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DSCSA FDA Pilot DRAFT Final Report

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Rymedi

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Executive Summary

In response to the FDA call for consortiums to pilot DSCSA compliance systems, a consortium led by healthcare technology company Rymedi was formed to include quality monitoring and tracking companies (Zebra Technologies), healthcare systems (WakeMed Hospitals and Health; and Indiana University Health) and supply chain innovation thought leaders (Center for Supply Chain Studies; Global Health Policy Institute at the University of California San Diego; and Good Shephard Pharmacy/Remedichain). The consortium developed a pilot to test interoperable DSCSA compliance technology in tracking specialty medicine transfers across large healthcare provider systems. This pilot design intentionally focused on this class of transfers because of heightened temperature sensitivity and lower tracking requirements for transfers across sites in a large healthcare provider system. Full deployment of the entire system was hampered by the COVID-19 coronavirus pandemic, however, the pilot process yielded significant findings crucial to the scalable adoption of quality monitoring tracking best suited for specialty medicine supply integrity through to patient use. The Consortium here presents the pilot activities and findings as a step towards enabling the integration of Quality Management System (QMS) automation and Real-World Evidence data capture in order to realize the promise of Learning Health Systems.

Pilot Design

Overview

This consortium developed a pilot that tests the implementation of interoperable DSCSA compliance technology, providing immutable genealogy and multi-partner data access, alongside the standard operating procedures within hospital and clinic networks after they take custody of medicines from wholesale distributors and third-party logistics providers (3PLs). Focusing on specialty medicines, the pilot tests DSCSA-required data capture, tracking and sharing of medicine transfers across different geographic sites within and between healthcare provider systems, while avoiding the need to move large amounts of data across the supply chain.

Goals

- Assess a blockchain-enabled hybrid data architecture solution for efficiently providing DSCSA compliance and additional tracking value propositions, including integrated sensors within barcodes to track proper temperature exposure, for healthcare provider systems transferring medicines within and between healthcare provider locations

- Evaluate adoption feasibility and supplemental value-propositions associated with implementation of the data architecture solution for both health systems specifically, and by extrapolation other "trading partners" as defined by the DSCSA

Consortium Entity Roles

Solution Providers

Rymedi
Type of Entity: Solution Provider – regulatory-specific life sciences and healthcare data capture, tracking and sharing

Temptime Corporation, now part of Zebra Technologies
Type of Entity: Temperature IoT sensors, signaling, data management, data capture, and labeling solutions

Pilot Location Partners

Indiana University Health, Indiana
Type of Entity: Large hospital and clinic network

WakeMed Hospitals & Health, North Carolina
Type of Entity: Medium-sized hospital and clinic network

Policy & Thought Leader Partners

Center for Supply Chain Studies
Type of Entity: Think tank

University of San Diego, School of Medicine, Global Health Policy Institute
Type of Entity: Research institute

Good Shepherd Pharmacy & Remedichain
Type of Entity: Nonprofit Pharmacy

Start & Finish Dates

Start: September 30, 2019 - Finish: March 30, 2020

Problem Focus

Drug Supply Quality Management in Healthcare Systems

The Consortium Pilot focuses on drug supply quality tracking across large healthcare systems in order to study potential gaps in healthcare system compliance with 2023 DSCSA requirements and gaps in DSCSA requirements of healthcare systems from the perspective of extending quality management traceability of prescription drugs through to the end patient.

Under the DSCSA, healthcare systems are typically treated as “dispensers” of drugs with the requirements attendant to that designation. Transfers of medicines across different locations within a healthcare system fall under the umbrella of distributions within entities “under common control”, and thus are exempt from the documentation of transfers of custody across locations and kinds of intra-health system organizations. When healthcare systems transfer to locations in other healthcare systems they are treated as “wholesale distributors” and have

custody transfer documentation requirements for the cross-system transfer, though not a chain of documentation of intra-system transfers. This applies whether the transfers to another health system are sales or donations. One exemption is when a healthcare system pharmacy transfers to another in order to meet the need of a specific patient. Documentation of that patient-specific need exempts that transfer. This does not apply to non-patient specific transfers to improve inventory management for general patient needs.

Most compliance with DSCSA requirements through 2019 have been included with wholesale distributor supplier relationships, particularly requirements that healthcare system pharmacies retain transaction information, transaction history and transaction statements for purchased medicines for six years. Both Indiana University Health and WakeMed Hospitals and Health procure most medicines from Cardinal Health who stores that information and provides the pharmacies reports when requested. Most DSCSA compliance vendors have healthcare system offerings focused on authentication and verification of medicines disbursed against that transaction record, and management of saleable returns requiring authentication and verification, as well as transfer of transaction records with the returned products.

The Consortium Pilot narrowed the focus further to explore another domain of potential quality tracking vulnerability: transfers of specialty medicines. Specialty medicines, increasingly biologics, often have special temperature sensitivities affecting their safety and efficacy. Therefore, traceability of temperature exposure alongside the transfers of custody across organizations can provide important quality control and assurance, in addition to supplemental data points in pharmacovigilance investigations of adverse events. Beyond greater sensitivity, specialty medicines are also often significantly more expensive than those not treated as specialty drugs. Therefore, the financial stakes and liabilities of quality maintenance across the value chain is greater with this class of medicines. Insofar as new systems for quality tracking may require greater costs and change management, a pilot focus on treatment categories with the greatest return-on-investment made practical and insight-revealing sense.

Insofar as the DSCSA implements a system to streamline actions and processes of ICHQ-9 risk management across the pharmaceutical supply chain, a pilot design focused on prospective

Quality Management System gaps became the focus of Consortium participants. The heightened sensitivity of specialty medicines and the growing role of large healthcare systems in the transport and management of specialty medicines as healthcare providers increasingly consolidate combines unique points of quality risk and opportunities to leverage emerging innovations in supply tracking to deliver both patient value in the form of higher quality assurance and bottom-line value for the organizations that would ultimately undergird the economics of those solutions as sustainable customers of solution providers.

An additional opportunity to investigate quality tracking in healthcare systems emerged from one of the Consortium partners, WakeMed Hospitals and Health, being the Federal Aviation Administration pilot site for medical drone delivery across healthcare provider sites. The pilot program grew to involve UPS and while it started with biological sample transfers has moved to include drone delivery of medicines. The Consortium agreed to include drone transfers of medicines in order to explore heightened quality monitoring value and implementation challenges in the emerging modality of drone and autonomous mobility transfers of medicine.

Approach

The Consortium developed a solution approach that integrates the blockchain-enabled tracking and data management technology of Rymedi with the temperature-monitoring barcoded intelligent label from Zebra Technologies, along with their industry-leading labeling and data capture solutions. Technology integration was part of the pilot, demonstrating interoperability between systems. However, the greater focus would be on workflow integration and business value identification in order to zero in on challenges for at-scale market adoption of heightened visibility in the quality tracking of medicines beyond the status quo in large healthcare systems and beyond.

One way of framing the pilot approach is the integration of Quality Management System (QMS) Automation with Digital Real-World Evidence (RWE) capture. The ideal scope would be to mirror the degree of supply quality monitoring visibility one gets with a structured phase 4

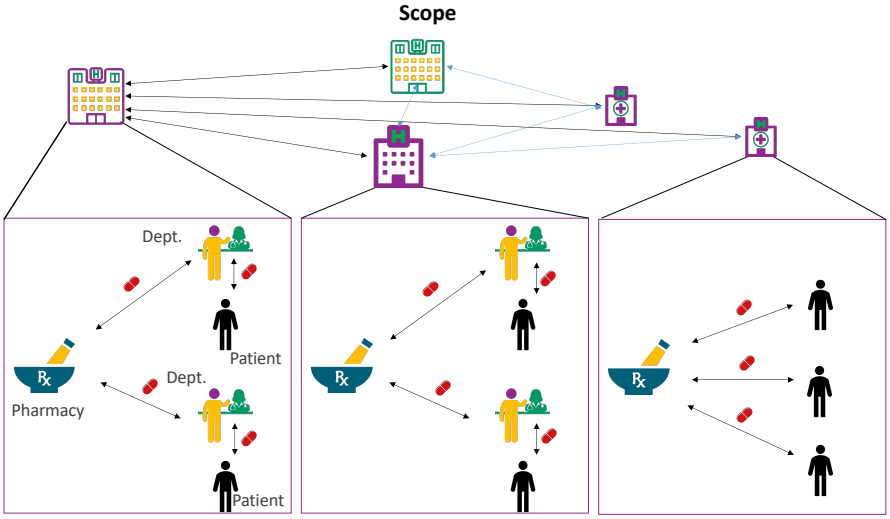
clinical trial. If appropriately integrated into clinical workflows and pharmacy operations supporting clinical care, the same QMS platform would provide RWE of value to many different organizations for different purposes, from clinical operations improvements to clinical research approval streamlining. The quality monitoring features would be part of an integrated platform delivering other kinds of value in order to justify added costs and change management efforts to achieve workflow adoption. Such an integrated e-health architecture instantiates the "Learning Health Systems" model healthcare system and regulator innovators have been envisioning since the late 2000s.

In the midst of the COVID-19 pandemic, the lack of such Learning Health System infrastructure worldwide is felt as a significant pain point hindering key elements of pandemic response: supply agility, quality monitoring of non-standard suppliers, rapid clinical response and contacting mapping for positive diagnoses, biostatistical reliability of RWE from clinical care efforts, missed opportunities for even faster therapeutic and vaccine development with better data sharing analytics and more distributed clinical trials.

In practice, as noted in the report findings, timing and resource constraints drove steady scope reduction in terms of the comprehensiveness of the proposed approach. Those reductions in scope were strategically defined in order to focus ongoing data capture and tracking efforts on points in the clinical supply value chain with the greatest QMS gaps. Healthcare system priority changes and the unfunded nature of the pilot which made healthcare system resource allocation a matter of finding openings in resource availability and schedules rather than a priority repeatedly delayed stages of the pilot. Digital data capture of medicine transfers en-route was ultimately delayed indefinitely beyond the scheduled pilot end date due to COVID-19 and healthcare system preparations beginning in February 2020.

The Consortium partners plan to continue to develop and implement the original design when the pandemic allows, and in the meantime are working to source additional resources in order to be able to pilot the entirety of the original envisioned scope.

Pilot Workflow



The FDA Pilot work flow was driven by the data capture of the drugs being tracked at WakeMed Hospital and Indiana University Hospital.

Solution Adapted for Hospital Environment

The software components of this pilot were designed to provide straightforward visibility of the pertinent data required by each stakeholder, from the nurses and clinicians requiring immediate information on the expiration and temperature compliance of the medicine they were administering, to the individuals in change of inventory and supply chain management within the organization.

As the provider of all of the hardware and labeling supplies, as well as some of the data transport mechanisms utilized in the pilot, Zebra's partnership was an important factor in this pilot. As a leading manufacturer of time-temperature indicators, labeling, data capture, and intelligent data solutions, Zebra's hardware and solutions are already prevalent throughout the hospital and supply chain environments, demonstrating that the hardware and supply technologies used in this pilot are already readily available for its target users.

WakeMed Hospital

The FDA Pilot will track the receipt and movement of 3 drugs (Retacrit, Zarxio, Curosurf) from receipt of Cardinal Health delivery to patient dispensing and saline solution for drone delivery at Wake Med's facility.
Zebra scanners will be placed at each of the work centers that encounter the movement of the drugs. The serial numbers of each scanner will be assigned to a unique physical location. At each stage, the items are processed by the hospital's traditional processes and application software.
Work centers and scanner quantity: Pharmacy Receiving (1), Medi-Cart (1), Pyxis Drug Dispensers (n<10)
Label Printing: Zebra Thermal Label printer will be installed at Wake Med's Pharmacy Receiving work space.
The process below will be performed in addition to the hospital's normal operating procedures.

Retacrit, Zarxio, Curosurf – Tracking
Work Center – Pharmacy Receiving:

1. Drugs are received by a Pharma Tech and scanned by the
   Rymedi application scanner.
2. The application presents the Pharma Tech with a "screen" to verify and/or add information to the drug's data (GTIN, Lot #, Exp Date, Serial#). No additional information will need to be added for Zarxio and Curosurf. A Serial# either needs to be added or generated for Retacrit.
3. Pharma Tech initiates a Barcoded intelligent label print to the Zebra printer.
4. Label is scanned by the Zebra Scanner.
5. Label is applied to the drug or attached to the outside of a bag that will contain the drug.

Work Center – Medi-Cart:

1. Drug is selected from Medi-Cart. Barcoded intelligent label is scanned by the Zebra Scanner for compliance and then scanned to initiate move to the next location.

Work Center – Pyxis:

2. Drug is selected from Pyxis. Barcoded intelligent label is scanned by the Zebra Scanner for compliance and then scanned to initiate move to the next location. Software operation of Barcoded intelligent label scanning: Upon receiving a Barcoded intelligent label scan, the Rymedi's Zebra Scanner API endpoint receives the scanned data structure, builds out the complete data fields and writes the record to the blockchain and the Rymedi Tracking database table.

A Dashboard UI will be developed to display current state of the tracked drugs and their historical tracking events. The Dashboard can be accessed from any internet connected device by addressing a specific URL with appropriate access credentials.

Saline Drone Delivery – Tracking

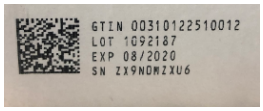
Initial testing with Saline Drone delivery was initially planned for late 2019 and later moved to Q2 of 2020. The initial drone route being from one building to another, less than a mile apart. The process to move saline via drone is similar process to 3 meds used at pharmacy with labels printed at the pharmacy and then scanned as they leave the pharmacy and into the drone box and scanned at second location upon arrival. A printer will be assigned to a work center in which the saline is scanned, Barcoded intelligent label is printed, and Barcoded intelligent label is scanned prior to packaging saline for Drone Delivery. At delivery and any additional movement of saline, Barcoded intelligent label is scanned for compliance.

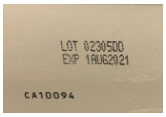
Barcoded intelligent label Print Software Process

- Scan Medication packaging label upon receipt of drug at Hospital Pharmacy

”GTIN": "05228200700532",
“Lot": "19R171",
"ExpirationDate"": “211231",
"SerialNumber": "NB1218P541309"

- Wake Medical (Zarxio, Curosurf, Retacrit, Drone Delivery – Saline)





<u>Barcoded intelligent label Print Software Process</u>

- Generate Label data structure and Barcode/QR Code and send to Savanna for Print

{"Quantity": "1",
"GTIN":"05228200700532",
“Lot":"19R171",
"ExpirationDate":"211231",
"SerialNumber":“NB1218P541309",
"Transaction":”**123456",}

- Print Label on Zebra ZT610 Printer stationed at Pharmacy Receiving Work Center
- Rymedi UI executing on TC52 Mobile Computer
  - Initial Data Capture
    - Scan/OCR medication labels
    - Generate Serial Number for Retacrit

- GTIN – 05015997010531
- Generate Label Data Structure
- Rymedi API initiates print to Savanna to print Zebra label

- Scan Zebra label
  - Savanna routes scan data to Rymedi API
  - Rymedi API writes scan records to database
  - Database records are hashed and written to blockchain
  - Blockchain TxID written to database

Software Users (loginID):

General Administration

Resource Mgmt (6000)

Wake Medical Hospital - WM

Dashboard Admin (6000WM)

Item Receiving (6002WM)

Drone Shipping (6003WM)

Drone Receiving (6004WM)

Indiana University Hospital - IU

Dashboard Admin (6000IU)

Item Receiving (6002IU)

Rymedi Software Work Flow:

Product is received from pharma distributer at hospital's Pharmacy Receiving work center. Product is scanned to obtain the GS1 identifiers (GTIN, Lot, ExpDate, Serial Number). Zebra label is printed for tracking. As product moves between work centers, Zebra label is scanned to ensure temperature compliance.

Medications being Tracked

Wake Medical Hospital (WM)

Retacrit (00878211080902)

Curosurf (00310122510012)

Zarxio (00361314318015)

Saline (xxxxxxxxxxxxxx)

Indiana University Hospital (IU)

Opdivo (00300033734133)
Keytruda (00300063026017)

Work Centers:

Wake Medical Hospital (WM)
Item Receiving (1)
Medi-Cart (1)
Pxyis Stations (4-6)
Drone Shipping (1)
Drone Receiving (1)

Indiana University Hospital (IU)
Item Receiving (1)
Patient Dispensing Stations

Operation of the FDA Pilot

Setup and Management of Work Centers and Zebra Devices
Resource Management (6000) – Work Centers are defined for the specific hospitals – Wake Medical Hospital & Indiana University Hospital. Each Zebra device (scanner, printer) is initially assigned to a Work Center.

Initial Receiving of the Drug at Hospital Pharmacy Receiving Work Center (WM & IU)
Item Receiving (6002WM & 6002IU) – Drugs are scanned to obtain GS1 identifiers. GS1 labels exist for Zarxio and Curosurf. Retacrit, Opdivo, and Keytruda will be scanned in the following manner – Barcode scan to obtain GTIN; OCR scan to obtain Lot and ExpDate; Serial Number to be auto-generated on Zebra Label Print. User will have ability to correct any failed scan by manually entering data. User initiates Zebra label "Print". One Zebra label is printed with the exception of Retacrit in which 10 labels are printed since the Retacrit package contains 10 vials of the drug. Once the Zebra label(s) are printed, a Zebra scan is required to validate the label(s) was printed properly.

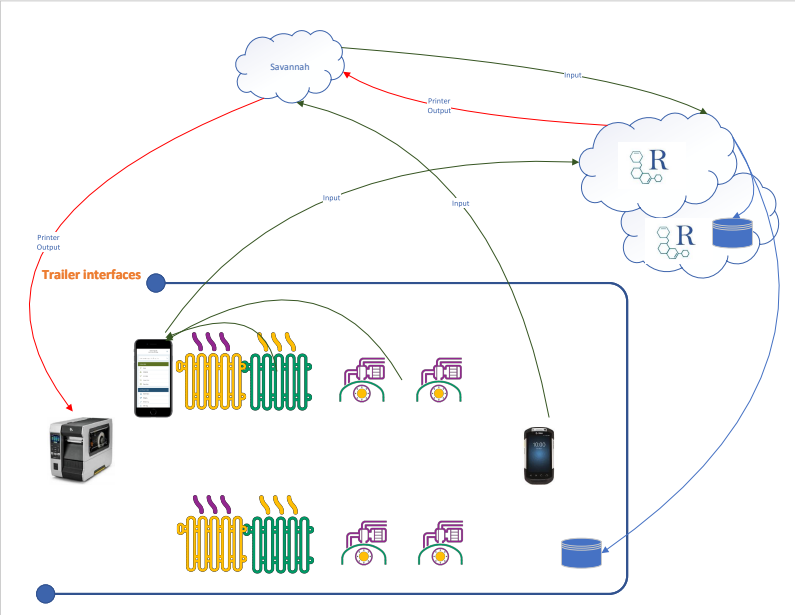
Drone Shipping & Receiving (WM)
Pre-printed Zebra labels will be available at the Drone Shipping Work Center to attach or include in the Saline package being transported by the Drone.

Drone Shipping (6003WM) – Tote ID tag is scanned along with a pre-printed Zebra label. If selected Zebra label scan fails, discard label and select new one. Use Tote ID tag to

secure the Package for shipment. Package is shipped by selecting the appropriate Drone Receiving Work Center.
Drone Receiving (6004WM) – Package is received at the Drone Station and the Tote ID tag is scanned. Package is opened and Zebra label is scanned. Confirm receipt of package shipped as maintaining temperature compliance or identify Damaged if temperature compliance has been violated.

Dashboard for Displaying Current Drug Tracking Status (WM & IU)
Administrator (6000WM, 6000IU) – User Interface provides access all the data obtained through the Zebra label scanning of the drugs as they move through the Work Centers. Status of each drug's inventory is displayed in addition to the status of an individual drug selected by serial number. User Interface also allows Zebra devices to be moved to different Work Centers.

Zebra Label Scanning



Each scan of a Zebra label will update the item (Drug Tracking) database and will write a transaction to the blockchain. The database record will include the timestamp, scanner device ID, physical location, GS1 label details and the temperature sensor indicator. Labels are printed via the Rymedi software which communicates directly with Zebra Savanna, which is a data services platform for aggregating and analyzing data for Zebra devices.

The Importance of Temperature Management

Proper handling of temperature sensitive medication is paramount to ensure drug efficacy and quality for patients. By ensuring that the drug manufacturer's specifications are met throughout the transport, storage, and administration of each particular medication, this adherence to quality control provides further assurance that the patient is receiving medication that has been properly handled throughout the supply chain. Furthermore, unit-level monitoring of the thermal disposition of medication can help prevent instances of waste where the proper thermal handling of the drug could not be otherwise determined. In addition, this technology can allow healthcare workers to make more informed decisions with respect to stock management of thermally sensitive medication.

Evaluation of OneScan App on Zebra TC52 Scanner Using Rymedi FDA Pilot Media

In advance of the Rymedi FDA Pilot, 2D barcodes thermally printed on a roll of label media with embedded 40°C threshold temperature sensors were used to evaluate the preliminary performance of the OneScan app downloaded onto a Zebra TC52 scanner. Results demonstrate proper performance and function of the OneScan app on Zebra TC52 scanner. When scanned before and after heat exposure, all individual 2D barcode sensors were appropriately read, and all required data associated with each scan was successfully transmitted from the OneScan app to the cloud, appearing in the OneScan web portal database.

Background and Scope

In preparation for the Rymedi FDA Pilot, 2D barcodes were thermally printed using a ZT610 thermal printer at Zebra, 6200 thermal transfer ribbon (as identified in the *Rymedi Ribbon Testing Results and Observations* report), and approved OneScan label media following the procedure detailed in *Rymedi Label Template – Quick Start Guide and Troubleshooting.* The resulting 2D barcode label media then were scanned using Zebra TC52 scanner with OneScan App v0.9.31 to assess:

- proper scanning and interpretation of 2D barcode sensor status on the label media using Zebra TC52

- complete transfer of 2D barcode data from the OneScan App on the TC52 to the OneScan web portal database. Data to include the following:

  o Date and time of 2D barcode reading
  o GTIN Product manufacturer and identifier
  o Manufacturer lot number and expiration date
  o Serial number of scanner device and product scanned
  o Longitude and Latitude
  o Status of 2D barcode indicator (i.e., “Sensor triggered”) o Full 2D Barcode string

  References (shown in Appendix)
  • OneScan Label Media Inspection Report for Rymedi FDA Pilot Media (26x26, 14dpm) • Rymedi Ribbon Testing Results and Observations
  • Use Instructions for the OneScan App for Rymedi Pilot
  • Rymedi Label Template – Quick Start Guide and Troubleshooting

Experimental Procedure
A roll of Rymedi FDA Pilot Media (26x26,14dpm) was manufactured and inspected for temperature response and dimensional conformance at Zebra. 2D barcodes were successfully thermally printed on the roll media using the ZT610 printer following the procedure outlined in *Rymedi Label Template – Quick Start Guide and Troubleshooting.*

Thirty (30) finished 2D barcode labels were peeled from the roll and placed on a PET sheet for assessment using a Zebra TC52 scanner with OneScan App v0.9.31. Initial testing (before heat exposure) was done at 21.5°C (room temperature) under controlled conditions using a stand (to keep the 2D barcode reading distance constant) inside an enclosed light box to ensure consistent lighting conditions on flat barcodes. Each individual barcode label was scanned once using the TC52 scanner.

The same sheet of thirty (30) 2D barcode labels was then heated above the threshold temperature (inside an incubator at 56°C) for 10 seconds. After brief heat exposure above the threshold temperature, the embedded threshold temperature sensor visually changed color (from colorless to black) and each individual barcode label was again scanned using the TC52

scanner. Table 1 shows an example of the appearance of 2D barcode labels before and after heat exposure.

Initial Appearance- Before Heating	End Point Appearance – After Heating
	

Table 1. Images showing 2D barcode threshold temperature sensor color change (before and after heating)

Results

After using OneScan v0.9.31 on the TC52 to scan each individual 2D barcode, all data was reviewed in the OneScan web portal database. The data in Table 2 was confirmed to be the same for each scan.

GTIN	Manufacturer Lot Number	Manufacturer Expiration Date	Serial Number of the Scanner Device	Longitude, Latitude	Full Barcode String
12345000102	123456	12/31/2021	579e694d99501629	40.82, -74.47	Yes

Table 2. Data from 2D barcode scans uploaded to the web portal database from the OneScan app on the TC52 scanner.

OneScan v0.9.31 on the TC52 was also able to accurately read all thirty (30) 2D barcodes tested before and after heat exposure. All the data collected from each scan (e.g., sensor status, scan date and time, 2D barcode serial numbers) was successfully uploaded to the OneScan web portal database. (shown in Table 3).

Serial #	2D Barcode Scans- Before Heating			2D Barcode Scans - After Heating		
	Scan Date	Sensor Triggered	Overall Status	Scan Date	Sensor Triggered	Overall Status
1003	8/27/2019 15:11	No	✓	8/27/2019 15:42	Yes	×
1019	8/27/2019 15:11	No	✓	8/27/2019 15:42	Yes	×
1020	8/27/2019 15:11	No	✓	8/27/2019 15:42	Yes	×
1021	8/27/2019 15:11	No	✓	8/27/2019 15:42	Yes	×
1029	8/27/2019 15:11	No	✓	8/27/2019 15:42	Yes	×
1033	8/27/2019 15:11	No	✓	8/27/2019 15:42	Yes	×
1034	8/27/2019 15:11	No	✓	8/27/2019 15:42	Yes	×
1035	8/27/2019 15:12	No	✓	8/27/2019 15:42	Yes	×
1037	8/27/2019 15:12	No	✓	8/27/2019 15:43	Yes	×
1038	8/27/2019 15:12	No	✓	8/27/2019 15:43	Yes	×
1004	8/27/2019 15:12	No	✓	8/27/2019 15:43	Yes	×
1039	8/27/2019 15:12	No	✓	8/27/2019 15:43	Yes	×
1040	8/27/2019 15:12	No	✓	8/27/2019 15:43	Yes	×
1042	8/27/2019 15:12	No	✓	8/27/2019 15:43	Yes	×
1044	8/27/2019 15:12	No	✓	8/27/2019 15:43	Yes	×
1060	8/27/2019 15:12	No	✓	8/27/2019 15:43	Yes	×
1061	8/27/2019 15:12	No	✓	8/27/2019 15:43	Yes	×
1062	8/27/2019 15:12	No	✓	8/27/2019 15:43	Yes	×
1022	8/27/2019 15:13	No	✓	8/27/2019 15:43	Yes	×
1015	8/27/2019 15:13	No	✓	8/27/2019 15:43	Yes	×
1005	8/27/2019 15:13	No	✓	8/27/2019 15:43	Yes	×
1024	8/27/2019 15:13	No	✓	8/27/2019 15:43	Yes	×
1036	8/27/2019 15:13	No	✓	8/27/2019 15:43	Yes	×
1048	8/27/2019 15:13	No	✓	8/27/2019 15:43	Yes	×
1049	8/27/2019 15:13	No	✓	8/27/2019 15:44	Yes	×
1050	8/27/2019 15:13	No	✓	8/27/2019 15:44	Yes	×
1052	8/27/2019 15:13	No	✓	8/27/2019 15:44	Yes	×
1053	8/27/2019 15:13	No	✓	8/27/2019 15:44	Yes	×
1054	8/27/2019 15:13	No	✓	8/27/2019 15:45	Yes	×
1058	8/27/2019 15:13	No	✓	8/27/2019 15:45	Yes	×
Overall Results: Prior to heat exposure, all thirty (30) 2D Barcodes show correct sensor status (Not Triggered)				Overall Results: After to heat exposure above the threshold temperature, all thirty (30) 2D Barcodes show correct sensor status (Triggered)		

Table 3. Summary data from OneScan web portal database showing results of 2D barcodes with individual serial numbers scanned before and after the threshold sensor was exposed to heat. The green checks indicate that the 2D barcode temperature sensor has not triggered, while a red "x" indicates that it has been triggered.

Conclusion

This preliminary study confirms that the materials to be used for the Rymedi FDA pilot (i.e., label media, Zebra ZT610 printer, OneScan app, Zebra TC52 scanner) work together to provide results that can be accurately and easily interpreted by the end user, facilitating the overall success of the FDA pilot. Results demonstrate the proper function of the following:

• Rymedi pilot media (with embedded 40°C threshold temperature sensor) used for thermally printing 2D barcodes

- OneScan app used on Zebra TC52 scanner
- Complete transfer of 2D barcode data from the OneScan app to the OneScan web portal

Attachments

Appendix	Reference Document Title
A	OneScan Label Media Inspection Report for Rymedi FDA Pilot Media (26x26, 14dpm)
B	Rymedi Pilot Label Media Template – Quick Start Guide and Troubleshooting
C	Rymedi Ribbon Testing Results and Observations
D	Use Instructions for the OneScan App on Zebra TC52 for Rymedi FDA Pilot

Appendix A

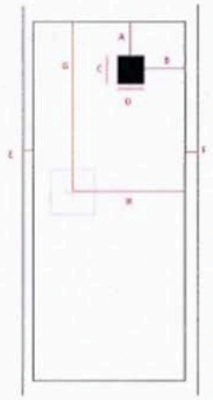
OneScan Label Media Inspection Report for Rymedi FDA Pilot Media (26x26, 14dpm)

Temptime
Improving Global Health

INSPECTION REPORT

Part Description	Rymedi FDA Pilot Media (26x26, 14dpm)			
Lot ID	19R220/1 (Lanes 1-5)			
Date of Manufacture	Printing	2019-08-08	Slitting	2019-08-09
Artwork Code	Rymedi FDA Pilot 2019_v2.0			

Test	Test Method	Expected Result	Result	
Appearance	Visual assessment	• Free of any foreign object debris • Uniform coating	☑ Clean ☑ Uniform	
Temperature Response Testing	WHO/PQS/ E006/IN04.VP.1 Test 3, Steps 2 through 3	≈ 40°C	Average: Minimum: Maximum:	40.5 40.0 40.5
A: Dimensional: Machine Direction (MD), Top of label edge to top of print area	Dino-Lite Digital Microscope; DinoCapture 2.0 v1.5.22.A	5.6 mm	Average: Minimum: Maximum:	5.0 4.8 5.3
B: Dimensional: Cross-web Direction, Right label edge to right edge of print area	Dino-Lite Digital Microscope; DinoCapture 2.0 v1.5.22.A	5.6 mm	Average: Minimum: Maximum:	6.1 5.8 6.3
C: Dimensional: Machine Direction, Top of print area to bottom of print area	Dino-Lite Digital Microscope; DinoCapture 2.0 v1.5.22.A	3.2 mm	Average: Minimum: Maximum:	3.1 3.0 3.2
D: Dimensional: Cross-web Direction, Side of print area to other side of print area	Dino-Lite Digital Microscope; DinoCapture 2.0 v1.5.22.A	3.2 mm	Average: Minimum: Maximum:	3.1 2.9 3.2
E: Left liner edge to left label edge	Dino-Lite Digital Microscope; DinoCapture 2.0 v1.5.22.A	1.5 mm	Average: Minimum: Maximum:	1.6 1.0 1.9
F: Right liner edge to right label edge	Dino-Lite Digital Microscope; DinoCapture 2.0 v1.5.22.A	1.5 mm	Average: Minimum: Maximum:	1.6 1.0 2.2
G: Center of Crosshair to top label edge	Dino-Lite Digital Microscope; DinoCapture 2.0 v1.5.22.A	22.5 mm	Average: Minimum: Maximum:	22.1 21.8 22.2
H: Center of crosshair to right label edge	Dino-Lite Digital Microscope; DinoCapture 2.0 v1.5.22.A	15.2 mm	Average: Minimum: Maximum:	15.5 15.2 15.8



A: MD, Top of label edge to top of print area
B: CW, Right label edge to right edge of print area
C: MD, Top of print area to bottom of print area
D: CW, Side of print area to other side of print area
E: Left liner edge to left label edge
F: Right liner edge to right label edge
G: Center of crosshair to top label edge
H: Center of crosshair to right label edge

Quality Personnel - Name	Quality Personnel - Signature	Date
Madeline Acevedo	Madeline Acevedo	2019-08-13
Project Rep. Reviewer - Name	Project Rep. Reviewer - Signature	Date
Nick Maas		2019-08-13

OneScan Label Media Template v0.2

Appendix B

Rymedi Pilot Label Media Template – Quick Start Guide and Troubleshooting

1. Purpose:

1.1. This guide defines the printer configuration settings and instructions for Rymedi pilot label media set up that can be followed by a first-time user in order to thermal print labels

2. Background and Scope:

2.1. Rolls of labels having temperature sensitive ink (e.g., Rymedi pilot label media) will be shipped to various facilities to be thermal printed using a ZT610 printer

2. 2.2. Personnel will load the Zebra Designer file onto a computer and thermally print its contents onto the labels
3. 2.3. Personnel will use a TC52 as a scanner to read barcode data in real time
4. 2.4. The overall objective of this is to determine if the labels (i.e. the product) have been

exposed above its threshold temperature

3. Label Characteristics

The roll contains sample labels having a small temperature sensitive region and is 5 modules by 5 modules located 6.5,6.5 thru 11.5,11.5. Refer to the diagram below.

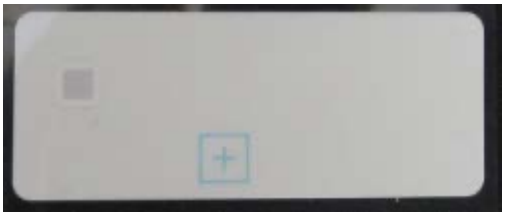


Figure 1. Rymedi pilot label media appearance prior to printing Zebra Designer contents

The roll will be placed into the ZT610 printer (follow the directional diagrams on the printer) in order to print a 2D data matrix barcode over the temperature sensitive region

of each label. It is very important to ensure that the roll is placed correctly into the printer as this will affect alignment of the 2D barcode on the sample label.

When the roll is correctly aligned, a 2D barcode will print in register and readings can be properly obtained. The alignment can be checked by verifying the placement of a printed crosshair relative to the preprinted crosshair. If the alignment of the roll is out of register, labels may have the following appearance and will produce invalid results. Refer to the diagrams below for examples of correct and incorrect placement of the crosshairs, and therefore the 2D barcodes on the label.

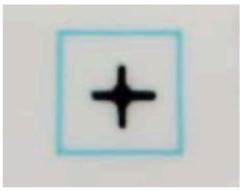


Figure 2. Proper placement of the target

Figure 3. Proper placement of the target

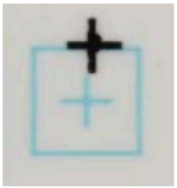


Figure 4. Improper placement of the target

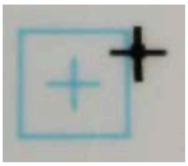


Figure 5. Improper placement of the target

4. Materials / Equipment:

4.1. Roll of Rymedi pilot label media (e.g., labels with temperature sensitive ink) 4.2. Roll of 6200 thermal transfer ribbon
4.3. ZT610 printer (600dpi)
4.4. Zebra Designer software Version 2.5.0

4.5. Laptop computer with Windows 10 operating system

5. Procedure:

5.1. Receipt and storage of Rymedi Pilot Label Media:
5.1.1. Sample rolls containing the temperature sensitive element are always active and

must be stored under typical room temperature conditions not exceeding 30°C prior to use.

5.2. Optimizing ZT610 Printer Settings
5.2.1. Open Zebra Designer software file on computer 5.2.2. Set printer settings

5.2.2.1.Darkness: 20
5.2.2.2.Speed: 2 inches per second (ips)

5.3. Printing 2D Barcodes on Rymedi Pilot Label Media Using Loaded Template

5.3.1. Remove Rymedi pilot label media sample rolls from room temperature storage conditions (at or below 30°C).

5.3.2. Place sample roll of label media on the printer by following the directional diagrams located on the printer

5.3.3. Follow the directional diagrams to correctly set up Zebra 6200 ribbon

5.3.4. When printing, ensure temperature sensor is located within the 2D barcode

6. Troubleshooting Steps

6.1. If personnel are experiencing difficulties with printing, attempt the following:

6.1.1. Ensure printer settings are correct
6.1.2. Ensure correct printer is selected in Label Setup (ZT610 600dpi)
6.1.3. Ensure sensor is under labels
6.1.4. Ensure 1 toggle is directly placed over the label media
6.1.4.1.Adjust pressure of toggle up/down, if challenges persist

6.1.5. Ensure labels remain aligned on roll during printing

6.1.6. Manually calibrate the printer by following this pathway on the printer: Home Menu -> Sensors -> Scroll to Media/Ribbon Calibration -> Follow directions to calibrate

Appendix C

Rymedi Ribbon Testing Results and Observations

1.1. The purpose of this testing is to determine what thermal transfer ribbon works best with the Rymedi pilot label media. The optimal darkness at the speed of 2 ips for each ribbon is determined as well.

2. Procedure:

2.1. Optimizing Print Darkness and Legibility:

2.1.1. Obtained a ZT610 600 dpi printer, label media, and 4 Zebra thermal transfer ribbons: 3200, 5095, 6200, and 5100.

2.1.2. Each ribbon was loaded into the printer and printed at varying darknesses, all at 2 ips.

2.1.3. The optimal darkness for each ribbon was determined based on the legibility of the text printed and the clarity of the barcode.

2.2. Testing for Durability of Each Ribbon at its Optimal Darkness

2.2.1. Each label was scratch tested, dry rubbed, and tape tested for ink adhesion and overall durability.

2.2.1.1. Scratch Test:

2.2.1.1.1. The wooden end of a cotton swab is rubbed across the print of the label 50X times, where one back-and-forth pass counts as one rub. 2.2.1.2. Dry Rub

2.2.1.2.1. The cotton end of a cotton swab is rubbed across the print of the label 50X times, where one back-and-forth pass counts as one rub.

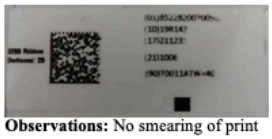
2.2.1.3. Tape Test

2.2.1.3.1. A piece of tape is placed over the label text and rubbed to make sure it is securely affixed to the surface.

2.2.1.3.2. Remove the tape with a brisk motion. Check the tape for removal of the text.

3. Results:

3.1. The table below shows the results of the durability testing at each ribbon's optimal

Test	3200 (25 Darkness)	5095 (15 Darkness)	6200 (20 Darkness)	5100 (25 Darkness)
Scratch	 **Observations:** immediately scratched off	 **Observations:** Little to no removal of print	 **Observations:** No visible removal of print	 **Observations:** No visible removal of print
Dry Rub	 **Observations:** Removal of print	 **Observations:** No removal	 **Observations:** No removal	 **Observations:** No removal
Tape test	 **Observations:** Some residue left on tape	 **Observations:** Light residue left on tape	 **Observations:** Light residue left on tape	 **Observations:** Light residue left on tape
IPA	 **Observations:** No smearing of print	 **Observations:** No smearing of print	 **Observations:** No smearing of print	 **Observations:** No smearing of print

4. Conclusion:

4.1. The most durable and most legible ribbon was determined to be the 6200 ribbon printed at 2 ips with darkness 20.

Appendix D

Use Instructions for the OneScan App on Zebra TC52 for Rymedi FDA Pilot

Starting Phone:

The Zebra TC52 as sent is turned off. To turn it on, press and hold the power button, located on the top right corner of the device. This will bring you to the “lock screen.”

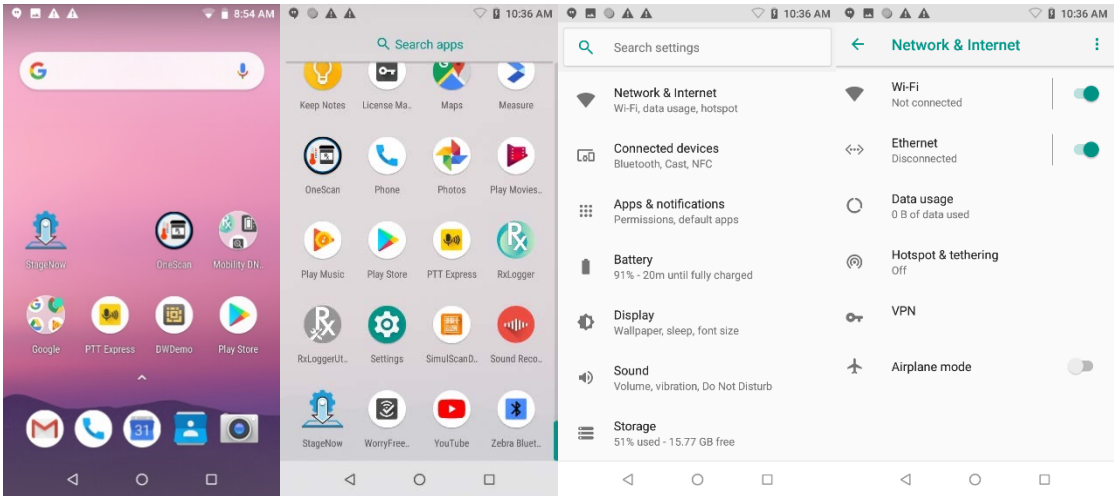
Place finger on lock icon on bottom center of lock screen. Swipe up from the lock icon to bring up the “home screen.”

Connecting to Wi-Fi:

You do not have to be connected to Wi-Fi when using the OneScan app. However, you must be connected to Wi-Fi when logging into the OneScan app for the first time. The TC52 will store the data from each reading and upload it to the online OneScan app database once it is connected to Wi-Fi again.

To get started connecting to Wi-Fi, begin by locating the settings icon. To do this, go to the home screen and swipe up from the bottom. This will open the “app drawer.” Scroll through the app drawer and locate the settings icon, which is a cog/gear. Tap the settings icon. Tap on “Network and Connection.” Then, make sure the slider, located on the right side of “Wi-Fi,” is positioned to the right. To check, below Wi-Fi, it should say “Not Connected.” If it says “Off,” the slider is not in the appropriate position. Tap “Wi-Fi.”

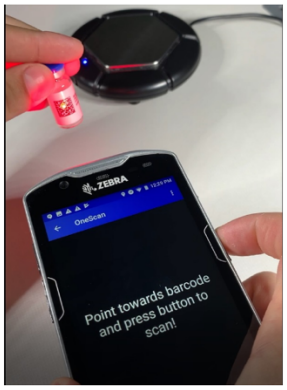
Then, tap the network you want to connect to. If prompted, enter the password for the Wi-Fi network, then press “Connect.” If not prompted for a password, just press “Connect.” After the Wi-Fi is connected, it will say the name of the network you are connected to below the word “Wi- Fi.”



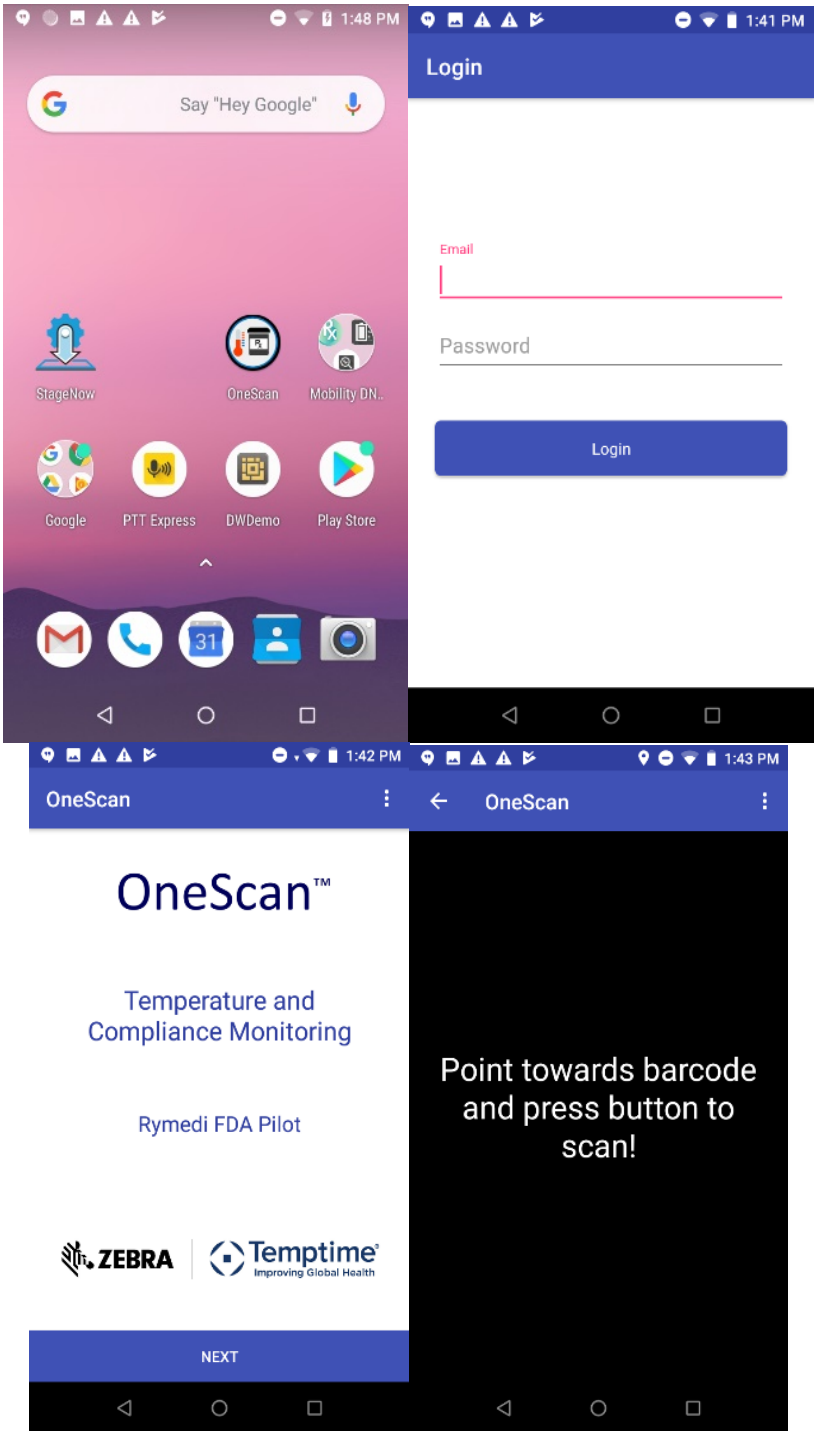
Launching and using the OneScan App:

On the Home Screen, locate the OneScan App. Tap the OneScan App to launch. Remember, Wi-Fi must be connected when signing into the OneScan app. Once launched, you will be prompted to log in. Enter the appropriate email and password and press “Login.” Once you are logged in, you will remain logged in unless you press “Log Out.” Pressing “Login” will bring you to the app’s opening screen. Tap “Next” on the bottom of the screen. This will bring you to a screen that says, “Point towards barcode and press button to scan!”

Scanning on the TC52 is accomplished by pointing the imager towards the barcode. The imager is located on the top of the device. To use the imager, press the scan button, which is found on both sides of the phone.

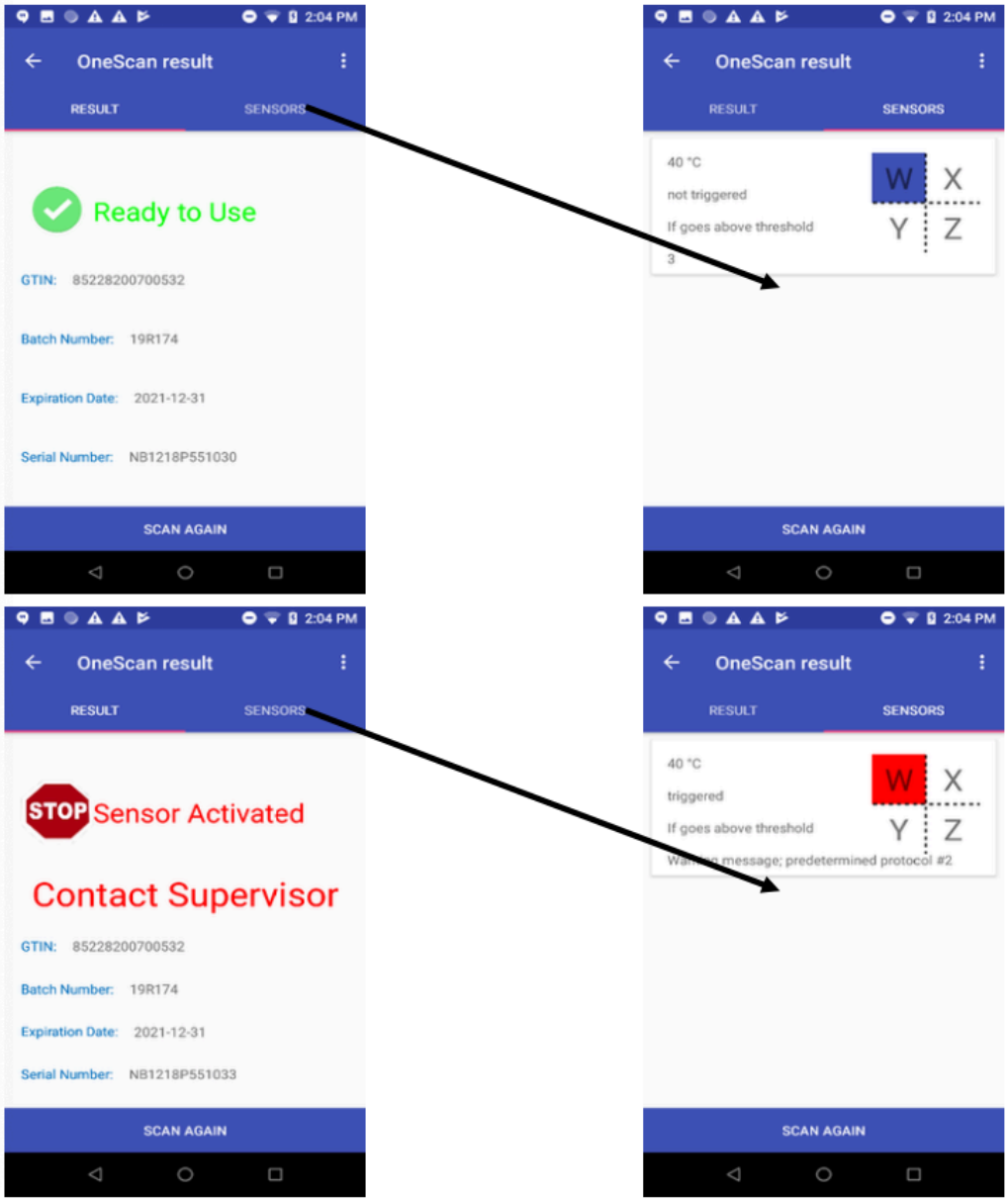


Point the imager towards the barcode. Then, press the side button to scan. A red light will appear atop the barcode as the device reads it. There is also an LED aimer that appears as a circle. Align this circle on the barcode to read.


1:48 PM
Say "Hey Google"
StageNow
OneScan
Mobility DN..
Google
PTT Express
DWDemo
Play Store
1:41 PM
Login
Email
Password
Login
1:42 PM
OneScan
OneScan™
Temperature and Compliance Monitoring
Rymedi FDA Pilot
ZEBRA
Temptime
Improving Global Health
NEXT
1:43 PM
OneScan
Point towards barcode and press button to scan!

The device will automatically bring you to the OneScan Results screen. The two possible results are “Ready to Use” or “Sensor Activated.” More information can be seen by pressing the “Sensors” tab.

To scan additional barcodes, you can press “scan again” and use the side button to scan. You can also scan the additional barcodes by just pressing the side button again to scan a new barcode without pressing “scan again.”

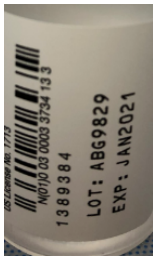


Indiana University

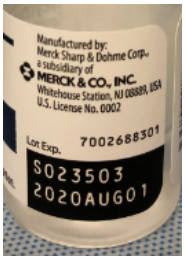
Rymedi – FDA Pilot : Indiana University Health Hospital

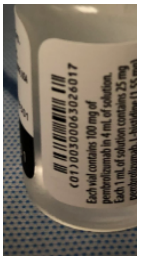
Medications Tracked

Opdivo

Keytruda





- Hospital Receives incoming Medication from Cardinal Health and stores in refrigerator.
  - Zebra “card” are stored with Medication
  - Rymedi Work Station present to perform Data Capture on initial receipt
    - Handler’s ID; PO Number from Invoice; Mfg or Cardinal as source

- Pharmacy Work Center requests Medication from Receiving
  - Medication shipped to Pharmacy Work Center
- Pharmacy Work Center (2) receives Medication from Receiving
  - Scan PO Number; Remove each item from box; Scan and gather or generate the necessary data (GTIN, Lot, ExpDate, SN-generate)
  - Print Zebra label
  - Scan Zebra label

- Medication order for Patient
  - Scans Zebra label
  - Medication (qty 2) mixed with Saline (unique identifier)
    - Auto generate new serial number for mixture
  - Print a new Zebra label for mixture; apply it to Saline bag
  - Mixture shipped to patient work center to dispense

- Patient Work Center
  - Scan the new Zebra label
  - Dispense to Patient

Pre-Printed Labels - Definition

- Generate Label data structure and Barcode/QR Code and send to Savanna for Print

{ "Quantity": "1",
"GTIN":"05228200700532",
“Lot":"19R171",
"ExpirationDate":"211231",
"SerialNumber":“NB1218P541309",
"Transaction":”**123456", }

Opdivo Label – Definition

- Scan Data from Medication Labelling

”GTIN": "05228200700532",
“Lot": "19R171",
"ExpirationDate"": “211231",
"SerialNumber": "NB1218P541309"

- Generate Label data structure and Barcode/QR Code and send to Savanna for Print

{"Quantity": "1",
"GTIN":"05228200700532",
“Lot":"19R171",
"ExpirationDate":"211231",
"SerialNumber":“NB1218P541309",
"Transaction":”**123456", }

Keytruda Label – Definition

- Scan Data from Medication Labelling

”GTIN": "05228200700532",
“Lot": "19R171",
"ExpirationDate"": “211231",
"SerialNumber": "NB1218P541309"

- Generate Label data structure and Barcode/QR Code and send to Savanna for Print

{ "Quantity": "1",
"GTIN":"05228200700532",
“Lot":"19R171",
"ExpirationDate":"211231",
"SerialNumber":“NB1218P541309",
"Transaction":”**123456",}

Opdivo Mixture Label – Definition

- Scan Data from Medication Labelling

”GTIN": "05228200700532",
“Lot": "19R171",
"ExpirationDate"": “211231",
"SerialNumber": "NB1218P541309"

- Generate Label data structure and Barcode/QR Code and send to Savanna for Print

{ "Quantity": "1",
"GTIN":"05228200700532",
“Lot":"19R171",
"ExpirationDate":"211231",

"SerialNumber":“NB1218P541309",
"Transaction":”**123456", }

Keytruda Mixture Label – Definition

- Scan Data from Medication Labelling

”GTIN": "05228200700532",
“Lot": "19R171",
"ExpirationDate"": “211231",
"SerialNumber": "NB1218P541309"

- Generate Label data structure and Barcode/QR Code and send to Savanna for Print

{"Quantity": "1",
"GTIN":"05228200700532",
“Lot":"19R171",
"ExpirationDate":"211231",
"SerialNumber":“NB1218P541309",
"Transaction":”**123456",}

Research Methods

Products Tracked by Pilot Location
Indiana University Health

- Opdivo (nivolumab), Bristol-Myers Squibb
- Keytruda (pembrolizumab), Merck

WakeMed Health

- Retacrit (epoetin alfa-epbx), Pfizer
- Zarxio (filgrastim-sndz Injection), Sandoz/Novartis
- Curosurf (poractant alfa), Chiesi

- Saline solution – drone delivery overlapping with FAA drone pilot

Activities

Medications selected for tacking, why they were chosen

September Key Accomplishments

- Technology integration completed between Rymedi software platform and Zebra sensors, scanners and cloud platform.
- Medicine selection with health system pharmacy leadership.
- Internal medicine transfer scope defined with health system leadership.

Issues/Challenges/Help Needed

- Health systems are cautious to impose additional activities on staff, especially in clinical settings
- Gaps in legacy tracking systems
- Operationalization within the health system organization of data value generated

October Key Accomplishments

- Walkthroughs of pharmacy and clinical care workflows with health system leaders.
- Design of workflow appropriate procedures for scanning and tracking of medicines.
- Sourcing and placement of labeling and scanning equipment.

Issues/Challenges/Help Needed

- Health systems are cautious to impose additional activities on staff, especially in clinical settings
- Gaps in legacy tracking systems
- Operationalization within the health system organization of data value generated

November Key Accomplishments

- Re-developed the User Interface (UI) after IUHealth and WakeMed walk-through and process mapping.
- Preparation of training materials for hospital system staff.

- Updated system integration capabilities to increase hospital ease-of-use and deployment efficiency.
- Equipment and software integration with current workflows and software systems.
- Monthly consortium team space and shared learnings conference calls.

Issues/Challenges/Help Needed

- Health systems are cautious to impose additional activities on staff, especially in clinical settings
- Gaps in legacy tracking systems
- Operationalization within the health system organization of data value generated

<u>December Key Accomplishments</u>

- Further updated system integration capabilities to increase hospital ease-of-use and deployment efficiency.
- Design of equipment and software integration with current workflows and software systems.
- Preparation of training materials for hospital system staff.

Issues/Challenges/Help Needed

- Health systems are cautious to impose additional activities on staff, especially in clinical settings
- Gaps in legacy tracking systems
- Operationalization within the health system organization of data value generated

<u>January Key Accomplishments</u>

- Equipment and software integration with current workflows and software systems.
- Initial training for hospital system staff.
- Initiated monthly consortium shared learnings conference calls.
- Alignment meeting with Indiana University Health leadership reveals significant delays and hesitation due to large internal changes that conflict with resource allocations to pilot: delayed large ERP implementation, new CIO, new Chief Pharmacy Officer. Status of continuation with pilot remains uncertain.

Issues/Challenges/Help Needed

- Health systems are cautious to impose additional activities on staff, especially in clinical settings
- Gaps in legacy tracking systems
- Operationalization within the health system organization of data value generated

Findings

The Promise of QMS-RWE Integration for Learning Health Systems

The Consortium solution of tracking of both products and processes exemplifies the integration of QMS and RWE systems and value propositions. The integration of Rymedi and Zebra technologies with advanced monitoring and tracking capabilities, as well as blockchain-enabled HIPAA/GDPR-compliant data transfers and management, provides healthcare supply, practice and research a variety of different value propositions: from improved specialty medicine quality control and operational efficiency improvements, to R&D streamlining and more agile standards compliance. Healthcare and pharmaceutical executives consulted throughout the project uniformly praised the ambition and rationality behind the solution design.

Technical integration across Rymedi and Zebra technology platforms took work and was well executed. As anticipated in the research design, the challenges to deployment and sustainable improvements to patient health ultimately lay in change management across organizations and divisions within organizations. The following findings detail lessons learned about the change management required to leverage the promise of QMS-RWE integrated technology systems. Those findings will be central to subsequent development of QMS-RWE integrated offerings, from UI design and on-boarding, to workflow integration and customer contracting. Technology solutions that promise improved health languish in the experimental sandbox quite often, failing to consider the full range of issues required for sustainable adoption in healthcare systems. The goals and findings of this pilot are geared towards taking steps to enable the integration of next-generation tracking technologies into the complex fabric of healthcare supply, practice and research.

Challenges in Adoption of Quality Tracking to Patient Use

While digital tracking in the pilot was indefinitely delayed by COVID-19 responses at the partner hospitals, collaborative solution design and implementation across the pilot period presented a variety of important findings for future implementations of high visibility QMS-RWE systems across healthcare systems for both streamlined DSCSA compliance and quality management and medical value above the regulatory standards required. Those challenges fall into several categories: workflow integration; interoperability; business case definition; administrative and organizational structure and responsibilities; permissions management and data rights; and change management for medication manufacturers and trading partners.

Workflow Integration

One of the key lessons from early EHR system deployments across healthcare systems between 2005 and 2015 involved the need for product feature and workflow integration design to be clinician-centered. Clinician-centered features and integration into workflows should avoid imposing additional burdens, and ideally generate point-of-care value that the clinician and patient can appreciate as they shift to new modes of clinical interaction and clinic-specific administrative processes. Leading EHR systems evolved from platforms focused on billing and reimbursement, adding clinical record features over time. Early system-wide deployments across large healthcare systems between 2005 and 2015 are rampant with stories of staff push-back and user errors due to the lack of clinician-centered feature design and workflow integration.

Therefore, one of the key pilot elements was to test approaches to clinical workflow integration. A key finding is that workflow integration approaches at various stages of activity are related to other technical and organizational adoption challenges addressed below. For example, where existing workflows involve data capture via label scanning or human entry into inventory or EHR systems, direct interoperability would obviate the need for otherwise redundant data capture activity. Insofar as workflow integration solutions involving

technologically mediated automated data capture via API integrations or IoT sensors increase deployment costs, the business case for greater supply quality visibility for a hospital directly affects hospital price tolerance for the simplest workflow integrations.

Workflow integration issues in the pilot arose around both hospital pharmacy operations and clinical activities. Pharmacy operations staff at both hospital systems were willing to work with the Consortium in adding data collection into workflows at points where it synchronized with documentation activities they already perform or points in their workflows where items are managed. There is wide variation in how pharmacy operations across hospital systems operate. Some processes lend themselves to lower-tech solutions for monitoring portions of the distribution chain than others. Standards for adapting technology platform workflow integrations to leverage these and have validation via tracking software need to be developed in order to make the modular adaptation of system implementation optimal for local organizational workflows while also satisfying process quality controls and monitoring.

One example of such a workflow workaround was Indiana University's Cancer Center pharmacy's boxing of oncology medicines for transport from the hospital pharmacy center managing shipments and inventory to the Cancer Center at another location in the same hospital complex. Rather than integrate serialized treatment-specific temperature monitoring labels at higher cost, a lower-cost temperature monitoring card was inserted into the transport boxes taking medicines from the inventory management center to the Cancer Center's clinic pharmacy preparing patient treatments. Workflows involving the opening and documenting of the medicines from the box would include inspection of the temperature monitoring card. IF, the workflow continued, it would signal that the card showed no temperature thresholds of concern crossed. Were the card to show temperature risk, then those medicines would not proceed further in the workflow and an investigation would follow. However, integration of a smart temperature monitoring label at the point of manufacturing or packaging would obviate the need for such a work around and provide even greater reliability in temperature controls by writing relevant temperature history directly onto digital records per serialized product.

In clinical workflows, nursing staff leadership buy-in is crucial. At WakeMed, coordination between the Consortium and WakeMed pharmacy leadership realized the centrality of needing to educate nursing leadership about the pilot and involve staff in joint-solutioning through clinical workflow design and implementation late. The need to work through nursing hierarchies and coordination meeting calendars imposed another set of unanticipated delays.

An important component of clinical and pharmacy operations workflow integration is appropriate training to use the tracking system. Pilot training planning focused on a small cluster of staff at selected medicine administration sites. Specialized Zebra scanners for the pilot were to be located with the temperature-controlled medicine dispensing equipment. Clinic staff would scan the medicine before administering.

While intentionally not a core feature of the pilot design for purposes of scope management, an other important component of workflow integration success is meaningful user experience. Comparative research on digital health implementations worldwide repeatedly show that product designs that provide the clinical user of the tool some kind of concrete value from their point of view eases or even promotes adoption. In the case of health system medicine tracking, some user interface notifications that assure the healthcare staff that they are safeguarding patient health via their activities would enhance user appreciation and understanding of the purpose of the system.

Interoperability

Technical interoperability between IT systems is an important aspect of tracking system adoption across healthcare systems. Originally envisioned as a key aspect of the pilot scope, the partial tracking across healthcare systems of only selected medicines made healthcare system leadership hesitant to put effort into enabling interoperability between the Consortium solution and legacy IT systems already in place. As a result, the pilot design shifted to implementing new tracking capabilities in parallel to current systems, with a priority on tracking across gaps in the current systems. This priority setting was based on Consortium leadership experience integrating with legacy tracking, inventory and e-documentation systems, noting the technical feasibility wherever there is organizational will to interoperate.

The pilot design thus noted where shipping, inventory, order management, EHR systems gathered data in the workflow and de-prioritized these data capture points with an eye toward feasible interoperability with data captured by those systems at a future point in time. Technical interoperability is most often hampered by legacy system company incentives against enabling interoperability in order to maintain customer lock-in and prevent competitor encroachment on some of the business value generated by the legacy IT offering already in place. Beyond standard-setting calls for interoperable systems, contractual innovation may actually incentivize interoperability by enabling legacy systems owners to have shared stakes in the business value creation enabled by connected across systems, whether in the form of upfront or deferred fees, data revenue rights sharing, and other forms of shared upside.

Business Case Definition

More sophisticated medicine tracking leveraging emerging technologies has a cost. Sustainable scaling of higher quality tracking visibility thus requires a business case in terms of value creation for end customers in order to undergird commercial contracting for those services by companies that would then mobilize those emerging technologies in order to meet the demand. As a result, the Consortium pilot design focused on testing cases where higher quality tracking to the patient could result in forms of Real-World Evidence of commercial value to various parties.

As pilot coordination proceeded and ever greater focus turned on internal administrative leadership permissions and delays, the Real-World Evidence focus of the pilot diminished in priority for purposes of implementation. However, discussions with administrators about the ongoing value of such a system did hinge on Real-World Evidence value propositions. For example, the ability to mirror CRO-monitored Phase 4 trial visibility into medicine supply all the way to the patient has significant commercial value for pharmaceutical companies looking to leverage new FDA guidelines for the submission of Real-World Evidence to streamline and in some cases obviate the need for new phase 4 trials of already in-market drugs in off-label prescribed use. One way of monetizing such tracking on the part of healthcare systems would

be for pharmacy purchase discounts or rebates tied to data sharing for specified medicines. Another approach would involve payment for data in the future after clinically significant efficacy signals for off-label use are detected. These two approaches are not mutually exclusive.

Other elements of a hospital business case for deployment include improved operations efficiencies and reduced risk. With the rise in value-based contracting, hospital budgets would retain most of the value incurred with such derisking. With appropriate HIPAA compliance, 3rd party data sales provide additional revenue streams. Another possible indirect return may accompany greater hosting of clinical trials and government and foundation research funding as a result of improved ability to conduct high quality medical research as a partial result of the tracking infrastructure installed.

Administrative and Organizational Structure and Responsibilities

Another challenge in implementation results from siloed administrative responsibilities within hospital administrative structures. Improved tracking of medicine quality has implications across hospital organizations. However, decision-making concerning system integration, hardware and software procurement, medicine and medical supply purchasing and specification-setting, are fragmented across different entities within hospital organizations. When aligned, all of the pieces required for the sort of tracking visibility piloted are feasible. However, without total alignment, important gaps can limit or even block implementation of these kinds of systems.

An important factor when healthcare system decision-making required for the system piloted is the reality that different parts of a hospital system have priorities that do not always align. For example, early delays at Indiana University Health resulted from lack of a clear understanding of what would be entailed due to leadership focus on specific inventory management system upgrades preoccupying pharmacy operations. This very reasonable focus at the core of their responsibilities meant that most discussions of potential value propositions and their associated business case were filtered through the lens of what it might mean for their

inventory management upgrade efforts. The most concerning point was whether there would be distraction or even resource pulls that would in any way hamper their efforts on that front.

Permissions Management and Data Rights

By intentionally bracketing the collection of any personal health information to avoid HIPAA issues in the pilot, patient data permission management and data rights did not make up a key part of the pilot. However, HIPAA and even GDPR compliant systems and agreements will need to form part of any Real-World Evidence collecting system for heightened quality supply visibility.

Change Management for Medication Manufacturers and Trading Partners

Another challenge revolved around securing the involvement of medication manufacturers for quality tracking to the patient, above the standards required by 2023 implementation of the DSCSA. Several top 10 pharmaceutical companies expressed both enthusiasm at the vision of the pilot – one Vice President stating “this is the future; you are building the systems we will all need in the future” – and hesitation at the operational, liability and budgetary implications of such heightened visibility. The prospect of integrating supply tracking, pharmacovigilance, Real-World Evidence capture, and streamlining product development trials made systemic sense to pharmaceutical executives. However, short-term implications of greater visibility floated very practical concerns.

For example, one Vice President expressly worried about departmental operational budget impacts across a large company and change management efforts that would be required to retool a large organization to optimize the value gained from greater, and more reliable, supply visibility to the patient. Illustrating the budgetary and change management challenge: Current pharmacovigilance investigation budgets are based on average adverse event reporting rates. Digital streamlining of adverse event reporting would likely involve more report investigations

alongside other kinds of business value created by the heightened visibility. However, the company would face departmental resource constraints and the need to innovate how pharmacovigilance is managed in order to more efficiently respond to reports. The fact that other forms of value accrue to other units in the company (e.g. streamlined phase 4 approvals for new indications; more effective and efficient trial matching; improved bargaining position in value-based contracting; and reduced litigation and regulator liability) does not automatically solve these challenges for the pharmacovigilance department. Therefore, systemic change management across the organization would be required to fully take advantage of the virtues of heightened supply visibility to the patient.

Consortium Next Steps

The Consortium partners agree to continue coordinating to advance the intended scope of the pilot as resources and opportunities allow. While healthcare partners are preoccupied with COVID-19 response for the coming months, other partners will be developing and submitting funding proposals to various government agencies and private foundations to fund implementation of the original scope of the pilot. FDA staff managing the DSCSA Pilot Program will be updated on those efforts in coming months and findings from the full implementation (likely early 2021) will also be shared with FDA staff.

Conclusion

The FDA DSCSA Pilot Program offered a unique opportunity for partnerships to explore novel systems for complying with DSCSA requirements scheduled for 2023. Those systems involve the both technology and organizational deployment of such technology. As a result, the Consortium partners designed a pilot focused on leveraging emerging technologies and addressing points of potential quality monitoring vulnerability: specialty medicine transfers across large healthcare systems.

Rymedi and Zebra Technologies integrated their technology platforms in order to provide heightened quality monitoring visibility for temperature sensitive specialty medicines all the way to points of patient use. In parallel, Consortium partners planned, tested and iterated

workflow integration across complex clinical settings. The vision was to pilot a quality monitoring system that would integrate QMS and RWE value propositions in order to undergird a sustainable market for tracking systems providing that level of heightened visibility across the entirety of the value chain to patient use.

As a result, the Consortium identified a plethora of findings relevant to scalable commercial adoption of QMS-RWE integrated platforms in order to comply with DSCSA requirements and provide heightened levels of quality monitoring visibility. Those findings ultimately pose questions of adoption in terms of change management across organizational structure and practice. Forthcoming collaboration among Consortium partners will focus on integrating lessons learned into technology design, on-boarding and professional services models to help organizations retool to take advantage of significant patient impact enabled by emerging tracking technologies and the reuse of captured data for ongoing health system learning.

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