The CenterWatch Monthly

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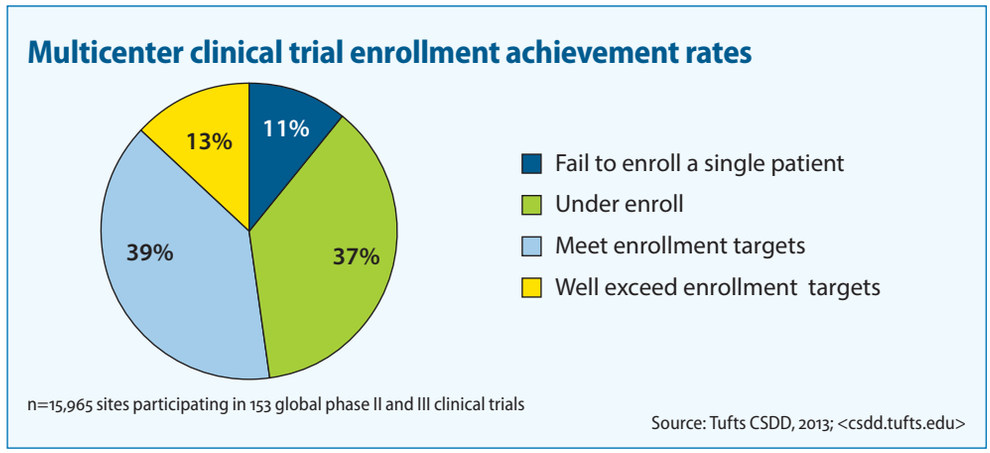
Balancing new with common recruitment tactics

Approaches shift to include social media and digital analytics

By Karyn Korieth



For sponsors and CROs, patient recruitment has become a moving target. Recruitment tactics are shifting from the use of traditional, centralized advertising to digital and online media. Outreach strategies have become more targeted and companies are moving toward leveraging networks of electronic medical records (EMRs) and other data to support more effective recruitment for clinical trials.

Yet there are mixed opinions about the value of digital or social media campaigns. While drug development executives expect EMRs and health records to play a major role in patient recruitment within five years, according to the Tufts Center for the Study of Drug Development (CSDD), much of the data needed to identify eligible clinical trial participants doesn't exist in EMRs. The systems weren't designed for simplifying searches across files.

"It's a really tough space to crack. The challenges are very well understood. The solutions are on a spectrum of expensive and ineffective to promising and unproven," said David Kronfeld, senior director, Corporate Development & Strategy, Medidata Solutions.

As clinical trials become increasingly complex and more difficult to recruit, requiring study participants to meet more detailed inclusion/exclusion criteria and companies increase their focus on rare diseases and personalized medicines with small patient populations, the industry needs to think critically about how to address patient recruitment challenges. What is needed in order to engage the patient using a particular technique?

"We certainly recognize a need for new approaches and more creative approaches," said Katie Shaw, director of Site and Patient Networks, IQVIA. "The positive is that we know the patients are out there. We

see **Patient recruitment** on page 7

Survey shows companies aim to increase range of patient data in clinical trials

By Zack Budryk

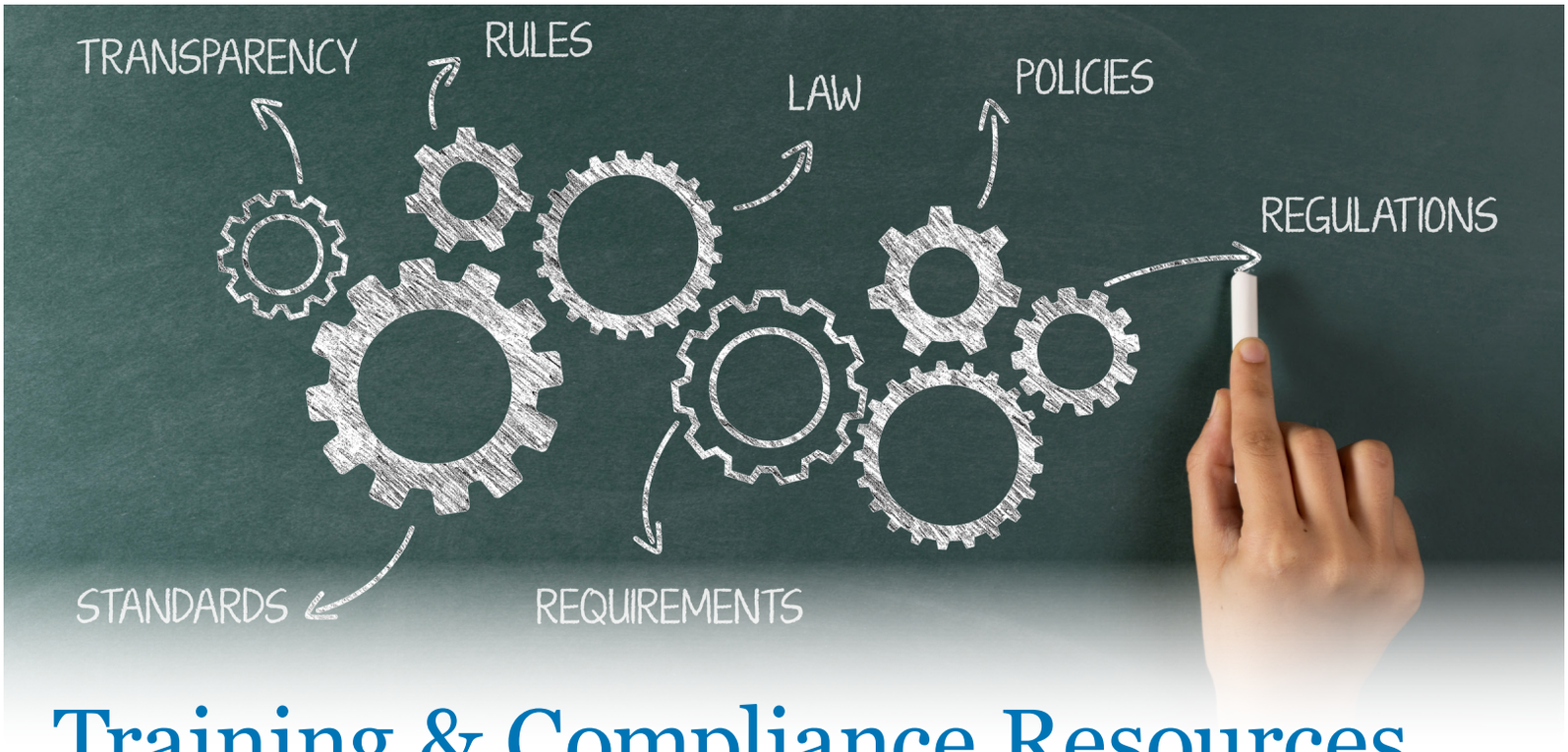
Most life sciences companies plan to significantly step up their use of real-world data sources over the next three years, according to a new survey by the Tufts Center for the Study of Drug Development.

In the second report from the 2017 eClinical Landscape Study, one of the largest, most in-depth surveys of clinical data management professionals, 97% of companies polled said they plan to increase their use of at least one source of clinical data to improve the accuracy of their decisions in the development process. Ninety-eight percent of respondents, however, report challenges with their clinical data management systems, indicating a greater need to prepare as they anticipate growth.

Most data companies currently gather is from electronic case report forms. But most respondents said they plan to source more data from electronic patient reported outcomes and electronic clinical outcomes assessments—two sources that currently account for only 4% of the data they manage.

On average, respondents rely on four sources for clinical data, but this is project-

see **Patient data** on page 12

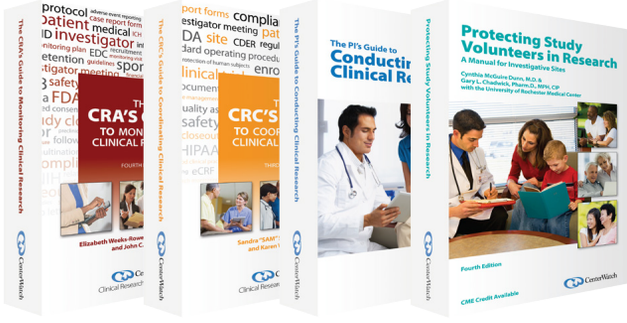


Training & Compliance Resources

CenterWatch has valuable resources for training and compliance purposes to help you succeed in conducting and managing clinical research programs.

Training

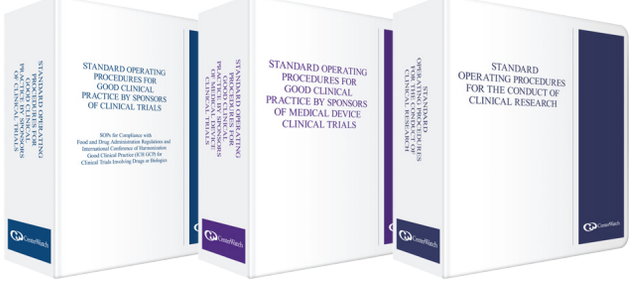
CenterWatch's training guides are for individuals interested in clinical research and for experienced professionals seeking to better understand their roles and improve the management of their clinical trials operations in a safe and ethical manner. *Volume discounts available.*



- Prepare for certification exams
- Train colleagues
- Teach clinical research courses
- Expand your skills and knowledge
- Study for college courses or internal programs

Compliance

Standard Operating Procedures (SOPs) are critical to an organization's quality performance and the ethical conduct of clinical trials, while helping to create and sustain a successful clinical trial program.



- Templates comply with federal regulations and requirements
- Each SOP is available digitally and includes forms, checklists and study management materials
- Optional binders with tab inserts available for separate purchase

Visit store.centerwatch.com

Dear Readers,

The holiday season is upon us! As we enter one of the most festive—and hectic—times of the year, give thanks for your friends, family and good food.

This December, keep an eye out for an upcoming FDAnews/CenterWatch webinar. "Sensors and Wearables in Clinical Trials: Critical Components for Success" launches Wednesday, December 20, from 1:30 p.m. to 3:00 p.m. ET. Visit www.fdanews.com/wearables to sign up.

We're ending the year on a high note. In this issue, our top feature tackles the necessary critical thinking for an industry looking to update patient recruitment tactics. While traditional methods have their place, the promise of Big Data and EMRs capture the attention of many. Another question addressed is: "Whose responsibility is it to recruit patients?" There's no perfect answer, but our top story offers food for thought.

For our second feature, we've dived into the use of read-world data sources in the life sciences. Several reports show that increased use is expected, with outstanding numbers of respondents looking toward the electronic informed consent space. The feature also covers mHealth and clinical data management systems.

Don't miss our January issue of *The CenterWatch Monthly*. Our primary feature is a showcase of 20 innovators changing the face of the clinical trials industry. These 20 were selected based on a key innovation they've crafted, developed, collaborated on, shepherded, released or expanded. We were beyond humbled at the truly outstanding submission response rate. While we received some amazing innovators and innovations—it was incredibly difficult to narrow down selection, and we were forced to leave out some incredibly worthy innovators—these top 20 are undeniable.

As you close the year, update your advertising campaigns with CenterWatch. Contact sales@centerwatch.com to develop a package to meet your business needs. We can help build brand awareness or promote a new product, service, webinar or white paper. It's your last chance to lock in 2017 advertising prices!

With appreciation,

Stephanie Hill
Managing Editor

In this issue

Coming in January

Top 20 Innovators showcase
Celebrating innovators driving change in the industry

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Regulatory Update

FDA Simplifies Requirements for Individual Patient Expanded Access

On October 3, 2017, the FDA updated Form FDA 3926 and its instructions, as well as other related guidance documents (below) regarding the institutional review board (IRB) review requirements for physician requests for individual patient expanded access treatment use of investigational drugs. The changes to Form 3926 are intended to allow for a waiver of the requirement for review and approval at a convened IRB meeting if the patient's physician obtains concurrence by the IRB chairperson (or designated IRB member) before the treatment use begins.

The Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers Guidance has been updated to address how FDA reviews adverse event data in the expanded access context and to reference the new requirement that expanded access policies be publicly posted. Other updated documents include:

- Individual Patient Expanded Access Applications: Form FDA 3926 Guidance
- Waiver of IRB Requirements for Drug and Biological Product Studies Information Sheet

The reasoning for this change was discussed in this notice from Dr. Scott Gottlieb, FDA's Commissioner: https://blogs.fda.gov/fdavoice/index.php/2017/10/expanded-access-fda-describes-efforts-to-ease-application-process/.

FDA Issues Final Guidance Documents

These new final guidance documents related to clinical trials include:

Minutes of Institutional Review Board Meetings

In the September 25, 2017, *Federal Register*, the FDA and the Office for Human Research Protections (OHRP) of the Department of Health and Human Services (DHHS) jointly issued a final guidance titled, "IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects." The guidance is intended for institutions and IRBs that are responsible for the review and oversight of human subject research conducted or supported by DHHS or regulated by FDA. To enhance human subject protection and reduce regulatory burden, OHRP and FDA have been actively working to harmonize their respective regulatory requirements and guidance for human subject research.

The purpose of the guidance is to assist institutions and IRBs in preparing and maintaining minutes of IRB meetings that meet the regulatory requirements set forth in FDA and DHHS regulations. The guidance also provides general recommendations on the type and amount of information to be included in the minutes. This guidance makes final the draft guidance of the same title dated November 2015. Significant changes in the final version reflect providing IRBs flexibility for not including certain information in minutes when the information is addressed in other IRB records.

Submit electronic comments at http://www.regulations.gov/ (enter the Docket Number below in the Search box). Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Identify your comments with Docket No. FDA-2015-D-3638. There are also instructions on how to submit confidential information. If those instructions are not followed, any submitted confidential information will be made public.

Age, Race and Ethnicity Data in Medical Device Clinical Studies

In the September 12, 2017, Federal Register, FDA issued a final guidance titled "Evalua-

tion and Reporting of Age, Race, and Ethnicity Data in Medical Device Clinical Studies." The purpose of this document is to outline FDA's recommendations and expectations for the evaluation and reporting of age, race, and ethnicity data in medical device clinical studies. This document makes final a draft version released on June 20, 2016. This document extends the policy established in the FDA's guidance titled, "Evaluation of Sex-Specific Data in Medical Device Clinical Studies" (August 22, 2014) to additional demographic subgroups of age, race and ethnicity

The guidance outlines the FDA's recommendations and expectations for patient enrollment, data analysis, and reporting of age, race, and ethnicity data in medical device clinical studies. Specific objectives of this guidance are to (1) encourage the collection and consideration of age, race, ethnicity and associated covariates (e.g., body size, biomarkers, bone density) during the study design stage; (2) outline recommended analyses of study subgroup data with a framework for considering demographic data when interpreting overall study outcomes; and (3) specify the FDA's recommendations for reporting age, race and ethnicity-specific information in summaries and labeling for approved or cleared medical devices. The FDA believes these recommendations will help improve the quality, consistency and transparency of data regarding the performance of medical devices within specific age, race, and ethnic groups as well as encourage appropriate enrollment of diverse populations including relevant age, race and ethnic groups. Proper evaluation and reporting of these data can benefit patients, clinicians, researchers, regulators and other stakeholders.

Submit either electronic or written comments at any time as described above. Identify your comments with Docket No. FDA-2016-D-0734.

The Regulatory Update is excerpted from Research Practitioner, *Volume 18, Number 05, November-December 2017.*

Month in Review

Top *CWWeekly* headlines from the past month:

- Voice assistant technology poised to fundamentally transform clinical research
- Don't fear for the orphan drug tax credit—it will survive
- Insys Therapeutics founder arrested on charges of racketeering
- GLOBE platform attempts worldwide standardization of clinical trial benchmarking
- Clinical research in the cloud, with help from Microsoft
- Circuit Clinical, ePatientFinder partner
- Investigator attrition and solving the "one and done" phenomenon
- Partnership aims to accelerate development of new immunotherapy strategies

Recent *Pulse* column topics:

- *The Pulse on Study Conduct*: Relationship development and their sustainability
- *The Pulse on Technology*: "Are we there yet?"—the long journey to paperless clinical trials
- *The Pulse on Study Startup*: Accelerating trials from the outset
- *The Pulse on Patient Recruitment*: Grasping for innovation—where should industry look?

Executives interviewed for the *Three Questions* column:

- Tim Kulbago, vice president of Imaging, ERT
- Gary Palgon, vice president Healthcare and Life Sciences, Liaison Technologies

For more information about any of the above articles, please refer to Volume 21, Issues 42-45. To subscribe to CWWeekly, *visit http://store.centerwatch.com, or contact sales@centerwatch.com.*

David Novotny
Senior Vice President
Medical Device &
Diagnostics Division
Novella Clinical

How to run a successful clinical trial for embolic protection devices

Because of the surge in the use of embolic protection devices (EPDs), the market for these devices is expected to grow into a billion-dollar industry. EPDs may protect patients from serious neurological damage that could occur during transcatheter aortic valve replacement (TAVR) procedures; they are designed to catch or divert valve debris that may travel to the brain. EPDs are commercially available in Europe, and the FDA cleared an EPD for the first time last June.

Despite their potential, EPD trials have shown mixed success. To compete in the growing TAVR market, EPD manufacturers must consider three factors to maximize their chances for trial success.

First, principal investigators will need to collect comprehensive patient health histories. This includes measuring the extent of their patients' illnesses, while accounting for factors that can cause attrition and risk a trial's viability. Investigators would, for example, ensure their patients' conditions are stable for at least 30 days prior to study enrollment.

Second, manufacturers should select trial sites based on their commitment and proven ability to dedicate significant time and resources to the study—more than is expected with a traditional device trial. We recommend building multidisciplinary investigative teams, including not only a heart failure/valve cardiologist, an interventional cardiologist, cardiovascular surgeons and imaging specialists, but also geriatricians, stroke neurologists, electrophysiologists, anesthesiologists and behavioral specialists.

Third, investigators must standardize their definitions of stroke and their criteria for diagnosing neurological complications. These standards should fall within existing and anticipated regulatory guidelines to streamline approval and adoption by payers.

For the EPD market to grow as anticipated, manufacturers must design their trials to more clearly demonstrate the effectiveness and safety of their devices. The strategies mentioned here will help manufacturers design better trials with more elucidating results that can help them develop EPDs more successfully.

Barbara Zupancic
Director, Global Patient
Recruitment Optimization
Worldwide Clinical Trials

Patient engagement key to improving Alzheimer's study success rates

Alzheimer's disease (AD) is the most common cause of dementia, contributing to 60% to 80% of cases. By 2050, the Alzheimer's Association expects the number of people diagnosed with dementia to increase from 46.8 million to 131.5 million. There is a clear need for continued drug development in this area.

However, AD trial recruitment is challenging due to medical comorbidities, extensive use of prescribed and OTC medications, behavioral complications of AD and many other factors. To address recruitment challenges, there are a number of tactics researchers can employ to maximize patient engagement.

We have seen much benefit from the utilization of digital media. Facebook and other channels provide a direct and low-cost way to reach millions of individuals seeking health-related information. By utilizing social media, forums, blogs, etc., and through the clever use of geo-targeted digital media programs, we help researchers promote study awareness, generate study interest and boost referrals.

Engagement and participation in community outreach events has also proven to increase interest and participation in AD clinical trials. For example, researchers can set up "Lunch and Learn" events for clinics, community screenings or other events in partnership with local support and advocacy groups where study information is made available to potential patients and their caregivers.

At Worldwide, we have found that following attendance at these events, we see an uptick in patient and caregiver interest, physicians that are more likely to actively engage with a study, and patient referrals to investigative sites, all resulting in a return on investment within two to three weeks.

By harnessing the power of the internet, engaging with the medical and patient communities, and utilizing insights gathered from patients and their caregivers, researchers can better engage with potential participants.

Seth B. Forman, M.D.,
Principal Consultant
Forsight Consulting

Everything you wanted to know about a clinical research site but were too afraid to ask

Clinical research is intense. Deadlines are tight. Protocols are complicated. But we all have the same goals: deliver safe and effective medications to patients who need them. Sometimes sites, monitors, CROs and sponsors collectively forget that there are human beings behind every email, but that's what every site has to keep in mind if the principal investigator wants a successful trial. Here's what else you should know about working with sites.

1. We work really, really hard. Enrolling appropriate subjects for a complicated trial consumes the administrative time and energy of 15 routine office (non-research) patients.

2. A reliable site sees every protocol. Our site routinely declines twice as many trials as we accept. The management and oversight of the trial are just as important as the contracting. After all, it is our responsibility to conduct the trial according to protocol and the CRO/Sponsor's responsibility to assist us when it comes to being "inspection ready."

3. Work with us. Sometimes it feels like sponsors and CROs are working against us. Please monitor us on schedule and keep up your end of the contract.

4. PIs want you to be a mensch. That's Yiddish for a human being. Develop protocols with open-label extensions. Offer the drug to subjects after FDA approval even if they are not insured or if insurance does not cover the medication.

I, like many others, am a clinical researcher and a practicing physician on the frontlines with patients who have no or inadequate therapy for their ailments. Our primary goal is to help our patients, which is why it's essential to remember the site is a crucial ally. Sites want sponsors and their studies to succeed, and working together—and keeping the mensch in mind—can get everyone there.

Patient recruitment

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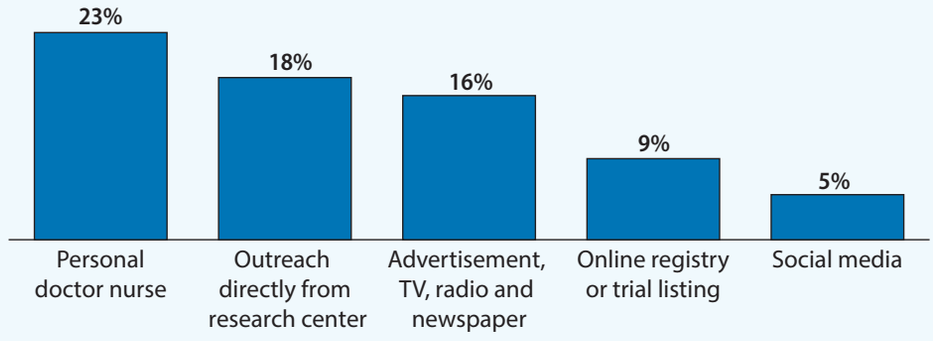
just need to be more precise, more targeted and strategic in how we find them and how we then take that next step to connect them to an investigator. There are a lot of different challenges in that whole progression."

Shift from traditional advertising methods

In 2011, a Tufts CSDD study identified centralized newspaper and radio advertisements as among the top patient recruitment tactics used by sponsor companies. Yet Joan Bachenheimer, founding principal and chief operating officer of BBK Worldwide, has observed that in the past few years, sponsor companies have returned to a strategy of hedging operating risk by increasing the number of investigative sites in a study and extending recruitment timelines, which has eroded the need for traditional, centralized advertising. Bachenheimer argued that media outreach is a far more effective tactic, but she said not all players in the space know how to garner a referral all the way through to enrollment.

Top five ways that study volunteers first learned about a clinical trial

Percent mention



Source: CISCRP 2017 Perceptions & Insights Study; n= 2,194 Past Study Volunteers

"There has been a huge lack of confidence in traditional, centralized media output," said Bachenheimer. "If they do traditional, centralized media outreach, they want it done at risk. They perceive so little value for it, they don't want to pay for it."

Big mass media campaigns are still used, particularly for large phase III studies where it's easy for patients to self-identify, but efforts have significantly shifted toward patient recruitment practices that employ digital and social media advertising techniques. New patient recruitment companies have emerged that specialize in social media and internet-based recruitment solutions, and traditional full-service firms have expanded services and technology to include digital approaches.

"Digital and social efforts are becoming a core part of recruitment efforts," said Matthew Howes, executive vice president, Strategy & Growth at PALIO, part of INC Research/inVentiv Health. "Digital and social should not be thought of as 'channels.' They should be thought of as modes and methods. They are how people communicate. With health being one of the leading topics online, it doesn't take a giant leap of faith to understand this is where patient recruitment should begin."

Social media targeting methodologies and digital campaigns have become more

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Patient recruitment

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sophisticated as companies use data from various sources, including patient databases and health information websites, to develop patient profiles and heat maps of potential study candidates, understand which channels and websites patients visit and how they talk about their condition to each other. An increasing number of online campaigns are directed at patient advocacy groups or rely on peer leaders to publicize their message and include educational material about clinical trials or disease areas to help create a dialogue with patients.

"Patient recruitment is about making and maintaining connections with people," said Martin Collyer, chief operating officer, Patient Recruitment and Retention, Bioclinica. "We don't spend a huge amount of money on marketing and outreach until we know that we've got the target audience that will respond. We develop a feasibility and use those in-depth insights to understand the unique study challenges and opportunities to create key messaging and positioning."

Tudor Reilly Health, a company that specializes in reaching self-referring patients for clinical trials, works with an international network of patient navigators, typically freelance clinical research associates (CRAs), to identify and reach out to patient groups that are focused on the particular disease area or condition. Tudor then invites them, on a goodwill basis, to take ethically-approved communication about a study and post a link to a website, mention the study in a newsletter or distribute flyers. Communications will contain the URL to the study website or, if they are not using a website, it will include contact details for the local investigator.

"We know from our own analytics that people who come to a clinical trial website from patient groups, as opposed to cold advertising, are 30 to 40 times more likely to complete the eligibility questionnaire successfully—as well as being a much more likely candidate for referral. Often, people who come through cold advertising fill in the questionnaire out of curiosity, not because they are serious about joining a clinical study. If they come from a patient group, they are much more engaged," said Peter Coë, managing director and co-founder of Tudor Reilly Health.

Although social and digital media campaigns reach large audiences, many remain skeptical about their ability to convert patients into study participants. Results from the Center for Information and Study of Clinical Research Participation's (CISCRP's) 2017 Perceptions & Insights Study, which builds on previous studies conducted in 2013 and 2015, found that only 5% of study participants first learned about a study through online patient communities or social media sites.

Significantly, metrics to support social media or online approaches often rely on the number of page views or click-throughs rather than patient enrollment rates. In addition, reaching patients through advocacy communities or running online ads in places they visit can result in filling the top of the so-called patient-recruitment funnel with interested patients, yet only a small percentage ever reach the bottom of the funnel to actual recruitment. For example, an analysis conducted by Clinical Performance Partners of a central recruitment campaign for a neurology indication, which used a combination of traditional and online/social media tactics, found that the effort resulted in 40,000 inquires. Yet after spending $1.3 million on the campaign, only 137 patients were enrolled, which was far fewer than the 850 subjects needed. As the model potentially creates more work for the study staff, 34% of referrals were not followed up on by the site.

"Enrollment rates with social media, with a few exceptions, have been unimpressive," said Mark Summers, chief executive officer, ThreeWire, a WIRB-Copernicus Group (WCG) company. "As an industry, we need to manage expectations properly. It's wrong for a recruitment firm to sell a million-dollar recruitment campaign without predictive metrics that can forecast its results. It's wrong and detrimental to the industry."

Some also consider online patient recruitment a limited strategy because it depends on patients actively searching for clinical trial information and exploring treatment alternatives beyond the recommendation of their physician.

"A patient who searches for a trial can find lots of resources. But what about the patients who aren't looking? What about patients who don't know about clinical trials? Basing an entire approach around

Investigative site activation and achievement rates

	Global activation rates (Percentage of sites randomizing at least one patient per trial)	Global achievement rates (Percentage of sites meeting patient enrollment target per trial)
Overall	89%	87%
Independent physicians	91%	96%
University/Hospital/ Government Clinics	87%	73%

Source: Tufts CSDD, 2013; <csdd.tufts.edu>

a patient who wants to find that information probably makes sense in some disease states. If a patient has cancer, they are very active in searching for treatment and alternative care pathways. But is the diabetic looking for a clinical trial when there many drugs out there that have worked for decades? It's a challenge," said Medidata's Kronfeld.

Nevertheless, in a roundtable discussion hosted by the Tufts CSDD, R&D executives said they expect use of social media, which already supports communication within patient communities, will grow as a recruitment tool by providing pathways between sites and specific populations.

"Social media is another part of the marketing mix and it's not going anywhere," said Scott Connor, vice president, Corporate Marketing and Strategy, Acurian, which was acquired by PPD in 2013. "The forms and methods will invariably shift over time but social media is about aggregation and ultimately it's becoming a more targeted channel across lots of goods and services, including clinical trials. Like any tactic, social media marketing requires vigilant tracking and adjustments. It can be wildly expensive in the wrong hands and extraordinarily cost effective in the right ones. As a single-threaded patient sourcing strategy, however, social media will have its volume and time limitations. To fill big trials fast, you need to leverage a wide variety of marketing channels and adjust them constantly during enrollment."

Promise of Big Data and EMRs

As access to health records and Big Data increases, the industry has begun to see a shift toward data-driven solutions to patient recruitment. Technology companies have begun to develop networks of electronic medical records and databases that could give sponsors or CROs objective data about available patient populations, rather than rely on estimates from sites, and identify investigators within health systems or geographic areas with the greatest access to those patients.

IQVIA has developed an approach that uses analytics and real-world data (RWD) to improve patient recruitment at all stages, not just when sites are open to recruitment. The strategy leverages data to select sites with the specific target patient population in their geographic area and to identify sites already treating patients that meet the study's high-level inclusion/exclusion criteria. Teams analyze data to help investigators set realistic recruitment goals during study initiation and determine whether sites will need additional tools and support. Site data is monitored to help develop strategies for identifying and engaging potential study participants. Similarly, data and analytics is used to develop and support referring physician networks in communities.

"It allows us to be more precise because we place the studies in the locations where we confidently know qualified patients already are. It becomes about being more targeted and cost-effective in how we help those sites connect and communicate to those patients," said Shaw. "With the data, we can help sites get a little farther down the road a little more quickly in the early days."

A major challenge in working with comprehensive data sets, however, is understanding how to translate the information into identifying and engaging individual patients for a clinical study. EMR-driven recruitment inherently uses de-identified data, which can guide development of study design, site identification, start-up methodology and geographic maps of potential patients. But it still relies on sites to review charts or mine electronic health

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Patient recruitment

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records to identify individual patients who meet the study's inclusion/exclusion criteria and to connect with those patients. In addition, even if the data suggests a patient would qualify for a clinical trial, that patient might not understand clinical research or be interested in participating.

"There is a move toward using electronic search tools to survey electronic health records and electronic medical records to identify patient candidates. Right now, none of these tools have advanced beyond the ability to conduct a high-level records survey or serve as a selection tool for good sites. Nobody has yet come up with an electronic tool that is a substitute for a human being looking at charts," said ThreeWire's Summers. "There is a real promise in this approach. But the technology is going to have to develop. There are legal and regulatory issues surrounding data privacy and how to re-identify data so that it can be used. There are also questions around who bears the cost of setting up a database at an institution so that these technology tools can be used. There are very real questions that have to be figured out. But given time, and managing everybody's expectations properly, I think that can occur."

Sites largely responsible for recruiting patients

For many trials, sponsor companies rely on sites to recruit the majority of patients from their own databases or in-house recruitment efforts. Experienced investigative sites typically combine traditional chart review with grassroots community outreach, physician referrals and social media campaigns. Many also use local advertising to build a brand in the community.

LCM|Manna Research, a network of fully owned and integrated clinical research sites in Canada, won the Society for Clinical Research Sites (SCRS) 2017 Site Patient Enrollment Innovation Achievement (SPRIA) award for its campaign to recruit pediatric patients into a type 1 diabetes trial. Due to the nature of the trial, the site built a program which differed from their traditional methods of physician chart review and data mining. Rather, the focus was on innovative methods such as community education about clinical trials, collaboration with patient advocacy groups, social media and a teen ski event to reach teens living with diabetes and their parents. As a result, sponsor timelines for study start and enrollment completion were exceeded with the site enrolling and randomizing 36 patients within six months.

"We've seen a shift in focus for patient recruitment," said Nazneen Qureshi, manager of Patient Engagement for LMC|Manna Research. "For many years, we've used traditional radio and print mediums, internal database searches and physician chart reviews. But more recently our approach has included the patient in the journey. We are building awareness around clinical research, as well as the therapeutic area in general, educating and empowering the community and having face-to-face conversations with people."

Although sites haven't necessarily seen an increase in their patient recruitment budgets, BBK's Bachenheimer said industry demand for outsourced patient recruitment and retention services has shifted toward offerings designed to ease site administrative burden. BBK's RSG Arrive global patient travel program, for instance, manages the logistical challenges of clinical trial participation for patients, which allows site staff to focus on patient care instead of booking hotels and airline flights or arranging for language translation services. In another example, ThreeWire offers an Enrollment Assistant service that places staff with the requisite skills at sites. The assistance may be recruitment related or back office support that frees up the study coordinator to spend more time recruiting study candidates.

"Some sites have all the candidates they want, they just don't have the resources and bandwidth to devote to a given study so that they can enroll patients as fast as sponsors and CROs want them to. Others don't have the requisite skills to identify the patients needed for a particular study," said ThreeWire's Summers.

Vendors in the patient recruitment space also support apps and other technology that assists sites with their recruitment efforts. In one example, TrialX, a clinical

Doubling planned timelines to achieve enrollment targets

	Increase in planned study duration to reach target enrollment
Overall	94%
Cardiovascular	99%
CNS	116%
Endocrine/Metabolic	113%
Oncology	71%
Respiratory	95%

n=627 global phase II and III clinical trials

Source: Tufts CSDD, 2014; <csdd.tufts.edu>

research informatics company, recently launched a product that allows sites or doctor's offices to create a playlist of video content, which would be broadcast on a television screen in the waiting room, that allows patients to learn about clinical research and treatments from their own healthcare provider. The private channel could be customized to include trial-specific advertisements or information about special therapeutic areas, such as recordings from TrialX's online talk show called CureTalks, which invites guests to discuss a wide range of medical and health issues.

"There isn't one magic bullet to find patients for trials," said Sharib Khan, co-founder and chief executive officer of TrialX. "We have created different tools and different ways to reach patients. You have to be available where patients are available."

As sponsors want to engage with sites that can produce enrollment, several top CROs have made investments in site networks and combined the ability to sell patient recruitment as an integrated service offering for its network. Bioclinica, which has 26 research sites in its network, acquired global patient recruitment and retention firm MediciGroup in 2015. In another example, after PPD acquired Acurian in 2013, the CRO's holding company acquired Synexus, which merged its operations with Radiant Research to become the world's largest clinical trial site network. Today, PPD offers its PatientAdvantage model that combines the CROs assets in site networks and patient recruitment to provide a fixed-price model where all CRO services, site services and patient recruitment are provided in a single price per patient.

"By reducing the number of sites needed and super charging those wholly owned sites with patients sourced by Acurian, PPD can offer a competitive development advantage. The competitive advantage to sponsors is certainty across budget, time/speed, data quality and patient delivery," said Connor.

Looking ahead

As the patient recruitment landscape evolves, those who closely watch the space agree there isn't one answer to solving the patient recruitment problem.

"There isn't any one tactic that will replace some other tactic. You can't replace radio ads. You can't replace newspaper ads. You can't replace online ads. You can't go away from chart reviews," said TrialX's Kahn. "There needs to be different avenues to reach different patients."

Going forward, as many of the recruitment tactics become more impersonal and automated, the industry needs to develop ways to engage patients identified through online media or data-driven recruitment campaigns, usher them through the recruiting process and enroll them as participants in clinical trials.

"The industry is changing rapidly and people are trying to figure out how we approach this," said Bioclinica's Collyer. "Although people are talking about patient centricity, they fail to put people first. It's only when they start realizing that they must understand who they are looking for and then develop a relationship with those people that they will be successful."

Karyn Korieth has been covering the clinical trials industry for CenterWatch since 2003. Her 30-year journalism career includes work in local news, the healthcare industry and national magazines. Karyn holds a Master of Science degree from the Columbia University Graduate School of Journalism. Email karyn.korieth@centerwatch.com.

Patient data

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ed to increase to six within the next three years, according to the survey.

Among the anticipated changes, nearly all (93%) respondents expect to use eInformed consent data (up 62 percentage points from today). Also, most companies plan to use mHealth and smart phone data and eSource data.

How much the data sources will change varied by business type. CROs responded that they anticipate using more data sources versus a lower amount from sponsors. Similarly, organizations with the highest trial volumes (greater than 15 trials per year) say they will use more sources of clinical data within the next three years.

"At the same time that clinical teams are managing traditional data from case report forms and local and central labs, they are being forced to step out of their comfort zone to manage, integrate, and analyze data from more diverse and less compatible sources, including smart phone and wearable devices, real-world evidence, and social media," said Ken Getz, research associate professor and director of the Tufts center.

Responding to questions about clinical data management systems, most respondents (30%) said cycle time was their biggest challenge, including time from protocol completion to first patient, first visit (FPFV) and time from last patient, last visit (LPLV) to database lock. Despite efforts to shorten the time, it still takes approximately 36 days from LPLV to database lock which is a longer period of time than 15 years ago (36 days vs. 33 days).

The second most cited challenge was costs (29%) followed by the number of clinical systems (18%). As trial volume increases, the number of companies that cite 'number of systems' as their single biggest challenge rose to 28%. As companies manage more trials, the ability to unify applications and processes will become increasingly important in improving trial efficiency.

"Life sciences companies want to collect more data from more sources, but are experiencing challenges managing the data they have now," said Richard Young, vice president of Veeva Vault EDC. "There is a significant opportunity for organizations to create a complete picture of their trials as new data points are generated or recorded so they can drive better decisions."

Veeva Systems sponsored the survey that included more than 250 companies, including sponsors and CROs.

Read the full survey results here: www.fdanews.com/11-08-17-Tufts.pdf.

Brexit may put U.K. at odds with new EU clinical trial regulations

By Zack Budryk

Because of delays in implementing the EU regulation, the U.K.'s compliance with future EU clinical trials rules will likely be subject to negotiation, as the country plans to only immediately implement EU regulations that were in place ahead of the planned March 2019 exit from the EU, according to a U.K. government official.

Robin Walker, a minister at the Department for Exiting the European Union, also cited a July letter from the Secretaries of State for Health and for Business, Energy and Industry Strategy that said the U.K.'s government is committed to continuing the working relationship and close collaboration between the EU and the U.K., which will include "any future EU regime on clinical trials."

Whether the latest EU clinical trials regulations are implemented before the exit date depends on a forthcoming EMA decision.

The EMA decided in July to postpone implementing the regulations from October 2018 to 2019 at the earliest due to technical difficulties. The agency has called the modernization process the most ambitious IT system it has required in the past decade. It further recently published guidance for drugmakers on dealing with the EMA after the Brexit process.

Read Walker's letter here: www.fdanews.com/11-06-17-Brexit.pdf.

China to allow use of overseas trial data in drug applications

By Zack Budryk

In a significant policy shift, China plans to accept data from foreign clinical trials in its drug approval process if the drug is already approved overseas.

The new policy will help the China Food and Drug Administration (CFDA) stretch its clinical research resources, replacing the current clinical trial center qualification system with a clinical trial filing system.

The change will "improve the efficiency of ethical reviews at the same time," according to Grace Palma, founder and CEO of Boston-based China Med Device, a firm specializing in assisting companies entering China.

The new approach also will speed up the approval process for urgently needed drugs, and drugs for rare diseases. Drugs for rare diseases with existing overseas approval will get the CFDA's approval with additional conditions.

China recently tightened up on its policing of clinical trials, with the Supreme People's Court requiring stricter punishments for companies that falsify clinical trial reports.

New Drugs in the Pipeline

The following drugs were added to CenterWatch's *Drugs in Clinical Trials Database* during the previous month. For additional information, please visit centerwatch.com/drug-information/pipeline/. Note: The database is a subscriber-only service. To request a free trial, you may visit centerwatch.com/drug-information/demo/. CenterWatch also prepares custom drug intelligence reports that cover a variety of medical conditions. Email marketresearch@centerwatch.com. Join the LinkedIn Drug Research Updates group!

Phase	Drug name	Indication	Company name
IND approved	Activated Allogeneic Donor Gamma-Delta (γδ) T cells	hematologic cancer following haploidentical stem cell transplantation	Incysus
I	HTI therapeutic HIV vaccine	HIV	Aelix Therapeutics
I	BBT-015	chemotherapy-related neutropenia and acute radiation syndrome	Bolder BioTechnology
I	CLDN18.2	pancreatic and gastric cancer	CARsgen Therapeutics
I	DS-1211	musculoskeletal diseases	Daiichi-Sankyo
I	Injectable Discogenic Cell Therapy	back pain	DiscGenics
I	H3B-6545	breast cancer	H3 Biomedicine
I	HTL16878	Alzheimer's disease	Heptares Therapeutics
I	IMA101	solid tumors	immatics biotechnologies
I	LT3001	acute ischemic stroke	Lumosa Therapeutics
I	MGA012	solid tumors	MacroGenics
I	MGD013	solid tumors	MacroGenics
I	MA-0211, MTB-1	muscular dystrophy	Mitobridge
I	PTI-125	Alzheimer's disease	Pain Therapeutics
I	PAT-1251	fibrosis	PharmAkea
Ib	ANS-6637	alcohol addictions	Amygdala Neurosciences
I/II	HER-Vaxx	gastric cancer	Imugene
I/II	Sym013	solid tumors	Symphogen
IIa	oral leuprolide	endometriosis	Enteris BioPharma
IIa	MSB-01	atopic dermatitis	Matrisys Bioscience
II	AAI101	urinary tract infections	Allecra Therapeutics
II	AMX0035	amyotrophic lateral sclerosis	Amylyx Pharmaceuticals
II	ATA230, CMV-CTL	cytomegalovirus	Atara Biotherapeutics
II	EB-001, serotype E botulinum	pain	Bonti
II	Biropepimut-S	squamous cell cancer	Gliknik
II	DRU-2017-5947 (vaccine)	brain cancer and multiple myeloma	MimiVax
II	TPU-006	pain	Teikoku Pharma USA
II	True Human antibody, MABp1, Hidradenitis Suppurativa	hidradenitis suppurativa	Xbiotech
III	vilaprisan	uterine fibroids	Bayer
III	AMT-061	hemophilia	uniQure
EU Approved	Wakix, pitolisant	narcolepsy	Bioprojet Pharma

FDA Actions

The following is a sampling of FDA regulatory actions taken during the previous month, compiled from CenterWatch and third-party sources including the FDA and company press releases. For more information on FDA approvals, visit www.centerwatch.com/drug-information/fda-approvals/. For custom drug intelligence reports, email marketresearch@centerwatch.com. Join the LinkedIn Drug Research Updates group!

Company name	Drug name	Indication	FDA action
Actuate Therapeutics	9-ING-41	neuroblastoma	Rare Pediatric Disease designation granted
ArQule	miransertib (ARQ 092)	Proteus syndrome	Rare Pediatric Disease designation granted
Atara Biotherapeutics	ATA230	congenital cytomegalovirus infection	Rare Pediatric Disease designation granted
Astellas Pharma	gilteritinib	acute myeloid leukemia	Fast Track designation granted
Alzheon	ALZ-801	Alzheimer's disease	Fast Track designation granted
Citius Pharmaceuticals	Mino-Lok	catheter lock solution	Fast Track designation granted
Cognition Therapeutics	CT1812	Alzheimer's disease	Fast Track designation granted
Geron	imetelstat	transfusion-dependent anemia due to Low or Intermediate-1 risk myelodysplastic syndromes	Fast Track designation granted
Heron Therapeutics	HTX-011	postoperative pain reduction	Fast Track designation granted
Medivir	MIV-711	osteoarthritis	Fast Track designation granted
Radius Health	elacestrant	advanced or metastatic breast cancer	Fast Track designation granted
BioMarin Pharmaceutical	valoctocogene roxaparvovec	hemophilia A	Breakthrough Therapy designation granted
MorphoSys	MOR208, lenalidomide	relapsed or refractory diffuse large B-cell lymphoma	Breakthrough Therapy designation granted
Novartis	Tafinlar (dabrafenib), Mekinist (trametinib)	stage III melanoma with a BRAF V600 mutation	Breakthrough Therapy designation granted
Achillion Pharmaceuticals	ACH-4471	paroxysmal nocturnal hemoglobinuria	Orphan Drug designation granted
Artemis Therapeutics	Artemisone	malaria	Orphan Drug designation granted
iVeena Delivery Systems	IVMED-80	keratoconus	Orphan Drug designation granted
Krystal Biotech	KB103	dystrophic epidermolysis bullosa	Orphan Drug designation granted
Lin Bioscience	LBS-008	Stargardt disease	Orphan Drug designation granted
Merrimack	MM-121	heregulin positive non-small cell lung cancer	Orphan Drug designation granted
Mobius Theraputics	Mitosol	refractory glaucoma	Orphan Drug designation granted
Neurocrine Biosciences	Ingrezza (valbenazine)	tardive dyskinesia	Orphan Drug designation granted
NewLink Genetics	indoximod	stage IIb-IV melanoma	Orphan Drug designation granted
Shire	SHP654	hemophilia A	Orphan Drug designation granted
Synlogic	SYNB1618	phenylketonuria	Orphan Drug designation granted
TiGenix	Cx601	perianal fistulas related to Crohn's disease	Orphan Drug designation granted
Zealand Pharma	glepaglutide	short bowel syndrome	Orphan Drug designation granted
Fortress Biotech	CEVA101	traumatic brain injury	Regenerative Medicine Advanced Therapy designation granted
AstraZeneca	Bydureon BCise (exenatide extended-release)	type 2 diabetes	Approved
AstraZeneca, Acerta Pharma	Calquence (acalabrutinib)	mantle cell lymphoma	Approved
Genentech	Zelboraf	anaplastic lymphoma kinase-positive metastatic non-small cell lung cancer	Approved
Genentech	Alecensa (alectinib)	Erdheim-Chester disease	Approved
GlaxoSmithKline	Shingrix (Zoster Vaccine Recombinant, Adjuvanted)	prevention of shingles (herpes zoster)	Approved

Study Lead Opportunities

CenterWatch analyzes data in its drug intelligence database to provide advance notice of clinical trials expected to enter the next phase of clinical development soon. Contact information is provided for follow up. **Sponsors/CROs:** To list an upcoming trial here, contact Stephanie Hill, (617) 948-5170, stephanie.hill@centerwatch.com; or to initiate a search to identify sites for an upcoming or currently active trial, email trialwatch@centerwatch.com or submit online at centerwatch.com/clinical-trials/trialwatch/. **Sites:** To be matched to sponsor/CRO requests, submit a brief online profile at centerwatch.com/news-resources/trialwatch/. For patient enrollment support on these studies, email sales@centerwatch.com. For site feasibility surveys, email marketresearch@centerwatch.com.

Drug name	Indication	Company name	Contact information
Phase I			
blinatumomab + pembrolizumab	relapsed or refractory diffuse large B cell lymphoma	Amgen	medinfo@amgen.com
AZD1775	solid tumors	AstraZeneca	information.center@astrazeneca.com
glucagon nasal powder	hypoglycemia	Eli Lilly	(877) 285-4559
Phase II			
BIIB074	onfirmed small fibre neuropathy that is idiopathic or associated with diabetes mellitus	Biogen	clinicaltrials@biogen.com
Brincidofovir	adenovirus	Chimerix	Garrett Nichols gnichols@chimerix.com
Ad26.RSV.preF	seasonal influenza	Janssen Vaccines & Prevention	JNJ.CT@sylogent.com
MCLA-128-based combinations	metastatic breast cancer	Merus	enquiries@merus.nl
AGN-242428	moderate to severe plaque-type psoriasis	Vitae Pharmaceuticals	IR-CTRegistration@allergan.com
Phase III			
Empagliflozin	chronic heart failure	Boehringer Ingelheim	clintriage.rdg@boehringer-ingelheim.com
Baricitinib	moderate to severe atopic dermatitis	Eli Lilly	(877) 285-4559
duloxetine hydrochloride	Japanese children and adolescents with depressive disorder	Eli Lilly	(877) 285-4559
pembrolizumab plus epacadostat	metastatic non-small cell lung cancer	Incyte	medinfo@incyte.com globalmedinfo@incyte.com
Tetravalent Dengue Vaccine	dengue	Takeda	medicalinformation@tpna.com
Levetiracetam	pediatric epilepsy subjects aged 1 month to less than 4 years of age with partial seizures	UCB Japan	UCBCares@ucb.com
Phase IV			
Volulyte 6%	hypovolemia	B. Braun Melsungen	studies@bbraun.com
emollient impregnated exam gloves	hand hygiene/dermatitis	Medline Industries, Inc.	Lori Rotolo lrotolo@medline.com
dabrafenib and/or trametinib	cancer	Novartis Pharmaceuticals	novartis.email@novartis.com

Compilation Reports Series

- **Data-driven**
- **In-depth journalistic reporting**
- **Categorized into strategic topics**

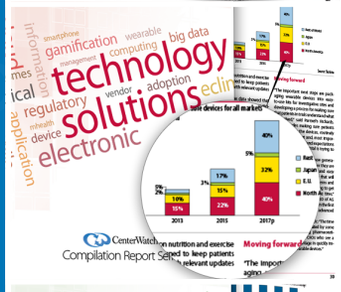
Each report may be used in business and marketing reports, conference presentations and more!

Sponsor

Covers the collaboration between Sponsors and CROs, outsourcing models, new initiatives, etc.

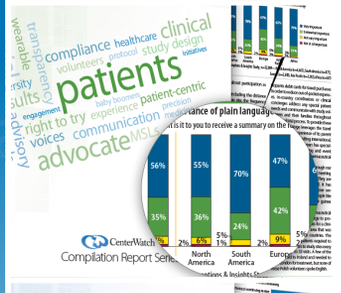
Contract Research Organization

Investigates the CRO landscape over the past 30 years—from evolution as a market trend to becoming a key player.



Technology Solutions

Discusses a variety of technology solutions and the role technology has played in clinical trials.

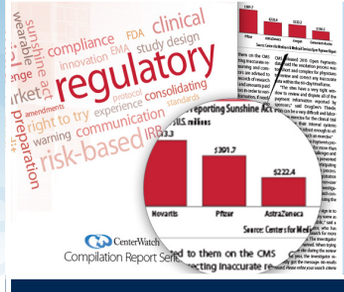


Patients

Focuses on patient engagement, patient diversity, dual enrollment challenges, etc.

Investigative Site Landscape

Covers its strategic element, job satisfaction, financial exigencies and the evolution of the clinical trials landscape.



Regulatory

Focuses on GCP and methods used to ensure compliance with regulatory requirements.

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