



Evidence-Based ONCOLOGY™

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ALSO IN THIS ISSUE



SP146

DATA EMPLOYMENT AND AI IN CANCER CARE. At AJMC's Institute for Value-Based Medicine meeting in Dallas, Texas, presenters discussed how artificial intelligence (AI) holds the promise of helping oncologists predict outcomes such as which patients will need pain management and which ones are at risk of depression, [SP146](#).



UPDATES FROM NCCN'S ANNUAL MEETING.

During the National Comprehensive Cancer Network (NCCN) annual meeting, presenters provided various clinical and policy updates from recommendations for germline testing to advances in biosimilars, [SP154](#).



PATEL

FROM TEAM BUILDING TO IMPLEMENTATION.

Authors from Carolina Blood and Cancer Care Associates discuss how to take approaches learned in team building and use them in the Oncology Care Model, [SP143](#).



NEW CLINICAL TRIAL GUIDANCE.

FDA recently updated its oncology clinical trial guidance documents to expand inclusion to pediatric patients as well as patients with comorbidities, [SP145](#).

APPROVAL FOR ATEZOLIZUMAB.

FDA has granted accelerated approval for atezolizumab (Tecentriq), in combination with nab-paclitaxel (Abraxane) for the treatment of adults with unresectable locally advanced or metastatic triple negative breast cancer, [SP168](#).

ADVERSE EVENT TRACKING

A Step in the Digital Direction: From Paper Logs to Electronic Data Capture

Nate Brown, BA; Evelyn Siu, BA; and Janet Donegan, ANP-BC, AOCN

RESEARCH DOCUMENTATION IS A critical aspect of running a clinical trial. Key patient information such as informed consent, adverse events (AEs), concomitant medications, and medical and surgical histories are collected and used to determine patient safety and efficacy as the trial proceeds. Ultimately, the sponsor may make decisions—ranging from modifying the dose of the investigational drug to closing the study due to AEs—based on the data collected.

Despite how critical this information is to a clinical trial, research documentation remains largely a cumbersome, paper-based process. The collection of paper research documentation, separate from the patient's medical chart, is often referred to as a "shadow chart"; this results in source documentation stored outside the patient's electronic health record (EHR). This information must be carefully tracked and transferred among all stakeholders who enter, edit, or sign off on any of these documents.

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ADVERSE EVENT TRACKING

A Step in the Digital Direction: From Paper Logs to Electronic Data Capture

Nate Brown, BA; Evelyn Siu, BA; and Janet Donegan, ANP-BC, AOCN

CONTINUED FROM COVER

One piece of documentation kept in this shadow chart is the AE log. AEs must be documented at every patient interaction and entered using standard terminology. The paper-based AE documentation (Figure 1) process is cumbersome in many aspects.

The Paper Log: A Conventional Solution

For decades, the paper log has been the accepted tool for clinical research staff, data coordinators, and primary investigators/sub-investigators (PIs/SubIs) for recording AEs in a prospective clinical trials. Each of those individuals is required to enter, edit, review, or sign off on every detail of log information. The clinical research coordinators (CRCs) first document the AEs in the paper log. Next, the PI/SubI reviews, completes, and signs off on these events before the data coordinator can use the written information to painstakingly type the exact data into the electronic data capture (EDC) system. However, each staff member physically sits in a different place, forcing a “hot potato” hand-off of the log throughout the day.

Potentially the Wrong Place at the Wrong Time

Additionally, AEs must be reviewed at every patient interaction (each visit, phone call, etc). This results in a risk that the CRC is interacting with the patient at the same time the PI/SubI is reviewing the log. Therefore, the CRC may not have the log on hand to immediately document the AE reported by the patient. Based on many conversations between Flatiron Health staff and those in clinical practices, it is clear that this cumbersome, multistep process means that the log may be in the wrong place at the wrong time.

Common Terminology Criteria Entry: A Manual Process

In addition to coordinating access to the paper log, recording the specific AE term is also a time-consuming process. All AEs must ultimately be reported using the standard Common Terminology Criteria for Adverse Events (CTCAE), a guideline that assesses the seriousness of the AE that occurred. Today, because the process is mostly paper-based, research staff must flip through about 800 terms and grades in PDFs and mini-booklets

Figure 1. Example of Today's Paper-Based Adverse Event Log

Adverse Event Log											
Patient ID											
#	Adverse event term (CTCAE 4.03)	*Is this a Serious Event?	Start/Stop date (ddmmyyyy)	Grade	Relationship to study treatment	Action taken with study treatment	Relationship to non-study treatment	Action taken with non-study treatment	Outcome	Concomitant or additional treatment given	Investigator Review
1		<input type="checkbox"/> Yes <input type="checkbox"/> No	Start Date: _____ Stop Date: _____	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	<input type="checkbox"/> Not related <input type="checkbox"/> Unlikely related <input type="checkbox"/> Possibly Related <input type="checkbox"/> Related	<input type="checkbox"/> Not applicable <input type="checkbox"/> Unknown <input type="checkbox"/> Dose not changed <input type="checkbox"/> Dose Reduced <input type="checkbox"/> Drug withdrawn	Non-study treatment: _____ <input type="checkbox"/> Not related <input type="checkbox"/> Unlikely Related <input type="checkbox"/> Possibly Related <input type="checkbox"/> Related	<input type="checkbox"/> Not applicable <input type="checkbox"/> Unknown <input type="checkbox"/> Dose not changed <input type="checkbox"/> Dose reduced <input type="checkbox"/> Drug withdrawn	<input type="checkbox"/> Resolved <input type="checkbox"/> Continuing <input type="checkbox"/> Resolved with residual effect <input type="checkbox"/> Unknown <input type="checkbox"/> Change in grade <input type="checkbox"/> Discontinued study due to AE		
2		<input type="checkbox"/> Yes <input type="checkbox"/> No	Start Date: _____ Stop Date: _____	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	<input type="checkbox"/> Not related <input type="checkbox"/> Unlikely related <input type="checkbox"/> Possibly Related <input type="checkbox"/> Related	<input type="checkbox"/> Not applicable <input type="checkbox"/> Unknown <input type="checkbox"/> Dose not changed <input type="checkbox"/> Dose Reduced <input type="checkbox"/> Drug withdrawn	Non-study treatment: _____ <input type="checkbox"/> Not related <input type="checkbox"/> Unlikely Related <input type="checkbox"/> Possibly Related <input type="checkbox"/> Related	<input type="checkbox"/> Not applicable <input type="checkbox"/> Unknown <input type="checkbox"/> Dose not changed <input type="checkbox"/> Dose reduced <input type="checkbox"/> Drug withdrawn	<input type="checkbox"/> Resolved <input type="checkbox"/> Continuing <input type="checkbox"/> Resolved with residual effect <input type="checkbox"/> Unknown <input type="checkbox"/> Change in grade <input type="checkbox"/> Discontinued study due to AE		
3		<input type="checkbox"/> Yes <input type="checkbox"/> No	Start Date: _____ Stop Date: _____	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	<input type="checkbox"/> Not related <input type="checkbox"/> Unlikely related <input type="checkbox"/> Possibly Related <input type="checkbox"/> Related	<input type="checkbox"/> Not applicable <input type="checkbox"/> Unknown <input type="checkbox"/> Dose not changed <input type="checkbox"/> Dose Reduced <input type="checkbox"/> Drug withdrawn	Non-study treatment: _____ <input type="checkbox"/> Not related <input type="checkbox"/> Unlikely Related <input type="checkbox"/> Possibly Related <input type="checkbox"/> Related	<input type="checkbox"/> Not applicable <input type="checkbox"/> Unknown <input type="checkbox"/> Dose not changed <input type="checkbox"/> Dose reduced <input type="checkbox"/> Drug withdrawn	<input type="checkbox"/> Resolved <input type="checkbox"/> Continuing <input type="checkbox"/> Resolved with residual effect <input type="checkbox"/> Unknown <input type="checkbox"/> Change in grade <input type="checkbox"/> Discontinued study due to AE		
4		<input type="checkbox"/> Yes <input type="checkbox"/> No	Start Date: _____ Stop Date: _____	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	<input type="checkbox"/> Not related <input type="checkbox"/> Unlikely related <input type="checkbox"/> Possibly Related <input type="checkbox"/> Related	<input type="checkbox"/> Not applicable <input type="checkbox"/> Unknown <input type="checkbox"/> Dose not changed <input type="checkbox"/> Dose Reduced <input type="checkbox"/> Drug withdrawn	Non-study treatment: _____ <input type="checkbox"/> Not related <input type="checkbox"/> Unlikely Related <input type="checkbox"/> Possibly Related <input type="checkbox"/> Related	<input type="checkbox"/> Not applicable <input type="checkbox"/> Unknown <input type="checkbox"/> Dose not changed <input type="checkbox"/> Dose reduced <input type="checkbox"/> Drug withdrawn	<input type="checkbox"/> Resolved <input type="checkbox"/> Continuing <input type="checkbox"/> Resolved with residual effect <input type="checkbox"/> Unknown <input type="checkbox"/> Change in grade <input type="checkbox"/> Discontinued study due to AE		

*Serious adverse events must be reported as per the protocol requirements (e.g. sending the SAE report form to safety within 24 hours of awareness)

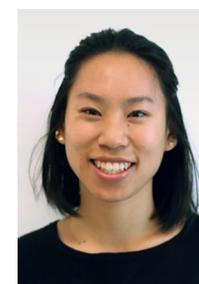
Investor Signature: _____ Investigator Signature Date (dd/mm/yyyy): _____

AE indicates adverse event; CTCAE, Common Terminology Criteria for Adverse Events.



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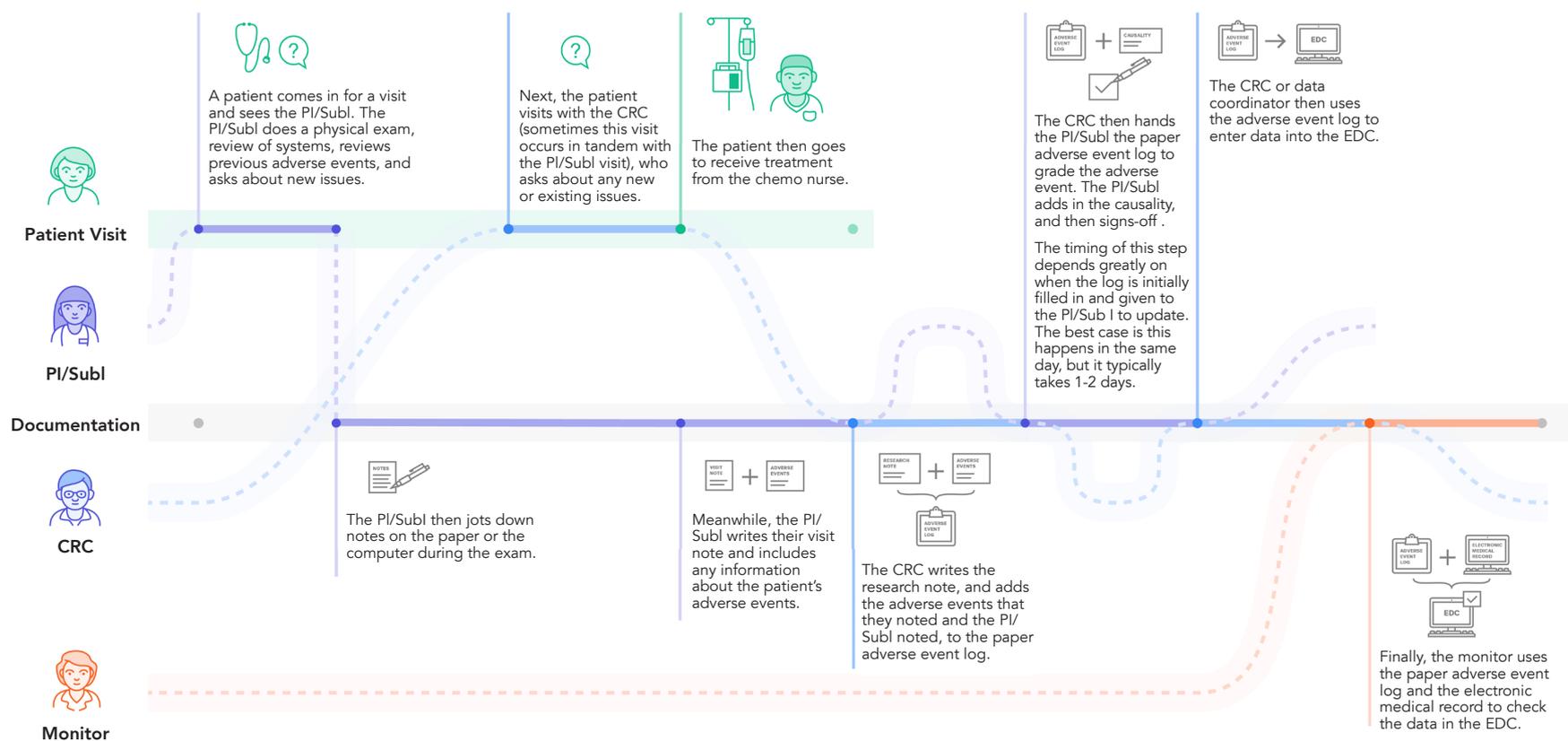
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ADVERSE EVENT TRACKING

Figure 2. The Journey of the Adverse Event Log



CRC indicates clinical research coordinator; EDC, electronic data capture; PI/SubI, primary investigator/subinvestigator.

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to find the correct term. Additionally, multiple versions of CTCAE are in use today, and each trial may reference a different version. Research staff must be careful to ensure that the version of the CTCAE term they use matches the CTCAE version of the trial.

Data Messiness and Interpretation

Finally, these logs quickly become crowded and messy due to the fact that multiple contributors write in and edit each log. Again, because of the manual and handwritten process, research team members and/or monitors often express frustration with the trouble of interpreting the data. This leads to questions that the research team spends time fielding, but these questions could have been avoided if the data had been more legible or easier to follow.

Trying a Different Approach: Integrating AE Documentation Into the EHR

Over the years, we've heard from the Flatiron Health network of community-based practices that for the reasons stated, paper-based research documentation—and specifically AE documentation—is a critical pain point. In 2017, we kicked off a brainstorming session with some of the 350-plus community leaders at our annual provider conference to explore different solutions. From these early conversations, it became clear that digitizing the AE workflow in the EHR could be a way to alleviate some inefficiencies of the paper-based workflow.

As the idea of electronic AE capture began to take shape, we conducted on-site user research with 10 selected practices. These sites represented a range of research practices, differing in size as well as phase (ie, early- through late-phase trial sites). We then partnered closely with 5 of these sites, which became our beta partners. A beta partner is a practice that tests our initial product versions and works closely with us throughout the product development process to ensure that our solutions are intuitive and effective for practices across the provider network.

At Flatiron Health, we believe that the only way to build an effective product is to start with a clear understanding of the problem. In this case, we needed to observe research teams' workflows and to conduct extensive interviews to better understand the current landscape of the AE documentation process. For the AE feature in OncoEMR® alone, we've spent more than 40 hours to date on the phone and in person (including several on-site visits), improving the workflow with our development partners.

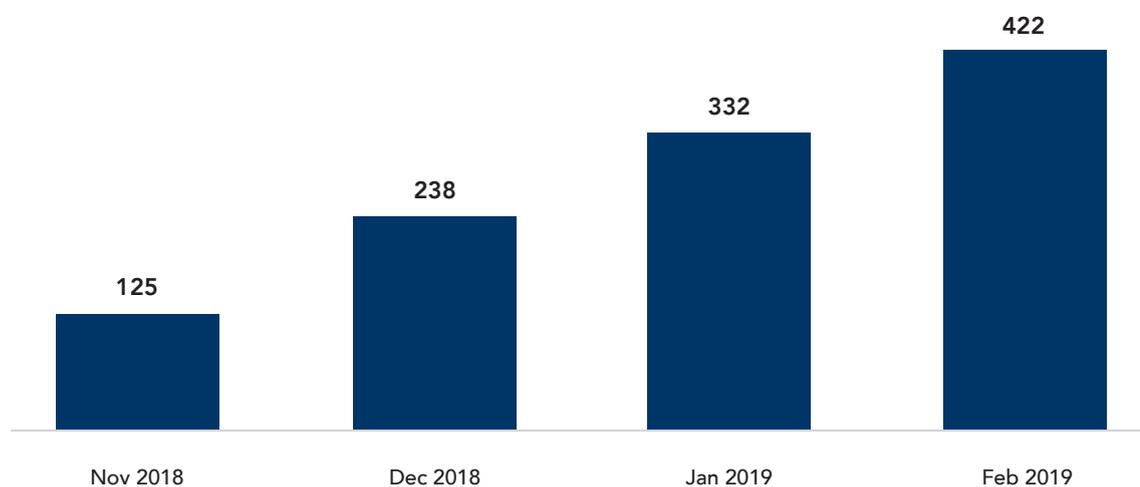
Across user research visits, we observed key trends in the core process for AE documentation (with slight variability) across sites (Figure 2). The research team at a site can find out about a patient's AE in several different ways: The patient may come to the practice for treatment and/or a physician visit and tell the physician, CRC, or chemo nurse; a patient's lab values may come back abnormal; the patient may call the practice to say

they are experiencing an issue; or the patient is hospitalized, which the practice learns from the patient, caregiver or hospital.

However, based on our beta partner research, it is most common for practices to find out about a patient's reported AE through the patient visit, so our user research focused primarily on this process:

- A patient comes in for a visit and sees the PI/SubI. A PI/SubI does a physical exam and review of systems, reviews previous AEs, and asks about new issues. The PI/SubI then jots down notes on paper or a computer during the exam. Next, the patient visits with the CRC (sometimes this visit occurs in tandem with the PI/SubI visit), who asks about any new or existing issues. The patient then receives treatment from the chemotherapy nurse.
- Meanwhile, the PI/SubI writes the visit note and includes any information about the patient's AEs. The CRC writes the research note, adding the AEs that they and the PI/SubI noted to the paper AE log. The CRC then hands the PI/SubI the paper AE log to grade the AE (eg, serious). The PI/SubI adds in the causality, then signs off. The timing of this step depends greatly on when the log is initially filled in and given to the PI/SubI to update. In the best-case scenario, this happens in the same day, but it typically takes 1 to 2 days. The CRC or data coordinator then uses the AE log to enter data into the EDC.

ADVERSE EVENT TRACKING

Figure 3. Number of Adverse Events Added in OncoEMR Over Time (Cumulative)*

*includes test patients

Finally, the monitor uses the paper AE log and the EHR to check the data in the EDC.

In each of these visits, we also learned about some overarching needs to address in an AE feature. For example:

- A need to show different users only the key information that is relevant to their needs:
 - PI/SubIs may want to see only information that requires action from them. For instance, “I don’t want to see the old or closed-out AEs,” said Ted Arrowsmith, MD, a PI at Tennessee Oncology, Chattanooga.
 - Previously in the paper logs, there could be several pages of resolved AEs that the PI/SubI would need to flip through before reaching AEs that required action from them.
 - However, monitors would need to see the comprehensive change history of who changed what, and when.
- A need for structure but room for some flexibility, such as the ability to:
 - Integrate with other physician workflows, yet not affect the workflows of physicians who are not involved in research.
 - Provide easy access to or the integration of CTCAE names and grades, such as with a smart-search or auto-suggest function.
 - Switch easily between CTCAE versions that differ based on the trial.
 - Allow for modifying previously entered data while tracking a comprehensive change history.

Moving From Initial Product to Real-World Readiness

In April 2018, we presented the first version of our feature to our beta partner practices. During this phase of feature development, we continued to learn more about the specific use cases for electronic AE documentation, and we gained more specific feedback about changes to our product. For example, some practices suggested specific termi-

nology changes. Another practice pointed out the importance of specifically calling out AEs that are dose-limiting toxicities (DLTs) for early-phase trials. Additionally, the paper log had other flexibilities that we hadn’t accounted for in the initial version of the electronic log, such as the ability to add an AE that was not listed as a standard CTCAE term. Gerald Falchook, MD, director, Sarah Cannon Research Institute at HealthONE, Denver, expressed that he “wouldn’t want to be boxed in” by the initial version of the digitized workflow.

The electronic AE capture that exists today in OncoEMR® includes functionality that is a direct result of feedback from our beta partners. These improvements include (but are not limited to):

- Specifying a unique AE term, in the cases when AE terms do not fit within the CTCAE terminology,
- Allowing capture of AEs by partial dates (month/year) when teams need to capture AE timestamps different from the month/day/year format,
- Displaying AEs in order of date added, not date edited, because users often prefer to find AEs by when they were added, and
- Adding the DLT, AE of significant interest, and serious AE labels for users to quickly see AEs of interest.

We know that the transition from paper to electronic documentation is not always easy. As burdensome as the paper-based AE documentation process is, it is familiar. Adopting new workflows requires staff training and time for learning, time that community oncology practices cannot always afford to spare. “We’ve used [the AEs feature] on 3 to 4 trials, and all the patients on the new trials. It takes a little getting used to,” said Wendy Koopman, a research manager at Cancer & Hematology Centers of Western Michigan. “It was helpful when we worked through different scenarios, and people could ask questions [to the Flatiron team]. Hands-on is [the] best way to learn.” To adopt this workflow, not only will the research staff and physicians need to change their process, but monitors will also have to adapt to a new electronic log.

That being said, even the FDA is beginning to communicate the benefits of capturing clinical trial data directly in the EHR. In a recently released guidance on the use of EHRs in clinical investigations, the FDA stated, “Fully integrated systems allow clinical investigators to enter research data directly into the EHR. This may involve, for example, use of research modules, use of research tabs built into the EHR system, or use of custom research fields within the EHR system for data that are entered for research purposes.”¹ This excerpt sheds light on the industry shift toward electronic research documentation workflows.

We are seeing continued uptake of the AE documentation feature among our beta partners, integrating it into their workflows. During the initial launch of the feature in November 2018, we observed 125 AEs added to clinical trial regimens, which grew to a total of 238 added by December 2018. By February 2019, a total of 422 AEs had been added using the feature in OncoEMR (Figure 3).

Our beta partners have also shared their enthusiasm about the benefits they have experienced from this change. A clinical research coordinator, Tiffany Cason, from Tennessee Oncology in Chattanooga, reported on the efficiency compared with her old CTCAE workflow: “I don’t use my paper CTCAE booklet anymore, because it’s faster to find the CTCAE term in OncoEMR.” Arrowsmith said he sees value in the consistency of the data captured: “The adverse event log in OncoEMR makes people choose actual adverse event terms. The more the source data from providers/coordinators can match the EDC, the better quality those data will be and the more bulletproof it is to audits and monitoring.”

Electronic AE documentation has recently become available to all practices that subscribe to OncoEMR, and we will continue to improve the feature’s functionality as we hear feedback. We recognize that this shift will require the participation of the entire research team in order for workflow changes to occur. We also recognize that digitizing this otherwise manual process is just one small step in helping research departments reduce the burden of research documentation. We’re excited to partner with our practices to develop something that generates such excitement for our research teams. In the words of Kim Tucker, MT HEW, a senior oncology site manager from Tennessee Oncology in Chattanooga, “[The] adverse event log is the best thing I’ve seen in 10 years. We can’t wait to start using this.” A long road waits ahead, but we’re constantly driven by the passion of our practices to move forward. ♦

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