Kneat

The Digital Validation Handbook

Your Guide to Faster, More Accurate Validation

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Introduction

Technology has been changing the way we communicate for almost as long as we've been able to send a message from one person to another. From cave paintings to emails, we now communicate faster, clearer, and from greater distances. Documentation has experienced the same incredible advancements and that has significant impacts on industries that are dependent on it, such as the life sciences industry, consumer packaged goods manufacturers, and businesses involved in other highly regulated fields.

Few areas of manufacturing require such stringent documentation practices and large volumes of documents as validation. Validation is the process of testing and establishing documentary evidence that a procedure, process, equipment or system operates as required. Validation includes the design and execution of tests, and management of deviations from expected results. Whether it's commissioning and qualification (C&Q), computer system validation (CSV), or a process particular to your business, validation professionals need to be able to develop, use, and share documents to keep operations running. That's why validation is perfectly situated to benefit from digital technologies that accelerate time to market, reduce costs, and provide more accurate results for lower risk of noncompliance.

Regulators and industry-groups agree. The U.S. Food and Drug Administration (FDA) established the Office of Digital Transformation[1] which aims to provide guidance on IT, data, and cybersecurity under the FDA's purview. This change will help the agency keep pace with the companies it regulates as the life sciences industry adopts practices under the Pharma 4.0 model.[2] Pharma 4.0 is an industry-specific framework that aims to bring the focus on digitalization and automation under Industry 4.0 to the life sciences sector. The model envisions deeper connection, transparency, and adaptivity through data.

In this guide, you'll learn about the various methods of digital validation, their benefits and drawbacks, and how your business can adopt a digital solution for faster, more accurate validation.

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1   (2022, December 5). *Office of Digital Transformation.* U.S Food & Drug Administration. https://www.fda.gov/about-fda/office-commissioner/office-digital-transformation
2   (n.d.). *Pharma 4.0.* International Society for Pharmaceutical Engineers. https://ispe.org/initiatives/pharma-4.0

Why Digital Validation

The workload of validation professionals is growing faster than their teams. In the 2022 State of Validation report[3] —a cross-sectional survey of validation professionals—74 percent of respondents said they expect their workloads to increase due to new products, changes to work processes, and organizational changes. With workload often surpassing human resource capacity, companies must turn to technology to empower professionals to handle the increased responsibility.

Validation relies heavily on two things: data and documents. Data is factual information, such as test results, time stamps, and temperature readings. Documents are how we communicate this data, such as User Requirements Specification (URS) documents. To accelerate validation productivity without raising the risk for error, validation teams must address both areas together.

Validation professionals face several logistical challenges in traditional paper-based validation, including:

▶ Lengthy delays as paper documents are distributed to key stakeholders
▶ Difficulties in obtaining wet signatures
▶ Required scanning of executed protocols
▶ Need for archiving to align with legal obligations
▶ Controlling document procedures
▶ Requirement for in-person supervision and execution

These logistical issues are compounded by intense scrutiny facing companies in highly regulated industries, opening them up to significant risks of brand damage and financial penalty imposed by regulators. This has been exemplified by the FDA's steady increase in data integrity warnings to drug manufacturers in recent years. In 2021, 65 percent of all warning letters issued by the regulator were for data integrity infractions.[4] Non-digital validation—both paper-based and hybrid solutions involving some paper—lack the document control procedures necessary to mitigate data integrity risks and achieve ALCOA compliance. A hybrid approach relies, in part, on manual activities as opposed to automation, facilitating the risk of human error, which also grows as workloads increase.

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3   Kay, J. (n.d). *State of Validation.* https://stateofvalidation.com/report/
4   Eglovitch, J. (2022, June 01). *Experts say FDA enforcement focus unchanged, use of alternative tools to grow.* Regulatory Focus. https://www.raps.org/news-and-articles/news-articles/2022/6/experts-say-fda-enforcement-focus-unchanged-use-of#:~:text=The%20US%20Food%20and%20Drug,on%20near%2Dterm%20enforcement%20trends

What Is Data Integrity?

Data integrity refers to the completeness, consistency, and accuracy of data and it is mandated by the FDA under federal regulation, CFR Title 21 Part 11.[5] Since 1997, this regulation has been the benchmark for electronic record keeping, establishing the need for password-protected signatures, ability to generate complete copies of records, time-stamped chronological record of all operations, and more. For life sciences and other regulated companies, data integrity is often synonymous with ALCOA[6] principles.

A	L	C	O	A
Attributable	**Legible**	**Contemporaneous**	**Original**	**Accurate**
Activity can be traced back to a specific individual	Data is readable and understandable	Data is recorded in a timely manner	Documents must be originals or "true copies"	The data must accurately reflect what was recorded

In recent years, ALCOA has expanded to ALCOA+, the new gold standard for data integrity with the addition of four new criteria:

- ▸ Complete
- ▸ Consistent
- ▸ Enduring
- ▸ Available

At a high level, these four additional principles reflect the need to maintain documentation in its entirety (Complete), ensure it is orderly and chronological (Consistent), stored for a significant period of time (Enduring), and accessible when needed (Available).

With the FDA's increasing scrutiny of data integrity, life sciences companies are increasingly looking to digital validation as a means to provide the highest standard of controls—a trend reflected in the State of Validation report, which found nearly 90 percent of companies[7] planned to adopt a digital solution or were currently using one.

5 (2022, Nov 29). *Code of Federal Regulations Title 21.* U.S. Food & Drug Administration. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11

6 (2018, December). *Data Integrity and Compliance With Drug CGMP Questions and Answers Guidance for Industry.* U.S. Food & Drug Administration. https://www.fda.gov/media/119267/download

7 Kay, J. (n.d). *State of Validation.* https://stateofvalidation.com/report/

Digital Validation & Data Integrity

Digital validation aligns well with ALCOA+ principles, but how well (if at all) a solution performs these functions should be a key consideration when choosing a partner. The following table represents what you should expect and how that expectation is met by Kneat's digital validation platform "Kneat Gx".

ALCOA+	Expectation	Kneat Gx Feature
Attributable	Who, when	Secure single sign-on and password protected signatures
Legible	Readable	No scanning or handwriting
Contemporaneous	Work time stamped when completed	Automatic time stamps
Original	Complete raw data information (avoiding transcriptions)	Data inputs directly into Kneat platform
Accurate	No errors and amendments are verified	Direct data entry, protected e-signatures, and revision feature with approvals
Complete	Record is represented in its entirety	Use of templates to ensure completeness
Consistent	Well-ordered and chronological	Uses unique IDs, automatically-generated timestamps or other features
Enduring	Stored long-term	Stored in Kneat's secure servers indefinitely
Available	Easily accessed for use	Accessible by approved parties as needed

Other Benefits of Digital Validation

Data integrity may be a major consideration for manufacturers, but the cost savings and increased revenue made possible by digital validation are also major draws. Merck Sharp & Dohme Corp. (MSD)—a subsidiary of Merck & Co.—was able to reduce its test execution cycle times by 50 percent and replace three different quality management systems (QMS) by adopting Kneat Gx.[8]

Another Tier One pharma company saw its productivity improve by over 100 percent using the same platform.[9] Highly efficient validation accelerates the release of equipment, computer systems, and facilities to production. Whether single product or multiproduct facilities, efficient changeover can result in higher yields, faster speed to market, and ultimately increased revenue.

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8   (2021, December 08). *MSD Global e-Validation Rollout.* Kneat. https://kneat.com/client-story/digitizing-validation-globally/

9   (n.d.). *Digitizing the entire validation life cycle: A productivity leap.* Kneat. https://kneat.com/client-story/tier-one-biotech/

Efficiency Across the Validation Lifecycle

Robust, digital validation systems that are built-for-purpose, allow users to manage the entire validation lifecycle by providing a range of features specifically designed to solve the unique challenges of validation documentation, from authoring documents to archiving them, and all the steps in between.

Document Authoring & Editing

▶ Leading digital validation systems allow the user to digitally author any required document (such as DQ, IQ, OQ, PQ, URS, FRS, DS, FAT, SAT, Risk Assessments, Change Controls, Logs and more) within the application, without reliance on APIs or wizards to external word processing software.

▶ Robust digital validation systems allow users to quickly and easily author, build, and edit validation-specific document features, such as step-based test-tables, link to other documents within the system, such as requirement specifications, and much more.

▶ Robust digital validation systems also enable automated document numbering, configurable within the application to a user's quality system requirements, to enable traceability.

**Document generation within Kneat Gx**
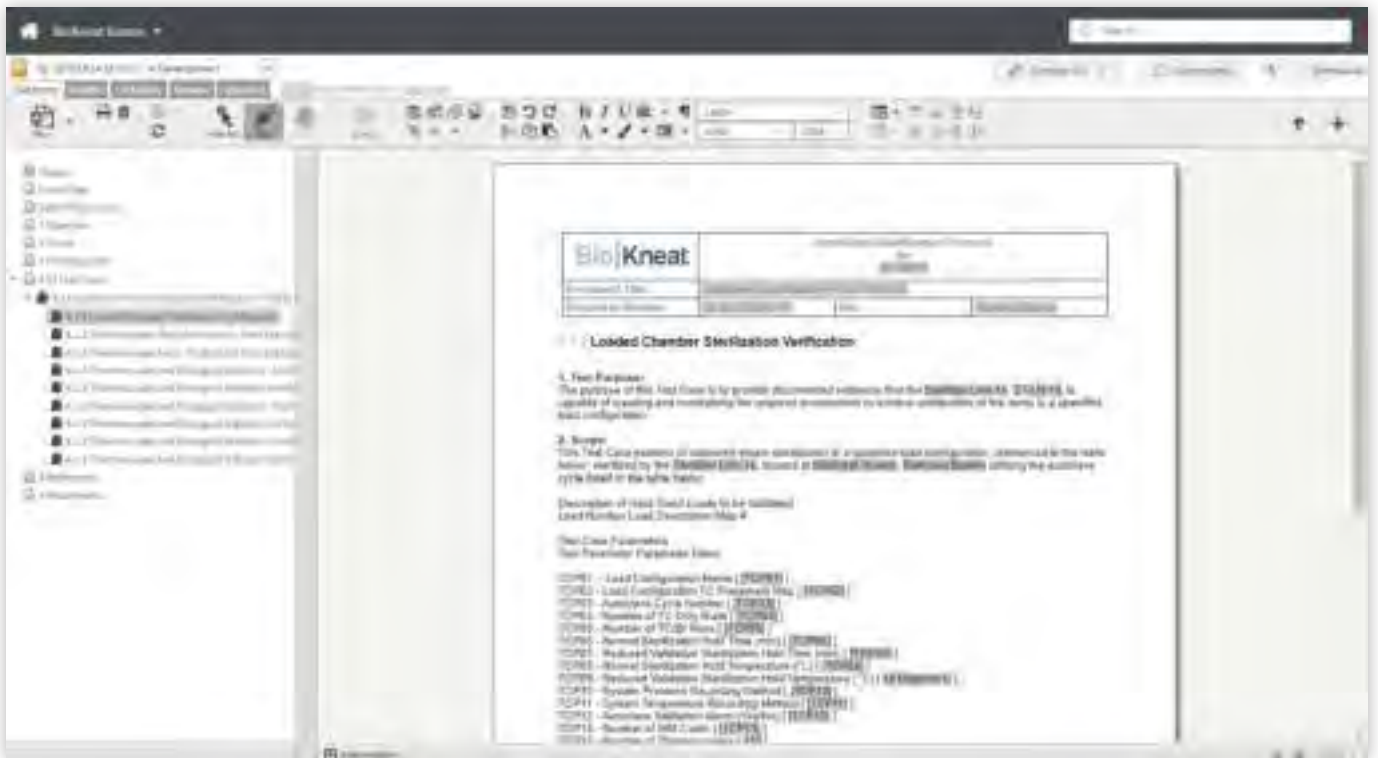
Templating

▸ Document templates, and document section templates such as test-cases, should be able to be created, stored, selected, and applied within the application.

▸ Robust digital validation systems also enable the "smart-import" of existing paper-based or digital document templates, transforming static features like tables into editable digital versions automatically.

Kneat's template library stores your document templates for easy access


Templated documents reduce cycle time
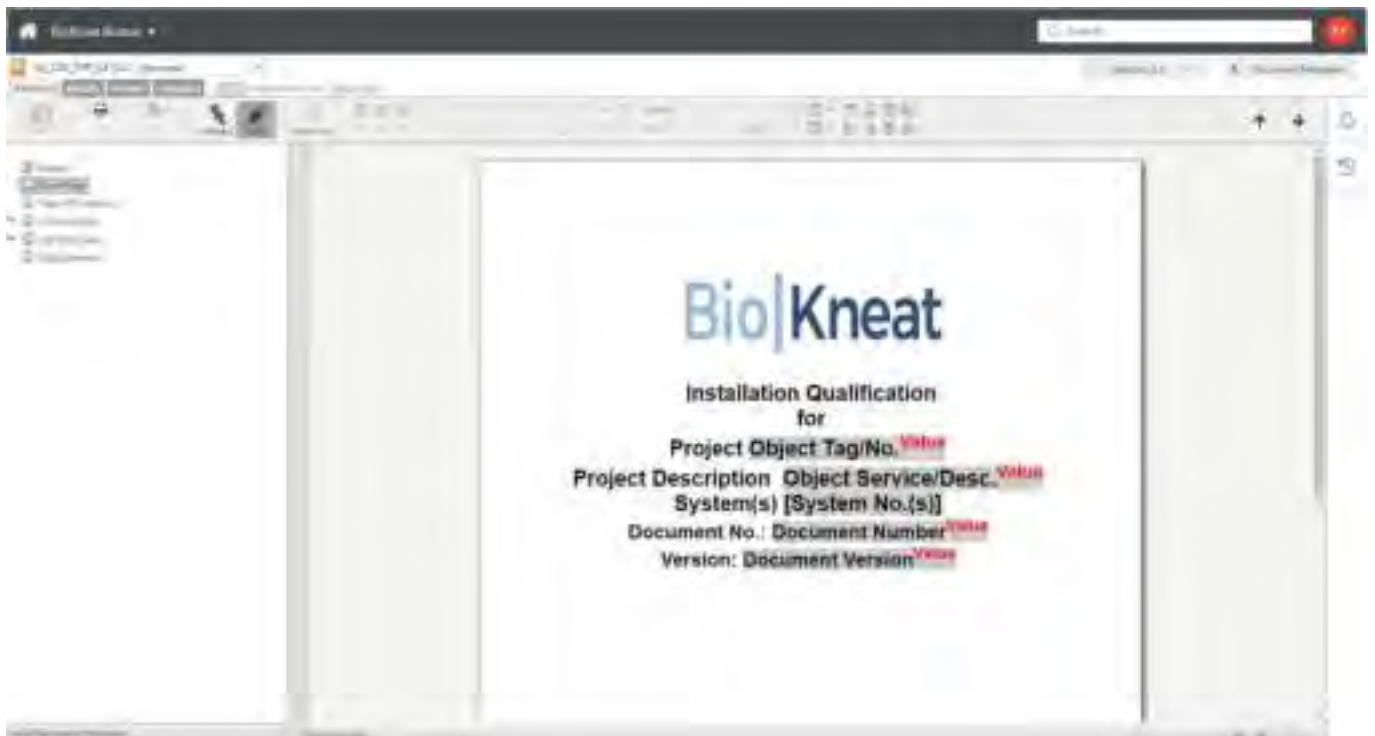
Workflow

▶ Built-for-purpose digital validation systems should enable some form of sequential documentation workflow, while enabling the appropriate level of flexibility to users with appropriate permissions, at the right times. At a high level these workflow stages should include in-development, review and approval, test-execution, and post-approval.

▶ Leading digital validation systems do not enforce workflow rules through software code (typically applied during system implementation). The most robust digital validation systems enable appropriate workflow restrictions to be applied via configuration settings within the application itself to enable appropriately permissioned and trained users to change pro-cesses independently when required, without reliance on vendors or software developers.

Review & Approval

▶ Leading digital validation systems enable documents to be issued digitally to other users for review, capturing reviewer's comments and author's responses, while allowing for side-by-side document version comparison.

▶ Robust digital validation systems allow for pre-approval and post-approval steps and include mandatory and non-mandatory password protected digital signatures for users involved in review and approval.

Send and receive documents for review and approval within Kneat Gx for near-instant sign off. Establish mandatory or non-mandatory use of password protected signatures to ensure data integrity compliance.
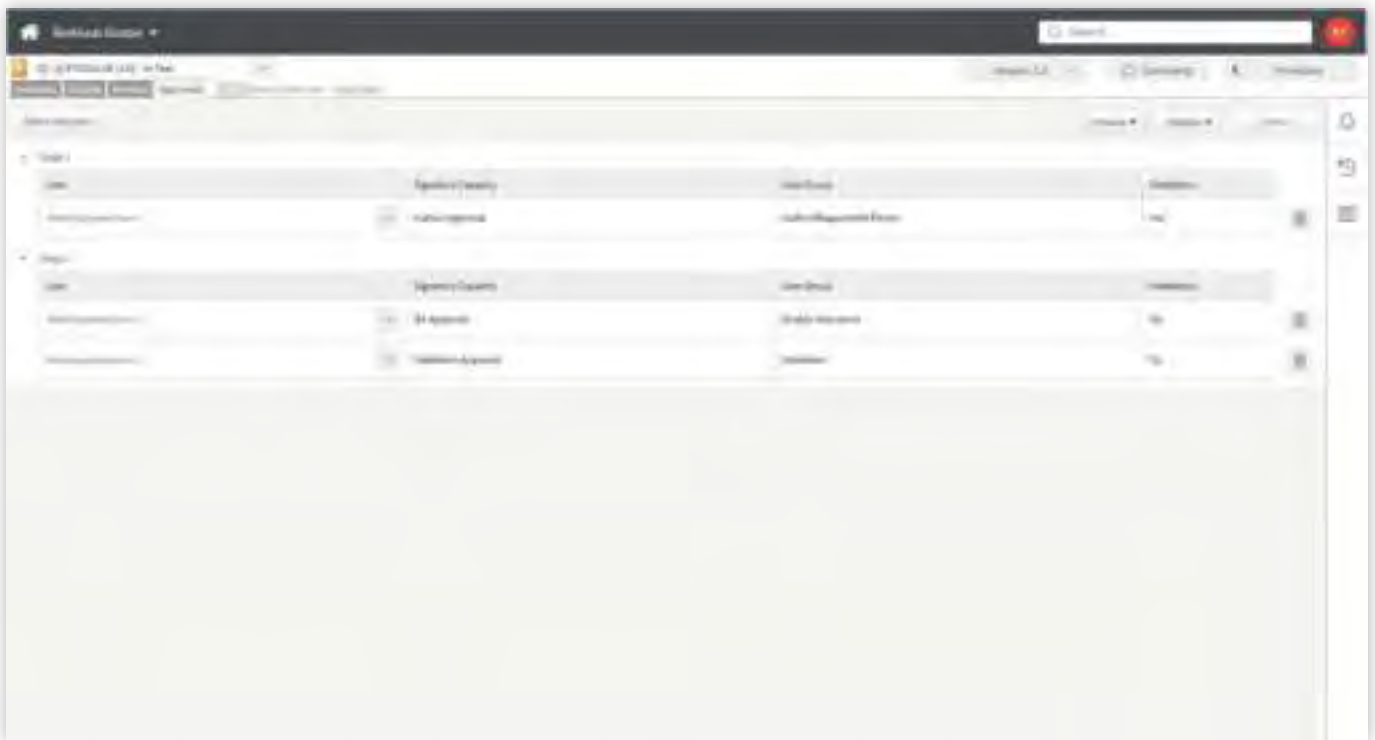
Test Execution

▸ Built-for-purpose digital validation systems should enable users to perform 21 CFR Part 11 compliant test execution within the application, facilitating password protected electronic signatures uniquely identifiable to a user's account.

▸ Leading digital validation systems should also allow users to attach test evidence in a wide range of file formats and link it directly to the test result given, in addition to documenting deviations and link these automatically against requirements for traceability purposes.

Execute tests directly in Kneat Gx in full 21 CFR Part 11 compliance and seamlessly attach test evidence, document deviations, and link for full traceability.
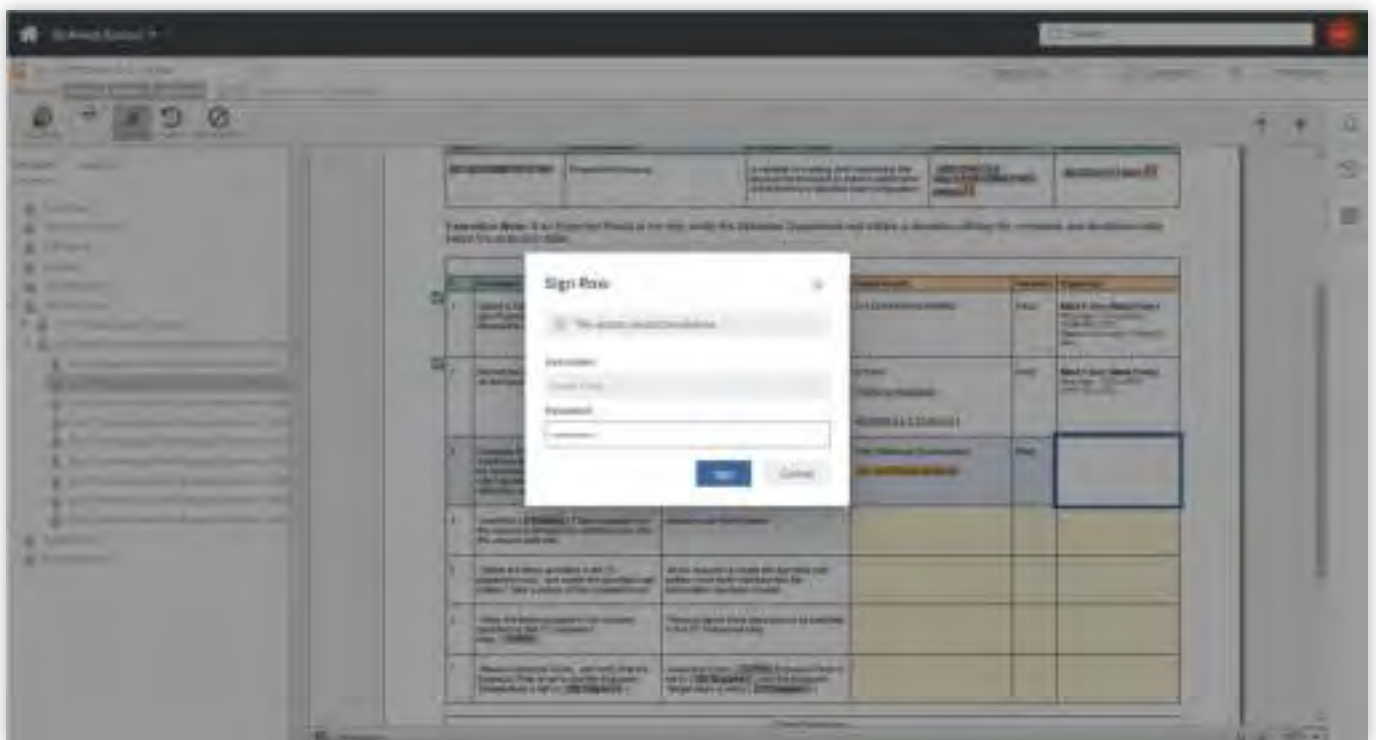
Traceability

▸ Robust digital validation systems should enable the automation of traceability matrices, to provide seamless tracking and access to all instances of documentation, such as requirements or any other document type, across an entire validation program.

▸ Within a document, leading validation systems will enable the linking of related or supporting documents wherever required, enabling visibility of all documentation across the lifespan of systems or equipment from within the latest document as required.

Prepare for Audits

▸ Leading digital validation systems enable instant audit readiness by automatically capturing and storing all user inputs, with a complete un-editable history of requirements, tests, deviations, and revalidation stored and instantly accessible to guest users.

Automatically generate a full audit trail in Kneat Gx.
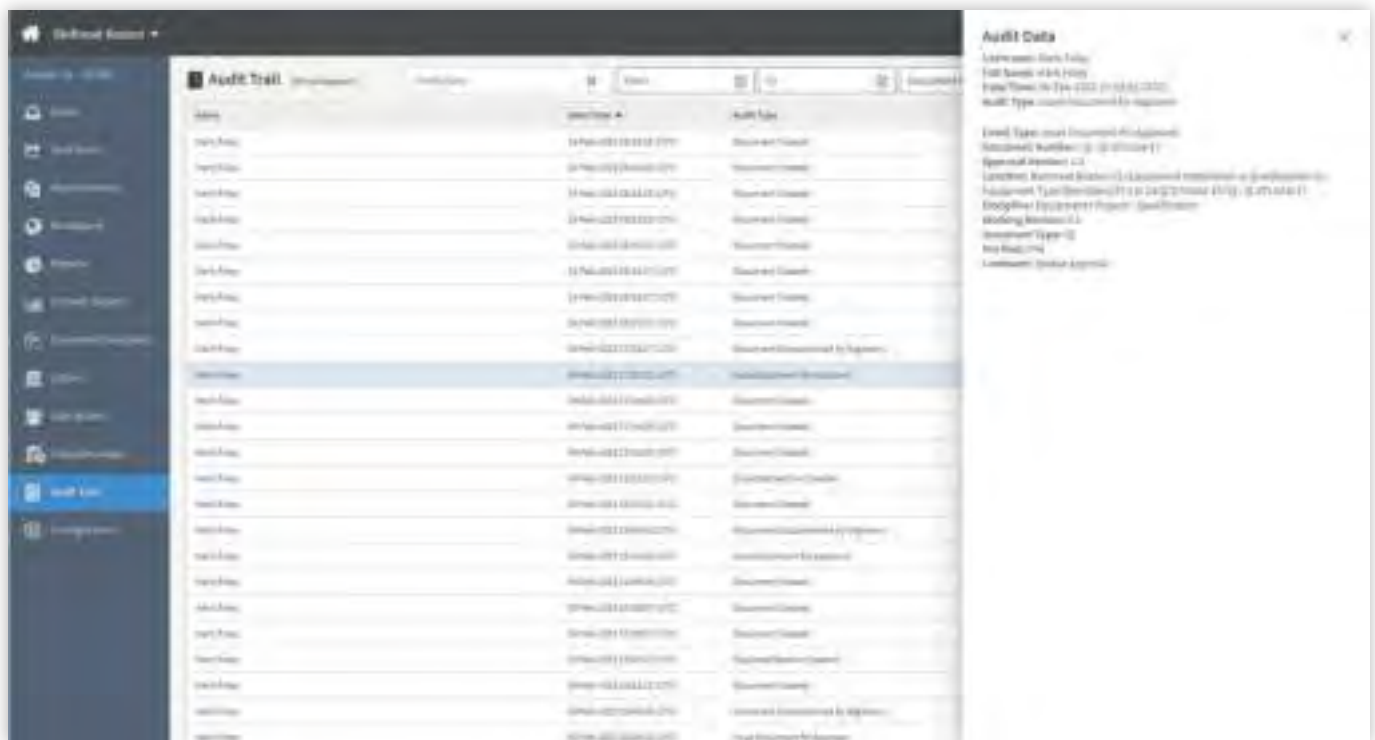
Harmonizing Validation Within an Organization

Digital validation helps to break down organizational silos and makes it possible for an organization to employ top-down, standardized validation processes across multiple sites and divisions. By harmonizing processes, no site is left hindered by inefficient process, mistakes are reduced and redundancies addressed, and managers may more easily monitor activities.

Reduce Deviations

Time efficiencies created by digitization allow validation teams to validate an increased rate of design phase activities, such as iterative prototyping and development, supporting higher "right-first-time" outcomes in later lifecycle stages. The digitization of process and procedure documentation enables greater accessibility to operators on the manufacturing floor, supporting a reduction in human error during implementation and execution. Better data, stronger documentation, and time efficiency all combine to help companies improve the odds against deviations and achieve more right-first-time results.

The Types of Digital Validation

There's no single way to digitize validation processes, but for the purposes of this guide we will examine four key dimensions:

- Hybrid digital validation
- Complete digital validation
- Paper-to-glass
- Paper-to-digital

In the majority of cases, a company's digital validation solution will be either hybrid or complete and either paper-to-glass or paper-to-digital. A company should select the solution right for its unique situation, evaluating criteria such as volume of work, available budget, and size of team.

Note: moving away from paper can happen in several different ways, but such a transition is frequently termed "paper-to-glass" as documents become readable on a screen. For the purposes of this discussion, we further differentiate digitization processes. **Paper-to-glass** represents a first step in digitization—with activities such as scanning or copying—whereas **paper-to-digital** refers to a transformation in which data and documents are leveraged in different ways not possible in their traditional form.

Hybrid Digital Validation

Hybrid digital validation is a mix of traditional, paper-based processes and digital systems. This is typically a starting point or a specific choice to address a narrower use case. Hybrid approaches understandably yield some of the benefits of digital validation for a lower price point, but they will also maintain the same drawbacks of paper-based validation, including longer cycle times and increased margin of error.

Expert Tip: Start Small by Going Big

Picking a work site or process to launch a digital validation solution is important. The greatest benefits will be realized where more work takes place. Look for processes with large volumes of documents, numerous hand-offs or lengthy cycle times.

Complete Digital Validation

When all or most of the necessary paper has been replaced by digital documents, a company may consider its validation fully digital. Depending on the size of the operation, this may be a lengthy staged process, or a rapid deployment. A complete transition will carry an upfront investment cost, but when chosen correctly, a digital validation solution pays for itself in increased productivity and reduced overhead costs. Data integrity and compliance concerns are also best met with digital solutions, and they will continue to be a key focus of regulators going forward.[10]

Paper-to-Glass

Paper-to-glass, in general, focuses on digitizing documents to make validation more efficient using scanners to help streamline document transfer and readability. The process typically involves scanning paper documents and transmitting their digital files to stakeholders. Some solutions allow for editing of a "layer" on top of the document, whereas others require the document to be printed, manipulated, and then rescanned.

This approach can remove the storage headaches of fully paper-based systems and greatly speeds the hand off of key documents. However, the scanning required means cycle times will still be longer than a fully digital solution, and data integrity risks remain as key aspects (such as approval signatures) happen offline and may not be time stamped accurately. This also does little to utilize data within the documents, which limits the efficacy of a paper-to-glass solution.

Paper-to-Digital

If paper-to-glass is simply viewing a paper document through a screen, paper-to-digital can be thought of as that paper *becoming* the screen, with computing power behind it. When a document becomes fully digital, the full advantages of technology are unlocked including:

- Automation
- Real-time visibility
- Controlled templates
- Rapid retrieval and traceability
- Error-proof handling for data integrity

In these scenarios, updates to a particular document or process can be pushed to all relevant documents instantly, removing the need to dig up buried documents or redo work. The key to benefiting from this approach is understanding the value of dynamic data.

> **Expert Tip: Use What You Know**
>
> A digital transformation is a big change, but it doesn't need to change everything. Look for a solution that allows you to leverage existing templates and familiar documents. This reduces implementation time, makes training easier, increases uptake across the organization, and ensures you aren't reliant on vendor involvement.

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10 (n.d.). *Warning Letters.* U.S. Food & Drug Administration. https://www.fda.gov/inspections-compliance-enforce-ment-and-criminal-investigations/compliance-actions-and-activities/warning-letters

Dynamic Data & Documentation in Kneat Gx

In a fully digital solution—such as Kneat Gx—both documents and data are manipulable, accessible, and stored electronically. This has wide scale impacts on validation activities, broadly ensuring compliance with data integrity regulations such as CFR 21 Part 11[11] and drastically reducing validation cycle times by removing barriers caused by paper-based or manual activity.

For example, test scripts can be designed, executed, and approved directly within Kneat Gx.

Step #	1
Test Procedure	Load the sterilizer with load configuration #3 dry goods maximum load and run it at a minimum temperature to a minimum time
Expected Result	▸ BI's show no growth after 7 days ▸ A minimum of 12 Fo were obtained at each TI location
Actual Result	▸ BI's showed no growth after 7 days ▸ Minimum Fo of 30 was found
Pass/Fail	Pass
Performed By	Richard Minco | 03 Jan 2023

A test template can be created in Kneat Gx and accessed by a validation professional. These templates can be populated automatically with relevant data, such as requirement codes, product names, and expected results. Using a device such as a laptop or tablet, the engineer can record the test result and sign their name using a password protected digital signature (a key requirement for data integrity.) Kneat Gx will automatically timestamp the signature and record the user's activities, making documentation instantly audit-ready. The engineer can send the test for approval to their supervisor who'll receive system and email notifications, containing a link to the document for review.

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11 (2022, Nov 29). *CFR - Code of Federal Regulations Title 21*. U.S. Food & Drug Administration. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11

Many activities require evidence, and the attachment of this evidence in paper-based validation processes is typically a time-consuming aspect of test execution, requiring printing, scanning, and collation. In Kneat Gx, testers can enter recorded results, create and process exceptions, and upload evidence (including necessary screenshots) without ever needing to leave the platform.

Every day, at sites around the world, thousands of steps across the validation lifecycle are performed. By increasing the efficiency of each step, even marginally, the net time and cost saving created by digital validation for large organizations can be significant.

Expert Tip: Online is Best

Some solutions require inputs to be entered offline and documents uploaded. Offline work carries data integrity risks as the time stamps may be missed or inaccurate.

Automated Documents and Audit Trails

A fully digital solution allows for automated documents which dramatically reduce the time it takes to complete validation cycles. By pre-loading templates, project maps, and other documentation, as much as 80 percent of required work can be done before validation begins.

Automated documents do more than streamline a process, they enable complex tracing related documentation, so users can see the full connectivity of any documents they wish to trace. Traceability matrices are time-consuming and cumbersome to produce and maintain manually, but when automated provide detailed visibility into, and control over, the interrelationships between documents without the workload.

ALCOA+ principles can automatically be applied as well—from attribution through unique logins to auto-generated timestamped e-signatures.

Audits are an inevitable part of manufacturing in highly-regulated industries and a digital validation solution can remove many pitfalls of audit preparation by automatically preparing an audit trail. Such steps include:

▶ Maintaining a revision history for any document
▶ Documenting changes, such as creation, deletion, or approvals
▶ Storing test results and events

The aforementioned traceability matrix also assists audit execution through the seamless navigation to relevant documents.

Align with Pharma 4.0

Pharma 4.0 makes a clear case for digitalization, not simply due to cost-savings and efficiency, but due to the intrinsic value of deep, available data. The driving idea behind Pharma 4.0 is that, by connecting sites, machines, and professionals to a central web, companies will have more transparency into their operations and generate data that can be used for critical business decisions that enhance product quality. Some areas that could benefit from such technology include:

▸ Predictive maintenance to decrease operational downtime
▸ Operational transparency for streamlined management
▸ "Smart" plant floors which can use automation and machine learning to enhance productivity and correct mistakes autonomously

While not an exhaustive list, these three benefits of Pharma 4.0 also show the versatility of a good digital validation solution such as Kneat Gx.

Predictive Maintenance

Many companies have a global footprint, with sites thousands of miles apart yet using the same machinery and processes. New insights can be unlocked by centralizing the data collected in day-to-day activities like validation. For example, an autoclave used at a site in Memphis is the same as one used at a facility in Mumbai. The Memphis autoclave experienced a part failure 18 months into operation and that same part in Mumbai is 12 months into its lifecycle.

When validation, part, test, and product data is stored together, engineers can be proactive to avoid failures. Parts used in the same machines for the same functions likely have the same lifespans. This would enable the Mumbai site to replace the part before it fails, thus minimizing downtime and productivity loss.

Expert Tip: Purpose-Built, But Flexible

When looking for a digital validation solution, look for solutions that are built on a foundation of understanding for your industry, but prioritize agility in your selection. Finding the balance between purpose-built functionality and agility of use will unlock new applications and enhance the value of your solution.

Operational Transparency

Every site requires validation, but validation disciplines can be managed remotely, allowing for global validation teams which decrease overall overhead, ensure alignment and quality across the organization, and streamline validation. Digital validation solutions can monitor validation activities and statuses across organizations enabling users to monitor entire lifecycles easily, no matter where they are.

"Smart" Plant Floors

"Smart" machines are those with increased functionality through digitalization. A key aspect of the Internet of Things (IoT), smart machines use software to provide new and exciting benefits to companies, but for life sciences companies, that also means the need to undergo Computer System Validation (CSV).

The regulatory requirements facing life sciences companies are a primary reason the sector has been slower than others to adopt innovative technologies—something the FDA specifically targeted in its guidance on Computer Software Assurance (CSA).[12]

That guidance provides a risk-based approach to CSV, meant to remove regulatory hurdles and encourage the adoption of technologies. To be effective, validation teams will need the ability to manage evidence, document reasoning, and keep validation documentation connected.

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12   (2022, Sept 13). *Computer Software Assurance for Production and Quality System Software.* U.S. Food and Drug Administration. https://www.fda.gov/media/161521/download
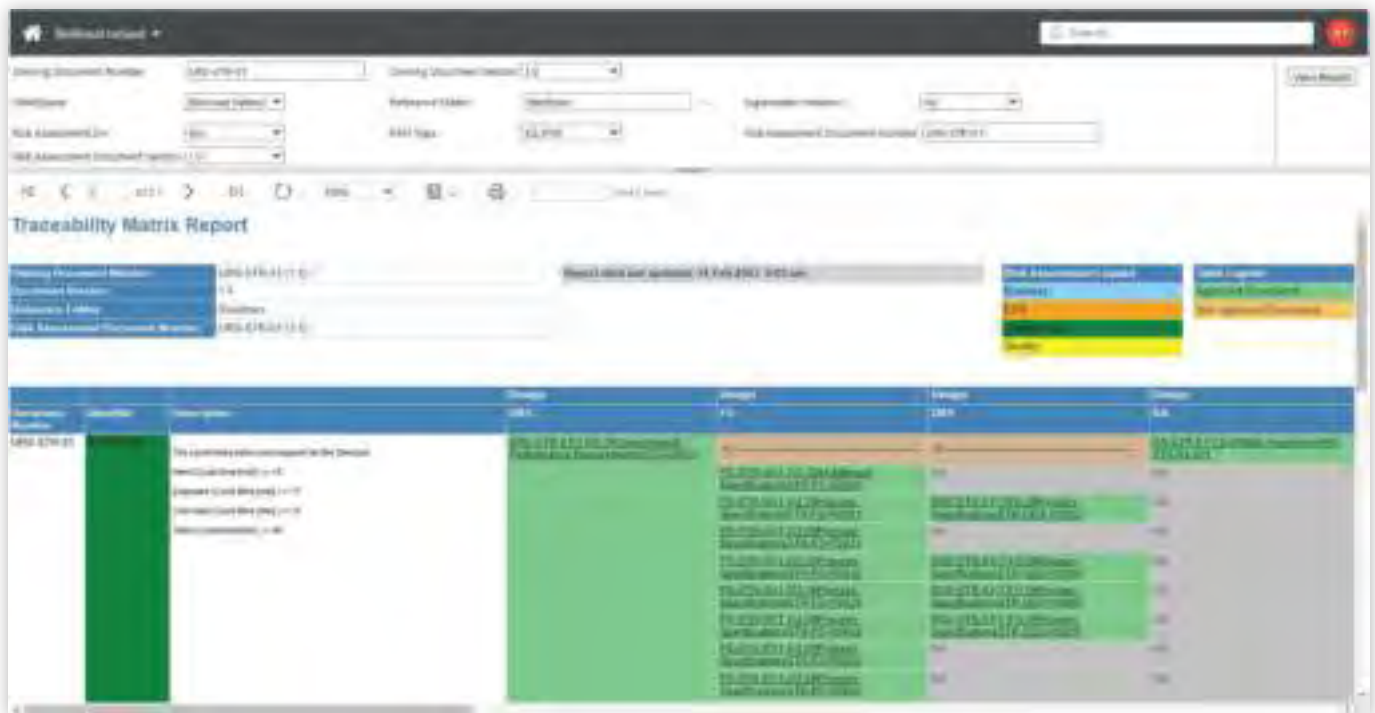
Kneat Gx

Kneat Gx is a SaaS Validation Lifecycle Management Platform designed to provide end-to-end digital validation to enable regulated companies to streamline their validation processes so they can make safer, high-quality products. Some key differentiators include:

Extensive Traceability Matrix

Close gaps in your program with a fully functional Risk Traceability Matrix for a live view of all traced requirements, tests, and documents.

If you can't access the data and documents you need you might as well not have them at all—and that means gaps in your risk assessment capabilities. Kneat Gx's Risk Traceability Matrix RTM) enables robust requirement management and risk tracing across an organization. The dynamic RTM delivers a live view of all traced requirements linked to associated completed tests. As lifecycle and project documents update (like URS, IQ, or OQ documents for example) these are auto-generated to all relevant entities.

This matrix not only streamlines navigation, but ensures changes or revisions seamlessly occur to all related documents, traces risks across processes, and integrates testing and change management activities.

Cloud-Based Capabilities

Kneat Gx is provided as a cloud-based Software-as-a-Service (SaaS) model, which enables near unlimited scaling for customers. Compared to on-premise models, SaaS solutions can be remotely managed from nearly anywhere in the world and are easier to extend to additional work sites and applications. Kneat Gx is faster to deploy, easier to train, and ready to scale to meet customers' needs.

Configurable Solutions

Kneat Gx is an out-of-the-box solution, meaning it comes readymade for quick deployment, but it's also easily configurable to meet numerous needs related to validation. Key applications include:

▸ Commissioning and Qualification
▸ Computer System Validation
▸ Equipment Qualification
▸ Cleaning Validation
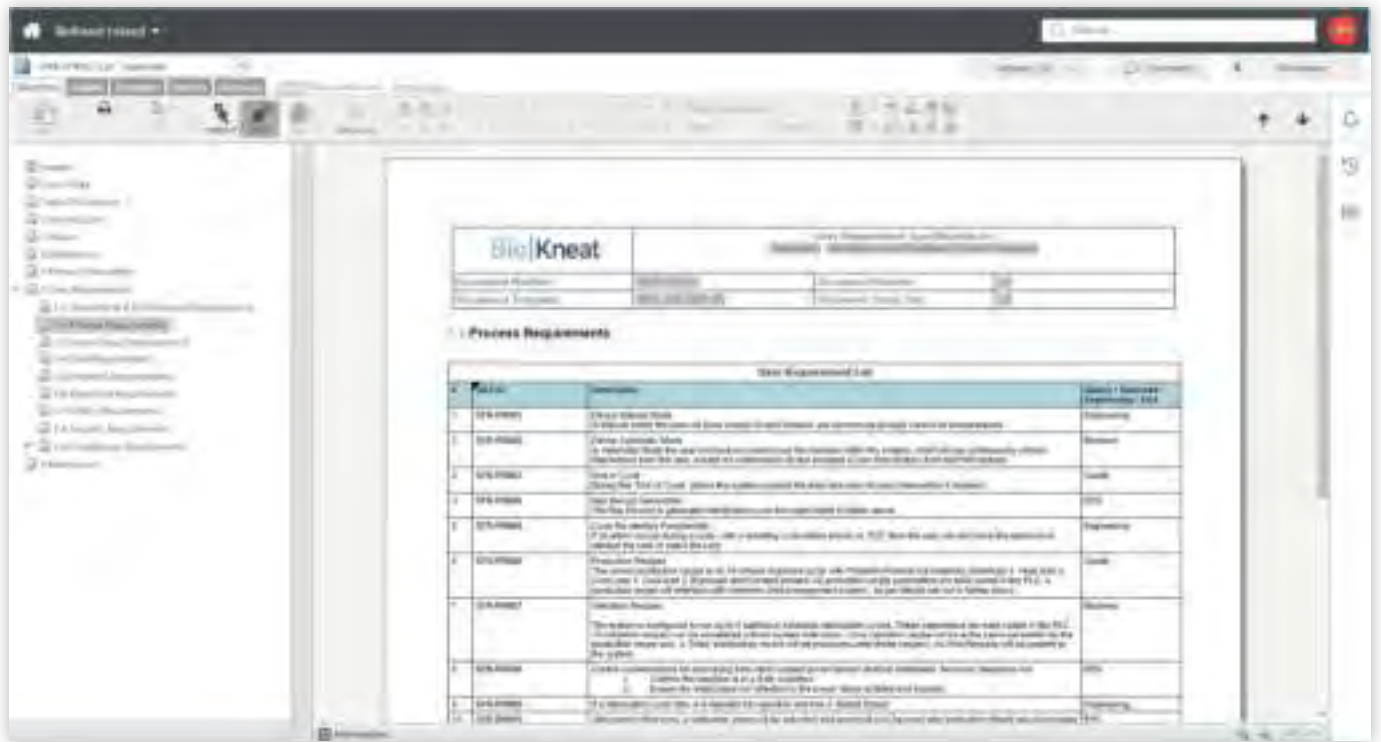▸ Electronic Logbook Management

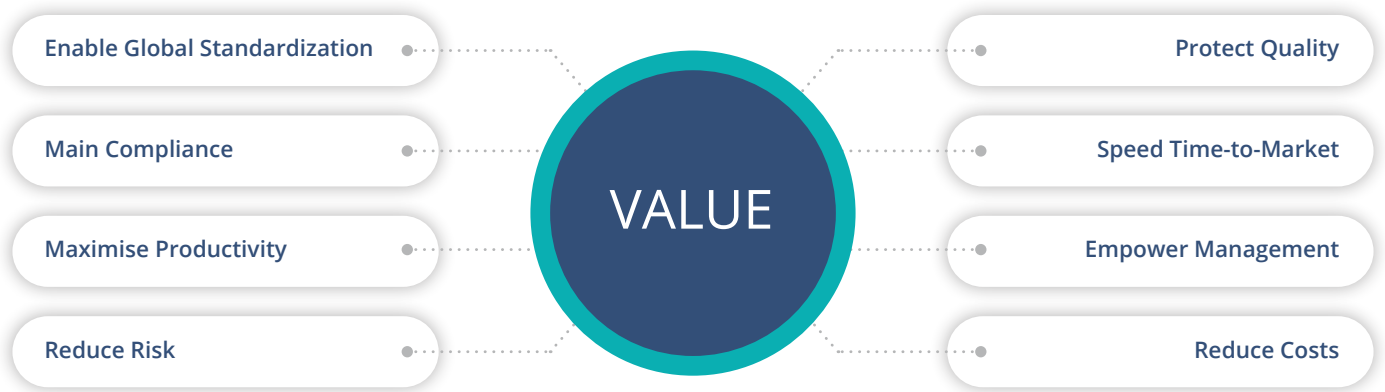**Kneat is fit for purpose for multiple disciplines.**
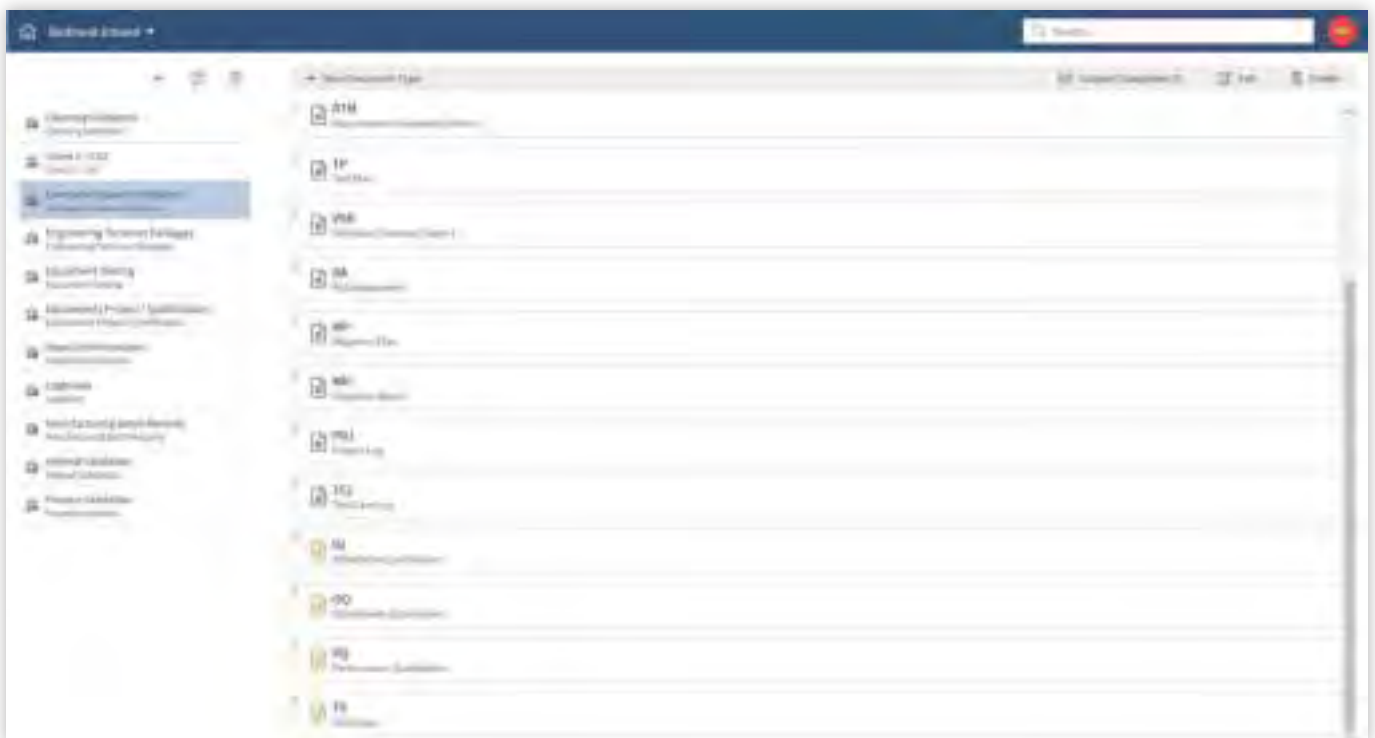
Easy to Use

Kneat Gx is built by people with a deep understanding of validation and the challenges facing highly regulated companies. Using familiar design, quick-to-create templates, and guided training, Kneat makes it easy to implement within your organization, map processes, and deploy across sites and disciplines.

Kneat Gx was specifically designed to look and feel familiar for validation professionals, while greatly enhancing the functionality of documents.

VALUE

Enable Global Standardization

Main Compliance

Maximise Productivity

Reduce Risk

Protect Quality

Speed Time-to-Market

Empower Management

Reduce Costs

> The advantage of Kneat is it gives us that end-to-end without paper, things are contemporaneous, the reviews and approvals are concurrent...for us it gives us that data integrity advantage we didn't have before.

Deborah Fullam, Director, IT Compliance, Global System
Merck Sharp & Dohme Corp.

Experience Kneat for Yourself

If you're looking for a digital validation solution for your company, Kneat Gx may be your answer. Contact us to book a personalized demonstration and see if Kneat is right for you.

Book My Demo

Kneat

Talk to Us

Find out how Kneat can make your validation easier, faster, and smarter.
Start your validation revolution by speaking to our experts.

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