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Enabling Technologies Consortium: Implementations of Wearable Enhanced Knowledge and Analytics Platforms for Pharmaceutical Laboratories

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Introduction

Core tools used for research and development in pharmaceutical laboratories, such as media capture, integration, and electronic notebooks, have not kept pace with the electronic multimedia tools and capabilities that are common in other personal and home-use technology. Within the Enabling Technologies Consortium, a collection of like-minded development scientists worked together on next-generation lab wearable and documentation solutions to align across pharmaceutical companies and influence vendors to meet future business needs. The use of wearable technology in laboratories and interface of devices with Electronic Laboratory Notebook (ELN) and other applications using a software agnostic approach was identified as a key opportunity. The subsequent assumptions, goals, results, and suggested next steps follow.

Background

Since the dawn of the scientific process, curious and enterprising scientists have needed the ability to record thoughts, observations and results in an easy and continuous way. Perhaps the most famous historical example of this is Leonardo da Vinci's notebook. Fortunately, technology improvements have made that process easier. Notably, about 20 years ago, professional scientists were able to take a big step forward with the maturation of the ELN.

In the last ten years computer and mobile technologies have advanced exponentially with processing power, connectivity, affordability and ease of use. However, pharmaceutical companies have been slow to adopt use of these new technologies. As a result, pharmaceutical professionals often do not have access to the same technology in their laboratories as they do in their homes.

The topic of transforming the way scientists document and capture data within the laboratory was raised within the Analytical working group of the IQ Consortium (*International Consortium for Innovation & Quality in Pharmaceutical Development*). Identifying and removing barriers to these technologies, and reaping the resulting productivity and quality gains is a priority for the IQ member companies.[1] As an outcome of a meeting on the subject at the IQ Summit in 2018, a working group was formed (*Next Generation Capture Working Group*).

The working group included 15 individuals from 12 mid to large pharmaceutical companies. The group focused on surveying and understanding the technology landscape within the industry by inviting each member company to share their respective informatics technology platform and visions. It was clear from these early discussions that while some details at each company differed, the members experienced highly similar struggles to take advantage of new information technology.

The next phase of the discussion was an open period for "blue sky thinking". To help the group consider the way in which these technologies could evolve, the conversation shifted to technical and organizational maturity.[2] The team examined the many dependencies and barriers to implementation for transformative ideas. This helped the team further organize the needs and potential technology solutions. The group then agreed to and published the transformation map that serves as a general guide to improving capabilities (Figure 1).

In late 2019 the working group leader met with IQ leadership to discuss the next steps. The outcome of this discussion was a decision to move this project into the Enabling Technologies Consortium (ETC) to focus on certain key areas in the transformation map. The ETC is a derivative of the IQ consortium that provides member ETC companies with a framework and funding mechanism to develop new technology. The guidance and best practices give a working team the framework needed to develop request for information, receive vendor responses and set a contract with partners for technology development.

The team published their request for information and within 60 days had multiple industry responses. After careful consideration by the project team and the ETC Board of Directors, the decision was made to move forward with two vendors that appeared to have complimentary areas of strength. Apprentice was selected for their experience with wearable implementations and strength in the execution of processes and procedures. Varya Technologies was selected for their lightweight and flexible information platform which matched design

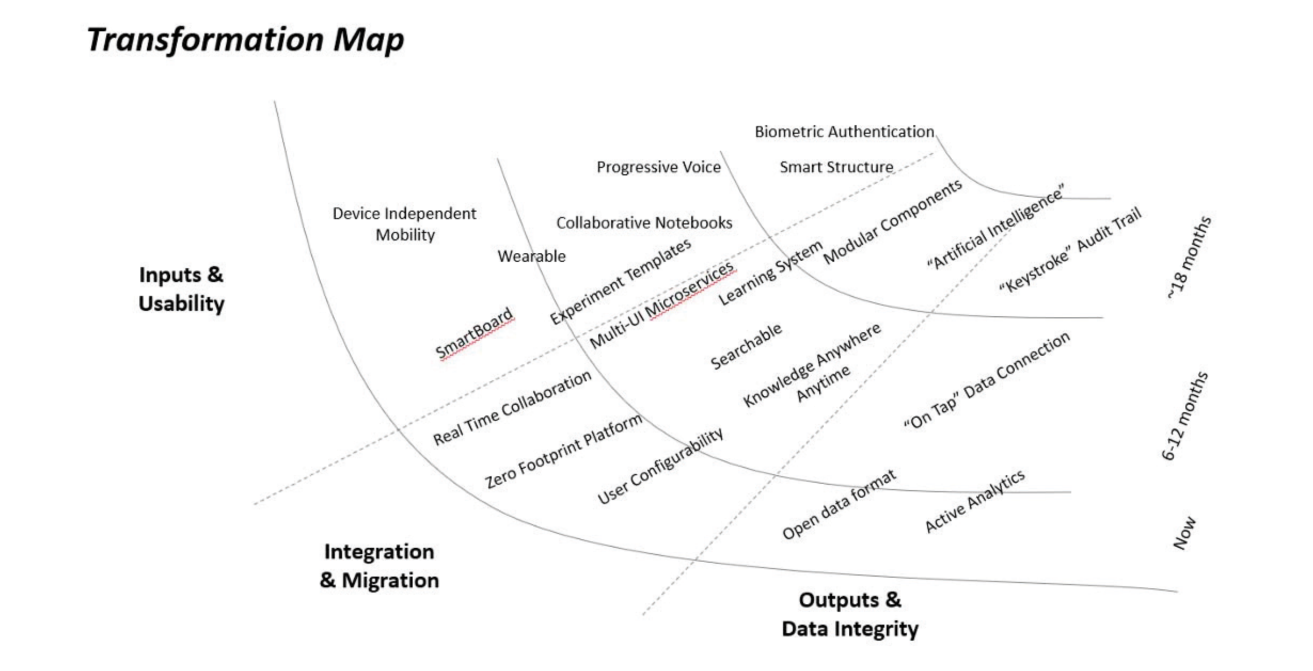


Figure 1. Transformation Map

and architecture principals of the consortium. After selection of these vendors, the team quickly moved into proof-of-concept (POC) implementations at four member companies.

Use Case: Integrated Laboratory Notebook

Having decided to move forward, the next step was to define use cases that explored the capabilities of emerging technology to transform the laboratory. The Bristol Myers Squibb (BMS) team focused on a new approach that combined wearable technology with a dynamic and flexible electronic laboratory notebook (ELN).

The ELN is a core tool used in research and development, however over the years its functionality and adaptability has not kept pace with other software tools and platform integration capabilities that we expect from our personal technology.

The use of wearables to collect experimental information logically requires linking with an ELN. The use case was to enable mobile, hands-free data capture via a real-time interface between headset wearable technology from Apprentice.io and an interface to devices and instrumentation with data platform in development by Varya Virtual documenting laboratory activities, (Figure 2). Anticipated benefits included a more immersive lab experience and learnings that would drive knowledge gathering efficiencies with improved workflows and consistent practices.

The Apprentice platform was already in place at BMS, utilizing a RealWear HMT-1 headset and an iPad to capture a wide range of lab activity information. This enables unencumbered procedure execution with video and audio recording along with automatic data capture using the Apprentice platform. Varya's platform, Iota, uses a Microsoft Office 365 (MS365) framework and a combined Teams and OneNote interface. The (MS365) platform is widely used within and beyond the healthcare industry, providing a familiar workflow and interface (ref 3). The setup and integration of Varya's ELN was through a Microsoft Teams portal hosted in a cloud environment and accessible via the web-based Teams client. After 2-3 hours of hands-on introduction and training, Varya's Iota became relatively easy to use based on previous ELN platform experience and familiarity with MS365 applications. One major concern encountered was that the desired real time interface between the Apprentice and Varya platforms was not possible within the time constraints of the POC, consequently indirect file uploads were used instead.

The overall structure and linkage of the two vendor platforms are shown in Figure 2. The evaluation by a handful of scientists demonstrated that with a small amount of planning most activities and data outputs of lab experiments could be easily captured in the ELN. The key takeaways were as follows:

- Apprentice tools enabled lab experiment stepwise information collection via video capture and dictation combined with templates and real-time data base connections.

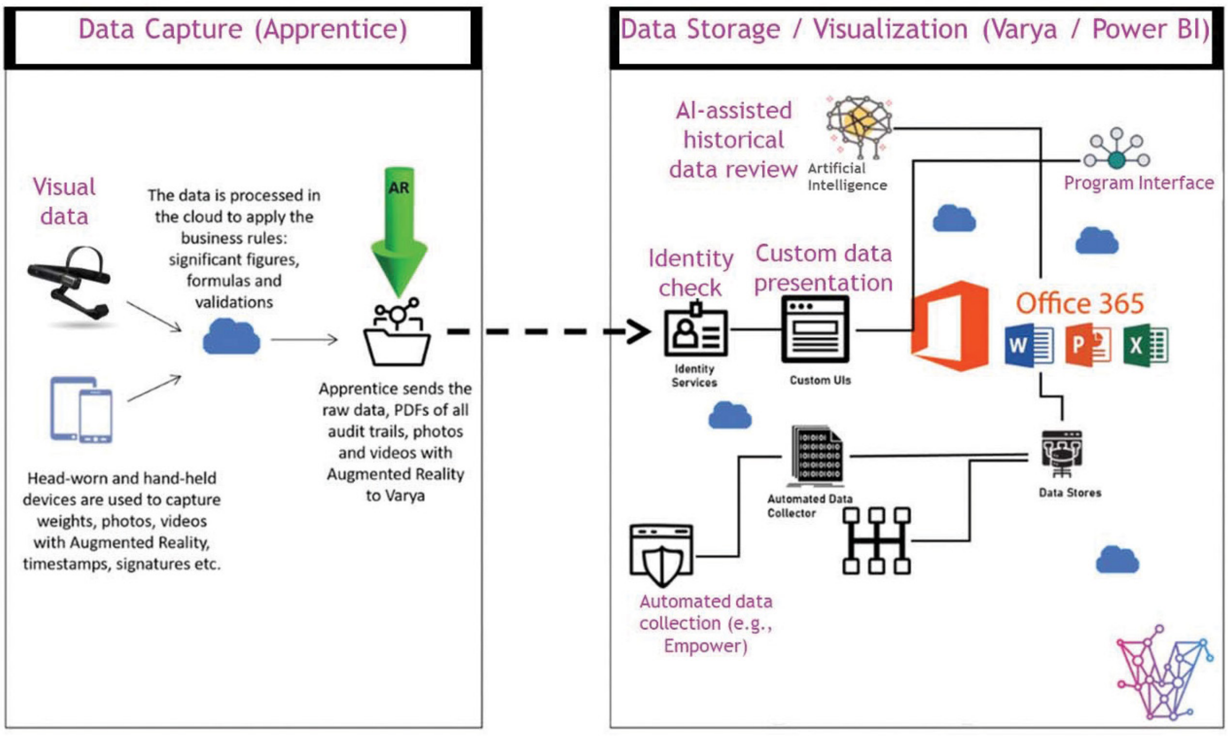


Figure 2. Connection of the Vendor Platforms

- Headwear integrated seamlessly with Apprentice online portal - collecting balance data, barcode-scanned reagents/instrumentation, images and transcribed notes.
  - » Annotated images using augmented reality was possible for more informative illustrations
  - » Apprentice files in various formats were uploaded into a Varya Iota notebook page – simple but not real time with lab activities
- Varya's Iota had diverse data capturing options (text, photo, video, audio/dictation) across MS365 programs using handheld devices, including iOS and Android phones.
  - » Use of QR codes to link and open experiments on any device, in any location, allowed real time collaboration within and across functional areas
  - » Many options for data processing, collation and visual interpretation within the ELN compared to standard ELN reporting, e.g., Empower data (either raw data or processed summaries) as a dynamic data source within the platform
  - » Multiple data sources with dynamic linkages and historical records are accessible within one ELN record

The different vendor collection processes were individually assessed before a combined experimental study was designed to leverage a full study workflow, as shown in Figure 3. A full analytical experiment (response factor determination/sample stability/robustness studies) was successfully demonstrated by performing an analytical experiment workflow that capture specific details of the activities and their results including detailed individual sample preparation capture with video, pictures, database linkage and combined dictation and keyboard entry with Empower raw data chromatography collection. HPLC instrument raw data outputs from the experiments were captured, documented and processed using Microsoft Power BI within the Varya ELN. Additionally, the results were presented as an interactive dashboard that could be used in a group meeting setting or incorporated directly into a presentation or summary report.

Through this endeavor, the team accomplished the objective by demonstrating the feasibility of the use of wearables and integrating with an ELN. We also recognized the future vision of using an ELN as a data repository, for data integration and experimental records. Within this we saw further opportunities as an immersive collaboration tool when working in the lab, reviewing or processing data, and for direct communication of results and conclusions.

Based on this experience, the team noted that the wearable and ELN space is rapidly evolving and there are different capability levels both

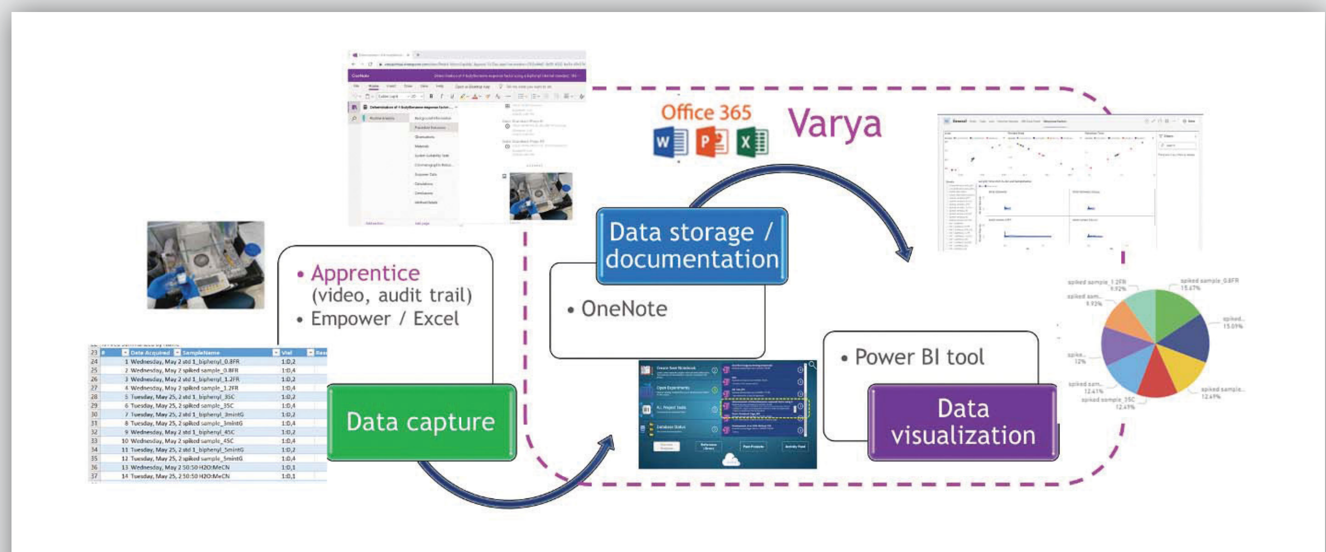


Figure 3. Study Information Workflow

from vendors and within pharmaceutical companies. This presents a need and opportunity to build an ELN infrastructure that is flexible, can meet the general requirements of most users and has the ability to evolve over time. Overall, our successful implementation and integration of these two powerful platforms, along with instrumentation and databases, demonstrates that both these vendors have platforms that can be connected, used and further developed to meet the future ELN needs of scientists.

Use Case: Dynamic Procedural Support

Biogen's interest in Next Generation Lab Capture operates on the premise of establishing a digital standard operating procedure (SOPs) for routine laboratory operation. We envision the digital SOP as one of two key input platforms for an information workflow that delivers scientific information into outputs such as reports and insights. The second platform involves standardized instrument data and file structures. A simplified schematic of the digital workflow is shown in Figure 4. With this approach, our expectation is that treating scientific information to make it FAIR (Findable, Accessible, Interoperable, and Reusable) will increase efficiency and create both direct and indirect value from the application of experimental data.

Currently, the written SOP is interpreted for practical use into makeshift spreadsheets or ELN templates that provide features of method guidance, preparative calculations, recording of materials and equipment, recording of experimental observations, capture of raw data, data analysis, and summarization of results. These tools are an interpretation of the written method and have the inherent risk of being inaccurate or not applicable to the exact laboratory setting. Moreover, because they require typing, information is often not recorded in real time. In most cases these tools are not transferred to receiving laboratories in Quality and CROs who have their own infrastructure for managing scientific information.

The Apprentice technology offers the promise of an interactive human readable document that aligns with our vision of a digital SOP. Listed in Table 1 is a series of features Apprentice offers that effectively captures the experimental metadata of a laboratory workflow and guide the operator through the method. Within the Apprentice environment, we were able to create an annotated SOP from an existing document (Figure 5). This allowed the document to be interactive, capturing the procedure in a stepwise workflow that can be consistently executed, tracked, and confirmed. We were able to complement the process

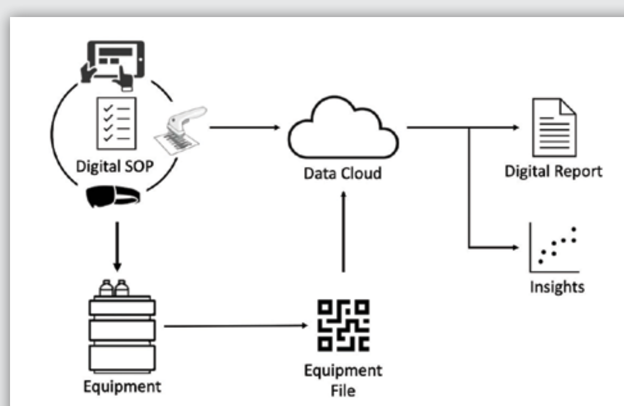


Figure 4. Laboratory Digital Information Workflow

using barcoding features to record equipment inventory and take advantage of the handsfree features by adding comments and observations using the VR headset. An additional feature that is only possible using VR technology is remote guidance. In our demo, we were able to independently onboard a novice user into the Tandem environment and use the RealWear headset to remotely provide guidance through a laboratory process despite no prior experience with the technology. The RealWear device was comfortable and had excellent video and photo quality.

Collectively, we feel believe Apprentice technology has the potential to enable our digital vision for managing the process of an analytical laboratory workflow. One area of development that will make this promising technology come to fruition is flexibility in the manuals feature where steps can be easily edited within a document and repurposed to procedures with similar steps. To complete our vision, we will look to integrate the experimental metadata from the Apprentice environment with analytical instrument data in a structured cloud-based environment. Once accomplished, analysis and reporting outputs can be automated independently or in conjunction with a suitable ELN.

Table 1. Digital Workflow Tool Features

Feature	Technology	Application
Method Guidance	• Apprentice Methods • Barcode • RealWear Headset • Tablet	Step by step workflow description and guidance for consistent execution and tracking of steps Information and step confirmation achieved by barcode
Preparative Calculations	• Apprentice Methods • RealWear Headset • Tablet	Calculations related to experiment scale completed with simple data entry or voice command
Simple Equipment Capture	• Apprentice Methods • RealWear Headset	Values entered by simple data entry or captured by photo or video
Recording Materials and Equipment	• Apprentice Methods • Barcode • RealWear Headset	Capture experimental materials and equipment hands free using a barcode reader.
Remote Guidance	• Apprentice Tandem • RealWear Headset	Remote guidance between lab personnel and deskside support for virtual training and troubleshooting

Use Case: Technical Transfer and Third-Party Organizations

The technical transfer of projects, methods, data and tests between Eli Lilly divisions can be a lengthy and resource intensive process (e.g., between development and manufacturing). The large number of computer-based systems and individuals (scientists and engineers) involved in a project provide complications to a process that is already highly detailed and regulated.

Eli Lilly leveraged wearables delivered by Apprentice and manufactured by RealWear to capture information that was then transferred to Varya's Iota platform. Iota allowed Lilly to build "notebooks" of research, experiments and results with few limitations. These notebooks included audio, video and images captured by the head-worn mobile devices. Through this interface Lilly was able to capture, locate, organize and perform analytics on this information to share and transfer to other parts of the Lilly organization. Iota's seamless

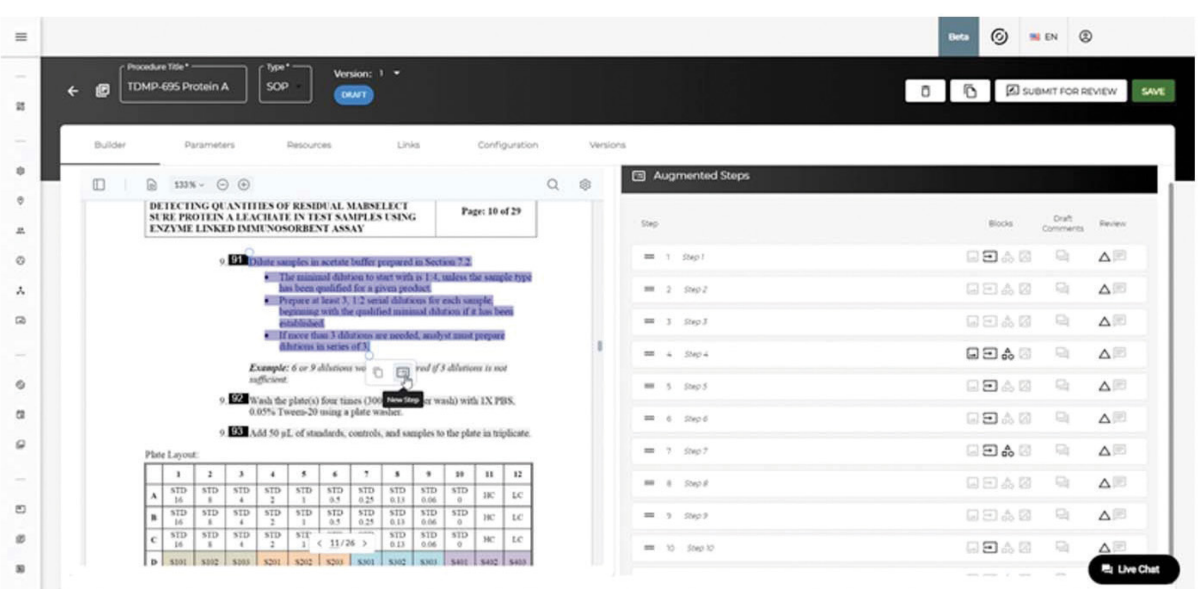
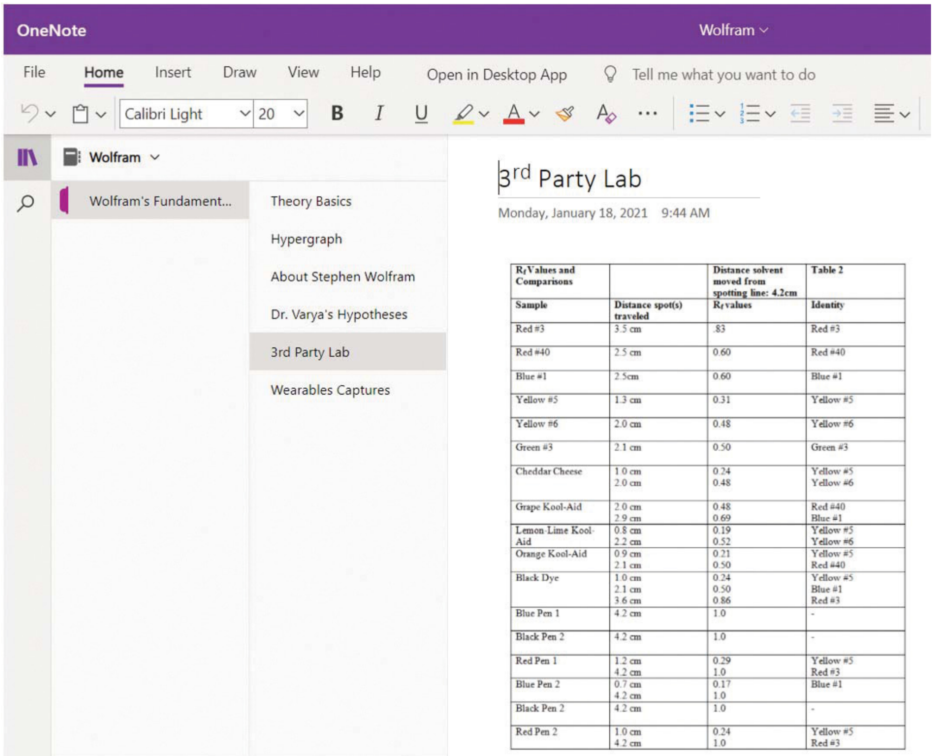


Figure 5. Apprentice Annotated SOP



R_f Values and Comparisons		Distance solvent moved from spotting line: 4.2cm	Table 2
Sample	**Distance spot(s) traveled**	**R_f values**	**Identity**
Red #3	3.5 cm	.83	Red #3
Red #40	2.5 cm	0.60	Red #40
Blue #1	2.5cm	0.60	Blue #1
Yellow #5	1.3 cm	0.31	Yellow #5
Yellow #6	2.0 cm	0.48	Yellow #6
Green #3	2.1 cm	0.50	Green #3
Cheddar Cheese	1.0 cm 2.0 cm	0.24 0.48	Yellow #5 Yellow #6
Grape Kool-Aid	2.0 cm 2.9 cm	0.48 0.69	Red #40 Blue #1
Lemon-Lime Kool-Aid	0.8 cm 2.2 cm	0.19 0.52	Yellow #5 Yellow #6
Orange Kool-Aid	0.9 cm 2.1 cm	0.21 0.50	Yellow #5 Red #40
Black Dye	1.0 cm 2.1 cm 3.6 cm	0.24 0.50 0.86	Yellow #5 Blue #1 Red #3
Blue Pen 1	4.2 cm	1.0	-
Black Pen 2	4.2 cm	1.0	-
Red Pen 1	1.2 cm 4.2 cm	0.29 1.0	Yellow #5 Red #3
Blue Pen 2	0.7 cm 4.2 cm	0.17 1.0	Blue #1
Black Pen 2	4.2 cm	1.0	-
Red Pen 2	1.0 cm 4.2 cm	0.24 1.0	Yellow #5 Red #3

Figure 6. Third Party Collaboration

integration with MS365 demonstrated the potential to speed the movement of molecule information from Research to Development (scale-up) and ultimately to manufacturing.

Related to this, but with its own unique nuances, is the transfer and sharing of molecule-based information with third party organizations. Over roughly the past decade the pharmaceutical industry has shifted a high percentage of its rule-based testing and an increasing amount of judgement-based work to contract research organizations (CROs). Scientists have struggled to effectively collaborate with CRO based scientists for activities like troubleshooting, method development, problem solving and knowledge transfer.

In the POC, Eli Lilly leveraged Iota to neatly organize and "package" this information for technical transfer internally (Figure 6). It would appear to our participants that this same capability could be leveraged with CROs in a similar fashion and allow for real-time collaboration. The key to this is the nearly ubiquitous use of RealWear MS365 applications across companies. Microsoft Excel has long been the desktop tool of choice for "discrete" numeric results and analysis. Cloud-based storage now allows, with security controls in place, authenticated users from anywhere in our partner network to access and contribute to this content. Additional tools like Teams, PowerApps and Power Automate allow citizen developers or solution providers to organize this information in a way that makes sense to our uniquely technical audiences. Iota demonstrated the ability to interface multiple partner organizations, maintain needed confidentiality and firewalls and develop apps, workflows and dashboards that enhanced the information workflow (Figure 7).

CROs also will find their burden eased by the use of this design. Many CROs have limitations on staff and budgets that increase the importance of being efficient. Again, with the ubiquity of MS365 many CROs should not require additional software support, installation or licensing to realize a positive impact. This allows both large and small organizations to bring their unique capabilities to bear in the pursuit of developing innovative health outcomes.

Eli Lilly found that the use of head mounted wearable devices from RealWear combined with the use of Varya's Iota platform greatly eased the transfer of technical information within the organization. Specifically, this meant significantly reduced technical transfers between Product Development organizations and Manufacturing. Similarly, the team identified significant opportunities to streamline our work with CROs, given the ease of which collaboration partners could share notes, results and methods. The combination of these improvements allowed our scientists to create multi-user, collaborative 'notebooks' where information could be expanded to include video, image and audio content and information could be exchanged internally and externally easily and securely.

Figure 7. "Transfer Ready" Artifacts

Conclusions and Next Steps

The original IQ working group envisioned a broad strategy for advancing laboratory informatics. The focus of this paper, and the ETC project, was centered on the evaluation of laboratory wearables. However, through this experience the member companies were able to expand to other areas of interest. Our discussions highlighted a synergistic approach using the expertise of two different vendors regarding wearables and platform technology to work in parallel. This created a dynamic environment where the consortia companies formulated complimentary use cases for their sites that evaluated the unique challenges for Integrated Laboratory Notebook, Dynamic Procedural Support and Technical Transfer and Third-Party Organizations. The ensuing collaborations extended the original use case goals with an overarching proof of concept leading to the following notable findings and accomplishments:

- The partners were able to create an immersive lab experience, using wearables, with a familiar workflow and interface that leveraged MS365. The premise of using the MS365 platform as a laboratory notebook is game changing to the industry. The ubiquitous nature of these tools makes the sharing of information much easier. Moreover, there is no need for additional infrastructure compared to a specialized ELN. The MS365 platform incorporates current state audio and visual technology that brings the tools scientist use at home to their laboratories.
- Use of annotated SOPs created dynamic procedure support with a digital stepwise workflow using the wearables to collect scientific information in a findable, accessible, interoperable, and reusable way. This led to successful evaluation of remote guidance, more independent use and transferability ease of procedures.
- The inherent familiarity of Varya's Iota platform coupled with Apprentice wearable technology enabled research, experiments and results to be captured easily. As the same MS365 capabilities are commonplace it creates real-time collaboration experience. This raises the possibility of more "bench work" collaboration and the possibilities of bringing unique skillsets, knowledge and experience closer together for innovation and problem solving.

An ETC project team comprised of members of multiple pharmaceutical companies has a clear advantage where members come from distinct aspects of the development organization and represent diverse organizational missions and institutional structures. Eli Lilly scientists were looking to orchestrate data for downstream uses. Biogen focused on internal lab efficiency through procedural execution. BMS sought to bring the two technologies together for a complete workflow experience. This diversity of the use cases enriched the pilot, and likely would have been insurmountable for a single company acting alone. Overall, each use case was a successful application of wearable technology that incorporated future-looking platform technology but also demonstrated opportunities for further development. Crucially this enables scientist to focus on experiments, collaboration, and innovation opportunities and not on burdensome laboratory communication technology.

Moving forward, the participants plan to continue discussions in other areas of interest and apply their learnings. Our first technology development experience was a highly successful demonstration of modern technologies and architecture. We determined that wearables and other mobile devices are valuable tools for enhancing the capabilities of a laboratory scientist if the right support is provided. We also discovered that having a vendor-agnostic and integrated approach for implementation will help us derive greater value. For example, MS365 readily offered an integration of tools on the same platform with familiar functionality, however this should be viewed as a floor and not a ceiling, with more and deeper capabilities that could be provided by vendors and partners with pharmaceutical domain experience. Additionally, getting two complementary vendors to integrate/interface together was also not as successful as we wished. For this reason, our group has realized that only a long-term focused industry engagement with vendors can enable the kind of solutions the industry truly needs. Otherwise, vendors will continue to focus on building monolithic solutions that fail to deliver on the promise of these technologies. The benefit of a "consortia-based" approach is that it allows the pharma industry to collaborate and achieve the level of consensus necessary to alter this course and avoid our industry's current environment where proprietary data, stored in closed systems limits our ability to freely execute the scientific process. Changing this course is perhaps the most impactful lever to pull in accelerating our industry's ability to bring life changing medicines to patients.

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