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White Paper Presented By ArisGlobal®

Automating Safety-to-Investigator Reporting

New alternatives to reducing costs, increasing productivity and ensuring regulatory compliance

EXECUTIVE OVERVIEW

Regulatory requirements mandate that Sponsors send a high volume of safety reports to a number of stakeholders, including authorities, IRBs /IECs and investigators. The challenge many Sponsors face is the balance between quality and high level of compliance, cost efficiency and the productivity of internal resources.

Traditional distribution methods currently used by Sponsors invariably fail to satisfy all the requirements of an ideal process such as rapid distribution, cost containment, security and reliability, high productivity and receipt tracking. To improve this situation, many companies engage in in-house development of IT systems; use inadequate software often designed for another purpose; or simply outsource the function to third parties such as CROs, incurring a high cost of distribution.

The advent and rapid adoption of electronic data capture (EDC) has changed the way industry conducts clinical trials completely. Investigators are now expected to use EDC for direct entry of clinical trial data. This acceptance of technology provides new opportunities for the distribution of clinical safety reports. Based on the concept of EDC, ArisGlobal® has developed agNotify™, the first commercial software specifically designed to support the online electronic distribution of safety reports to all stakeholders.

Through agNotify™, clinical safety reports (SUSARs) are distributed automatically from the Sponsor to all stakeholders—authorities, IRBs /IECs and investigators—according to user-defined distribution rules. Email notifications are sent to all recipients, and after logging in to the secure and reliable investigator portal, users open the report with a single mouse click, which triggers an automated acknowledgement of receipt to be sent to the Sponsor.

agNotify™ allows Sponsors to free up high-qualified resources for more value-adding work; save and control distribution costs; increase the level of compliance; and save time that can be better used for pharmacovigilance and clinical safety activities. agNotify™ is offered as a hosted solution with all the required IT-related services, including 24*7*365 help desk for investigators. A simple and transparent pricing model gives the user flexibility while reducing fixed costs.

COMMON CHALLENGES WITH SAFETY-TO-INVESTIGATOR REPORTING

Once a new substance has entered clinical development, Sponsors have to inform—depending on the region indications under study, these regulations require companies to send out large volumes of reports. A challenge many Sponsors face with the distribution of these reports is the balance between quality and high level of compliance, cost efficiency and productivity of internal manpower. Many Sponsors mail or send by courier thousands of reports and track the corresponding number of acknowledgements received. Depending upon the trial, a single serious advent event (SAE) report can manifest into hundreds of reports that need to be collated, addressed and distributed.

Shipping costs, especially if courier services are used, can be very expensive. Further, proving to inspectors and auditors that all recipients who should have been informed actually received and read the safety report can become challenging. Often it falls on the clinical research associate (CRA) to document if all reports have been received and filed correctly. Moreover, there are high error rates inherent in every manual process and the business impact can be difficult to estimate.

The solutions chosen by different companies differ significantly, indicating there is no one best way of solving the challenge.

Current distribution processes used in the industry

In order to understand how Sponsors currently handle safety alert reports, it is important to look at how they prove that all investigators received and read the report. In principle, there are two different processes in use by Sponsors.

The first method is a manual process that does not allow rapid verification of the receipts (Figure 1).

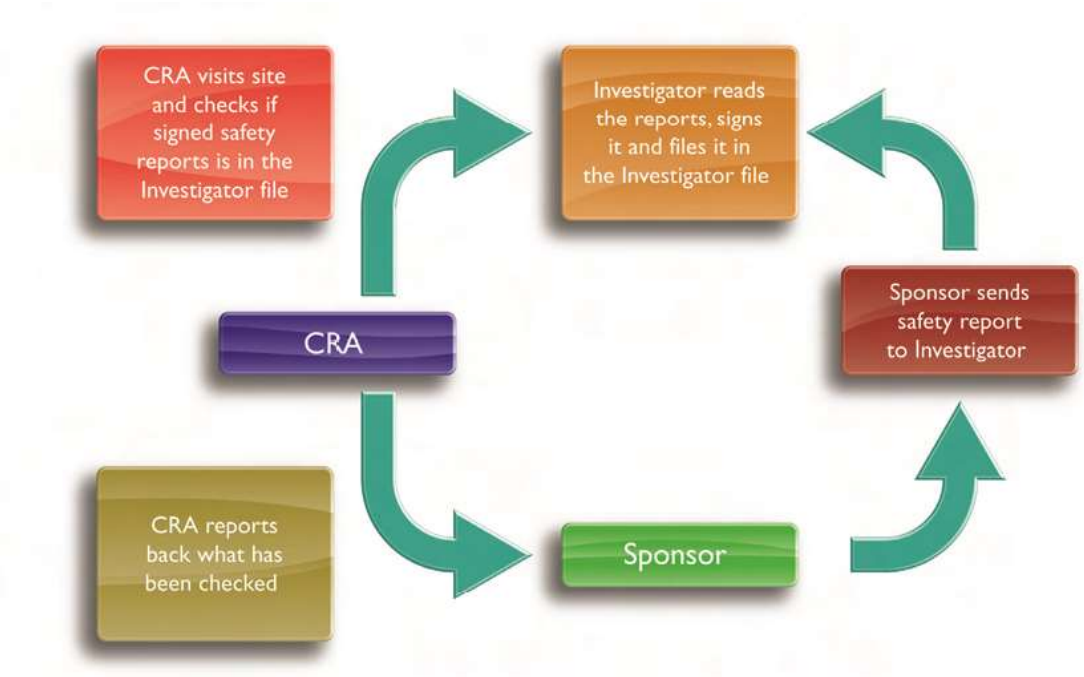

Figure 1. Verification of receipt by CRA

During a monitor visit, CRAs check if the safety reports that have been distributed are in the investigator file and are appropriately signed, proving they have read them. While this sounds simple, the drawbacks of this process are evident. CRAs often do not visit the sites immediately after the reports were sent out. In case a report has not been received, they will typically discover this quite late in the process and, as such, the site may not be informed about the safety issues within the timeframe required by regulatory authorities, leading to high risk and potential safety concerns.

Furthermore, highly paid CRAs need to spend valuable time just for checking receipts—time they could use much better while they are on site for other work on the often-crowded agenda of a monitoring visit.

Figure 2 shows the second process that companies typically follow. Following this process, Sponsors can achieve almost immediate acknowledgment. Sponsors either use a courier service, which confirms they have delivered the report to the investigator, or they ask the investigator to confirm they have read the report, e.g., via fax or email. However, this process is quite expensive and does not prove the investigator actually read the report (courier service), or it leaves the investigator with the additional administrative burden of acknowledging receipt of the report. There is also the risk that investigators forget to acknowledge receipt, resulting in an increase in the administrative workload for the Sponsor to remind them.

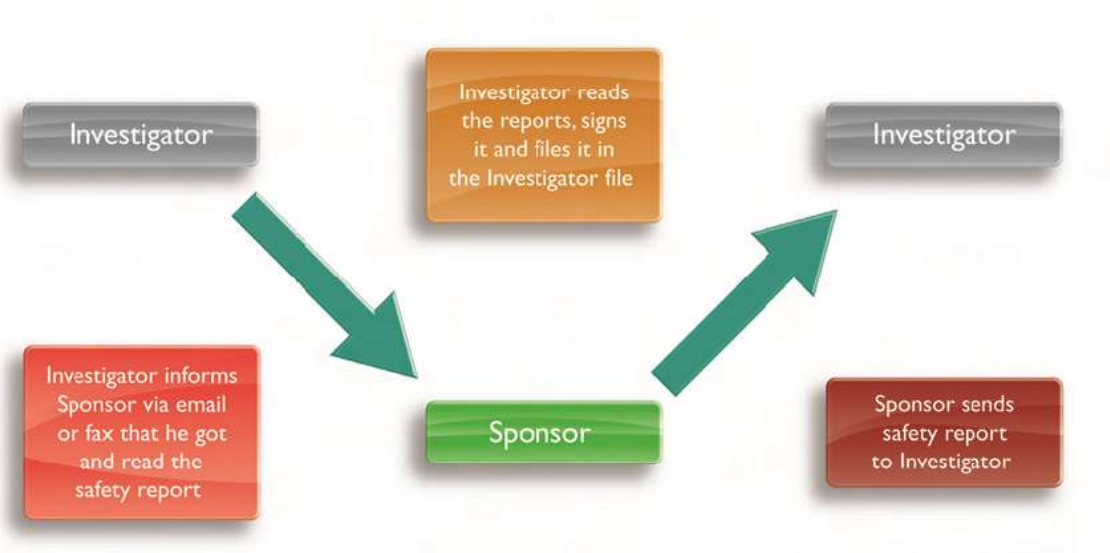

Figure 2. Near-time verification of receipt

The ideal distribution process

The ideal process to distribute safety reports should fulfill many different requirements. First of all, it needs to be easy to set up and maintain, as well as support the differing regulatory obligations for notification. It should be cost effective, reliable and highly secure. Any process should also be easy for the investigator and support each investigator's preferences for receipt.

Media used for distributing safety reports

Looking at the current media used by most Sponsors, none of them are efficient and cost effective. Distributing reports via courier service fulfills most of the quality-related requirements but is very

expensive. Worldwide distribution via normal mail has severe drawbacks in terms of reliability and speed, since letters can get lost and intercontinental postal service may well take several days to deliver.

Fax-based processes rely on the 24*7*365 availability of the recipient's fax machine, which is not under the Sponsor's control. Furthermore, while fax allows user to track that the report was received by the investigator's fax machine, it does not allow tracking if and when the investigator actually received and read the report.

Without doubt, email distribution is the fastest and least-costly distribution channel. However, tracking of receipt acknowledgement is semi-automatic at its best, leaving the user still with a lot of manual work. Creating overviews and distribution reports from different perspectives require tedious manual data entry into some kind of database. Furthermore, security issues question the reliability of a purely email-based process.

Whatever media used, a good documentation of all the process steps is not supported, thus making it work intensive to show inspectors and investigators which safety reports were sent when to which recipients, and when they received them.

Many in the life sciences industry are not satisfied with the current situation and are looking for alternative solutions. Despite the general and increasing trend in the industry to focus on core competencies, some companies engage in in-house IT development projects and use self-developed databases. Other companies use software originally designed for a different purpose. This "off-label use" of software helps, but leaves many open issues, since the software does not support the special aspects of the safety report distribution to investigators.

agNotify™: FIRST COMMERCIAL SOLUTION

agNotify™ is the first commercial software solution specifically designed to automate the electronic distribution of clinical safety reports to investigators, IRBs/IECs and other stakeholders with a high level of security and reliability.

The process of distributing safety reports using agNotify™

Using agNotify™, the process of informing investigators about safety issues is fast and easy. Safety reports are typically generated within the pharmacovigilance system, e.g., ARISg™. The user then either uploads the report manually into agNotify™ or saves it in a specified folder where it is picked up automatically. Predefined distribution rules within agNotify™ control the distribution process.

Cover letters are generated automatically based on user-defined templates, with different templates available for the country and investigator. When a report is distributed, the investigator is notified via email that a new safety report is available. Upon entering the investigator portal, the investigator opens the report with a single mouse click, which in turn generates the acknowledgement of receipt within the system. An automated reminder function helps to ensure the investigator does not forget to read the report.

For investigators that do not have reliable access to the Internet, fax or email-based distribution is supported, including automatic tracking of successful or failed fax transmissions.

Figure 3. The process of distributing safety reports using agNotify™

Comprehensive safety report distribution system

agNotify™ provides extensive capabilities to support the distribution of safety reports to investigators, ethics committees, review boards and other stakeholders. Key features include:

• Automated or manual distribution of safety reports to investigators, IRBs, IECs and any other stakeholders
• Notification by portal, email or fax dependent upon investigator preferences
• Distribution of individual case reports and/or aggregate summary reports
• User-defined distribution rules
• Distribution based on study and/or product
• Automated read acknowledgements
• Templates for cover letters for initial notification and reminders
• Archival of safety reports

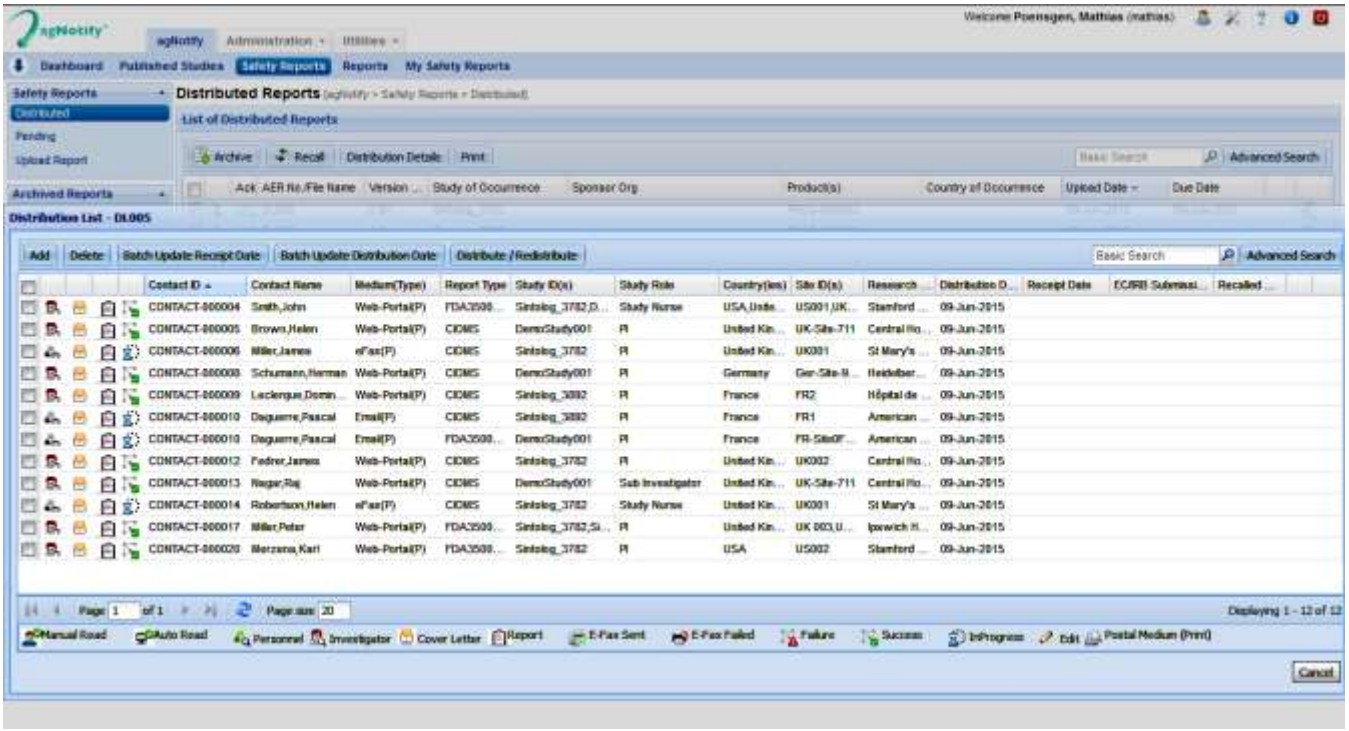

Figure 4. Tracking of reports and receipts

Services

ArisGlobal® recognizes that companies are requiring more and more services around IT-based solutions in order to help them focus on their core business. agNotify™ is offered as a managed, hosted software solution, eliminating the burden from the Sponsor to deal with all the basic IT tasks such as hardware maintenance, backup and disaster recovery. Users access and use the solution remotely and securely via the Internet, using their existing hardware from any location in the world without the need to install any additional piece of software on their computers. System availability is 24*7*365 with 98% uptime due to full server redundancy. Infrastructure management services follow IT Infrastructure Library (ITIL) guidelines. A multilingual support desk is provided by skilled personnel from ArisGlobal®, leveraging its long-standing leadership experience in safety and pharmacovigilance to deliver superior 7*24*365 assistance to the investigator community and the Sponsor's users, ensuring a high, first-call resolution rate. Training can be provided to users of the Sponsor and to investigators.
Service is delivered according to predefined service level agreements (SLA) by dedicated support teams.

BUSINESS BENEFITS

The Web-based safety report distribution system leverages ArisGlobal®'s 20-plus years of clinical safety experience and is the first such system to be designed specifically for expeditious and reliable safety reporting. agNotify™ saves costs, reduces the workload of the employees and helps the Sponsor to increase regulatory compliance.

Enable your highly qualified resources to perform more value-adding work

By implementing agNotify™, Sponsors can distribute increasing volumes of clinical safety reports while reducing the burden on staff. Taking advantage of the inherent productivity benefits of electronic communication, much effort is saved in preparing and sending up to thousands of letters to investigators. Distribution lists can be generated automatically and there is no need for the tedious manual tracking of acknowledgements, which usually is either done by members of a central group specializing in safety alert distributions or by the CRAs at their next visit at the site. No paper-based confirmations of receipts need to be archived in the trial master files. Creating the reports, which show all the details to auditors and inspectors, is just a matter of a few mouse clicks. Additional savings can be realized by integrating agNotify™ with the user's clinical trial management system (CTMS), allowing to transfer automatically the necessary study and investigator data.

Cost savings

agNotify™ allows electronic distribution of safety reports at a very low cost level. Two aspects add to these cost savings. First, there are no costs for sending paper-based safety reports via mail or expensive courier services. Second, and perhaps less visible but important to recognize, is the cost companies usually incur for the internal manpower needed to prepare, distribute and manually track acknowledgement of safety reports.

Increased level of regulatory compliance

As regulatory agencies focus more and more on safety-related issues, ensuring a high level of compliance is of utmost importance to Sponsors. The automatic tracking of acknowledgements helps Sponsors to have full control over the process with real-time data and ensures all investigators received and read the report within the short timelines set by the regulations for alerting stakeholders of safety reports.

Every manual process has an inherent error rate, regardless on how well it is designed and standard operating procedures (SOPs) are written. Estimating how high the error rate can be very difficult in paper-based environments. The automated electronic process supported by agNotify™ reduces the error rate and enables users to track every single transaction to its lowest level of detail in case anything went wrong.

Since all the information is stored in a central database, users can easily generate reports and answer all the questions auditors and inspectors might have using predefined reports. Questions such as which safety reports were delivered to a site within the last x weeks, or a complete list of all reports and their recipients, including when they received the reports for a specified product, are available within a few mouse clicks.

Designed from an investigator's perspective

After receiving a notification via email, investigators log in to a user-friendly and easy-to-use portal, giving them an overview of all new, and relevant clinical safety information at a glance. Upon reading a report, an acknowledgement is automatically sent to the agNotify™ portal. System-generated reminders ensure no information gets lost in an investigator's busy and sometimes hectic working days.

Automated password management functionality reduces the need to call for help desk support. Investigators can learn very quickly how to use the system.

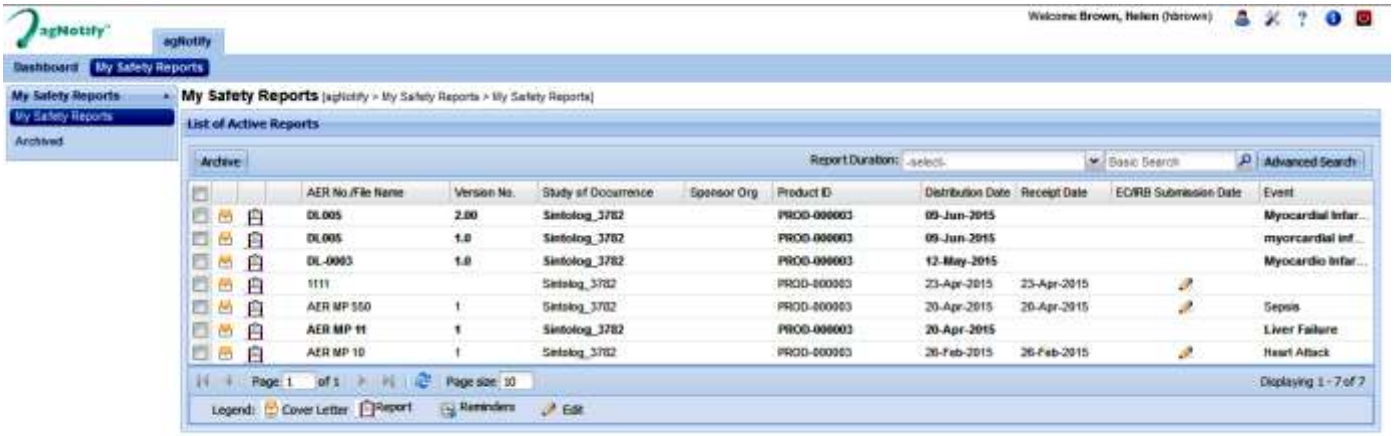

Figure 5. The investigator has a complete overview of all safety reports and can access each report within a single mouse click

More time for assessment of cases before distribution

Distributing reports using agNotify™ takes only a few minutes, which is considerably faster compared to expensive, overnight courier services or postal mail, which takes upwards of several days to cross continents. Given the tough timelines for alert reporting, agNotify™ frees valuable time for collecting more information about the case from the reporting investigator and doing all the assessment work necessary.

Fast implementation and attractive financial profile

agNotify™ is offered as a managed, hosted software solution, eliminating the investment in new hardware, software and application infrastructure support staff. As part of the agOnDemand™ offering, agNotify™ can be quickly deployed as an out-of-the-box solution or configured and integrated with other systems, such as any clinical trial management and pharmacovigilance system.

The solution and managed services free the Sponsor from the burden of IT-related tasks.
A simple and transparent pricing model gives maximum flexibility and scalability by reducing fixed costs and eliminating hidden ones. The solution provides low cost compared to any paper-based process—guaranteeing a fast return on investment.

Support is delivered by ArisGlobal®, a company 100% committed to supporting life science industries and whose core business is to develop and support new software solutions that facilitate regulatory compliance, manage risk and improve operational efficiency.

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SUMMARY

Distribution of safety reports to investigators is a labor- and cost-intensive process. Many Sponsors still send paper-based letters via normal mail or via expensive courier services, which require people to print reports and cover letters, sort and collate them. Some companies require their investigators to fax or email back an acknowledgement of receipt. Additional workload is needed to track the acknowledgments of receipt and to create the documentation required to prove regulatory compliance.

Questions that Sponsors need to ask include:

> Is my organization's current process for safety report distribution fully ensuring my compliance with regulatory requirements?
>
> Can we quickly and easily create the documentation required to show our compliance to auditors and inspectors?
>
> Have we factored in and analyzed all of the costs involved with our current process?
>
> Are possible time delays in alert notification and the difficulty in adequately tracking receipt and read acknowledgement placing patients at greater risk?

At ArisGlobal®, our experts understand the challenges and are ready to demonstrate how agNotify™ can streamline and automate safety-to-investigator report distribution and thereby deliver a quick return on investment from labor, paper, and courier/mailing costs; reduce the workload of your employees; and help increase regulatory compliance.

For more information

ArisGlobal® invites you to participate in a more detailed discussion tailored to your unique requirements. Please contact your ArisGlobal® representative or contact us at info@arisglobal.com.

About ArisGlobal®

For over 25 years ArisGlobal (www.arisglobal.com) has been a leading provider of integrated software solutions for pharmacovigilance and safety, regulatory affairs, clinical research and quality & compliance for medical inquiries. Solutions are available on premise or on a regulated Cloud platform. Life science companies using ArisGlobal's solutions can better build and maintain the trust they need with their customers, medical practitioners and regulatory bodies around the world.

agNotify™ is part of the Total Clinical™ cloud-based eClinical platform designed to streamline clinical operations and clinical data management to drive down costs and optimize trial outcomes.

For information on ArisGlobal® solutions, visit www.arisglobal.com.

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