Trusted Research Environment (TRE)

Making research secure and accessible

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> This gives a short introduction to the ways in which NTT DATA is building on the Microsoft Azure TRE concept to enable dynamic research projects that bring together experts from different backgrounds and locations. NTT DATA provides secure online collaborative environments, with the tools, management support and oversight needed to facilitate research, while ensuring the complete security that public health related projects need.

Healthcare challenges

The entire healthcare marketplace worldwide is going through the most intense period of disruptive change for several decades. Despite the many differences in such key factors as funding and market participation, these changes are taking place in every developed and most developing countries. We are seeing:

- A move to much more patient-centred, personalised care, with treatments increasingly focused on the individual and, in some cases, directly linked to their own DNA.
- A gradual change over from a centralised, hospital-based model for healthcare delivery, towards more decentralised locations and methods.
- Increased use of technology to provide everything from secure research platforms to remote monitoring systems.

These changes are designed to address major trends in healthcare management worldwide, including the three most important of all:

1. **Growing numbers of people living with Long Term Conditions, multiple morbidities and longer life expectancy.**
2. **The consequent pressure on budgets, making conventional methods of delivery increasingly unaffordable.**
3. **The power of emerging technology, with growing capability to target conditions more accurately and fine tune treatments to individual needs.**

Balancing the needs of general medicine and personalised targeted medical care is a unique challenge, and requires the most effective and appropriate research tools. Trusted Research Environments are a crucial enabler of research into personalised care, together with successful development of new treatments and methods.

Healthcare professionals are now focusing on “insight-driven patient care pathways”, which are personalised treatments, including medicines and other regimes, to surround the individual with the best possible options for their own specific needs and conditions. This approach moves away from the generalised medical model of the past, in which a common, best practice treatment would be offered to all patients, with only minor variations possible.

Today, we are helping create the conditions in which the many different players within the health economy can work together on treatments that are tailored to an individual’s needs, because they include insights based on detailed data related to that individual patient.

Real patient data is essential for this approach, providing not just the rich insights needed to develop new treatments and refine those that exist, but also fitting novel treatments to a known individual. Many of us will eventually benefit from this new approach, but turning it into a reality is not simple, and requires a new approach to research- which is *collaborative* but also *uncompromisingly secure.*

Secure Ecosystem Research

Making significant advances in targeted treatments is, by definition, a highly collaborative process. It requires input from specialists of many different kinds, together with a high degree of innovation and creativity, in a space where multiple scenarios can be developed and tested, and where continuous development is possible.

> “ Yet this flexible, joint working can only take place in spaces that are highly secure.

The key to achieving higher levels of targeting and personalisation is to use real patient data as the basis for research, but that leads to some significant issues in terms of safe, ethical management. These include:

Secure collaboration

One of the drivers for fast and effective development of new compounds and delivery systems is joint working between large pharma companies and often much smaller specialist innovators. Creating secure shared workspaces has been historically challenging, yet the need for these workspaces continues to grow.

Development spaces

This form of efficient ecosystem working requires secure virtual development spaces that can be shared by teams from multiple partners, with maximum efficiency- yet with assured security and data integrity. There is a current lack of such spaces, and that is inhibiting rapid treatment development.

Security, ethics, regulation

There is growing public concern about use of patient data- and that is perfectly understandable. Individual people are the owners of their own data: they want it used only for ethical purposes, and with their permission. The demand for tightly controlled, secure and ethical management of data is enforced by regulations, which are becoming tougher by the year.

Technology understanding

It is fair to say that many interested parties, from government departments to citizens, have limited understanding of the technologies and methods involved in use of real-world data. There needs to be a real effort to educate stakeholders and accelerate adoption, as we develop new and more advanced methods.

> The industry should move rapidly towards more effective use of secure, shared development spaces, and NTT DATA is leading the way in developing practical, proven solutions.

Building a successful solution

The idea of collaborative development platforms is not new. There are existing solutions across many industries which enable researchers from different organisations, in widely distributed locations, to meet in a common space, work together and build shared solutions. No matter what the objective or who the participants, all these ecosystem-based partnerships require strong security guidelines and agreed rules for access to tools and data.

The challenge of patient data

When dealing with real patient data, however, the security requirements are higher than ever, so the need for maintaining data integrity is absolute and non-negotiable. Viable solutions must combine the ability to share data access openly enough to make significant medical breakthroughs, with the need to safeguard patent privacy without compromise.

Cloud-native approach

NTT DATA has built its own strategy for healthcare collaborative secure research on the Microsoft Azure Trusted Research Environment (TRE), which is a flexible accelerator designed to help technology partners build their own, customised and unique research solutions on the Azure Cloud platform.

This has enabled NTT DATA to build solutions that are cloud-native by design, enabling access from geographically distributed locations, by teams that include an exceptional variety of skills and specialisations, all working with rich data sources and modern data platforms, yet with assured security in place at all times.

NTT DATA customises its approach to the precise technical and workflow needs of each different customer, based on Microsoft's Trusted Research Environment code. Solutions include accelerators to support rapid deployment and configuration of an individual customer's bespoke collaborative environment.

White label solutions

NTT DATA provides a white label, Azure Application Portal that enables researchers and administrators to create, access and orchestrate tools for virtual environments. Using an out of the box workspace and workstation configuration, with baseline tools such as R, Python and OHDSI Atlas provided as standard.

What makes this approach so flexible and effective is its simplicity and usability. Researchers have the freedom to select from a range of selected custom templates to meet their own exact needs and objectives. Just as healthcare professionals of every kind are now working to deliver tailored treatments that precisely address patient needs, so NTT DATA ensures that their own research environments give them access to cloud elasticity and agility, enabling them the freedom they need to transform healthcare outcomes.

NTT DATA's Trusted Research Environment

NTT DATA provides the technical capability to customise workspace templates to meet the various needs of researchers across the industry. Providing assured and tested workspaces is a key factor in enabling a consistent and stable environment for researchers to achieve their research goals successfully.

This means research organisations using NTT DATA's solution build on proven best practice, with access to a highly respected and successful collaborative research platform, but with exceptional freedom to develop, extend and tailor their platform to their exact requirements. The structure of a typical solution can be seen in figure 1 below:

Figure 1: basic layout of a TRE solution

The logical structure of the environment is simple and, in its outline, is likely to stay consistent, no matter how different and varied the individual solutions may be. The core components are:

Data platform

Data is the driving force for all research projects, and that data can come from a very wide range of sources. For collaborative healthcare research, much of this will be related to real patient data, which will be contained within the Data Platform and governed by strict security protocols.

As with all complex research environments, access to the richest sources of data is the most basic necessity, but data integrity has to be completely assured at all times. Researchers will be able to query data that has been made available using modern Profile Based Access or Role Based Access. This is through a combination of Cohort Query tools and Structured Query Languages.

In most cases data will be restricted through access controls directly across the data products, including features like data masking. Researchers will be able to bring data into their workspace for use with their analytical tools through querying the Data Platform and through the Airlock “Bring Your Own Data” workflow. Any linking of data is done within the workspace. Any data leaving the workspace is processed through the Airlock workflow, ensuring compliance with the agreed ethics and contractual commitments.

For this reason, the structure of the data layer, itself, is extremely important, comprising tools for ingestion, then integration and finally publishing. This means data can be ingested from any authorised source, while meeting the strictest regulatory standards to maintain patient confidentiality.

Infrastructure-as-code (IaC)

Using IAC to provision and manage cloud resources brings significant benefits to the research environment operators. By defining infrastructure, such as virtual machines, storage and databases programmatically, IaC ensures consistent deployments of research services in Azure, reducing the risk of human error. This automation allows the implementation of new services on demand, which minimises the management overhead associated with TRE administration.

The ability to easily define new templates for workspaces puts IaC at the heart of what makes a cloud-based research environment truly agile, and therefore capable of quickly adapting to new requirements and evolving tool sets.

TRE. The figure shown earlier illustrates the simplest form of TRE, but solution provides a wide range of features and tools, covered in the next section, to accelerate and simplify on-boarding and high efficiency working. This means administrators have considerable freedom to design and manage the collaborative activities that take place within their workspace and researchers have great discretion in setting up and managing their environments.

Joint working, therefore, takes place in ways that are not prescribed by the TRE, except for the absolute and non-negotiable need to conform with security and access requirements. The space provided within the TRE is highly flexible and available in organisationally approved locations. This means researchers from approved worldwide locations can enter the virtual space and collaboratively work within it, as long as their authorisation to do so remains valid.

In practice, the leadership of each individual research team will set the ground rules for the team, exactly as for any physical research laboratory. Individuals retain freedom to follow up on promising developments, again in just the same way as for any other project.

Output

The aim of the TRE, exactly as for any other research environment, is to produce insights that can be used as input to such essential uses as product development (for example, novel treatments and medicines) or further research projects that have been identified as new priorities.

The same issues exist at the output side of the environment as for the input. Data integrity must be assured, and so must ownership of proprietary materials, methods and knowledge. This is especially important inside a TRE, as different researchers may (or quite probably will) come from different organisations, bringing their own distinctive IP and insights, which must also be respected.

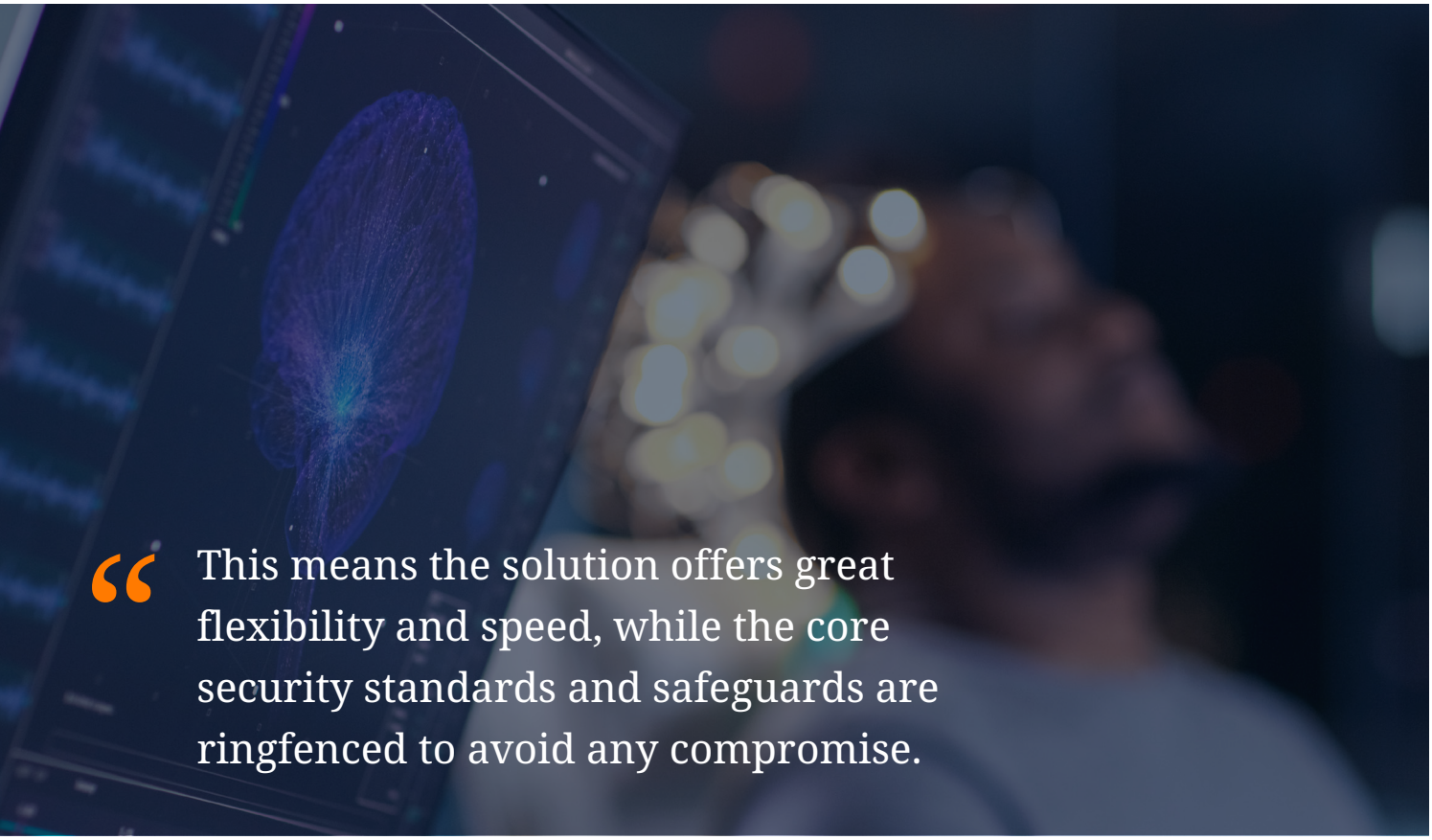
NTT DATA TRE: Key features and benefits

Every enterprise or research centre that adopts the NTT DATA TRE solution gains immediate access to toolsets and accelerators designed to enable fast start and high efficiency operations. Each feature of the solution is designed to focus on key priorities for effective research. These include:

Secure access

The TRE solution focuses on striking the best available balance between high speed and highest security. It therefore includes tools for managed access and authentication, which help ensure fast onboarding and a rapid start to joint working, starting with Active Directory, for federated access. This is in addition to all the established features of Azure AD to control policy and access provide a great degree of assurance to organisations.

Terms and conditions can be customised to the exact needs of each individual team, while research sponsors are permitted to set the IAM rules best studied to their team and its needs, but only for their own specific collaborative working space.



Effective collaboration

The key to high performance working inside the TRE lies in the definition of individual workspaces, each focused on a specific project or stage. This makes it simple to define which individuals have permission to enter which workspaces, simplifying creation of project-based workspaces, with access to each of them confined to nominated team members.

The tools provided by NTT DATA enable workspace/project managers to set their agreed rules for access and working protocols, while also providing essential technology services. The solution, for example, accelerates provision of virtual machines and also for setting up physical workstations.

The solution includes an option to provide and manage dedicated physical workstations that come complete with data science-based analytics tools, such as R, STATA and Python. Finally, the solution offers a wide range of options for configuring workspace-based services. Tools such as Gitea, Atlas or Guacamole are provided as standard.

Secure Data Environment (SDE)

The NTT DATA solution includes administration practices and tools designed to help manage and govern collaborative environments, with a strong focus on agreed joint objectives. Given the complexity and sensitivity of healthcare-based TREs, it is clear that flexible but strong and very clear governance of all key management activities is a vital necessity.

Among the options managed by SDE administration are workstation creation and secure management; managing airlock requests; delivering cost reporting on request; and general management reporting and associated insights.

> In this way, research leaders have the confidence that a complex shared environment is always meticulously managed, with full reporting available to enable analysis.

One remaining key feature is the provision of Airlocks, which provide proven and auditable separation between different parts of the TRE, together with the people working within in it. This means customers and users, alike, can be confident that their operations meet all regulatory requirements in detail, and assures privacy and data integrity at all times.

Security management inside the environment includes the following list of standard features:

- **Controlled access.**
  Manages access to the secure environment through effective application of authentication and validation.
- **Threat detection and prevention.**
  Monitors data flows continuously to identify and immediately block potential threats such as malware.
- **Data leakage prevention.**
  Prevents unauthorized transmission of sensitive information, protecting against data breaches- a key requirement for demonstrating data integrity.
- **Compliance and audit.**
  Supports regulatory compliance by tracking data transfers and access, with a reviewable audit trail to provide clear evidence of compliance, and rapid follow up on any transactions that seem unusual.
- **Process and workflow management.**
  Uses workflows to review and approve data or code transfers. This ensures that full governance and oversight are in place at all times, reducing any potential for leakage or faults due to rule breaches or ignorance.
- **Isolation and containment.**
  Isolates security incidents to prevent spread and enable targeted responses. This is based on the reality that even the very strongest systems cannot ensure absolute and total security, so we build in a rapid and effective response mechanism, designed to stop damage spreading and restore normal working fast.

The toolset that comes as standard with NTT DATA TRE is designed to ensure fast start to any project, maximum agility inside the research environment, all backed by a set of governance rules and procedures that ensure security, with data integrity as a basic feature of the environment. The goal is to help researchers work collaboratively, efficiently and effectively, without spending too much of their time on administration and governance- because the solution does that as a matter of course, on their behalf.

Figure 2 below provides an overview of how the airlock process works from the user perspective.

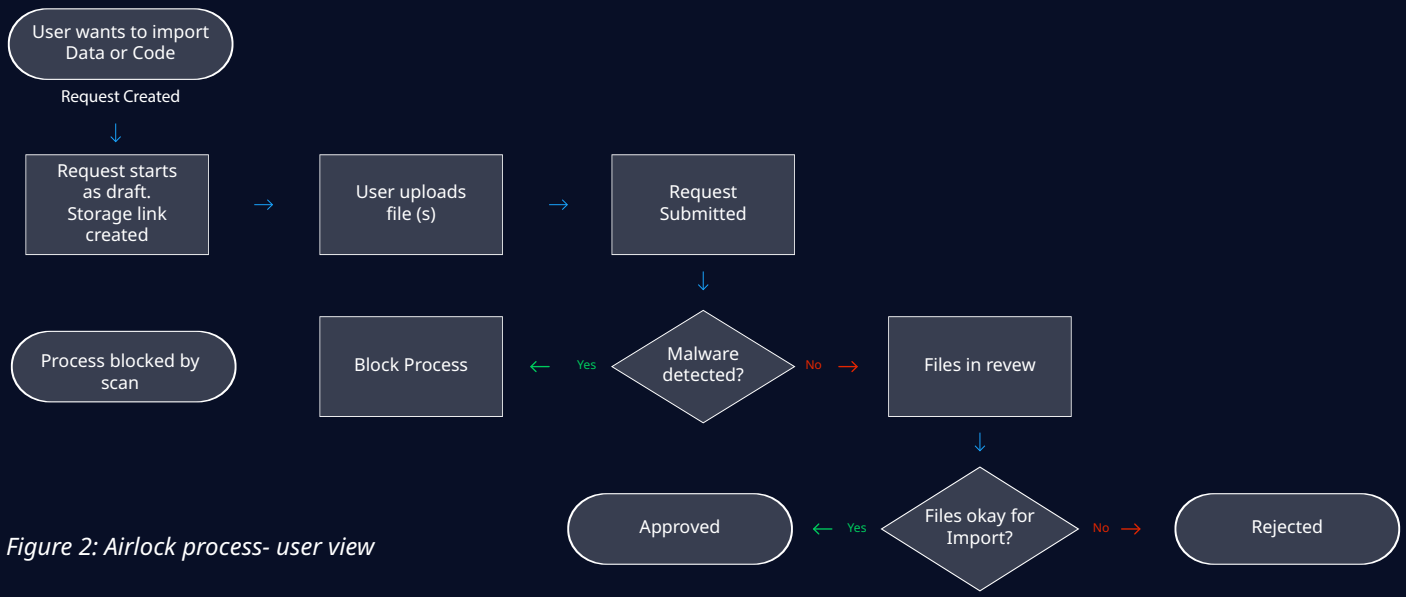


Figure 2: Airlock process- user view

The key benefits

The goal of the TRE is to help all stakeholders in the wider healthcare economy achieve their own scientific and commercial goals, in ways that ensure mutual benefit and support to them all.

Academic innovators

Can work collaboratively with their peers and colleagues across rich innovation ecosystems to make scientific breakthroughs, as they seek to turn truly personalised care into a lived reality.

Pharmaceutical companies

Can build on this work to identify new compounds and development options, turning these into effective treatments for targeted delivery.

Healthcare providers

Use these advances to build integrated treatments and pathways that deliver better outcomes for society. That enables patients to receive treatments that improve quality of life and enable Long Term Conditions to be managed, while improving efficiency to reflect difficult budget realities.

Society

Is the ultimate beneficiary, in a world where public health is the single most important indicator for personal security, prosperity and contentment.

The common factor for all these stakeholders is the need to work collaboratively and to access the most sensitive patient data, without compromising privacy and data integrity. NTT DATA's TRE solution addresses these needs by building on Microsoft Azure's own TRE Accelerator approach to deliver:

- **Secure collaboration.**
  Open access to collaborative workers, ensuring risk-free data sharing among authorized users, with reduced data transfer to avoid leakage.
- **Scalability and flexibility.**
  A platform that is scalable by design, so it can adapt to growing data and changing research needs without disruption or new engineering.
- **Innovation and insights.**
  NTT DATA recognises that innovation is the key to secure collaborative research, and has designed its solution to enable safe research that improves the potential for new discoveries.

In summary

NTT DATA works closely with advanced research establishments and experts in healthcare, and has built up a deep understanding of their requirements. The NTT DATA TRE solution has been designed with input from healthcare researchers and with their needs at front of mind.

Above all, it is based on the reality that real patient data is at the heart of the most important scientific breakthroughs in this field. There is a clear understanding that the move to highly personalised treatments requires access to real patient data, but that the privacy of patients is a top priority, which cannot be compromised under any circumstances. This solution is designed to combine speed, agility and scalability with absolute data security and assured regulatory compliance. This is how NTT DATA can offer perhaps the fastest start available to essential research projects, without compromise.

Real world experience

The NTT DATA approach is now being proved in action through client experience, with one of Europe's largest healthcare research institutes. The initial success of the first joint project have led to extension of work scope and time duration.

Trusted Research Environment (TRE)

The UK remains one of the world's leading centres for healthcare research, but the lessons learned from projects such as these have universal application. As an adviser to the European Commission for the European Health Data Space (EHDS) project, NTT DATA has exceptional insights to the way that public health provision is rapidly evolving across highly varied nations and economies. These lessons are factored into development of the TRE solution for the future.

Building on experience

NTT DATA's TRE solution is built on the engineering work carried out by Microsoft Azure to establish a framework for fast project initiation. NTT DATA uses its role as a global platinum Microsoft partner, with deep knowledge of Azure, a platform we have used since its inception, to inform and enhance the quality of our own offerings.

NTT DATA decided to build its own Trusted Research Environment solutions on MS Azure due to the added value Azure brings, including assured compliance with key regulations in all major geographies.

General Data Protection Regulation (GDPR)

Azure facilitates compliance with GDPR, providing tools and documentation to help protect personal data and ensure privacy.

Health Insurance Portability and Accountability Act (HIPAA)

For healthcare applications, Azure offers specific features to safeguard patient information, supporting organizations in meeting HIPAA requirements.

Federal Risk and Authorization Management Program (FedRAMP)

Azure is certified under FedRAMP, meeting the strict security criteria required for processing U.S. federal government data.

ISO/IEC 27001

Compliance with this international standard indicates Azure's commitment to managing information security systematically.

Researchers have the benefit of knowing that Azure already meets care standards as a matter of basic design.

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Why NTT DATA?

NTT DATA is committed to healthcare in the widest sense, worldwide. We are active in:

- Helping to create the secure research framework across the European Union, as a trusted partner to the European Commission.
- Implementing advanced concepts in remote patient monitoring, helping to develop less intrusive and costly forms of healthcare delivery.
- Pioneering uses of AI in targeted pharmaceutical applications, with proven use cases in this field.

We are a trusted partner to NHS England, arm's length bodies and individual trusts across the country, where our work in delivering trusted, secure environments is well established. Because we work across the entire healthcare research ecosystem, we have a more rounded view of the different stakeholders in healthcare than most technology players.

Finally, as part of the wider NTT Group, we share in a research budget of more than $3 billion per annum, dedicated to developing innovative concepts and solutions. For partners in the UK NHS, we understand the funding model, the issues and pressures, how different interest groups work, and we support them as a committed, long-established industry insider. We strongly support the 5 Safes:

Safe people

With a relentless focus on the wellbeing of everyone involved.

Safe projects

Ensuring that every activity is lawful, compliant and managed to the highest standards of care.

Safe data

Allowing no compromises on patient privacy and the integrity of personal information.

Safe settings

establishing strong governance and mission guidelines.

Safe outputs

Delivering materials and strategies that can be implemented at once with no risk to any participant.

The NTT DATA TRE solution is designed and engineered for fast onboarding; with technology infrastructure built for speed and responsiveness; workspaces that are both highly flexible and meticulously audited; high levels of *automation and scalability*; with support tools, including exploration dashboards to enable easier collaboration; and provides Azure based industry leading encryption, which conform to the latest ISO security standards.


NTT DATA