM Getting Started Portal

B. Sponsor Portal Use Case Toolbox

C. Agency Portal Use Case Toolbox

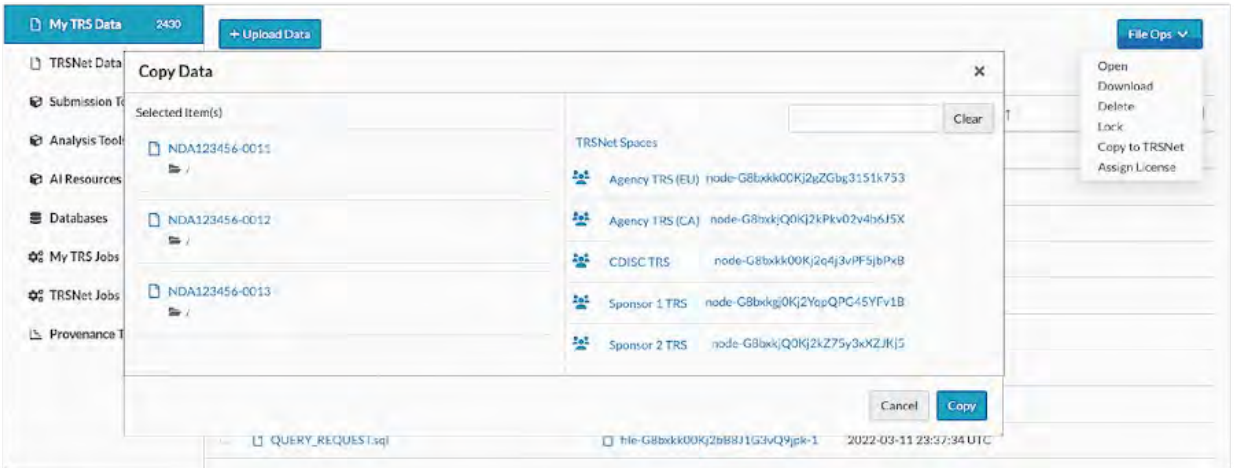
D. Multi-Agency Portal Use Case Toolbox

Figure 8: TRS Portals



A. Data and File Operations Menu

B. Provenance Tracking



C. Copy Data to Space

Figure 9: Data

Data in the TRS

Files and folders are provided for users to upload, analyze, organize, and download data (Figure 9a). Data, once uploaded, is immutable and uniquely identified with a Globally Unique Identifier (GUID), and the provenance of all data objects is tracked (Figure 9b). The provenance tracking spans TRSnet nodes reflecting where data resides and is processed. Files can be private, accessible only to the user that uploaded or generated the file, or they can be copied to other TRSnet users via Spaces (Figure 9c). Files are stored in a cloud provider's object store (e.g. S3) but all access to the data is controlled through the TRS.

TRS Applications, Workstations, Executions

Users can work with files using batch applications and interactive workstations (Figure 10). Each execution of an application or workstation is accessible only by the user that launched it. Execution takes place on cloud compute instances within a hardened container environment that is destroyed upon completion. All applications are immutably versioned with each version uniquely identified with a GUID. Developers can create and share Linux-based applications using the application development web interface. Users can select from a range of cloud compute instance types, including GPUs, for execution of batch applications or deployment of interactive workstations.

Figure 10: Applications

TRS Licenses

TRS Licenses provide the means to establish terms of use between TRS users for access to data, applications, and workstations, and provide the mechanism by which interchange contracts are implemented. The creator of an object can create a terms of use agreement and attach it to the object they want to share (Figure 11). Users that have access to the shared object can discover and view it, but they cannot open the object until they have agreed to the terms of the agreement. Use agreements can be either click-through or require the approval of the licensor to grant access to the object. This can support a range of interchange contract use cases including controlled access to RWD, and sponsor authorization for agency work-sharing.

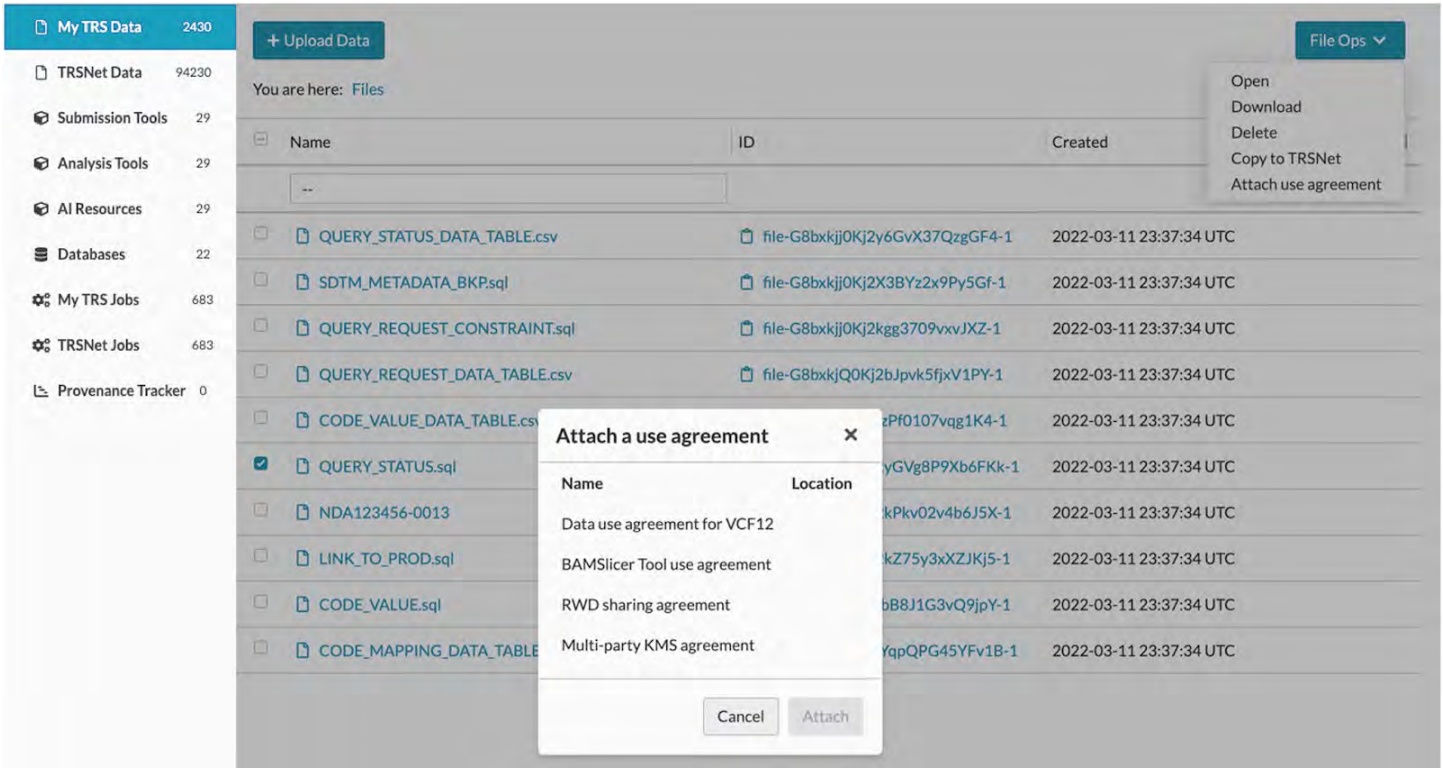
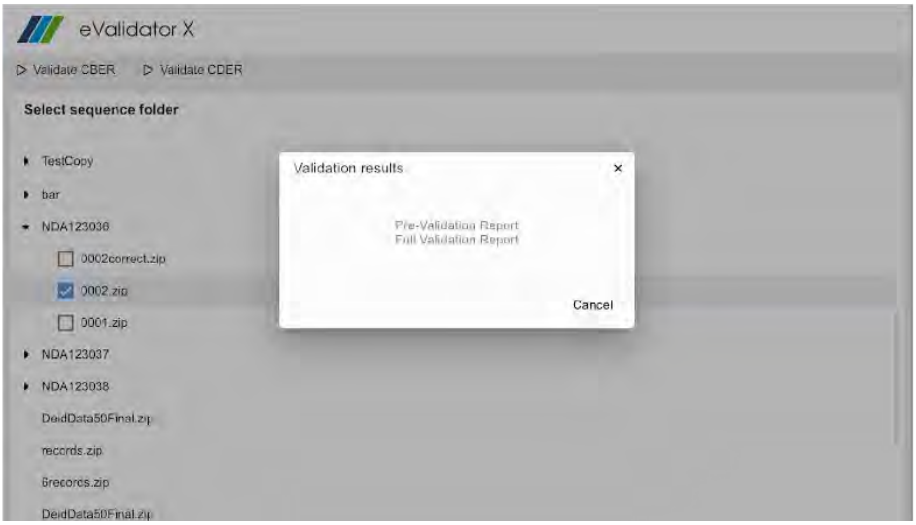


Figure 11: TRS Use Agreement Assignment

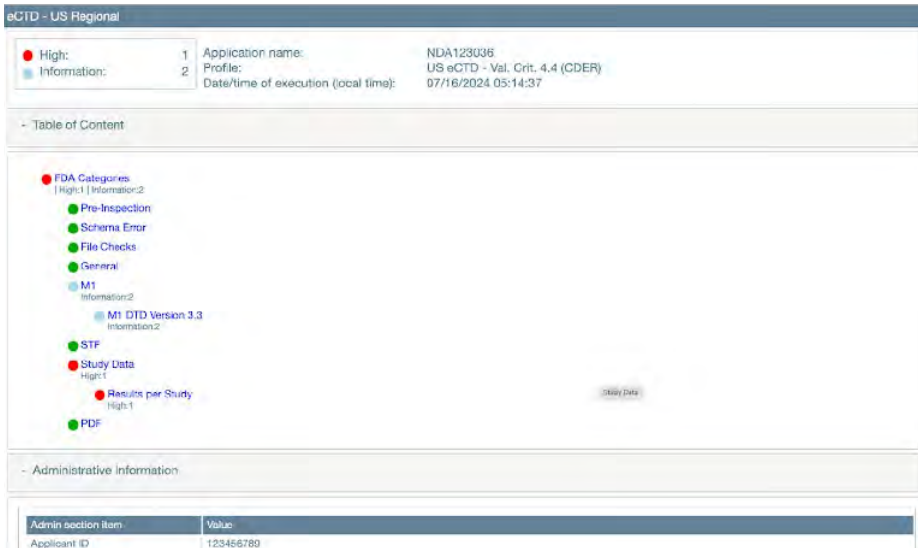
SUBMISSION TOOLS

LORENZ eValidator

LORENZ has deployed their gold standard eCTD validation software, eValidator, on the DNAnexus platform for presentation as a TRS application. LORENZ provided a Linux-compatible version of eValidator using the DNAnexus API for filesystem interactions and deployed it on a workstation (Figure 12a). The eCTD XML backbones and referenced content files, meta data, etc. are verified against selected published criteria, and a validation report is generated (Figure 12b).



A. LORENZ eValidator Workstation



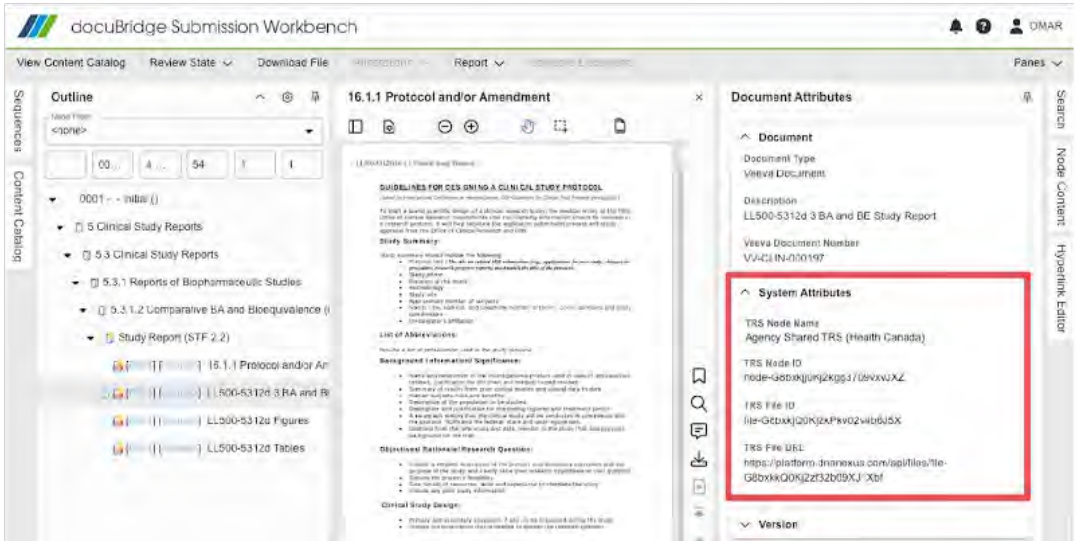
B. Validation Report

Figure 12: LORENZ eValidator

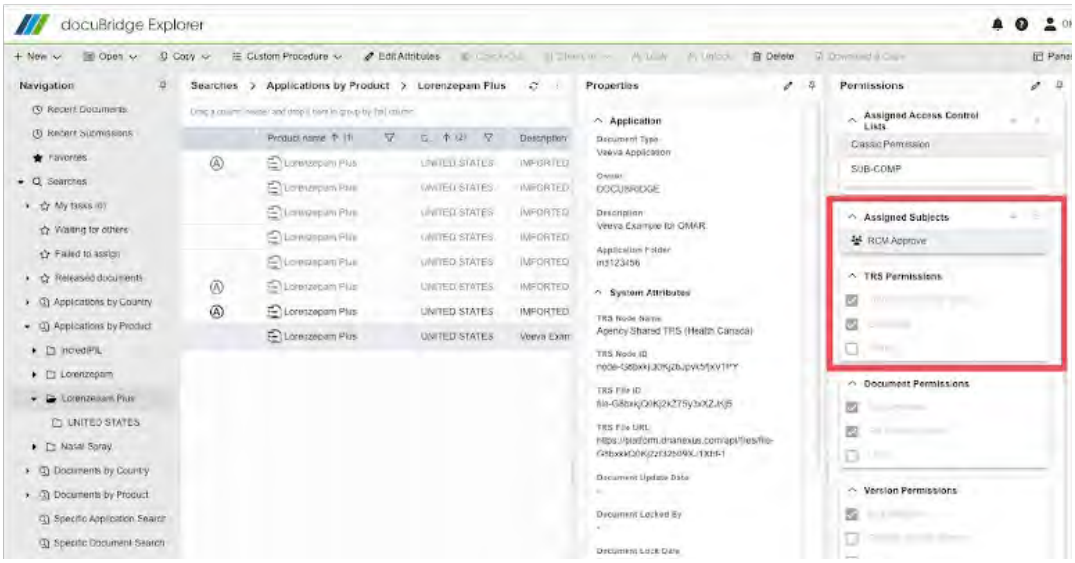
LORENZ docuBridge-DSM

LORENZ is developing docuBridge-DSM, a TRSnet-aware version of their gold standard electronic submission management and regulatory content management system for compiling, publishing, importing, and reviewing eCTDs. Submission package objects will be accessible from multiple TRS nodes to review in aggregate presenting TRS-related system attribute properties for node name and ID, file ID, and URL for the object on the remote TRS node (Figure 13a). A new layer of TRSnet-based permissions is being added to the docuBridge document, version, and object permissions model, to confer remote TRS node permissions for operations such as data transfer, downloading, and sharing (Figure 13b).

Submissions will be created using docuBridge-DSM to construct and review the package from objects on multiple TRS nodes, accessing them by their globally unique identifiers to compile and publish an integrated submission package once review is complete.



A. docuBridge-DSM TRS System Attributes



B. docuBridge-DSM TRS Permissions

Figure 13: LORENZ docuBridge-DSM

Analysis Tools

A wide range of data analysis and regulatory software is available for sponsors, researchers, and reviewers. The open-source CDISC-CORE validation application analyzes Study Data Tabularization Method (SDTM) and other CDISC dataset formats using a CDISC open rules engine. Jupyter Notebooks provide Python and R, and Tensorflow for GPU-enabled AI applications. Open-source R-based and commercial SAS-based interactive analysis applications are available for authorized users to run on workstations (Figure 14).

An open-source FHIR Clinical Data Repository workstation is provided with Jupyter Notebooks for analysis and visualization of RWD in the HL7 Fast Healthcare Interchange Resources (FHIR) format.

Platform Cost Controls

Administrators can limit the total amount that a user may incur consuming cloud compute and storage and limit the amount any single application or workstation can incur in compute costs. Administrators can also control users' access to specific compute and database instance types. Detailed reports of user activity and costs are extracted from the platform and presented to operational and contracting stakeholders.

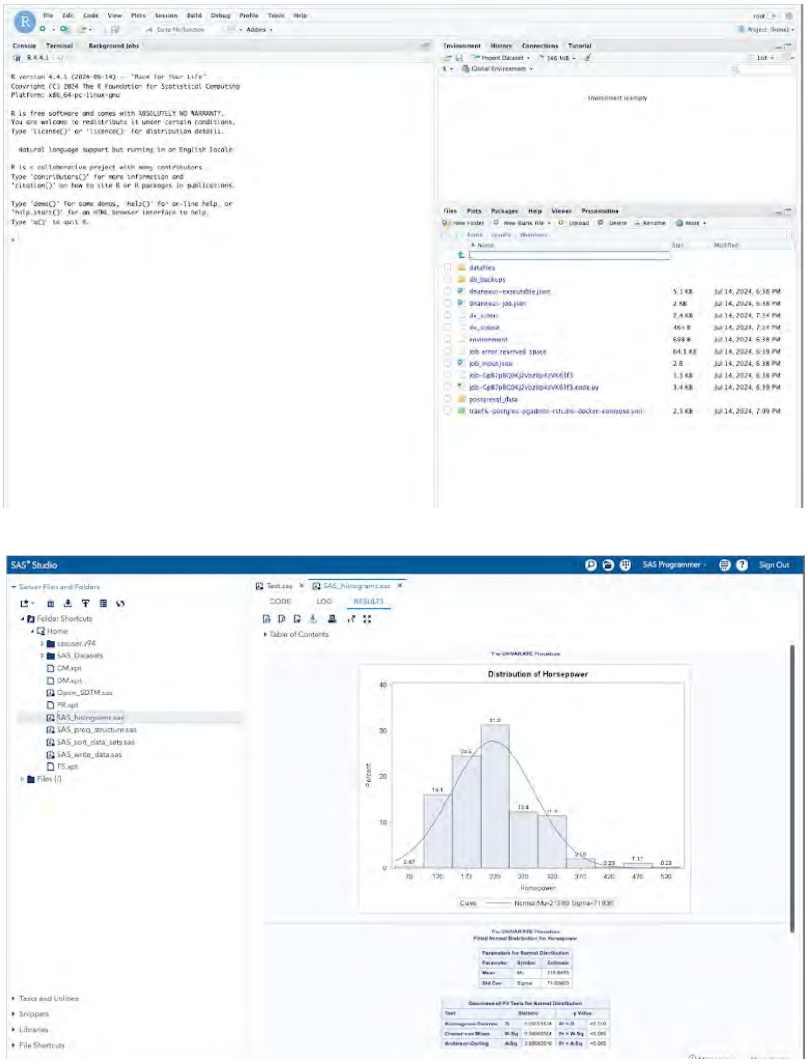


Figure 14: Analysis Tools Workstations

Use Cases Mapped to the TRSnet

In order to visualize how regulatory use cases can be implemented using a TRSnet, a regulatory reliance and work-sharing use case is mapped to the proposed TRSnet design to demonstrate sponsor and multi-agency interactions. First, a simple example is described to demonstrate the TRS regulatory information system capabilities that enable use cases to be built on a TRSnet.

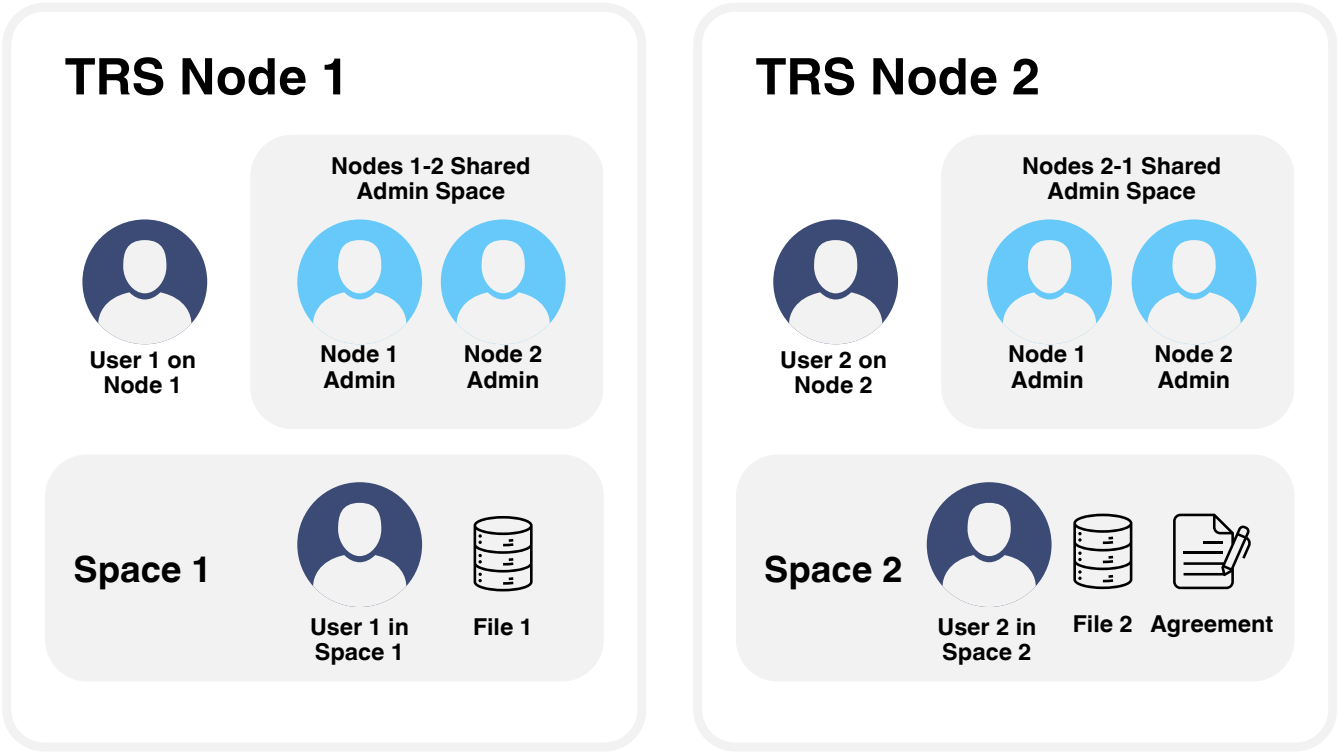


Figure 15: TRSnet Example Configuration

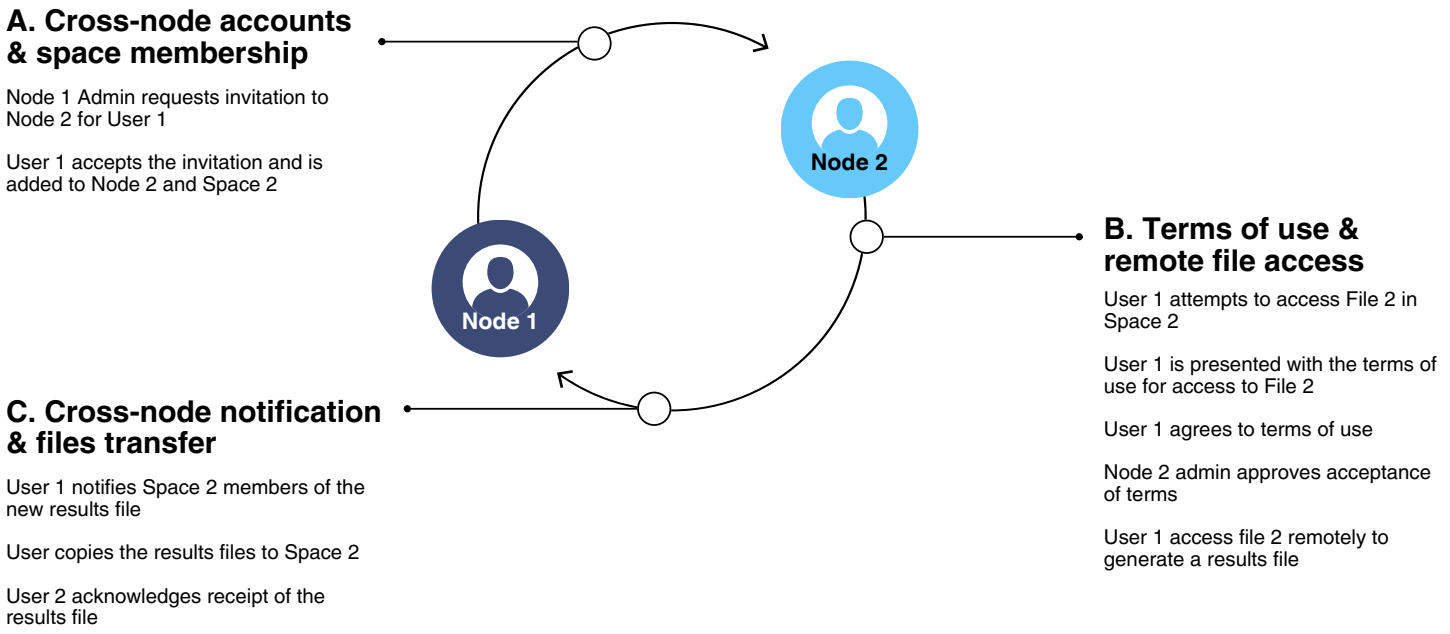


Figure 16: TRSnet Example Interactions

TRSnet Example

A TRSnet example configuration is used to illustrate how TRS nodes, user accounts, files, use agreements, and threads enable collaboration across nodes (Figure 15). The example configuration consists of two TRS nodes, with an established interchange contract that authorizes interaction, each with administrators that interact through discussion threads in the bilateral Shared Admin Spaces on each node. Each node has a user who is a member of a space on their respective node. The file in Space 2 has a use agreement with terms that need to be agreed to in order to access the file.

The Node 1 Admin initiates a thread in the Shared Admin Space requesting that the Node 2 administrator invite User 1 to also become a user on Node 2. User 1 receives and accepts the invitation and now has an account on Node 2 that is added to Space 2. Reciprocal transactions are initiated by the Node 2 administrator to obtain a Node 1 account and Space 1 membership for User 2. (Figure 16a)

User 1 attempts to access File 2 in Space 2 and is presented with terms of use to which they agree. Based upon this agreement, the Node 2 administrator approves access to the file, and User 1 can now run an application on Node 1 that accesses File 2 remotely in order to generate a Results File in Space 1. (Figure 16b)

User 1 initiates a discussion thread to notify both Space 1 and Space 2 members that the Results File is ready. User 2 receives the notification, reads the thread and copies the Results File to Space 2, and responds to the thread to acknowledge receipt of the file. (Figure 16c)

The TRS CLI supports writing and reading of threads so that workflows can be programmed with TRS applications and workstations using threads for inter-process communication. Using the capabilities presented in this simple example, complex regulatory use cases can be implemented using TRS nodes.

TRSnet for Reliance and Work-Sharing

A model TRSnet design supporting regulatory reliance and work-sharing between agencies is described. Three agencies have created a TRSnet dedicated to their joint review capabilities enabling a sponsor to make a single submission and perform combined information request handling with all three agencies.

TRSnet Design

A TRSnet design for a model reliance and work-sharing use case is presented (Figure 17).

This TRSnet comprises three agency nodes, a single sponsor node, and a multi-agency node that acts as the control tower for this TRSnet. Although only a single sponsor is modeled, the design can support multiple sponsors. Each node can be located as appropriate for the company or agency based on data residency, security, privacy, and risk categorization requirements. Since the multi-agency node will not store any actual submission data, the constraints for its location are not as stringent as the sponsor nor agency nodes.

As part of establishing the cross-node membership agreements that interconnect the TRS nodes, each node will require appropriate authorization and auditability to establish trusted relationships between nodes. Core TRS capabilities that enable this use case are:

- Spaces providing the foundation for secure collaboration between groups of users across nodes
- Globally Unique Object Identifiers, data immutability, and chain of provenance tracking to enable trusted cross-node data sharing
- Web-based Portals providing use case-specific workflows and tools presenting SOPs for stakeholder interactions
- A Licenses presentation and acceptance framework to enable the codification, enforcement, and tracking of stakeholder interactions
- Discussion Threads to support user-to-user, application-to-user, and application-to-application cross-node interactions
- Workstations, Applications, and Data resources in the cloud to enable interactive review of submissions and confirmatory analysis of accompanying data

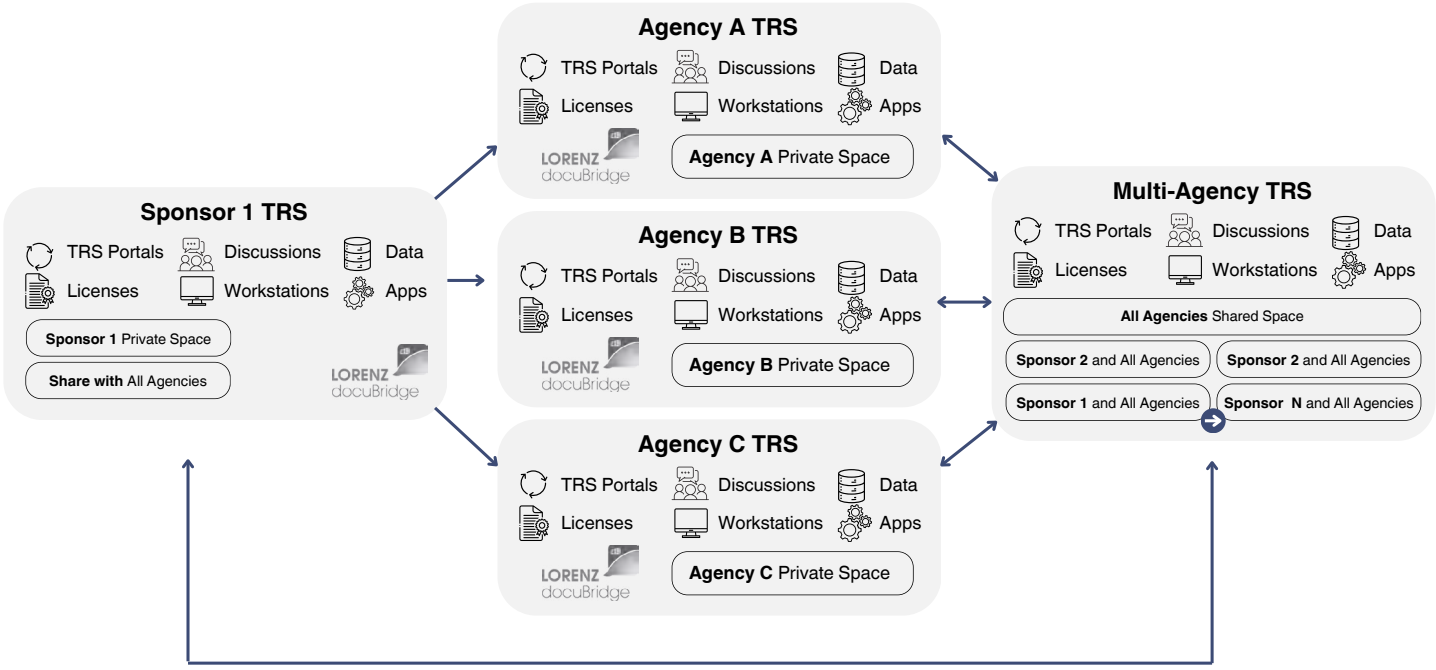


Figure 17: TRSnet for Reliance and Work-Sharing

The multi-agency TRS node is the central hub for stakeholder relationship management and stakeholder communications, though submission data is never shared across it. The All Agencies Shared Space includes members from all of the participating agencies and is used for all multi-lateral interactions between agencies. There are individual spaces for each sponsor with membership from the single sponsor's organization and all participating agencies, used for bi-lateral interactions between all agencies and individual sponsors. Since provenance is tracked and reportable on all spaces and their data, application, and discussion activity, the multi-agency TRS node serves as the system of record and reporting for all stakeholder interactions throughout the submission process.

The multi-agency TRS portal presents workflows for agency and sponsor network setup, creating a submission plan, establishing data use agreements, presenting and reviewing eCTDs, combined information request handling, and presentation of a submission recommendation.

Each sponsor node is dedicated to a single sponsor and provides a portal presenting sponsor-specific workflows and tools. Each sponsor node provides a shared space for presentation of eCTD submissions where agencies are able to navigate and review the submission directly in the sponsor's space. Each agency node is dedicated to a single agency and provides a portal presenting agency-specific workflows and tools. Agency nodes do not present any shared spaces, and coordinate all of their interactions with sponsors through the multi-agency node. Sponsor and agency nodes both provide the docuBridge-DSM workstation that enables collaborative review of submissions across nodes using globally unique identifiers to reference objects in sponsor-to-agency shared spaces.

Multi-Agency TRS Setup

Once the TRS administrators on the nodes have established their cross-node user accounts and shared administrative spaces memberships (as described in the TRSnet Example), they can bootstrap the reliance and work-sharing TRSnet by presenting and executing the agreements and provisioning the cross-node user accounts and spaces required for the use case. The Cross-Node Membership Agreement specifies the governance requirements (data residency, security, privacy, and risk categorization) that each node must comply with in a demonstrable manner (e.g. formal authorization, audit evidence).

The Multi-Agency Common Reliance Agreement specifies how each agency regards the review outputs of the others and what level of additional review a relying agency may have to carry out for suitability in their regulatory domain. While the primary challenges to establishing multi-agency agreements are legal and commercial in nature, this example demonstrates how the multi-agency TRS would enable the management and execution of agreements in a consistent, trackable, and non-repudiable manner. This example presents a multi-lateral agreement applicable to all agencies without modification, but agency-specific bi-lateral reliance agreements could also be implemented.

Agency administrators use the multi-agency TRS (MA-TRS) portal to carry out the SOPs to execute cross-node membership and common reliance agreements that have been mutually agreed to and presented on the MA-TRS. MA-TRS administrators provision requested agency users on the MA-TRS and add them to the All Agencies Shared Space (Figure 18a). Sponsor administrators use the MA-TRS portal to carry out the SOPs to execute cross-node membership agreements presented on the MA-TRS. MA-TRS administrators provision requested sponsor users on the MA-TRS and add them to their individual Sponsor and All Agencies space (Figure 18b).

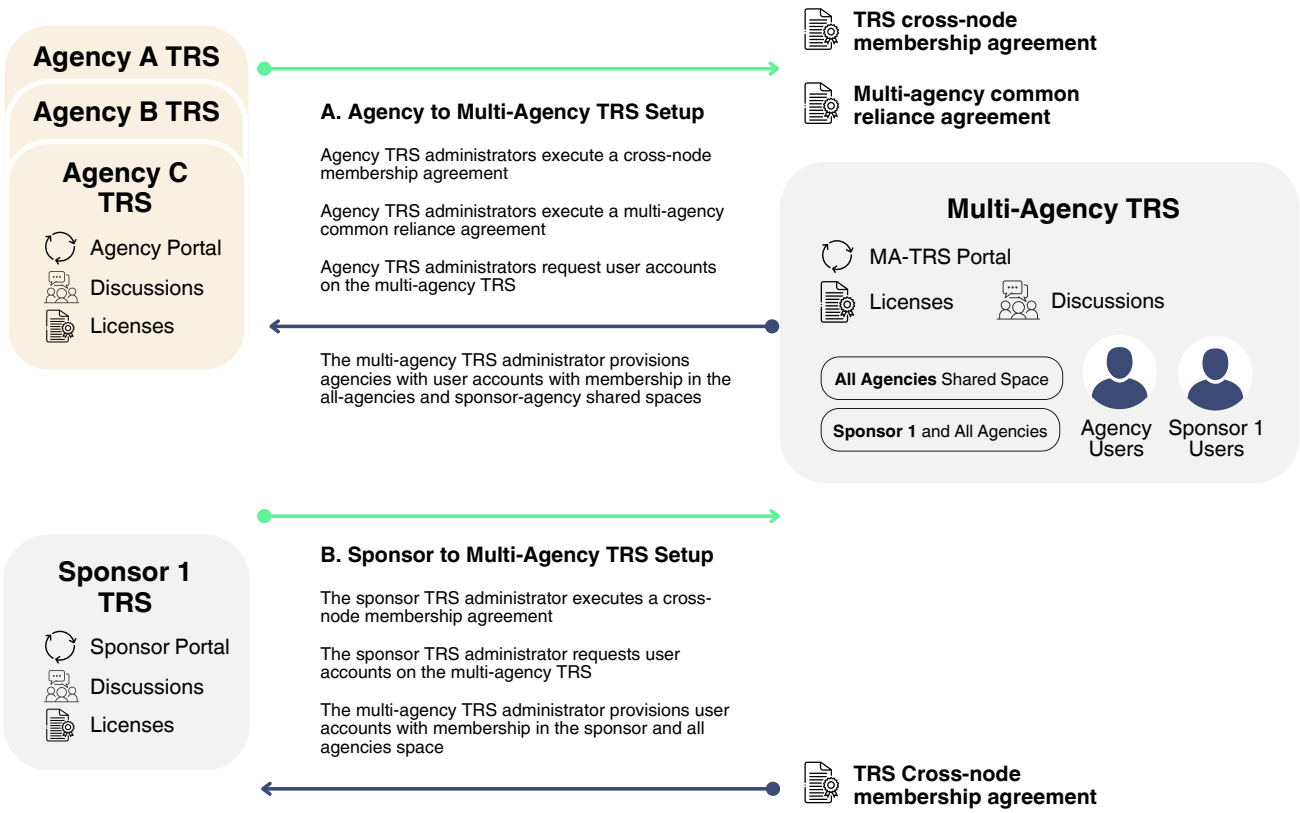


Figure 18: Multi-Agency TRS Setup

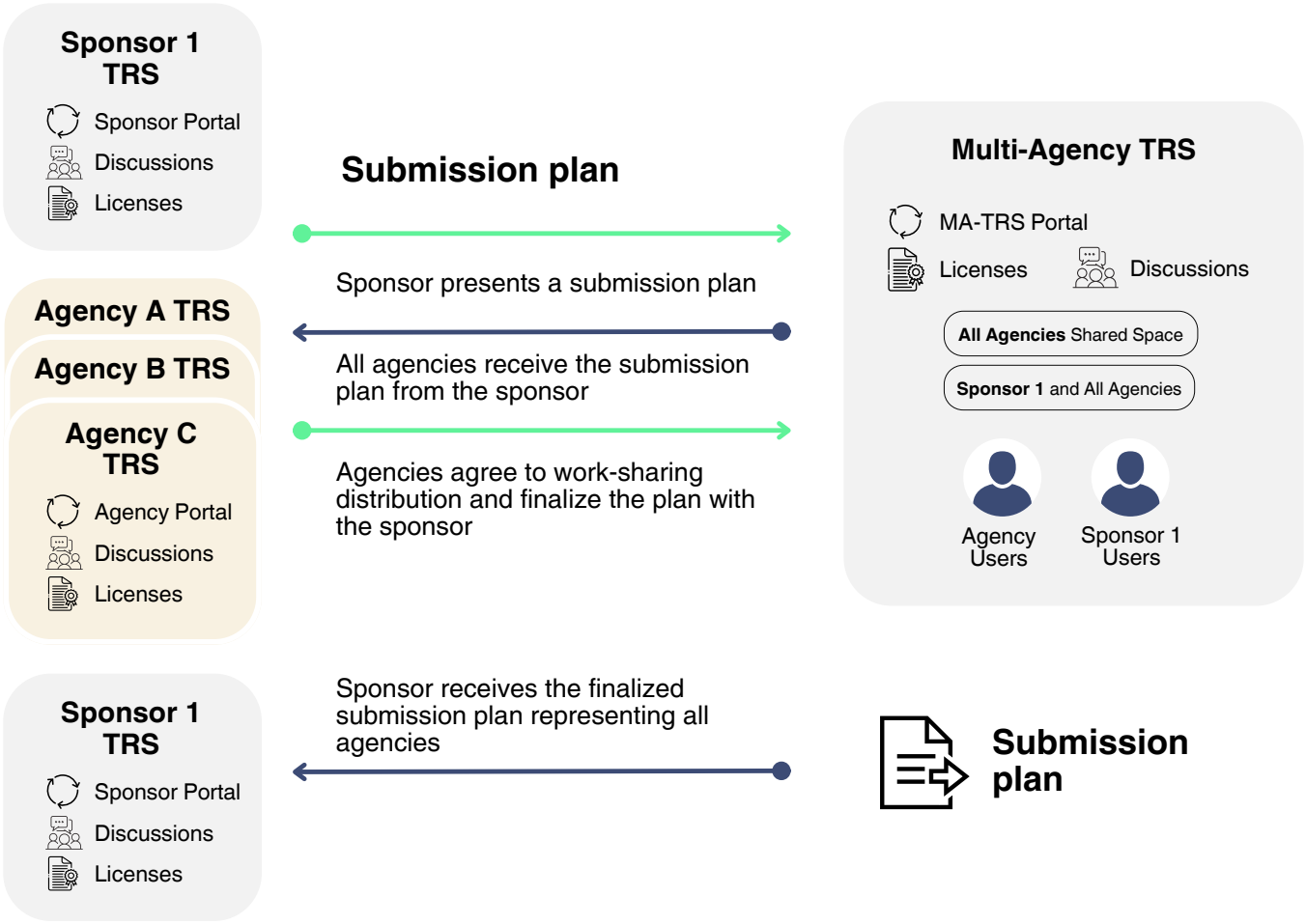


Figure 19: Submission Plan

Submission Plan

The sponsor regulatory team uses the MA-TRS portal to obtain, prepare, and present a global submission plan (Figure 19). The plan is presented to all the agencies requested by the sponsor in the Sponsor and All Agencies shared space. The plan is copied to the All Agencies shared space for work-sharing assignment and finalization. The resulting final plan is presented to the sponsor in the Sponsor and All Agencies shared space.

Data Use Agreements

The sponsor regulatory team and agencies use the MA-TRS portal to execute bi-lateral data use agreements with each agency (Figure 20). The sponsor's proposed data use agreement is presented to all the agencies in the Sponsor and All Agencies shared space. The agreement is copied to the All Agencies shared space and downloaded for execution by each agency. Each agencies' executed agreement is presented to the sponsor in the Sponsor and All Agencies shared space.

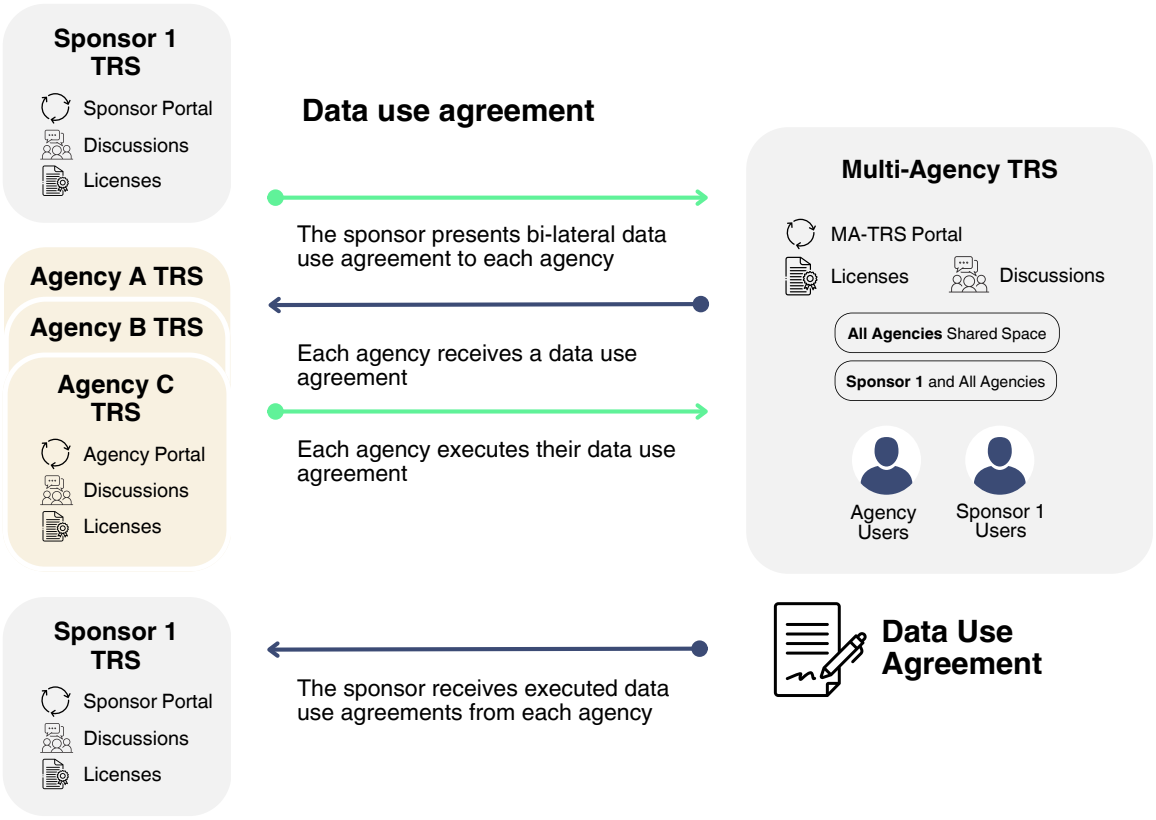


Figure 20: Data Use Agreement

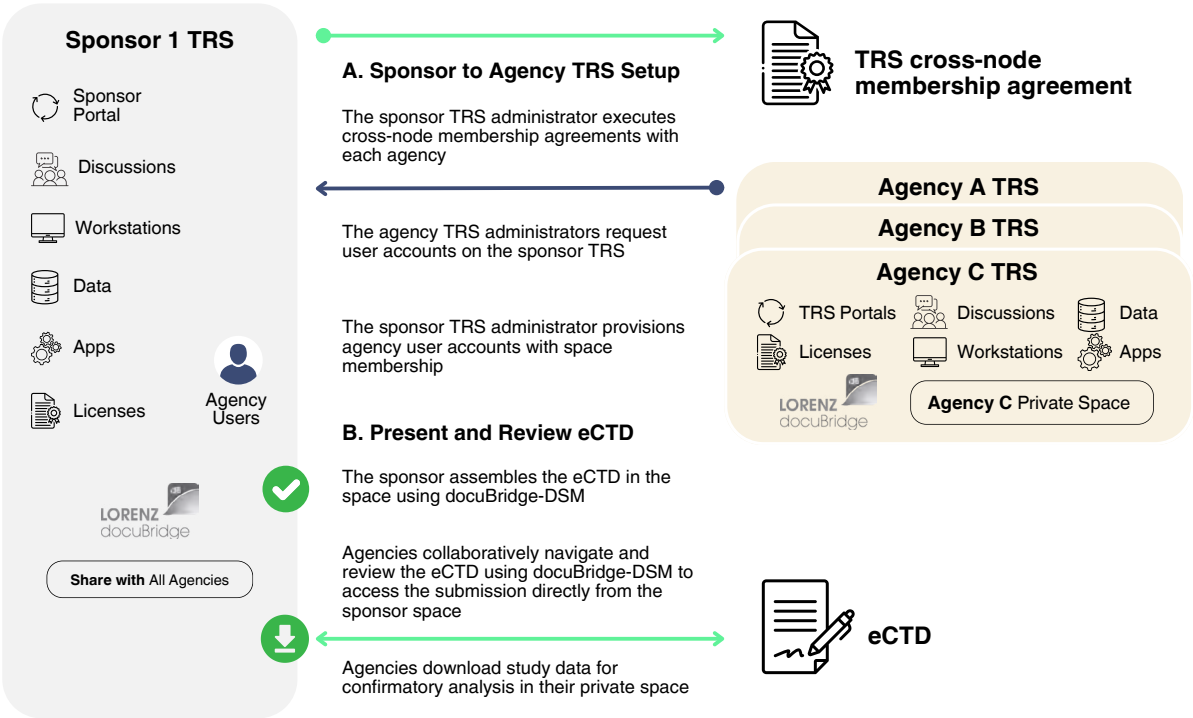


Figure 21: Sponsor to Agency TRS Setup and eCTD Presentation and Review

Sponsor to Agency TRS Setup and eCTD Presentation and Review

Once the data use agreements have been executed, the sponsor uses their portal to execute cross-node membership agreements with each agency (Figure 21a). This establishes the trust relationships required for the sponsor to provision agency users with membership in the Shared with All Agencies space.

The sponsor uses docuBridge-DSM running on a workstation in their own TRS to construct the eCTD submission in the Shared with All Agencies space (Figure 21b). Each agency uses docuBridge running in their own TRS to navigate and collaborative review the eCTD accessing it directly in the sponsor's TRS shared space without copying it to the agency's TRS. For confirmatory analysis of datasets, each agency downloads only the data they need from the sponsor's TRS for analysis in the agency's authorized TRS environment.

Combined Information Request Resolution

Agency reviewers use the MA-TRS portal to collaborative construct a combined information request (IR) for presentation and resolution with the sponsor (Figure 22). They construct the IR in the All Agencies Shared Space and present it to the sponsor in the Sponsor and All Agencies shared space. The sponsor provides an IR response that is copied from the sponsor to the all-agencies space for review. The agencies collaboratively construct an IR resolution confirmation in the all-agencies space and present it in the individual sponsor shared space.

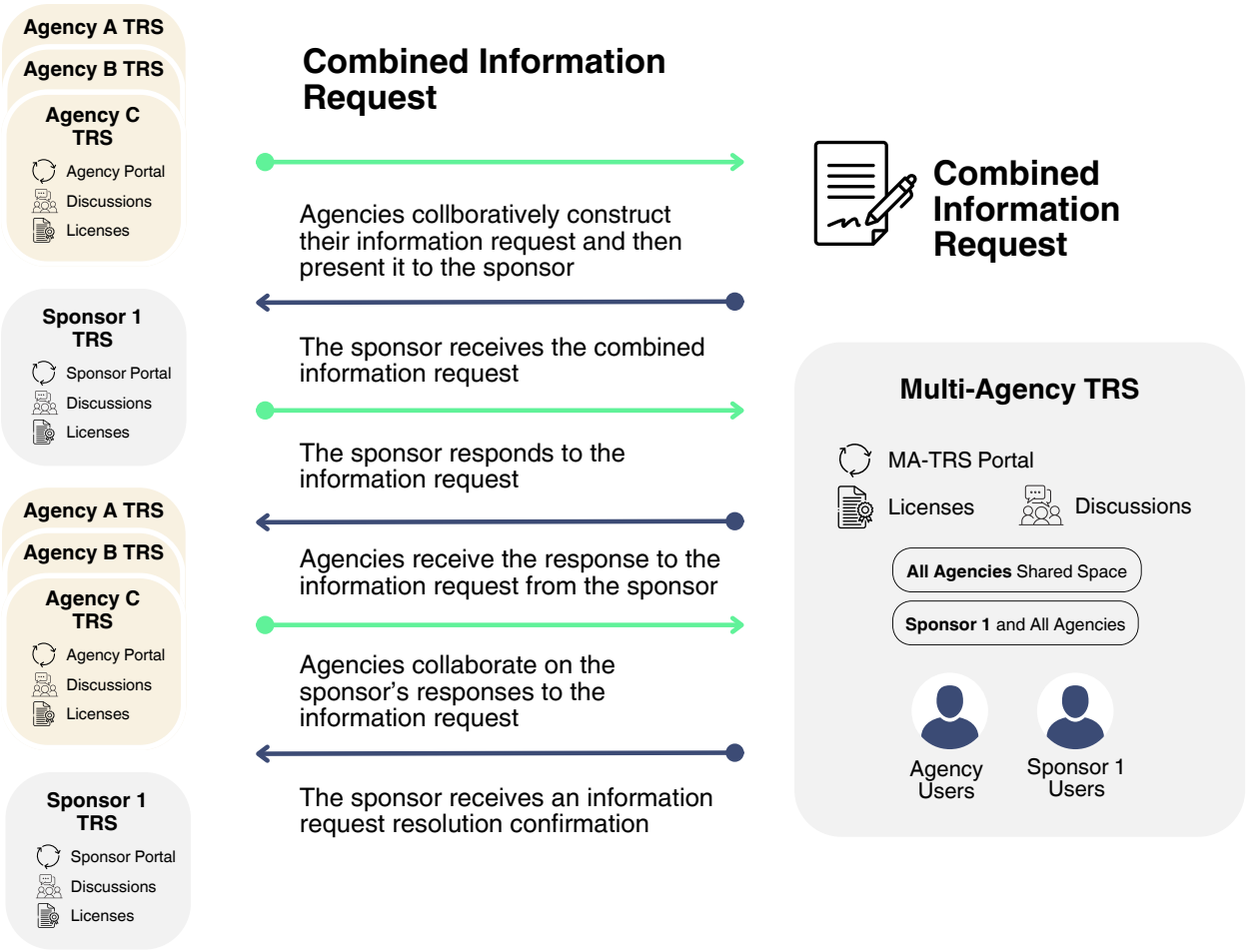


Figure 22: Combined Information Request Resolution

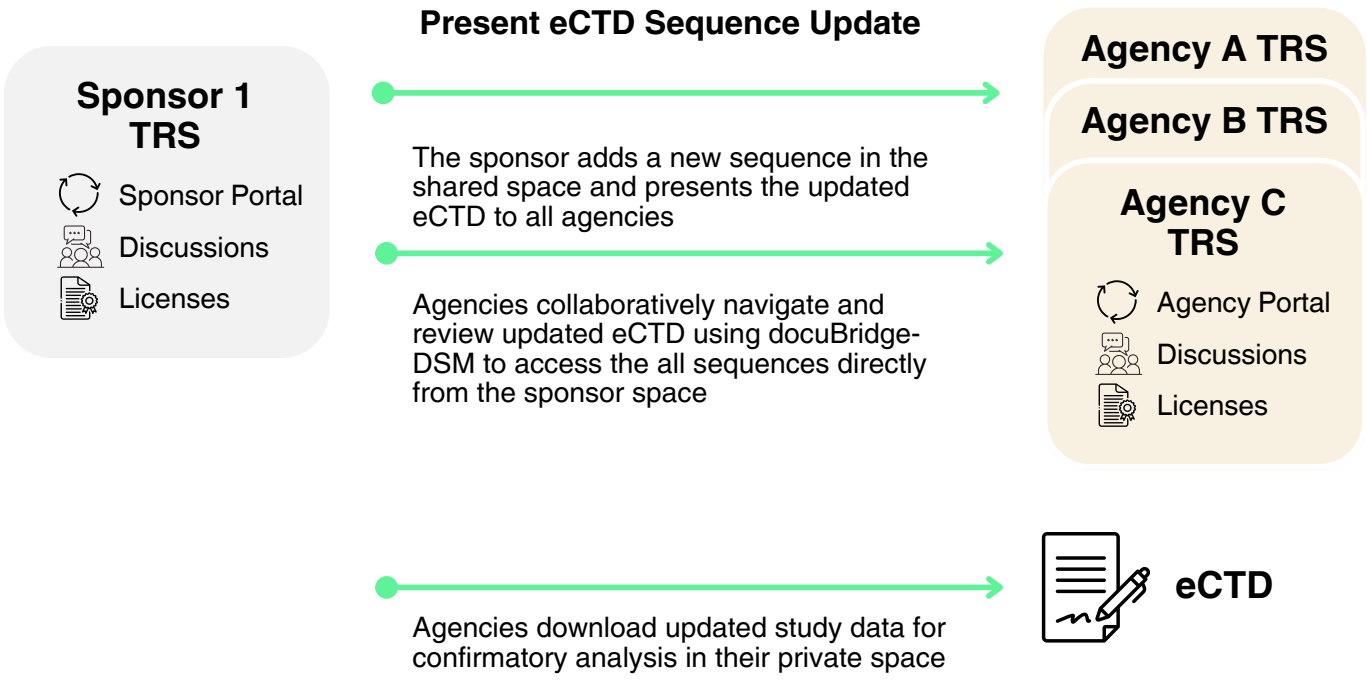


Figure 23: Present eCTD Sequence Update

Present eCTD Sequence Update

The sponsor uses docuBridge-DSM running on a workstation in their own TRS to add a new sequence to the eCTD submission in the Shared with All Agencies space (Figure 23). Each agency uses docuBridge running in their own TRS to navigate and collaborative review the updated eCTD with access to all sequences directly in the sponsor's TRS shared space without copying them to the agency's TRS. For confirmatory analysis of updated datasets, each agency downloads only the data they need from the sponsor's TRS for analysis in the agency's authorized TRS environment.

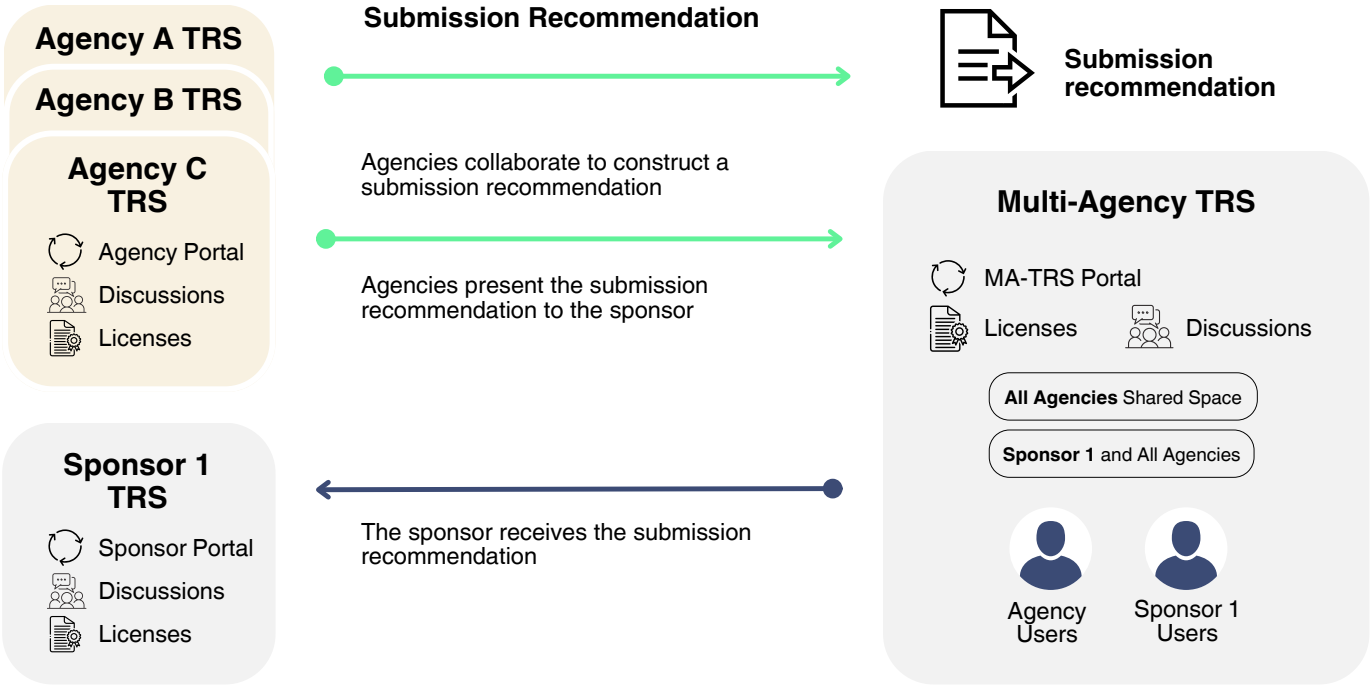


Figure 24: Submission Recommendation Interactions

Submission Recommendation

Agency reviewers use the MA-TRS portal to collaboratively construct a combined submission recommendation in the all-agencies shared space for presentation in the Sponsor and All Agencies shared space.

Summary and Next Steps

Summary

The cloud has transformed how most industry and government organizations perform business and provide public service, including pharmaceutical sponsors developing and bringing drugs and devices to market, and global health regulatory agencies. In the arena of global regulatory interaction however, cloud adoption has been slow due to the security, privacy, and quality requirements spanning global, regional, national, industry, and agency boundaries. Even within a single major agency there are many separate cloud solutions serving individual centers' internal needs, while globally there are very few collaborative regulatory cloud solutions in production.

As cited in research and demonstrated in production projects exploring inter-agency reliance and work-sharing, it is clear that a global cloud-based platform supporting regulatory collaboration use cases spanning sponsors and their real-world data providers, regulatory agencies, and standards development organizations, could provide significant regulatory process efficiency gains. Design principles for cloud-based regulatory collaboration are proposed along with a pragmatic archetype for regulatory information systems and the governance and services they provide.

Mapping a model regulatory reliance and work-sharing use case to the design for a network of Trusted Regulatory Spaces (TRSnet) envisions a platform built using open-source and commercial software running on diverse cloud service providers. Platform support for a globally unique object identification mechanism enables Dynamic Submission Management (DSM) for secure construction and interactive review of submissions while reducing the burden and risk of replication and repeated data transfers throughout the submission process. As a result, data can be securely shared in the cloud between regulatory stakeholders with confidence in security and provenance.

This design has been proven to demonstrate the transformative capabilities and efficiencies of cloud-based regulatory collaboration in a production setting. By providing a networked regulatory-grade platform with rich user services, and the required security, privacy, quality, and risk management attributes, the proposed design enables the creation of global Trusted Regulatory Spaces Networks to collaboratively advance sponsor, agency, and standards development organization use cases.

Next Steps with the TRS Commons

To advance the TRSnet vision, LORENZ is sponsoring the TRS Commons Platform on DNAnexus. This platform will allow sponsors, RWD providers, agencies, and standards organizations to join a secure global network to explore regulatory use cases in the cloud. It will include tools like LORENZ docuBridge and eValidator for Dynamic Submission Management.

Commons members can create their own protected spaces to test and deploy TRSnet designs with their selected regulatory partners. These spaces will also provide discussion groups for members-only communications. LORENZ and DNAnexus are working with industry, agencies, and standards organizations to create initial communities on the platform.

Sponsors, agencies, and organizations are invited to join the TRS Commons to advance regulatory use cases of their interest at their own pace, using the latest cloud tools to improve the delivery of safe and effective drugs and devices. Additional use cases could include regulatory process co-pilots based on conversational AI, harmonization of post-approval manufacturing change submissions across global agencies, and the transition to eCTD 4.0.

For more details, join the TRS discussion at https://www.lorenz.cc/trs/.

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A Transformative Approach to Dynamic Submission Management: Trusted Regulatory Spaces
https://20779781.fs1.hubspotusercontent-na1.net/hubfs/20779781/Solutions_Brief_DNAx_LORENZ.pdf

Glossary

Trusted Regulatory Spaces (TRS):
Secure cloud-based environments where sponsors, health agencies, and standards organizations collaborate to exchange, validate, and standardize regulatory information.

Dynamic Submission Management (DSM):
A streamlined process for submitting regulatory documents using cloud-based platforms and AI technologies to enhance efficiency and reduce timelines.

Cloud Technology:
Internet-based computing platforms that provide services like data storage, sharing, and analysis for regulatory submissions and collaboration.

Artificial Intelligence (AI):
Advanced algorithms used to analyze large datasets, refine trial methodologies, scrutinize safety protocols, and enable Real-World Data (RWD) analysis.

FDA Orbis and PRISM Projects:
Initiatives by the U.S. Food and Drug Administration aimed at global collaboration in regulatory review and reliance to streamline drug approval processes.

Access Project (Health Canada):
A multi-agency program to enhance collaboration and reliance for regulatory decision-making among countries.

World Health Organization (WHO):
A global organization advocating for international regulatory convergence to ensure timely access to safe and effective medicines.

International Federation of Pharmaceutical Manufacturers and Associations (IFPMA):
An industry group promoting collaboration, regulatory harmonization, and the implementation of global pharmaceutical standards.

Regulatory Collaboration:
Cooperative efforts between countries, agencies, and organizations to share expertise, resources, and data for regulatory purposes.

Regulatory Reliance:
The practice where one regulatory authority uses the decisions or expertise of another to make its own regulatory decisions.

Real-World Data (RWD):
Data collected outside traditional clinical trials (e.g., electronic health records, observational studies) used for regulatory submissions and confirmatory analyses.

Multi-Regional Submissions:
Simultaneous submissions of regulatory documents to multiple regional agencies, leveraging global cloud-based platforms to reduce sequential delays.

Post-Approval Changes (CMC - Chemistry, Manufacturing, and Controls):
Adjustments made after a product's approval that require globally harmonized submission processes to streamline regulatory updates.

Structured Data Standards:
Harmonized, standardized data formats designed to digitize and normalize regulatory information for global interoperability and AI-readiness.

Submission Timelines:
The timeframes associated with the regulatory process, which can be reduced using cloud collaboration and dynamic submission systems.

Collaborative Contracts:
Agreements established within TRS networks that define terms for sharing regulatory data, analyses, and resources securely.

Cloud Service Providers (CSP):
Companies that offer cloud platforms (e.g., AWS, Microsoft Azure, Google Cloud) for hosting TRS networks and supporting global collaboration.

Normalization and Harmonization:
The process of standardizing regulatory data formats to facilitate global interoperability and digitization.

Global Regulatory Synergy:
Alignment and cooperation among global agencies to ensure efficient regulation, as demonstrated during the COVID-19 pandemic response.

AI-Ready Information:
Standardized and digitized data that can be processed by AI for analysis, enabling faster and more accurate regulatory decision-making.

Regulatory Use Cases:
Scenarios where cloud-based collaboration enhances regulatory workflows, including submission processes, Real-World Data (RWD) integration, and multi-sponsor/agency research projects.

Regulatory Cloud Design Principles:
Foundational guidelines for creating secure, scalable, and collaborative cloud-based regulatory environments to address industry and agency needs.

Archetypical Regulatory Information System Model:
A proposed system design for regulatory cloud networks that aligns with key requirements and standards for secure information exchange.

TRS Network (TRSnet):
A cloud-based network composed of open-source and commercial software that enables distributed regulatory submission management and collaborative workflows.

Standards Development Organizations (SDOs):
Organizations that define and evolve standards for data exchange, such as ICH for eCTD submissions.

Pharmaceutical Regulatory Leaders:
Decision-makers in the pharmaceutical industry responsible for regulatory policy, IT systems, and operations.

Risk Management Specialists:
Professionals who assess and mitigate risks in cloud-based regulatory systems, ensuring compliance with security and privacy standards.

LORENZ Life Sciences Group:
A company providing software solutions for regulatory information management, including product registration, submission assembly, validation, and review.

DNAnexus:
A cloud-based platform for precision health, genomic analysis, and regulatory research, recognized for its secure, collaborative capabilities.

precisionFDA:
A secure, cloud-based collaborative research platform powered by DNAnexus to support regulatory science and innovation.

FedRAMP Authorization:
A U.S. government security compliance standard that ensures cloud service providers meet stringent privacy, security, and quality controls.

LORENZ Cloud:
A Software-as-a-Service (SaaS) solution by LORENZ providing managed AWS environments for regulatory information management.

DNAnexus Precision Health Cloud:
A multi-tenant cloud Platform-as-a-Service (PaaS) enabling secure collaboration, analysis, and management of scientific and healthcare data.

UK Biobank Research Analysis Platform (UKB-RAP):
A cloud-based Trusted Research Environment (TRE) enabling global researchers to analyze UK Biobank's biomedical data securely.

Trusted Research Environment (TRE):
A secure cloud environment that controls data access, prevents data extraction, and adheres to privacy regulations to minimize re-identification risks.

Access Management System (AMS):
A system used by platforms like UKB-RAP to control data access on a project-by-project basis for authorized researchers.

System Security Plan (SSP):
A document outlining the security controls applied to a cloud-based system to ensure compliance and mitigate risks.

Privacy Impact Assessment (PIA):
An assessment that identifies and mitigates privacy risks associated with data handling in cloud systems.

ISO 27001:
An internationally recognized standard for information security management systems (ISMS) ensuring robust data security practices.

Multi-Factor Authentication (MFA):
A security protocol requiring multiple verification methods (e.g., password and mobile code) to grant access to a system.

Single Sign-On (SSO):
A user authentication process allowing individuals to log in to multiple systems using a single set of credentials.

Data Residency Controls:
Measures that allow cloud platforms to manage where data is stored globally to comply with regional regulations.

Data Governance Controls:
Policies and processes that ensure data security, quality, and compliance within cloud systems.

eValidator:
LORENZ software for validating electronic submissions against industry standards like eCTD.

eCTD (Electronic Common Technical Document):
A globally recognized format for submitting regulatory information electronically to health agencies.

ICH (International Council for Harmonisation):
An organization that develops guidelines for pharmaceutical regulatory processes, including eCTD formats.

Next Generation Sequencing (NGS):
A technology for high-throughput genomic sequencing, used in platforms like precisionFDA for regulatory research.

QMS (Quality Management System):
A system that ensures quality standards are maintained during development, deployment, and operations in cloud environments.

Product Development Life Cycle (PDLC):
A framework followed by organizations like LORENZ to manage software development processes.

Enterprise Performance Life Cycle (EPLC):
A framework employed by DNAnexus to align cloud platform operations with FDA compliance standards.

Data Use Terms:
Agreements specifying how research data can be accessed, used, and shared within Trusted Research Environments.