The Art and Science of Site Monitoring Visit Reports
By John Mitchell

An experienced CRA may follow all the rules and requirements for writing a site monitoring visit report (SMVR), but there are nuances that can make the difference between a report that simply follows that formula and one that really paints a picture its audience can understand.

Roslyn Hennessy, senior project manager at Westat describes the ideal SMVR as “a snapshot in time of what’s happening at the site.” To develop that snapshot, start by asking who will read the report, she advises. There are several types of audiences for SMVRs, all of which have slightly different interests:

- The sponsor wants to know about the performance of the site — is it in compliance with the protocol, are improvements needed, are there any major concerns;
- The PI and site staff want to know if additional training or procedural changes are needed;
- Regulatory authorities and auditors want to know if the site is in compliance and, if not, what corrective action was taken;
- Future monitors need enough information to ensure a smooth hand-off from one CRA to another.

It’s important to give all of the key stakeholders the “heart or the core of the information that they are most interested in,” she says. And although an SMVR should be comprehensive, it also needs to be concise to see Site Monitoring on page 4

Expert Q&A: Effective Patient Recruitment

Mark Summers, WCG president of patient engagement and founder/CEO of WCG ThreeWire, and Molly Hair, ThreeWire director of site engagement and management, provide their take on subjects ranging from forecasting study enrollment to ensuring reasonable return on investment.

**Question: What is the best way to realistically forecast new study enrollment?**

**Summers:** The way to realistically forecast is to literally develop a flowchart, beginning with study candidate identification and following that all the way through to scheduling the initial office visit, attending office visits, all of the sites’ screening processes. And then when you get into the processes that have to happen at the site, mapping out who’s going to do each of those steps and how much time that’s going to take. Because identifying patient candidates is often easier than solving the problem of a site’s bandwidth.

**Hair:** Sites really do need to be honest with themselves about what competition is at their site — not just competition for the patient, but the competition for their team’s time and competition against maybe less obvious sources, like standard of care.

**Question: What are the best methods to advertise to or recruit patients located in rural areas?**

**Summers:** The first thing I would say is, unless you have a patient population where the patients are going to predominate in see Expert Q&A on page 5
Health Canada Issues Guidance on Off-Label Uses of Drugs in Trials
Health Canada released new guidance that the agency hopes will make it easier to study the off-label benefits of drugs in clinical trials. Canadian regulations currently require any treatments purchased for clinical trials for their off-label properties to be designated “investigational drugs.” But Canadian officials worry that’s adding unnecessary hurdles that slow life-saving or life-changing research.

Under the new guidelines, Canadian officials will ask a series of questions about a given treatment before deciding whether it has to be designated an investigational drug, including:
- Does the drug have “an established safety profile when used off-label in the study population?”
- Is it being used as part of a comparator arm in a clinical trial, as supportive or rescue therapy, or whether it’s part of a standard therapy “that another investigational drug is being used to supplement in the investigational arm of the trial?”
- Is there any uncertainty about the risks and benefits of the off-label use?
- Is the drug already authorized in Canada and will trial doses will be bought in Canada?
- Does the off-label use increase the risks for patients beyond the normal risks of taking the medicine, and
- Is it “otherwise clear that the drug to be used off-label is not being tested in the clinical trial.”

Sponsors will have to provide the proposed off-label drug’s Notice of Compliance or Drug Identification Number and explain what the original indication was for. They also will have to explain the proposed off-label use in the trial, how the proposed use is “consistent with current or recognized medical practice,” why the off-label use shouldn’t be considered as a separate clinical trial, and the risks of off-label use, the agency says.


French Titan Dassault Acquires Health Software Firm for $5.8 Billion
Tech giant Dassault Systèmes is buying health software company Medidata Solutions in a whopping $5.8 billion arrangement.

Medidata brings to the table cloud-based technology and clinical expertise that helps fuel the development of therapies for a host of customers, including CROs, drugmakers, biotech firms, and medical centers and sites. The company says it recently has branched out into real-world evidence and analytics.

Janssen Offers Patient-Centered Communication Training
Janssen has developed a training platform aimed at helping clinical trial professionals and patients communicate effectively.

The “HealthCaring Conversations” program currently is in the pilot stage, being used only by a selection of Janssen-sponsored trials, but the company plans to begin rolling it out to all of its trials worldwide in October.

Based on behavior science and a large literature review, the program offers digital learning courses, on-site training and webinars to help trials increase enrollment and retention by teaching them how to communicate with potential trial subjects.

Janssen plans to offer the program to non-Janssen trials eventually and invites site managers to attend its workshop on patient communication at the Society for Clinical Research Sites conference in October.

Dutch Hospitals Test Performance-Based Payment for Off-Label Cancer Treatments
A cancer patient who responds well to an off-label treatment in a clinical trial should not have to pay out of pocket for the drug just because it is not considered as standard of care, a Dutch research institute believes.

The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital is launching a pilot study in which drugmakers and health insurers will share the cost of a drug that has proven effective for an individual even though it isn’t indicated for that person’s type of cancer.

The pilot study will use Bristol-Myers Squibb’s cancer drug Opdivo (nivolumab) for off-label treatment of various rare tumors. The drugmaker will guarantee the medication costs for a patient’s 16-week evaluation phase, and the health insurers will reimburse patients for whom the off-label medicine appears safe and effective after the evaluation period.

“It is becoming increasingly clear that every tumor is biologically unique and that treatment must therefore increasingly be customized to the individual patient,” the institute says.

Large-scale comparative drug studies usually needed for the approval of new indications cannot be conducted for rare tumors, the institute says.

Performance-based drug payments are gaining traction elsewhere, including the US. In November 2018, the Centers for Medicare and Medicaid Services approved Michigan’s plan to allow its Medicaid program to negotiate payment arrangements with drugmakers based on patient outcomes.
This feature highlights changes in clinical research organizations’ personnel.

Zyla
Zyla Life Sciences has announced the appointment of H. Jeffrey Wilkins as senior vice president and chief medical officer, effective immediately. Dr. Wilkins most recently served as the chief medical officer at Lycera.

Akrevia Therapeutics
Joseph Farmer has been appointed chief operating officer at Akrevia Therapeutics. Prior to joining Akrevia, Farmer was the senior vice president, general counsel and corporate secretary at Tesaro.

Altimmune
Will Brown has been named the chief financial officer at Altimmune. Brown has been serving as the acting chief financial officer since May 2018.

Mersana Therapeutics
Mersana Therapeutics has announced Brian C. DeSchuytner as senior vice president of finance and product strategy. DeSchuytner was previously at Tesaro, where he was vice president responsible for the ZEJULA (niraparib) commercialization.

Grail
Hans Bishop has been appointed chief executive officer at Grail and Joshua Ofman has been named chief of corporate strategy and external affairs. Bishop was previously the chief executive officer at Juno Therapeutics. Ofman was most recently at Amgen as senior vice president, global value and access and policy.

Roche
Roche has announced that Thomas Schinecker has been promoted to chief executive officer of Roche Diagnostics, effective August 1. Schinecker is currently head of centralized and point-of-care solutions at Roche.

Celsius Therapeutics
Tariq Kassum has been named president and chief executive officer of Celsius Therapeutics. Kassum was formerly the co-founder of Obsidian Therapeutics and served as chief operating officer and head of corporate development.

Signant Health
Signant Health has appointed Lawrence Miller as chief technology officer. Miller was most recently chief security officer for Symphony Communication Services.

eGenesis
Ariel Jasie has been named chief business officer and general counsel at eGenesis. Jasie was previously chief business and strategy officer at Dermavant Sciences.

PMV Pharmaceuticals
PMV Pharmaceuticals has named Deepika Jalota head of regulatory affairs. Jalota was formerly the global regulatory strategy head of Oncology I at Bayer HealthCare Pharmaceuticals.

SCWorx Corp.
Tad Schweikert has been appointed chief operating officer of New York-based SCWorx Corp. Schweikert was most recently a senior principal of enterprise solutions at Vizient.

Paradigm
Paradigm has promoted Kevin Turner to chief executive officer of the Catastrophic Care Management division. Turner previously served as chief sales and marketing officer for Catastrophic Care Management. Karen Jones has been appointed to the newly created role of chief human resources officer. Jones was most recently senior vice president, HR business partner for Experian, Inc.

Dicerna
Steven A. Kates has been named vice president, regulatory affairs at Dicerna. Kates was most recently the director of regulatory affairs at Takeda Pharmaceuticals. David J. Caponera has been appointed head of patient advocacy and patient services. Caponera was formerly vice president, patient engagement and access support at Catalyst Pharmaceuticals.

Freeline
Freeline has announced the departure of Anne Prener, its chief executive officer. Prener joined the company in 2017. An executive search is underway for the chief executive role. In the interim, Freeline chairman Chris Hollowood will act as executive chairman.

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avoid burying important information or tiring the reader. Writing an SMVR is an exercise in deciding what information needs to go in and what needs to stay out.

“We really need to get more efficient in terms of going just from point A to B,” she says, “but in that A to B, we need to include some important things.”

Hennessey recommends starting at the end. A monitor usually will have an overall message to convey in the report and should choose the information that supports that message. “Know what you want to say ahead of time and write to your conclusion,” she says. “What do I need to say to get me to that conclusion?”

Be analytical in what you write, she advises. A good SMVR is more than an “information dump.” When writing the report, provide the reader with some context instead of just transcribing notes. Explain what those notes indicate, Hennessey urges. Look for common denominators in the findings and identify root causes of problems. Pay attention to trends, from a single visit and across several visits.

In addition to being analytical, an SMVR should be objective. Elizabeth Weeks-Rowe, a clinical research training consultant, advises SMVR authors to keep the human factor in mind. A monitor may encounter many different personalities in a trial, but they should not be reflected in the site report.

“Taking the emotion out of verbiage is critical,” says Weeks-Rowe. “Be factual, not emotional.” If, for example, a principal investigator is less than professional, this impression should not be included in the report. Instead, address any outcome of that behavior. Making sure that all findings are actionable helps avoid an emotional narrative, she says.

Hennessey notes that an attentive monitor can enhance communication between the site and the sponsor. “Sometimes the investigators feel like the sponsor is too far removed,” she says, and wonder “where is my voice heard?” The investigator may feel more comfortable communicating with the CRA, who then passes the information on to the sponsor via the SMVR.

The last step in writing an effective SMVR is recommending corrective actions, Hennessey says. All issues/findings noted in the report should have an associated action and/or resolution. Have a “no finding left behind” policy, she advises. But, she cautions, don’t be overly prescriptive. It’s important that the PI and site staff take responsibility for problems and solutions.

Both Hennessey and Weeks-Rowe stress taking care of the basics, carefully reviewing the SMVR for misspellings and grammatical errors. Flaws in the presentation, Hennessey says, distract from the content and message and ultimately hurt the credibility of the monitor and the company.

Ultimately, the SMVR must be able to stand the test of time, Hennessey says. Trials can last for years and go through several CRAs along the way. “It’s not often that a CRA gets to work with a site from initiation to closeout,” she notes. And a regulatory request for further information or an audit can come at any time. In one case, she says, the FDA came back to question the SMVR 10 years after the fact.
Expert Q&A
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rural areas, then don’t pick sites in rural areas because recruiting in a rural area is very difficult. So this is really more a question the answer to which entails going upstream into the site selection process. If you have to choose patients in rural areas, conduct a very careful site selection process. You should be picking sites that have patients in their database or have ready access to patients without advertising for the study. You have a very sparsely distributed patient population. Media costs are going to be amortized over those patients and it’s going to be very expensive. If you do have to advertise, then local advertising is going to be the way to go. Meaning, local newspapers or small town newspapers. Interestingly, the page-per-page readership of small town newspapers tends to be a lot higher than it is in big cities.

Hair: There needs to be a reason that you go to a rural site, and there may be very logical ones depending on what your protocol is. What I would recommend to the sponsor or CRO, in order to set the site up for success, is that they engage in discussing recruitment earlier on in the process and maybe interact with the recruitment vendor or other places where they can consult with some expertise about recruitment earlier in the process because the information that they get about the strategy may better equip the sponsor for adjusting the timeline for recruitment and enrollment, give them a more realistic notion of when the timelines can be achieved within a rural setting.

Question: Clinical trial agreement contracts play a huge role in patient recruitment. Which is better: a cost-reimbursable or fixed-price model?

Summers: From our perspective, the cost-reimbursable model is better than the fixed-price model that may be great for a CRO or sponsor, may be great for the internal budgeting process. But the economic equation has to work for sites. So if it turns out that this fixed-price model is going to become detrimental to the site — either in terms of the site incurring costs that they had not forecasted when they contracted for the study or perhaps putting that study at a disadvantage from a reimbursement standpoint compared to other studies that the site is engaged in — I think cost reimbursable is virtually always a better way to go.

Question: Does your approach include recruitment at any cost? Where are the limitations of that approach?

Summers: Well, the short answer is no. It’s not recruitment at any cost, it’s recruitment at a cost that represents an ROI that is acceptable to the sponsor or CRO, whoever’s paying for recruitment. And so the limitations are really going to be set by that ROI. And that’s going to depend on each individual study. It’s possible to calculate the value of each enrolled patient. There’s a simple spreadsheet tool we’ve developed to do that. And then you can build a recruitment funnel and enrollment funnel and evaluate the cost and compare the cost of enrolling each patient against the value of that enrolled patient and determine return on investment. We try to do that up front.

Some projects we have a cost per enrolled patient of $4,000 or $5,000, and that’s acceptable. For some, it’s $25,000 or $30,000, and that can be acceptable. But if it should be $5,000 or $6,000, that’s not acceptable. So no, it’s not recruitment at any cost. That has to be reasonable and it has to make sense and represent that reasonable return.
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At WCG, we use our evidence-based insights to help set you up for success from the start. From strategic site selection to accelerating enrollment, our solutions empower you to anticipate problems, make better decisions and gain greater control over the key elements of your clinical study startup.

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## Drug & Device Pipeline News

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<td>TERN-101 non-alcoholic steatohepatitis (NASH)</td>
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<td>OnKure, Inc.</td>
<td>OKI-179 advanced solid tumors</td>
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<td>Purdue Pharma, L.P.</td>
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<td>Goldfinch Bio, Inc.</td>
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<td>Aerpio Pharmaceuticals, Inc.</td>
<td>AKB-9778 primary open angle glaucoma (POAG)</td>
<td>Phase I/II trial initiated enrolling 48 subjects</td>
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<td>Adocia</td>
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<td>Phase I/II trial initiated enrolling 24 subjects in Germany</td>
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<td>Tolero Pharmaceuticals, Inc.</td>
<td>TP-0903 previously treated chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL)</td>
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<td>Pharming Group N.V.</td>
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<td>Noveome Biotherapeutics, Inc.</td>
<td>ST266 persistent corneal epithelial defects (PEDs)</td>
<td>Phase II trial initiated</td>
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<td>Ivenix, Inc.</td>
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<td>CorMatrix Cardiovascular, Inc.</td>
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<td>Bolder Biotechnology, Inc.</td>
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<td>Palatin Technologies, Inc.</td>
<td>PL-8177 non-infectious intermediate, posterior, pan and chronic anterior uveitis</td>
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<td>Genentech</td>
<td>Rituxan (rituximab) in combination with glucocorticoids (GCC) granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) in children two years of age and older</td>
<td>Priority Review granted by the FDA</td>
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<td>SpeeDx Pty. Ltd.</td>
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<td>Innovative Health Solutions, Inc.</td>
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<td>Polivy (polatuzumab vedotin-piiq) in combination with bendamustine plus Rituxan (rituximab) diffuse large B-cell lymphoma (DLBCL)</td>
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<td>Merck</td>
<td>KEYTRUDA metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC)</td>
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<td>Senseonics Holdings, Inc.</td>
<td>Eversense Continuous Glucose Monitoring System diabetes</td>
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For news on trial results, FDA approvals and drugs in development, Join the LinkedIn Drug Research Updates group!
Upcoming Event Highlights

Conferences

JUNE 23-27, 2019
Drug Industry Association 2019 Annual Conference
San Diego, CA

SEPTEMBER 4-5, 2019
Clinical Trial Risk & Performance Management Summit
Philadelphia, PA

SEPTEMBER 27-29, 2019
Society of Clinical Research Associates 2019 Annual Conference
San Antonio, TX

OCTOBER 23-25, 2019
FDA Inspections Summit
Bethesda, MD

OCTOBER 27-30, 2019
MAGI Clinical Research Conference 2019 West
Las Vegas, NV

[ VIEW ALL CONFERENCES ]

Webinars

JUNE 26, 2019
Collect All the Money You’re Owed: Put Financial Audits to Work for You
11:00 a.m. – 12:00 p.m. EDT

Chances are, yours is one of the many research sites leaving money on the table. Maximize what you collect with this free, not-to-be-missed webinar.

› How to perform financial lookbacks on open studies and those in close-out
› How to insert language into your CTAs to ensure the study sponsor/CRO provides you with all necessary documentation associated with payment
› And more

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