Development of the Respiratory Disease Dashboard for the Identification of New and Emerging Respiratory Pathogens

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Center (AFHSC-GEIS), asked the Johns Hopkins University Applied Physics Laboratory (APL) to develop a system that would allow for easier collection and visualization of respiratory disease data collected from their worldwide laboratories. As part of the Suite for Automated Global Electronic bioSurveillance (SAGES) program, APL developed the Respiratory Disease Dashboard (RDD) as a secure Internet-accessible database with user-friendly entry, analysis, and visualization of infectious disease laboratory data. Global AFHSC-GEIS laboratories, as well as other partner laboratories in various countries, use RDD to submit their weekly respiratory disease laboratory data to AFHSC-GEIS; RDD also serves as their central repository for these data.

INTRODUCTION

Since the 1940s, there has been a significant rise in occurrences of infectious diseases emerging in the human population for the first time.¹ Emerging respiratory diseases can spread rapidly and globally, especially with international air travel.² This rapid spread is primarily a result of the diseases' mode of transmission: infected people produce aerosolized droplets when coughing or sneezing, and others inhale those droplets or infect themselves by touching contaminated surfaces and then touching their eyes, mouths, or noses. Resistance to antibiotics³ and antivirals⁴ is increasing at a rate that threatens to limit the arsenal of drugs to fight respiratory diseases caused by bacteria and viruses, respectively. For viral respiratory diseases, vaccination is usually effective if it occurs at least 2 weeks before initial exposure and if the vaccine contains the same or similar antigens as the current circulating virus. Influenza viruses are of particular concern because their high rates of mutation mean that vaccines must be reformulated at least annually. Rapid identification of emerging respiratory diseases can provide longer lead times for the development of prevention strategies such as drugs and vaccines. The 2003 Severe Acute Respiratory Syndrome (SARS) outbreak and the 2009 H1N1 influenza pandemic emphasize the importance of improved global disease surveillance.

After the 2009 influenza pandemic, the Global Emerging Infections Surveillance and Response System, a division of the U.S. Armed Forces Health Surveillance Center (AFHSC-GEIS), asked the Johns Hopkins University Applied Physics Laboratory (APL) to develop a system that would allow for easier collection and visualization of respiratory disease data from U.S. DoD laboratories on five continents around the world. These laboratories, along with their partner network laboratories, support global surveillance for febrile and vector-borne infections, gastrointestinal infections, antimicrobial-resistant organisms, sexually transmitted infections, and respiratory infections. Among these surveillance objectives, monitoring influenza and other respiratory infections is a continuing priority for the AFHSC-GEIS network.^{5,6} The respiratory disease surveillance network coordinated by AFHSC-GEIS was dramatically expanded in 2008, processing more than 26,000 specimens from 491 collection sites in 75 countries.⁷ This expansion of respiratory disease surveillance within the AFHSC-GEIS partner network has underscored the need for a robust data management system to log, analyze, monitor, and visualize trends among respiratory pathogens. Management of data generated by such a diverse collection of partners requires a flexible system that is user friendly for a wide array of personnel. This article describes the Respiratory Disease Dashboard (RDD), an Internet-based system designed to serve as a central database for visualizing and tracking respiratory pathogens collected in the AFHSC-GEIS partner network. RDD makes significant contributions to the AFHSC-GEIS global respiratory disease surveillance network by strengthening the current portfolio of global public health surveillance systems, including targeting unique populations in resource-limited regions.

DEVELOPMENT AND FEATURES OF RDD

Original RDD Prototype

The initial web-based RDD application was built on a Grails stack. Grails (http://grails.org) is an open-source "coding-by-convention" web framework that allows programmers to develop web applications quickly. Coding by convention, also known as "convention over configuration," allows for rapid prototyping with maximum flexibility. Grails applications are mainly written in Groovy (http://groovy.codehaus.org),8 an open-source dynamic language for the Java Virtual Machine⁹ platform. To support users' requests for geographic information system (GIS) mapping capabilities, PostgreSQL (http://www.postgresql.org) geographic object-relational databases, along with the PostGIS (http://postgis.net) spatial extensions, were added on the server to support location-based SQL queries. OpenLayers (http://openlayers.org), a JavaScript mapping library, was added on the client to integrate mapping interface components. The front end was updated to use the open-source framework ExtJS (http://www.sencha. com/projects/extjs/) to provide interactive JavaScript widgets for additional flexibility with the interface.

The initial RDD prototype focused on rapidly communicating reports of novel respiratory pathogens from AFHSC-GEIS partner labs. In the case of influenza,

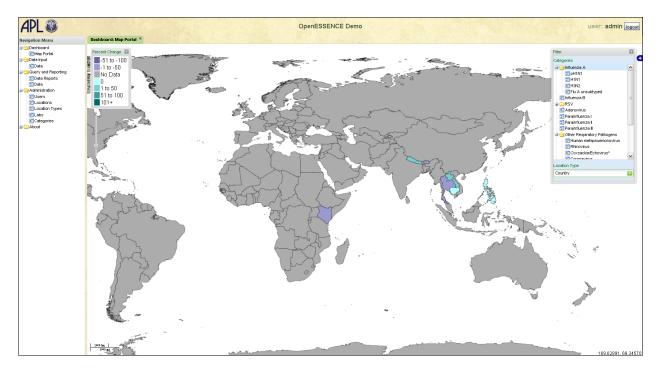


Figure 1. Original RDD map portal showing different countries highlighted by occurrences of different types of respiratory disease.

isolates are identified using nomenclature established by the International Committee on Taxonomy of Viruses.¹⁰ Two types of influenza viruses are known to cause seasonal epidemics in humans: influenza A and influenza B. Influenza A viruses are further divided into subtypes that are classified by their two proteins (antigens) called hemagglutinin (H) and neuraminidase (N). A particular influenza virus is then identified as H1N1, H3N2, etc. It was important for RDD to have an easy means of organizing and tracking changes in these subtypes, as their classification and tracking aids in vaccine development and monitoring of disease transmission. Therefore, prototype algorithms were established to identify and highlight on a map (Fig. 1) the greatest percent change in the number of new cases during the most recent 2-week interval compared with the previous 2-week interval. In the case of influenza, algorithms were used to determine the number of new cases in the current week for an influenza subtype divided by all new cases reported for the current week (e.g., the number of H1N1 influenza cases/the number of all influenza cases) subtracted by the number of cases in the previous week for the same influenza subtype divided by all the cases reported for the previous week. A positive result was displayed as an increase from week A to week B, whereas a negative result was displayed as a decrease. Users could then use the map display to observe and monitor the region or country flagged with the greatest percent change over the last 4 weeks of data. The map provided a filter window for users to look at all observed categories, category groups (user-defined sets of categories), and individual categories. Built using the GeoExt (http://geoext. org) JavaScript toolkit for integrating OpenLayers with ExtJS, this interactive map provided zoom, pan, and selection capabilities. Selection via click-through displayed a time series with 90 days of observed values for the selection as well as an informational tab detailing the labs supplying data to the region/country. The system was configured to allow AFHSC-GEIS administrators to access data at the country level to observe counts. The other available user roles, denoted lab and dashboard, could access only calculated percentages by week at the country level.

RDD DEVELOPMENT

As often happens with information technology initiatives, once users were able to visualize their initial requirements via the prototype, they realized they desired additional features and capabilities. After the RDD prototype began to be used, the APL development team proposed migration of the RDD prototype to leverage components of the ongoing Suite for Automated Global Electronic bioSurveillance (SAGES) OpenESSENCE (OE) development effort.^{11,12} Using the OE backbone for RDD took advantage of OE's data-agnostic design that could easily incorporate the RDD data sources. Therefore, RDD was migrated from Grails to OE. However, additional functionality was needed within OE to support several of the customized visualizations and interfaces required by RDD, such as a conditional report panel, interactive dashboard map, and role-based access to data. These features were initially developed as static, custom interfaces but were later incorporated within the core OE system so that any data source in addition to RDD could use these features.

Flexibility for Use by Both AFHSC-GEIS and Partner Global Laboratories

To more closely match data collection by the global partner laboratories, RDD has undergone several redesigns of the back-end data models. Initially, the data were to be collected by AFHSC-GEIS regional labs, where each laboratory reported information for one or more countries. The report's web form was arranged in a tabular format, with categories listed vertically in rows and each associated country in a column. Although data were and continue to be reported weekly, data were submitted only as an aggregate count by category, with each country's disease information supplied by a regional AFHSC-GEIS lab. The data collection model was later modified to allow the creation of additional in-country laboratory sites so that one or more labs within each country can submit a data report. So that non-AFHSC-GEIS labs can be included in the future and retain the correlation with past AFHSC-GEIS data collection, the new in-country site can be associated with a AFHSC-GEIS regional laboratory. Therefore, the new RDD version can continue to incorporate results from AFHSC-GEIS laboratories as well as those from in-country laboratory sites. In addition, the new RDD version allows information to be provided via separate country and category reports. That is, when entering data via a new web-based report, users can choose from filtered pick lists to select a country and then an associated in-country site. In most cases, these site associations are currently limited to a single country and one reporting site; however, RDD can now accommodate the need for a single regional AFHSC-GEIS site to report information from one or more countries and/or in-country sites.

Automatically Accounting for Lags in Test Results

The latest data model in RDD is designed to align better with how test results are captured by different laboratories. Although a patient's respiratory specimen may be tested as soon as it is collected, different tests take varying amounts of time. For example, rapid influenza diagnostic tests may give results within 30 minutes, indirect or direct fluorescent antibody tests take several hours, polymerase chain reaction may take from one to several hours, and viral culture takes several days or even weeks. These different types of tests are all useful because they have different capabilities for identifying different diseases. Furthermore, each lab may be capable of performing only certain types of tests. Because of the lag in availability of test results, laboratory personnel previously had to backfill data and recalculate counts manually. The users had to manually edit several weeks of reports for each new week of data. RDD now uses the sample collection date to take into account these lags in availability of test results, and it automatically backfills previous weeks' data and updates the counts.

Enhancing Data Accountability and Reliability

For accountability and reliability, RDD also provides robust information about the data. Multiple fields routinely used by the laboratories were isolated to allow RDD to collect information from the results of individual lab samples and use that information to calculate the multiple fields that users previously computed manually. Therefore, RDD now allows the labs to submit more information for tests during the current reporting week instead of inputting only aggregate data for a lab. Sometimes a single test may report multiple results because patients may have more than one pathogen (e.g., coinfection). Therefore, RDD now provides the user with the ability to add information about each test, including a sample identifier, the type of test and how it was performed, and whether the results revealed more than one pathogen. These data are automatically added to the RDD disease counts so that the total values, including data from co-infections, are computed automatically. The new system now automatically associates results with the relevant reporting week/date by using information from the sample identifier and the collection date and location to compute values for co-infections and total pathogens isolated by week. Therefore, labs can submit data as results become available, and the new RDD eliminates manual data backfill. Another advantage of submitting data in a single report as results become available is that data could theoretically be submitted daily if individual labs see large numbers of samples. The user can also submit lab reports in bulk across multiple weeks of data without the manual post-processing required to compute and update values across multiple weeks of data. Having more information available about each laboratory test serves as a check on the accountability and reliability of data entry from each laboratory. For example, one can observe that the entered results are consistent with the type of test described.

Accommodating Differences in Weekly Data Reporting

Although each laboratory reported its results weekly, many labs used different definitions for the beginning of the week, and these definitions varied depending on local reporting requirements. It became apparent in the original version of RDD that such reporting could cause discrepancies in the way the disease presence was represented across multiple laboratories. To avoid this problem, the new version of RDD allows the user to record the actual collection date for the test and keeps track of that date when the results become available. Therefore, RDD does not have to rely on each lab's definition of the reporting week and can instead standardize the weekly reporting to allow for more accurate comparisons of disease activity across multiple labs and regions. To allow for data comparison, the U.S. Centers for Disease Control and Prevention uses a standardized method for counting weeks (http://wwwn.cdc.gov/nndss/document/ MMWR Week overview.pdf). The first "epi week" of each year is defined as ending on the first Saturday in January as long as that Saturday falls at least 4 days into the month. After week one, then each "epi week" begins on a Sunday and ends on a Saturday. Actual collection dates are used and then translated within RDD. The user now has the ability to use the CDC "epi week" definition or one that is requested by his or her sponsoring agency.

Allowing Easier Data Tracking and Mapping

The newer version of RDD allows the use of several other data attributes to help track and map the data. For example, a user can include a data flag to exclude mapping of multiple mobile or ship-based laboratory stations. Doing so allows the user to exclude labs that are considered too mobile, thereby avoiding tracking inconsistencies.

Other attributes include the ability to denote the incountry site populations and assay classifications. These in-country site populations include categories used for disease surveillance purposes, such as U.S. military, local civilian, those presenting with influenza-like illnesses, etc. An assay classification is a group of diagnostic tests (i.e., assays) assigned to each lab by AFHSC-GEIS on the basis of local lab capabilities. For example, a particular lab may be capable of only certain types of tests, whereas other labs may be able to do tests that are more sophisticated. One or more tests may be available per site and are included in the assay classification for that site. These assay classifications are used in the new RDD to maintain compatibility with previous aggregate disease reporting so that data can be compared over multiple years.

Flexibility in Laboratory Data Collection Modalities

Another challenge was that different laboratories used various data collection and storage modalities. The RDD user-defined template mirrored how sample information was already being collected at most labs, but other labs incorporated sophisticated local databases that require assistance to export the data into the correct weekly reporting template for RDD. For example, some labs record their test results in text files, Microsoft Excel files, Microsoft Access files, Statistical Analysis Software (SAS) files, or other file types. These labs may be submitting their results to multiple entities in addi-

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tion to AFHSC-GEIS. One of the requirements of the redesigned RDD data collection system was to reduce overhead in collecting and submitting information to AFHSC-GEIS. Working with AFHSC-GEIS and their partner labs, APL created an Excel template to standardize weekly data collection. This Excel template, which is now used for weekly data submission, makes it easier for users to migrate their bulk data by converting to comma-separated value (CSV) files for bulk uploading. In addition, software scripts were written for large database users to allow different types of data collection modalities (e.g., Microsoft Access) to be used to generate standardized CSV files for bulk data upload.

Bandwidth Challenges in Resource-Limited Settings

Another challenge has been the speed of RDD in resource-limited settings. Although many of the reporting laboratories are operating on U.S.-acquired equipment, the labs themselves are still located in resource-limited settings where data transmission may encounter slow speeds and limited bandwidth. The team examined the RDD data structures for ways to reduce the bottlenecks in the RDD web application and found that certain code and debugging libraries could be eliminated. For example, some of the JavaScript library and debug files were more than 2 MB. These JavaScript libraries could be minified to sizes less than 200 KB. Doing so reduced the bandwidth requirements while maintaining data accountability and reliability.

User Interface and Data Input

In the latest version of RDD, the customized data entry panel provides a role-based access control interface for AFHSC-GEIS partner laboratories to enter data directly into RDD. This role-based approach, implemented with Spring Security (http://projects.spring.io/ spring-security/), means that the permissions for accessing different features are based on the job functions of the user. The access control interface also filters the lab and country reporting fields to those the site administrator has assigned to the particular user role. For secure data transmission, Hypertext Transfer Protocol Secure (HTTPS) is used. A custom data entry grid with reporting countries as columns and reporting categories as rows provides users with an interface that is aligned with reporting requirements. The grid also provides a means to dynamically adjust the number of columns and rows as countries and/or categories are added or removed from the system. Figure 2 illustrates the data input interface, showing the location and different types of influenza.

Data Visualization

The RDD map portal enables filtering of data to show various category groups and data for different time periods. For example, the results could be filtered by type of respiratory disease, such as influenza A, influenza, other non-flu pathogens, all pathogens, and all specimens. In addition to countries, the user can select regions including

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	3	3 S	Site A(145), Site B(15), Site C(38)	Low	09/01/2011	01/28/2012	admin admin	07/23/2013	07/24/2013				
	14		Site A(310), Site B(62), Site C(180)			09/27/2012			09/19/2013				
	13	3	Site A(210), Site B(22), Site C(57)	Low	12/08/2010	06/13/2011	admin	07/16/2013	08/01/2013				
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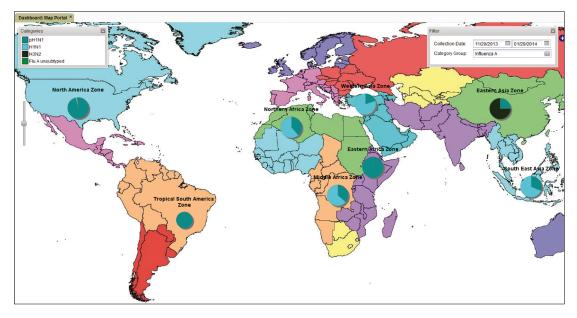


Figure 3. RDD global influenza report map.

multiple countries for aggregate results. In response to user requests, the new RDD map now displays results using the World Health Organization (WHO) regional disease transmission zones provided in the WHO Global Health Observatory Map.^{13, 14} Figure 3 shows the percentage of reports positive for influenza A, color-scaled by WHO flu zone. In addition, pie charts can be overlaid to show the distribution of different respiratory diseases (e.g., influenza A subtypes and influenza B). Because of their similarity to the WHO Global Health Observatory Map, maps produced by RDD are in a format familiar to global users.^{13, 14}

RDD supports time-series graphing and the application of outbreak detection thresholds that assist the user in visualizing weekly biosurveillance results (Fig. 4). Either single or multiple pathogen results can be plotted over time. Figure 4 uses simulated data for H1N1, pandemic H1N1 (pH1N1), H3N2, influenza B, and adenovirus to illustrate plots of multiple pathogens. The plots for each type of pathogen may also show warnings (yellow dots) or alerts (red dots) based on particular algorithm thresholds for that pathogen. These algorithms are described in detail elsewhere (e.g., Ref. 15).

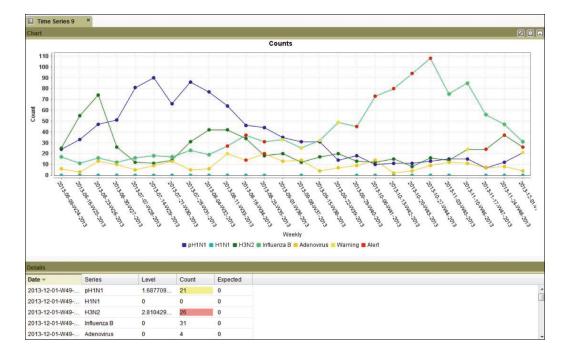


Figure 4. RDD screenshot showing time-series plots of different pathogens.

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Because RDD can now integrate the older aggregate reports with the newer data entry methods, users can make year-over-year comparisons, allowing them to compare past seasons with each other and with the current season (Fig. 5). These data can also be filtered by specific pathogens (including different influenza subtypes), pathogen groups (e.g., all influenza), country, region, assay type, surveillance population, etc. Examination of these time series may also allow users to spot sudden changes in disease reporting.

Role-Based Data Analysis and Results Reporting

In addition to the visualization of analytical results described above, RDD supports data reporting at different levels that vary with the role of the user. Countrylevel reporting allows laboratory users role-based access to data for all countries aggregated to the country level but not below. In-country laboratory users are allowed role-based access to more detailed all-level report data but only for their particular countries. Individual laboratories can view their own data at the individual sample level with a tabular view and can export weekly data capturing all fields specific to their weekly reporting needs. A combined report allows users to query both legacy aggregate data and the newly adopted individual lab sample reporting data. These data were combined by aggregating the individual lab samples to align with the legacy aggregate report data. In the combined data reports, users are able to run multiple queries that span the transfer to the new collection system, including site comparison reports and a newly developed year-overyear time-series plot. RDD also supports tabular output of data, including pivot tables, for more advanced analysis in other statistical software packages commonly used in epidemiology.

Administrative Functions and Determining Reporting Latency

Several administrative reports and site maintenance portals have been added to the RDD web application. Via the web interface, administrators have the ability to create and modify almost all attributes related to continuing system expansion. These functions include administering user accounts, managing reporting sites, and updating all reported data fields labels, associations, and colors. For example, administrators can use the rolebased access control to assign individual users to different roles that allow different types of data access.

To maintain the timeliness of the submitted reports, an administrator can perform a time-series analysis (Fig. 6) to determine the number of days from an expected report date to the actual date the report was submitted and the number of days since the last modification to the expected report date. RDD allows the administrator to determine minimum, maximum, and average values for both of these metrics. The administrator can thereby monitor reporting quality by observing latency in reporting and modifications/backfilling of data.

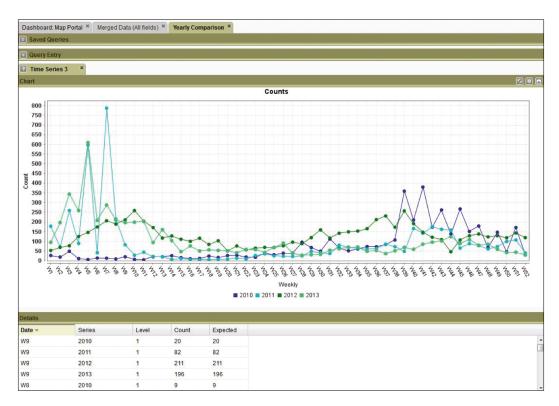


Figure 5. Year-over-year time-series plot showing seasonal disease variations.

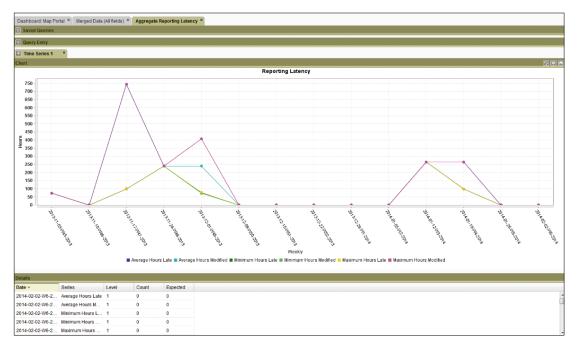


Figure 6. Time-series analysis of results reporting latency.

In addition, an administrator can generate a highlevel lab/week report to quickly view reporting statuses by week. This report includes a grid (Fig. 7) styled with colored checkmarks and "X"-marks to help quickly identify latent reporters. Data can be aggregated/grouped by region, country, AFHSC-GEIS laboratory hub, and incountry site.

Future Efforts and Sustainability

There are continuing efforts to migrate the custom elements of RDD into the core OE open-source release. To quickly respond to sponsor/end user requirements, features are often developed statically and loaded into the web application dynamically, outside of the core OE code base. When users identify desirable features, the features are typically folded back into the core OE code base and integrated with the Groovy data source configurations for inclusion in other SAGES projects/efforts.

APL designed RDD so that local administrators can use the interface to configure essentially all components needed for day-to-day system administration. This includes any fields that have associated colors, labels, groupings, and user accounts. APL still typically handles additional reporting components requiring core system changes, and the system will likely always require a developer in the loop. An ongoing effort for the core OE project is to redesign the core system to adhere to accepted and well-documented standards so that it is easier to transition future development efforts to the user community.

CONCLUSIONS

APL developed RDD as a secure Internet-accessible means of collecting and sharing laboratory results in a respiratory disease database with user-friendly entry, analysis, and visualization of infectious disease data. RDD serves as the central repository for respiratory disease specimen data generated by the AFHSC-GEIS laboratories. These laboratories support surveillance efforts on five continents, test hundreds of respiratory isolates each week, and report influenza subtype information to AFHSC-GEIS headquarters. Additionally, many partner laboratories perform an expanded panel of respiratory pathogen tests that include other viral and

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Figure 7. Grid showing AFHSC-GEIS hub site reporting.

bacterial agents. Medical laboratory technicians at partner institutions can enter data directly into RDD via a web-enabled form. These data become instantly available for analysis by the laboratory user. Through RDD, the user can tabulate disease prevalence, distribution of influenza subtypes, and the frequency and distribution of other respiratory pathogens. These tabulations can be filtered by geographic region, assay type, and surveillance population. To provide an instant visual snapshot of influenza subtype distribution worldwide, the main RDD page overlays pie charts on global maps that can also depict the WHO disease transmission zones (Fig. 3).

The development of RDD has helped the APL team to identify a number of informatics issues that provide overarching benefit to many similar initiatives at APL. Using the OE backbone benefited both the SAGES and RDD projects by minimizing duplicative architecture and security efforts. In addition, the overall ability of both systems to ingest data improved, as did the team's ability to analyze and test the systems. The decision to merge the projects was based on the sponsor's desire to continue the RDD effort, the available resources currently working on the OE platform, and the similarities in system requirements. Instead of building in parallel two separate systems with similar functionality, APL made better use of sponsor funding to ultimately provide far more functionality in a single aligned application.

RDD may be used in a variety of global settings to improve the timeliness of data collection, the efficiency of analyzing results by disease and country, the tracking of disease spread, and the communication of results among different users at different locations. RDD enhances the early detection of disease outbreaks, allowing more time for mitigation of the effects of these outbreaks.

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