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Leveraging Today's Technology for Clinical Trial Imaging

Over the last decade, medical imaging has been playing a greater role in the diagnosis of disease and, logically, there has been an analogous increase in the use of imaging in all phases of clinical trials to evaluate new drug candidates. In most cases, the images taken during each patient visit during the study need to be sent to a Centralised Core Lab, which specialises in image review and analysis. The conventional method of transporting compact discs (CDs) with diagnostic image scans (including radiographs, magnetic resonance imaging (MRI), computerised axial tomography (CAT) and ultrasounds), even over short distances, is an expensive, opaque and environmentally unfriendly process. Leveraging telecommunication tools for file transfer and integrating imaging with electronic data capture (EDC) has the potential to transform the manner in which imaging is used in clinical trials. New tools are now available that make this integration a reality and could provide better transparency for sponsors, improve data quality, reduce costs, give more de-identification options, and even reduce a firm's carbon footprint.

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The primary method used today to transmit diagnostic image scans is to physically ship the scans to central labs for review. This process has been identified for years as costly and inefficient by clinical trial sponsors. Previous attempts at electronic transport used ineffective

technologies such as File Transfer Protocol (FTP) or Hypertext Transfer Protocol Secure (HTTPS), which are simply file transfer processes that do not provide the workflow, redundancy, persistence and reliability necessary to allow for the fast submission of de-identified image exams as is needed in clinical research.

In fact, no method in use today that runs exclusively over the open, unmanaged internet can achieve the reliability and efficiency needed in a global clinical trial. The point-to-point limitation of FTP and the Digital Imaging and Communications in Medicine (DICOM) standard, and their inability to achieve redundant and persistent connections over wide area networks, requires users to closely monitor and facilitate these lengthy transactions. While most people think of these technologies as “free”, this perception comes at a high cost. If the service is unmanaged, the management, in practical terms, is simply shifted to the individual users. Given the nature of investigator sites and the burden that's already imposed on their staff, sites have been reluctant to adopt these “free” and unreliable solutions, which do not provide robust support at the technical and customer care levels.

These electronic file transfer protocols can be particularly untrustworthy in global studies that have sites in locales with poor public internet infrastructure. If the internet connection drops, the entire file transfer process has to be initiated from start and cannot be resumed mid-transfer.

Relying on the traditional standard courier service also has severe limitations. Burning clinical trial images onto a compact disc (CD) after patient visits and then physically mailing the CD to a central reviewer — typically a core laboratory — for analysis is an expensive, time-consuming process that stresses clinical trial productivity. This labour-intensive process is also impeded when images need to be quickly transported to an international locale — all but eliminating the possibility of conducting global adaptive and eligibility trials that require fast turnaround and better control of subject data.

It is easy to conclude that clinical trial sponsors need a way to transport patient images more quickly and efficiently for less

cost and with real-time capability to track and manage the images.

Driving the Need for a New Solution

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Imaging can be effectively used to make drug development “go/no-go decisions” regarding the potential efficacy of a drug, so as to end or continue projects before they become too costly. Additionally, there has been an increased use of imaging as surrogate markers — that is, a biomarker that is a substitute for the actual clinical end result (often used when the actual end result would be undesirable, such as the death of a patient).

Oncology, neurology and cardiovascular trials, in particular, benefit from the use of imaging. Positron emission tomography (PET) scans, for example, are used to detect whether a cancer has spread, which can help determine the effectiveness of a therapy or drug. And various imaging techniques can provide insight into the vascular system and the hardening of arteries, and identify blockages that are key to uncovering therapies for cardiovascular issues.

The success of imaging in diagnosing diseases and therapy has only accelerated its use in clinical research and uncovered novel applications for the technology — imaging is already being used for such

vital clinical activities as patient selection, optimisation of dose and schedule, and safety assessments.

Trial Efficiency and Harmonising Image and Clinical Data

With the increased use of imaging in clinical research, the challenges associated with traditional image transfer methods have also been exacerbated, namely, the costs associated with managing and reconciling images, and trial efficiency.

It is expensive for sponsors to pay a courier service to transport images burned on a CD, and this can also negatively impact trial efficiency, mainly because of time delays and the fact that the sponsor has little insight into the location of the image, or its quality, until after the results are sent back in a report.

Manually matching or reconciling image results back to the remainder of the clinical data is a laborious process that can significantly delay final analysis and data review. The reconciliation effort is a necessary step in the process, as images sent out for review must be de-identified from any subject reference to meet regulatory standards. Study personnel have to remove specific identifiers (up to 18 in all) from the image file before it can be shipped, in order to anonymise the image. Once the de-identified image has been analysed, the sponsor has to manually link the image results back to the clinical trial data. Before the image can be “re-identified” it must be extracted from either the CD or a file system and then imported into the trial repository. Because the clinical data and the imaging data are being transferred separately and require human intervention to synchronise the data, the process is opaque and often rife with error.

The combination of all of these factors — increased use of imaging, inefficient and opaque processes with high costs — has been driving the need to replace the traditional methods for capturing and transferring images.

The Future is Now

As so often happens, it takes a novel approach to a problem to find the appropriate solution. In terms of diagnostic image transfer, it was the realisation that moving diagnostic image scans over long distances is really a telecommunications challenge and not a file transfer issue. A telecommunications-based solution with significant control over the infrastructure and bandwidth available for transfers, coupled with advanced workflow capabilities and technology to overcome local firewall constraints, can be an effective way to conduct these complex data transfers.

Boston-based AG Mednet has developed just such a fully-managed

telecommunications solution. In contrast to standard courier services and FTP/HTTPS applications, the AG Mednet solution allows trial managers to receive images directly into their repositories, receive form data directly into their subject trackers without having to do data re-entry, and easily track the state of image submissions from every investigator site.

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It is in use by Phase I, II and III clinical trials across therapeutic areas that include oncology, cardiovascular, neurology and respiratory. The rate of adoption by investigator sites is accelerating as more and more sponsors, sites, trial managers, imaging core labs and clinical research organisations realise that the value of this methodology is not just in the important cost reduction in transport. Just as critical to the trial is the new-found ability to reduce submission errors caused by non-validated pen-and-paper based forms, lack of proper de-identification, inability of sponsors and imaging core labs to extract images from CD, and, most importantly, the reduction in site queries.

While this telecommunications approach solves many of the issues associated with physically (or electronically) transferring the actual images, it is the integration of a highly available image transfer network with a robust EDC system that provides sponsors the ability to fully synchronise the trial’s clinical and imaging data. This combination gives the sponsor insight into when images are shipped, tracked and received, improving the reconciliation process and leading to quicker database lock. AG Mednet has teamed up with Phase Forward, a leading provider of data management solutions for clinical trials and drug safety, to bring sponsors this integrated solution.

AG Mednet’s image transfer platform queries Phase Forward’s InForm™ EDC system each time an investigator begins to process the scans, and provides him with well-defined options for completing de-identification and eCRF tasks. Once the data is submitted, the imaging network reports back to the EDC system, which in turn can update the status of image

submissions on its repository.

This integration is presently being deployed as part of two clinical trials — oncology and cardiovascular technology assessments (TAs) — and should have a positive impact on the reconciliation tasks required to close a trial’s database. The process of mapping patient and image ID should be vastly streamlined; images cannot be sent without required information; and sponsors will be able to see when an image was shipped and received.

The advent of AG Mednet’s managed network dedicated to the acquisition and transfer of imaging data, coupled with Phase Forward’s InForm EDC solution could transform the way in which imaging is utilised in clinical research. ■

ABRAHAM GUTMAN
PRESIDENT AND CEO
— AG MEDNET

Abraham has had a long career in technology management worldwide. Prior to founding AG Mednet in 2005, he founded Emperative, Inc., a telecommunications software startup of which he was the President and CEO. Mr. Gutman has a Bachelor of Arts degree in Computer Science from Cornell University and a Masters in Computer Science degree from Yale University. He is the inventor on US Patent 6449355 for the Method and system for providing assistance to users of a service, and has a number of Patents Pending related to both the technology and business processes associated with the exchange of diagnostic image studies across long distances between unrelated hospital and research entities. Mr. Gutman is a member of the Board of Trustees at Facing History And Ourselves, as well as the Community Advisory Board at WGBH.



ROBERT QUINN —
HEAD OF SOLUTIONS
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For the last four years, Mr. Quinn has been in charge of managing all aspects of product launches for Phase Forward’s clinical data management and safety solutions, including product positioning and customer research. Prior to Phase Forward, Mr. Quinn worked for The MathWorks, Parametric Technology and Raytheon providing enterprise process improvement solutions to scientific and engineering professionals. He started his career as a design and project manager/engineer building missile systems for the United States military. Mr. Quinn holds a B.S. degree in mechanical engineering.

